Société Chimique de France
Le réseau des chimistes

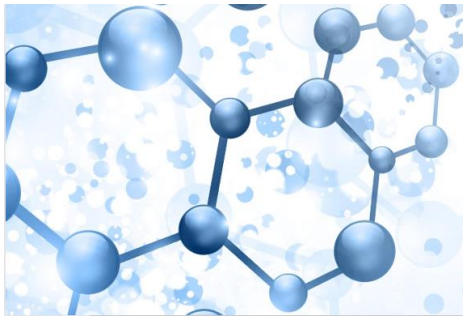
N° 11

ECHO DCO

Septembre 2021

La lettre du bureau de la Division de Chimie Organique

SOMMAIRE



LE MOT DE LA PRÉSIDENTE

Chers sociétaires,

Je suis très heureuse de vous écrire au nom du nouveau bureau de la DCO, qui vous remercie tous pour la confiance accordée à travers vos nombreux votes pour ce mandat.

Avant toute chose, j'adresse également nos plus chaleureux remerciements au précédent bureau, notamment à Matthieu Sollogoub, son président, ainsi qu'à Elsa Anselmi, Philippe Dauban et Muriel Durandetti ; ils ont montré un dévouement sans faille et une énergie à toute épreuve pour animer la vie de notre communauté en nous proposant des manifestations scientifiques d'excellente qualité dans une ambiance conviviale. Quand la pandémie nous a contraints, les web-séminaires organisés avec notre partenaire EurJOC ont pris très efficacement le relais avec une audience extrêmement forte.

Nous nous engageons à poursuivre ce travail d'animation par l'organisation de manifestations scientifiques au cours desquelles nous espérons bien nous retrouver de visu, tout en tentant de maintenir un système bimodal, qui a prouvé son intérêt pour en faciliter la diffusion. Nous continuerons à proposer les prix aux chimistes adhérents à la SCF, qui sont importants pour promouvoir la chimie organique française autour de nous et à l'International. Nous souhaitons renforcer nos contacts au niveau européen et nous affichons une attention particulière à la diversité, la parité et la mise en valeur des jeunes dans notre communauté. Vous lirez dans cette gazette que nous avons créé deux Vice-Présidences qui traiteront particulièrement de ces points.

J'ai aussi le plaisir de vous annoncer la date de notre prochaine journée d'automne qui aura lieu **le 1er décembre prochain** sur le Campus des Cordeliers de Sorbonne Université pour nous retrouver. Save the date !

Cette division de la SCF est la vôtre, n'hésitez pas à nous contacter, à venir nous rencontrer pour échanger des idées et nous aider à rendre plus visible encore notre belle communauté de chimistes organiciens. Bonne rentrée à tous !

Très cordialement

Emmanuelle Schulz, Présidente de la DCO

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ELECTION DU NOUVEAU BUREAU DE LA DCO 2021-2024

Le verdict des urnes est tombé le dimanche 20 juin 2020. Suite au vote pour le renouvellement du bureau de la DCO, une nouvelle équipe s'est constituée pour travailler à la promotion et l'animation de la chimie organique française pour les trois prochaines années. Nous nous sommes réunis le 8 juillet dernier pour en déterminer la composition, ainsi que les rôles joués par chacun.

- **Emmanuelle Schulz** : Présidente du bureau
- **Frédéric Lamaty** : Vice-Président en charge de la diversité, de la parité et du lien avec le réseau Jeunes
- **Olivier Baslé** : Vice-Président en charge du lien avec l'international
- **Xavier Guinchard** : Vice-Président en charge de la communication
- **Damien Bonne** : Trésorier
- **Kevin Cariou** : Secrétaire

Ce bureau restreint est complété par :

- **Sandrine Piguel** : Assistante pour la trésorerie
- **Jeanne Crassous** : Assistante pour les questions internationales et le lien avec les autres sections de la SCF
- **Morgan Donnard** : Assistant pour la communication et responsable du Prix Yves Chauvin
- **Cyril Ollivier** : Assistant communication et responsable du Prix Jean Normant
- **Emmanuel Gras** : Assistant pour le secrétariat et responsable du lien avec les sections régionales
- **Sébastien Vidal** : Assistant pour les questions de diversité, parité et du lien avec le Réseau Jeunes et Responsable du Prix Jean-Marie Lehn
- **Stéphanie Norsikian** : Responsable des Prix de thèse Dina Surdin et Henri Kagan
- **Anis Tlili** : Responsable du Prix Marc Julia
- **Samir Messaoudi** : Responsable du Prix Jean-Pierre Sauvage
- **Matthieu Raynal** : Chargé de mission pour le groupe thématique de Chimie Supramoléculaire
- **Boris Vauzeilles** : Chargé de mission pour le groupe thématique de Chémobiologie

AVOS AGENDAS : Journée d'Automne de la DCO 2021

La Division de Chimie Organique a le plaisir de vous annoncer que la **Journée d'Automne de la DCO 2021** se déroulera le mercredi **1er décembre 2021** à l'amphi Pasquier du campus des Cordeliers de Sorbonne Université (métro Cluny-La Sorbonne ou Odéon).

Pour fêter le plaisir de nous retrouver, nous avons choisi de célébrer la chimie française en favorisant les communications orales des récipiendaires de prix de la DCO, ainsi que les communications orales des jeunes chercheurs. Le programme comprendra:

- 1 conférencier invité: **Prof. Christof SPARR** de l'Université de Basel (Suisse).
- 4 lauréats des prix de la DCO 2020 :

Jeanne CRASSOUS	Prix de la DCO 2020, ISCR, Rennes
Julie OBLE	Prix Jean NORMANT 2020, IPCM, Paris
Julien LECLAIRE	Prix Jean-Marie LEHN 2020, ICBMS, Lyon
Yannick GEIGER	Prix de thèse Henri KAGAN 2020, IPCMS, Strasbourg

- 3 lauréats des prix de la DCO 2021 :

Sophie FEUILLASTRE	Prix Marc JULIA 2021, CEA Saclay
Charlotte LORTON	Prix de thèse Dina SURDIN 2021, ICSN, Gif sur Yvette
Davide AUDISIO	Prix Jean-Pierre SAUVAGE 2021, CEA Saclay

- 4 communications orales jeunes chercheurs. Retrouvez l'appel à candidature ci-dessous et sur notre site web https://new.societechimiquedefrance.fr/divisions/chimie-organique/

Toutes les informations sont disponibles sur le site https://dco-automne2021.sciencesconf.org/

Pour rappel, ces journées de la DCO sont gratuites, même si l'inscription est obligatoire, et réservées aux adhérents de la SCF. Pour les non-adhérents, elles constituent une occasion pour rejoindre la SCF. https://new.societechimiquedefrance.fr/adherer-a-la-scf/
Cette journée sera également accessible en visioconférence. Les informations seront disponibles sur le site web.

APPEL A COMMUNICATION ORALES POUR LA JOURNEE D'AUTOMNE 2021

Dans le cadre de sa prochaine **Journée d'Automne 2021** (mercredi 1er décembre 2021), la Division de Chimie Organique lance un appel à candidature pour des communications orales auprès de ses membres sociétaires occupant une position permanente depuis moins de 7 ans.
Le bureau de la DCO sélectionnera 4 personnes qui seront invitées à présenter une communication orale à la Journée d'Automne. La DCO invitera les lauréats au déjeuner ainsi qu'à un dîner la veille, le 30 novembre. Les frais de voyage et d'hébergement seront à la charge des lauréats.

Critères d'éligibilité :
- Être sociétaire de la SCF depuis au moins 3 ans.
- Occuper une position permanente (académique ou industrielle) depuis moins de 7 ans (nomination à partir de septembre 2014).

Procédure :
- Communication en anglais de 15 minutes (questions comprises).
- Les résumés des communications (1 page max. en pdf suivant le template) doivent être envoyés sous forme électronique uniquement avant le 22 octobre 2021 à midi à : Morgan Donnard donnard@unistra.fr

L'appel à candidature et le template peuvent être trouvés sur le site internet de la DCO : https://new.societechimiquedefrance.fr/divisions/chimie-organique/

PARITE, DIVERSITE ET RESEAU JEUNES

Le Bureau de la DCO-SCF a mis en place une **vice-présidence chargée de la parité, de la diversité et de la relation avec le réseau RJ-SCF**. Notre mission sera notamment de veiller à maintenir la meilleure représentativité de notre communauté de chercheurs et enseignant-chercheurs dans les conférences organisées ou soutenues par la DCO, mais aussi dans les prix décernés ou autres processus de sélection. Notre action sera aussi tournée vers le réseau des jeunes RJ-SCF pour donner une plus grande visibilité aux actions qu'ils pourront mettre en œuvre en leur apportant le soutien nécessaire pour les mener à bien, mais aussi en se nourrissant de leurs initiatives. La place des jeunes adhérents est primordiale dans notre communauté scientifique car ce sont eux qui continueront à animer et à enrichir cette vie scientifique dans le futur.
Afin de pouvoir agir au mieux et au plus près des attentes de notre communauté, nous sommes à votre disposition pour vos demandes, informations ou idées d'action dans le cadre de cette vice-présidence.

N'hésitez pas à nous contacter par e-mail.

frederic.lamaty@umontpellier.fr
sebastien.vidal@cnrs.fr

SOUTIEN DE LA DCO

Créé en janvier 2020 et rattaché à la Division de Chimie Organique, le groupe de Chémobiologie SCF-ChemBio (https://new.societechimiquedefrance.fr/groupes/groupe-de-chemobiologie/) est désormais membre de l'**European Federation for Medicinal chemistry and Chemical biology** (EFMC).

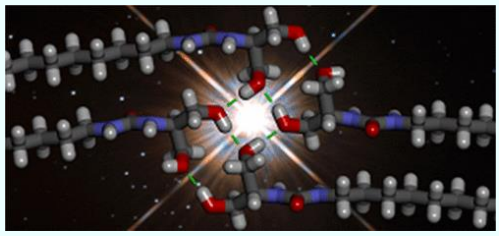
La DCO a soutenu cette démarche, qui vise à s'inscrire dans une évolution récente de l'EFMC en direction de la chémobiologie (Chemical Biology Initiative).

LES HIGHLIGHTS DE LA CHIMIE DE LA DCO

Le bureau de la Division de Chimie Organique se propose de mettre en valeur chaque semestre les articles les plus significatifs dont les auteurs correspondants sont membres de notre division.
Vous trouverez dans les pages suivantes un choix d'articles publiés sur la période octobre 2020-juin 2021 dans les journaux suivants :
- *J. Am. Chem. Soc.*
- *Chem. Sci.*
- *Angew. Chem. Int. Ed.*

Nous avons conscience que ce choix d'articles est arbitraire. N'hésitez pas à nous faire part de vos remarques, et, éventuellement, à nous soumettre des propositions de travaux à « highlighter ».

Hydroxy Channels–Adaptive Pathways for Selective Water Cluster Permeation

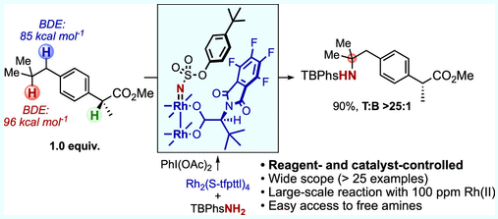


Li-Bo Huang, Arthur Hardiagon, Istvan Kocsis, Cristina-Alexandra Jegu, Mihai Deleanu, Arnaud Gilles, Arie van der Lee, Fabio Sterpone, Marc Baaden, Mihail Barboiu* *J. Am. Chem. Soc.* **2021**, *143*, 4224-4233

https://dx.doi.org/10.1021/jacs.0c11952

Artificial water channels (AWCs) are known to selectively transport water, with ion exclusion. Similarly to natural porins, AWCs encapsulate water wires or clusters, offering continuous and iterative H-bonding that plays a vital role in their stabilization. Herein, we report octyl-ureido-polyol AWCs capable of self-assembly into hydrophilic hydroxy channels. Variants of ethanol, propanediol, and trimethanol are used as head groups to modulate the water transport permeabilities, with rejection of ions. The hydroxy channels achieve a single-channel permeability of 2.33×10^8 water molecules per second, which is within the same order of magnitude as the transport rates for aquaporins. Depending on their concentration in the membrane, adaptive channels are observed in the membrane. Over increased concentrations, a significant shift occurs, initiating unexpected higher water permeation. Molecular simulations probe that spongelike or cylindrical aggregates can form to generate transient cluster water pathways through the bilayer. Altogether, the adaptive self-assembly is a key feature influencing channel efficiency. The adaptive channels described here may be considered an important milestone contributing to the systematic discovery of artificial water channels for water desalination.

Catalytic Intermolecular C(sp3)–H Amination: Selective Functionalization of Tertiary C–H Bonds vs Activated Benzylic C–H Bonds

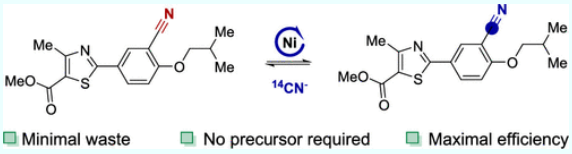


Erwan Brunard, Vincent Boquet, Elsa Van Elslande, Tanguy Saget, and Philippe Dauban* *J. Am. Chem. Soc.* **2021**, *143*, 6407–6412

https://dx.doi.org/10.1021/jacs.1c03872

A catalytic intermolecular amination of nonactivated tertiary C(sp^3)–H bonds (BDE of 96 kcal·mol^{-1}) is reported for substrates displaying an activated benzylic site (BDE of 85 kcal·mol^{-1}). The tertiary C(sp^3)–H bond is selectively functionalized to afford α,α,α-trisubstituted amides in high yields. This unusual site-selectivity results from the synergistic combination of Rh_2(*S*-tfpttl)$_4$, a rhodium(II) complex with a well-defined catalytic pocket, with *tert*-butylphenol sulfamate (TBPhsNH_2), which leads to a discriminating rhodium-bound nitrene species under mild oxidative conditions. This catalytic system is very robust, and the reaction was performed on a 50 mmol scale with only 0.01 mol % of catalyst. The TBPhs group can be removed under mild conditions to afford the corresponding *NH*-free amines.

Direct Carbon Isotope Exchange of Pharmaceuticals via Reversible Decyanation



Minghao Feng, Joao De Oliveira, Antoine Sallustrau, Gianluca Destro, Pierre Thuéry, Sebastien Roy, Thibault Cantat, Charles S. Elmore, Jorg Blankenstein, Frédéric Taran, and Davide Audisio* J. Am. Chem. Soc. 2021, 143, 15, 5659–5665

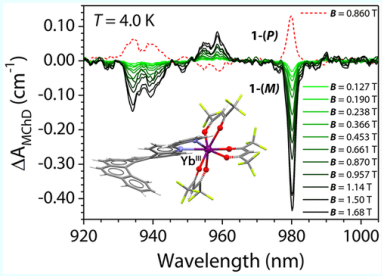
https://dx.doi.org/10.1021/jacs.1c01923

The incorporation of carbon-14 allows tracking of organic molecules and provides vital knowledge on their fate. This information is critical in pharmaceutical development, crop science, and human food safety evaluation. Herein, a transition-metal-catalyzed procedure enabling carbon isotope exchange on aromatic nitriles is described. By utilizing the radiolabeled precursor Zn([^{14}C]CN)$_2$, this protocol allows the insertion of the desired carbon tag without the need for structural modifications, in a single step. By reducing synthetic costs and limiting the generation of radioactive waste, this procedure will facilitate the labeling of nitrile containing drugs and accelerate ^{14}C-based ADME studies supporting drug development.

Helicene-Based Ligands Enable Strong Magneto-Chiral Dichroism in a Chiral Ytterbium Complex

Matteo Atzori*, Kais Dhbaibi, Haiet Douib, Maxime Grasser, Vincent Dorcet, Ivan Breslavetz, Kévin Paillot, Olivier Cador, Geert L. J. A. Rikken, Boris Le Guennic, Jeanne Crassous*, Fabrice Pointillart*, Cyrille Train *J. Am. Chem. Soc.* **2021**, *143*, 2671–2675

https://dx.doi.org/10.1021/jacs.0c13180

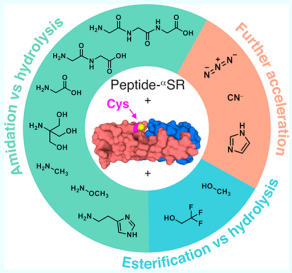


Here we report the first experimental observation of magneto-chiral dichroism (MChD) detected through light absorption in an enantiopure lanthanide complex. The *P* and *M* enantiomers of [Yb^{III}((*X*)-**L**)(*hfac*)$_3$] (X = *P*, *M*; **L** = 3-(2-pyridyl)-4-aza[6]-helicene; *hfac* = 1,1,1,5,5,5-hexafluoroacetylacetonate), where the chirality is held by the helicene-based ligand, were studied in the near-infrared spectral window. When irradiated with unpolarized light in a magnetic field, these chiral complexes exhibit a strong MChD signal (g_{MChD} ca. 0.12 T^{-1}) associated with the $^2F_{5/2} \leftarrow {}^2F_{7/2}$ electronic transition of Yb^{III}. The low temperature absorption and MChD spectra reveal a fine structure associated with crystal field splitting and vibronic coupling. The temperature dependence of the main dichroic signal detected up to 150 K allowed, for the first time, the disentanglement of the two main microscopic contributions to the dichroic signal predicted by the MChD theory. These findings pave the way toward probing MChD in chiral lanthanide-based single-molecule magnets.

Acyl Transfer Catalytic Activity in De Novo Designed Protein with N-Terminus of α-Helix As Oxyanion-Binding Site

Elise A. Naudin, Alastair G. McEwen, Sophia K. Tan, Pierre Poussin-Courmontagne, Jean-Louis Schmitt, Catherine Birck, William F. DeGrado*, Vladimir Torbeev* *J. Am. Chem. Soc.* **2021**, *143*, 3330–3339

https://dx.doi.org/10.1021/jacs.0c10053

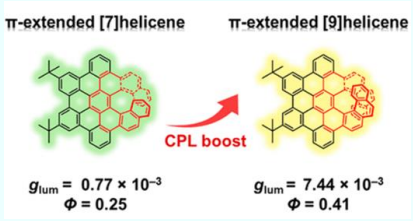


The design of catalytic proteins with functional sites capable of specific chemistry is gaining momentum and a number of artificial enzymes have recently been reported, including hydrolases, oxidoreductases, retro-aldolases, and others. Our goal is to develop a peptide ligase for robust catalysis of amide bond formation that possesses no stringent restrictions to the amino acid composition at the ligation junction. We report here the successful completion of the first step in this long-term project by building a completely de novo protein with predefined acyl transfer catalytic activity. We applied a minimalist approach to rationally design an oxyanion hole within a small cavity that contains an adjacent thiol nucleophile. The N-terminus of the α-helix with unpaired hydrogen-bond donors was exploited as a structural motif to stabilize negatively charged tetrahedral intermediates in nucleophilic addition–elimination reactions at the acyl group. Cysteine acting as a principal catalytic residue was introduced at the second residue position of the α-helix N-terminus in a designed three-α-helix protein based on structural informatics prediction. We showed that this minimal set of functional elements is sufficient for the emergence of catalytic activity in a de novo protein. Using peptide-$^{\alpha}$thioesters as acyl-donors, we demonstrated their catalyzed amidation concomitant with hydrolysis and proved that the environment at the catalytic site critically influences the reaction outcome. These results represent a promising starting point for the development of efficient catalysts for protein labeling, conjugation, and peptide ligation.

Amplification of Dissymmetry Factors in π-Extended [7]- and [9]Helicenes

Zijie Qiu, Cheng-Wei Ju, Lucas Frédéric, Yunbin Hu, Dieter Schollmeyer, Grégory Pieters*, Klaus Müllen*, and Akimitsu Narita* *J. Am. Chem. Soc.* **2021**, *143*, 4661–4667

https://dx.doi.org/10.1021/jacs.0c13197

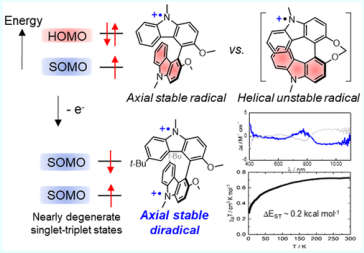


π-Extended helicenes constitute an important class of polycyclic aromatic hydrocarbons with intrinsic chirality. Herein, we report the syntheses of π-extended [7]helicene 4 and π-extended [9]helicene 6 through regioselective cyclodehydrogenation in high yields, where a “prefusion” strategy plays a key role in preventing undesirable aryl rearrangements. The unique helical structures are unambiguously confirmed by X-ray crystal structure analysis. Compared to the parent pristine [7]helicene and [9]helicene, these novel π-extended helicenes display significantly improved photophysical properties, with a quantum yield of 0.41 for 6. After optical resolution by chiral high-performance liquid chromatography, the chiroptical properties of enantiomers 4-*P*/*M* and 6-*P*/*M* are investigated, revealing that the small variation in helical length from [7] to [9] can cause an approximately 10-fold increase in the dissymmetry factors. The circularly polarized luminescence brightness of 6 reaches 12.6 M^{-1} cm^{-1} as one of the highest among carbohelicenes.

Axially and Helically Chiral Cationic Radical Bicarbazoles: SOMO–HOMO Level Inversion and Chirality Impact on the Stability of Mono- and Diradical Cations

Sitthichok Kasemthaveechok, Laura Abella, Marion Jean, Marie Cordier, Thierry Roisnel, Nicolas Vanthuyne, Thierry Guizouarn, Olivier Cador, Jochen Autschbach*, Jeanne Crassous, Ludovic Favereau* *J. Am. Chem. Soc.* **2020**, *142*, 20409–20418

https://dx.doi.org/10.1021/jacs.0c08948

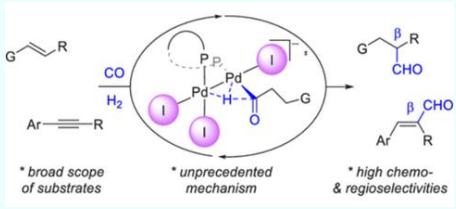


We report persistent chiral organic mono- and diradical cations based on bicarbazole molecular design with an unprecedented stability dependence on the type of chirality, namely, axial versus helical. An unusual chemical stability was observed for sterically unprotected axial bicarbazole radical in comparison with monocarbazole and helical bicarbazole ones. Such results were experimentally and theoretically investigated, revealing an inversion in energy of the singly occupied molecular orbital (SOMO) and the highest (doubly) occupied molecular orbital (HOMO) in both axial and helical bicarbazole monoradicals along with a subtle difference of electronic coupling between the two carbazole units, which is modulated by their relative dihedral angle and related to the type of chirality. Such findings allowed us to explore in depth the SOMO–HOMO inversion (SHI) in chiral radical molecular systems and provide new insights regarding its impact on the stability of organic radicals. Finally, these specific electronic properties allowed us to prepare a persistent, intrinsically chiral, diradical which notably displayed near-infrared electronic circular dichroism responses up to 1100 nm and almost degenerate singlet–triplet ground states with weak antiferromagnetic interactions evaluated by magnetometry experiments.

Binuclear Pd(I)–Pd(I) Catalysis Assisted by Iodide Ligands for Selective Hydroformylation of Alkenes and Alkynes

Yang Zhang, Sebastian Torker*, Michel Sigrist, Nikola Bregović, Paweł Dydio* *J. Am. Chem. Soc.* **2020**, *142*, 18251–18265

https://dx.doi.org/10.1021/jacs.0c09254

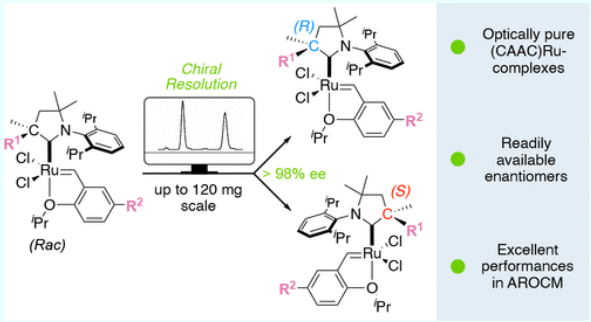


Since its discovery in 1938, hydroformylation has been thoroughly investigated and broadly applied in industry (>10^7 metric ton yearly). However, the ability to precisely control its regioselectivity with well-established Rh- or Co-catalysts has thus far proven elusive, thereby limiting access to many synthetically valuable aldehydes. Pd-catalysts represent an appealing alternative, yet their use remains sparse due to undesired side-processes. Here, we report a highly selective and exceptionally active catalyst system that is driven by a novel activation strategy and features a unique Pd(I)–Pd(I) mechanism, involving an iodide-assisted binuclear step to release the product. This method enables β-selective hydroformylation of a large range of alkenes and alkynes, including sensitive starting materials. Its utility is demonstrated in the synthesis of antiobesity drug Rimonabant and anti-HIV agent PNU-32945. In a broader context, the new mechanistic understanding enables the development of other carbonylation reactions of high importance to chemical industry.

Optically Pure C1-Symmetric Cyclic(alkyl)(amino)carbene Ruthenium Complexes for Asymmetric Olefin Metathesis

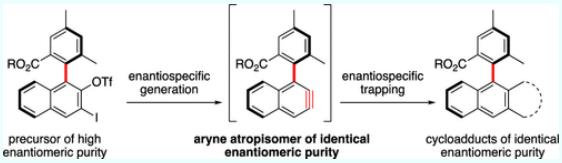
Jennifer Morvan, François Vermersch, Ziyun Zhang, Laura Falivene, Thomas Vives, Vincent Dorcet, Thierry Roisnel, Christophe Crévisy, Luigi Cavallo, Nicolas Vanthuyne, Guy Bertrand*, Rodolphe Jazzar*, Marc Mauduit* *J. Am. Chem. Soc.* **2020**, *142*, 19895–19901

https://dx.doi.org/10.1021/jacs.0c10705



An expedient access to the first optically pure ruthenium complexes containing C_1-symmetric cyclic (alkyl)(amino)carbene ligands is reported. They demonstrate excellent catalytic performances in asymmetric olefin metathesis with high enantioselectivities (up to 92% ee). Preliminary mechanistic insights provided by density functional theory models highlight the origin of the enantioselectivity.

Enantiospecific Generation and Trapping Reactions of Aryne Atropisomers

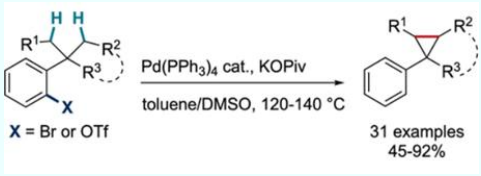


Yun-Long Wei, Guillaume Dauvergne, Jean Rodriguez*, Yoann Coquerel* *J. Am. Chem. Soc.* **2020**, *142*, 16921–16925

https://dx.doi.org/10.1021/jacs.0c08218

Enantioenriched aryne atropisomers having a biaryl stereogenic axis vicinal to the reactive triple bond are demonstrated to exist. These reaction intermediates are easily produced in situ and can undergo the standard aryne cycloaddition chemistry in an enantiospecific manner. Notably, the aryne atropisomers herein have allowed the practical syntheses of a small nanographene as well as some triptycene and anthracene derivatives that embed stereogenic axes of controlled absolute configurations.

Direct Synthesis of Cyclopropanes from gem-Dialkyl Groups through Double C–H Activation

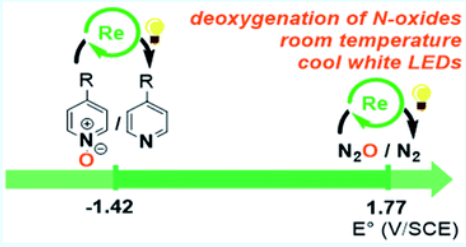


Antonin Clemenceau, Pierre Thesmar, Maxime Gicquel, Alexandre Le Flohic, Olivier Baudoin* *J. Am. Chem. Soc.* **2020**, *142*, 36, 15355–15361

https://dx.doi.org/10.1021/jacs.0c05887

Cyclopropanes are important structural motifs found in numerous bioactive molecules, and a number of methods are available for their synthesis. However, one of the simplest cyclopropanation reactions involving the intramolecular coupling of two C–H bonds on *gem*-dialkyl groups has remained an elusive transformation. We demonstrate herein that this reaction is accessible using aryl bromide or triflate precursors and the 1,4-Pd shift mechanism. The use of pivalate as the base was found to be crucial to divert the mechanistic pathway toward the cyclopropane instead of the previously obtained benzocyclobutene product. Stoichiometric mechanistic studies allowed the identification of aryl- and alkylpalladium pivalates, which are in equilibrium via a five-membered palladacycle. With pivalate, a second C(sp^3)–H activation leading to the four-membered palladacycle intermediate and the cyclopropane product is favored. A catalytic reaction was developed and showed a broad scope for the generation of diverse arylcyclopropanes, including valuable bicyclo[3.1.0] systems. This method was applied to a concise synthesis of lemborexant, a recently approved anti-insomnia drug.

Photocatalytic deoxygenation of N–O bonds with rhenium complexes: from the reduction of nitrous oxide to pyridine N-oxides

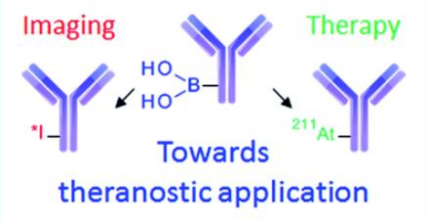


Marianne Kjellberg, Alexia Ohleier, Pierre Thuery, Emmanuel Nicolas, Lucile Anthore-Dalion,* Thibault Cantat * *Chem. Sci.* **2021**, DOI 0.1039/D1SC01974K

https://dx.doi.org/10.1039/D1SC01974K

The accumulation of nitrogen oxides in the environment calls for new pathways to interconvert the various oxidation states of nitrogen, and especially their reduction. However, the large spectrum of reduction potentials covered by nitrogen oxides makes it difficult to find general systems capable of efficiently reducing various *N*-oxides. Here, photocatalysis unlocks high energy species able both to circumvent the inherent low reactivity of the greenhouse gas and oxidant N_2O ($E^0(N_2O/N_2)$ = +1.77 V *vs.* SHE), and to reduce pyridine *N*-oxides ($E_{1/2}$(pyridine *N*-oxide/pyridine) = −1.04 V *vs.* SHE). The rhenium complex [Re(4,4′-*t*Bu-bpy)$(CO)_3$Cl] proved to be efficient in performing both reactions under ambient conditions, enabling the deoxygenation of N_2O as well as synthetically relevant and functionalized pyridine *N*-oxides.

Investigation on the reactivity of nucleophilic radiohalogens with arylboronic acids in water: access to an efficient single-step method for the radioiodination and astatination of antibodies

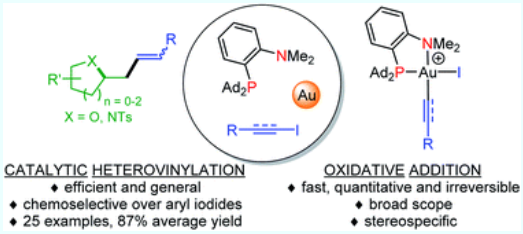


Marion Berdal, Sebastien Gouard, Romain Eychenne, Severine Marionneau-Lambot,Mikael Croyal, Alain Faivre-Chauvet, Michel Cherel, Joelle Gaschet, Jean-François Gestin, * François Guerard * *Chem. Sci.* **2021**, *12*, 1458-1468

https://dx.doi.org/10.1039/D0SC05191H

Easy access to radioiodinated and ^{211}At-labelled bio(macro)molecules is essential to develop new strategies in nuclear imaging and targeted radionuclide therapy of cancers. Yet, the labelling of complex molecules with heavy radiohalogens is often poorly effective due to the multiple steps and intermediate purifications needed. Herein, we investigate the potential of arylboron chemistry as an alternative approach for the late stage labelling of antibodies. The reactivity of a model precursor, 4-chlorobenzeneboronic acid (**1**) with nucleophilic iodine-125 and astatine-211 was at first investigated in aqueous conditions. In the presence of a copper(II) catalyst and 1,10-phenanthroline, quantitative radiochemical yields (RCYs) were achieved within 30 minutes at room temperature. The optimum conditions were then applied to a CD138 targeting monoclonal antibody (mAb) that has previously been validated for imaging and therapy in a preclinical model of multiple myeloma. RCYs remained high (>80% for ^{125}I-labelling and >95% for ^{211}At-labelling), and the whole procedure led to increased specific activities within less time in comparison with previously reported methods. Biodistribution study in mice indicated that targeting properties of the radiolabelled mAb were well preserved, leading to a high tumour uptake in a CD138 expressing tumour model. The possibility of divergent synthesis from a common modified carrier protein demonstrated herein opens facilitated perspectives in radiotheranostic applications with the radioiodine/^{211}At pairs. Overall, the possibility to develop radiolabelling kits offered by this procedure should facilitate its translation to clinical applications.

Oxidative additions of alkynyl/vinyl iodides to gold and gold-catalyzed vinylation reactions triggered by the MeDalphos ligand



Jessica Rodriguez, Alexis Tabey, Sonia Mallet-Ladeir, Didier Bourissou* *Chem. Sci*. **2021**, *12*, 7706-7712

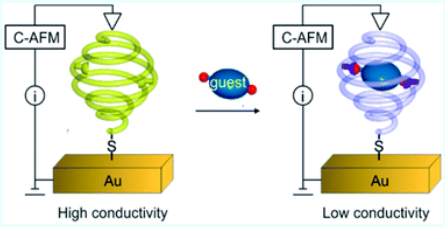
https://dx.doi.org/10.1039/D1SC01483H

The hemilabile $Ad_2P(o\text{-}C_6H_4)NMe_2$ ligand promotes fast, quantitative and irreversible oxidative addition of alkynyl and vinyl iodides to gold. The reaction is general. It works with a broad range of substrates of various electronic bias and steric demand, and proceeds with complete retention of stereochemistry from *Z* and *E* vinyl iodides. Both alkynyl and vinyl iodides react faster than aryl iodides. The elementary step is amenable to catalysis. Oxidative addition of vinyl iodides to gold and π-activation of alkenols (and *N*-alkenyl amines) at gold have been combined to achieve hetero-vinylation reactions. A number of functionalized heterocycles, *i.e.* tetrahydrofuranes, tetrahydropyranes, oxepanes and pyrrolidines were obtained thereby (24 examples, 87% average yield). Taking advantage of the chemoselectivity for vinyl iodides over aryl iodides, sequential transformations involving first a hetero-vinylation step and then a C–N coupling, a C–C coupling or an heteroarylation were achieved from a vinyl/aryl bis-iodide substrate.

Sensing a binding event through charge transport variations using an aromatic oligoamide capsule

Pedro Mateus, Antoine Jacquet, Alejandro Méndez-Ardoy, Alice Boulloy, Brice Kauffmann, Gilles Pecastaings, Thierry Buffeteau, Yann Ferrand, Dario M. Bassani,* Ivan Huc* *Chem. Sci.*, **2021**, *12*, 3743-3750

https://dx.doi.org/10.1039/D0SC06060G

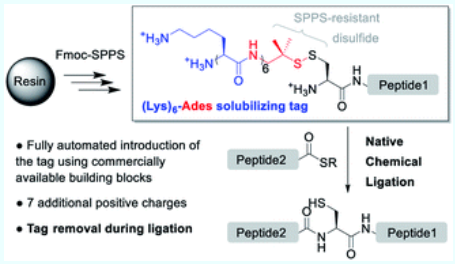


The selective binding properties of a 13-mer oligoamide foldamer capsule composed of 4 different aromatic subunits are reported. The capsule was designed to recognize dicarboxylic acids through multiple-point interactions owing to a combination of protonation/deprotonation events, H-bonding, and geometrical constraints imparted by the rigidity of the foldamer backbone. Compared to tartaric acid, binding of 2,2-difluorosuccinic acid or 2,2,3,3-tetrafluorosuccinic acid resulted in symmetry breaking due to deprotonation of only one of the two carboxylic acid groups of the encapsulated species as shown by NMR studies in solution and by single-crystal X-ray diffraction in the solid state. An analogous 14-mer foldamer capsule terminated with a thiol anchoring group was used to probe the complexation event in self-assembled monolayers on Au substrates. Ellipsometry and polarization-modulation infrared absorption-reflection spectroscopy studies were consistent with the formation of a single molecule layer of the foldamer capsule oriented vertically with respect to the surface. The latter underwent smooth complexation of 2,2-difluorosuccinic acid with deprotonation of one of the two carboxylic acid groups. A significant (80-fold) difference in the charge transport properties of the monolayer upon encapsulation of the dicarboxylic acid was evidenced from conducting-AFM measurements (S = 1.1 × 10^{-9} *vs.* 1.4 × 10^{-11} ohm^{-1} for the empty and complexed capsule, respectively). The modulation in conductivity was assigned to protonation of the aromatic foldamer backbone.

A straightforward methodology to overcome solubility challenges for N-terminal cysteinyl peptide segments used in native chemical ligation

Skander A. Abboud, El hadji Cisse, Michel Doudeau, Hélène Bénédettia, Vincent Aucagne* *Chem. Sci.* **2021**, *12*, 3194-3201

https://dx.doi.org/10.1039/D0SC06001A

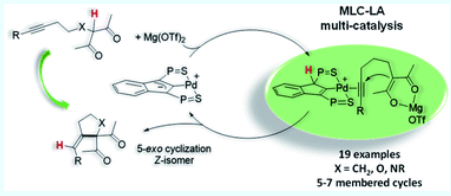


One of the main limitations encountered during the chemical synthesis of proteins through native chemical ligation (NCL) is the limited solubility of some of the peptide segments. The most commonly used solution to overcome this problem is to derivatize the segment with a temporary solubilizing tag. Conveniently, the tag can be introduced on the thioester segment in such a way that it is removed concomitantly with the NCL reaction. We herein describe a generalization of this approach to N-terminal cysteinyl segment counterparts, using a straightforward synthetic approach that can be easily automated from commercially available building blocks, and applied it to a well-known problematic target, SUMO-2.

Metal–ligand–Lewis acid multi-cooperative catalysis: a step forward in the Conia-ene reaction

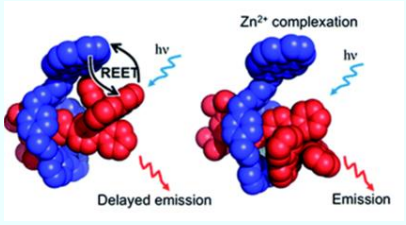
Arnaud Clerc, Enrico Marelli, Nicolas Adet, Julien Monot, Blanca Martín-Vaca* Didier Bourissou* *Chem. Sci.* **2021**, *12*, 435.

https://doi.org/10.1039/D0SC05036A



An original multi-cooperative catalytic approach was developed by combining metal–ligand cooperation and Lewis acid activation. The [(SCS)Pd]$_2$ complex featuring a non-innocent indenediide-based ligand was found to be a very efficient and versatile catalyst for the Conia-ene reaction, when associated with Mg(OTf)$_2$. The reaction operates at low catalytic loadings under mild conditions with HFIP as a co-solvent. It works with a variety of substrates, including those bearing internal alkynes. It displays complete 5-*exo vs.* 6-*endo* regio-selectivity. In addition, except for the highly congested ^{t}Bu-substituent, the reaction occurs with high *Z vs. E* stereo-selectivity, making it synthetically useful and complementary to known catalysts.

Damming an electronic energy reservoir: ion-regulated electronic energy shuttling in a [2]rotaxane

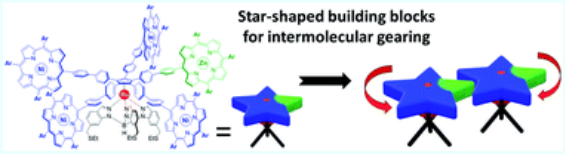


Shilin Yu, Arkady Kupryakov, James E. M. Lewis, Vicente Martí-Centelles, Stephen M. Goldup,* Jean-Luc Pozzo, Gediminas Jonusauskas, Nathan D. McClenaghan* *Chem. Sci.* **2021**, *12*, 9196-9200

https://dx.doi.org/10.1039/D1SC02225C

We demonstrate the first example of bidirectional reversible electronic energy transfer (REET) between the mechanically bonded components of a rotaxane. Our prototypical system was designed such that photoexcitation of a chromophore in the axle results in temporary storage of electronic energy in a quasi-isoenergetic "reservoir" chromophore in the macrocycle. Over time, the emissive state of the axle is repopulated from this reservoir, resulting in long-lived, delayed luminescence. Importantly, we show that cation binding in the cavity formed by the mechanical bond perturbs the axle chromophore energy levels, modulating the REET process, and ultimately providing a luminescence read-out of cation binding. Modulation of REET processes represents an unexplored mechanism in luminescent molecular sensor development.

Desymmetrised pentaporphyrinic gears mounted on metallo-organic anchors

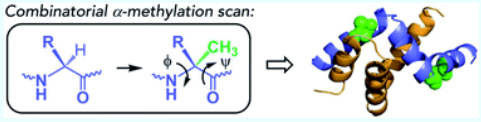


Seifallah Abid, Yohan Gisbert, Mitsuru Kojima, Nathalie Saffon-Merceron, Jérôme Cuny, Claire Kammerer,* Gwénaël Rapenne * *Chem. Sci.* **2021**, *12*, 4709-4721

https://dx.doi.org/10.1039/D0SC06379G

Mastering intermolecular gearing is crucial for the emergence of complex functional nanoscale machineries. However, achieving correlated motion within trains of molecular gears remains highly challenging, due to the multiple degrees of freedom of each cogwheel. In this context, we designed and synthesised a series of star-shaped organometallic molecular gears incorporating a hydrotris(indazolyl)borate anchor to prevent diffusion on the surface, a central ruthenium atom as a fixed rotation axis, and an azimuthal pentaporphyrinic cyclopentadienyl cogwheel specifically labelled to monitor its motion by non-time-resolved Scanning Tunneling Microscopy (STM). Desymmetrisation of the cogwheels was first achieved sterically, *i.e*. by introducing one tooth longer than the other four. For optimal mechanical interactions, chemical labelling was also investigated as a preferential way to induce local contrast in STM images, and the electronic properties of one single paddle were modulated by varying the porphyrinic scaffold or the nature of the central metal. To reach such a structural diversity, our modular synthetic approach relied on sequential cross-coupling reactions on a penta(*p*-halogenophenyl)cyclopentadienyl ruthenium(II) key building block, bearing a single pre-activated *p*-iodophenyl group. Chemoselective Sonogashira or more challenging Suzuki–Miyaura reactions allowed the controlled introduction of the tagged porphyrinic tooth, and the subsequent four-fold cross-couplings yielded the prototypes of pentaporphyrinic molecular gears for on-surface studies, incorporating desymmetrised cogwheels over 5 nm in diameter.

Conformational editing of intrinsically disordered protein by α-methylation



Valentin Bauer, Boris Schmidtgall, Gergő Gógl, Jozica Dolenc, Judit Osz, Yves Nominé, Camille Kostmann, Alexandra Cousido-Siah, André Mitschler, Natacha Rochel, Gilles Travé, Bruno Kieffer , Vladimir Torbeev* *Chem. Sci*. **2021**,*12*, 1080-1089

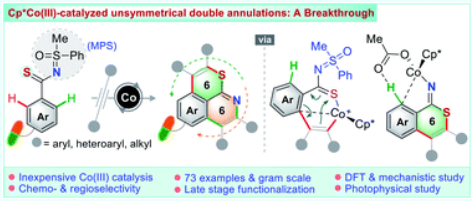
https://dx.doi.org/10.1039/D0SC04482B

Intrinsically disordered proteins (IDPs) constitute a large portion of "Dark Proteome" – difficult to characterize or yet to be discovered protein structures. Here we used conformationally constrained α-methylated amino acids to bias the conformational ensemble in the free unstructured activation domain of transcriptional coactivator ACTR. Different sites and patterns of substitutions were enabled by chemical protein synthesis and led to distinct populations of α-helices. A specific substitution pattern resulted in a substantially higher binding affinity to nuclear coactivator binding domain (NCBD) of CREB-binding protein, a natural binding partner of ACTR. The first X-ray structure of the modified ACTR domain - NCBD complex visualized a unique conformation of ACTR and confirmed that the key α-methylated amino acids are localized within α-helices in the bound state. This study demonstrates a strategy for characterization of individual conformational states of IDPs.

Harnessing sulfur and nitrogen in the cobalt(iii)-catalyzed unsymmetrical double annulation of thioamides: probing the origin of chemo- and regio-selectivity

Majji Shankar, Arijit Saha, Somratan Sau, Arghadip Ghosh, Vincent Gandon,* Akhila K. Sahoo * *Chem. Sci.* **2021**, *12*, 6393-6405

https://dx.doi.org/10.1039/D1SC00765C

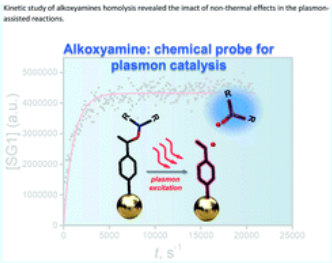


An unconventional cobalt(III)-catalyzed one-pot domino double annulation of aryl thioamides with unactivated alkynes is presented. Sulfur (S), nitrogen (N), and o,o′-C–H bonds of aryl thioamides are involved in this reaction, enabling access to rare 6,6-fused thiopyrano-isoquinoline derivatives. A reverse 'S' coordination over a more conventional 'N' coordination of thioamides to the Co-catalyst specifically regulates the formation of four [C–C and C–S at first and then C–N and C–C] bonds in a single operation, a concept which is uncovered for the first time. The power of the N-masked methyl phenyl sulfoximine (MPS) directing group in this annulation sequence is established. The transformation is successfully developed, building a novel chemical space of structural diversity (56 examples). In addition, the late-stage annulation of biologically relevant motifs and drug candidates is disclosed (17 examples). The preliminary photophysical properties of thiopyrano-isoquinoline derivatives are discussed. Density functional theory (DFT) studies authenticate the participation of a unique 6π-electrocyclization of a 7-membered S-chelated cobaltacycle in the annulation process.

Establishing plasmon contribution to chemical reactions: alkoxyamines as a thermal probe

Olga Guselnikova, Gérard Audran, Jean-Patrick Joly, Andrii Trelin, Evgeny V. Tretyakov, Vaclav Svorcik, Oleksiy Lyutakov, Sylvain R. A. Marque,* Pavel Postnikov * *Chem. Sci.* **2021**, *12*, 4154-4161

https://dx.doi.org/10.1039/D0SC06470J

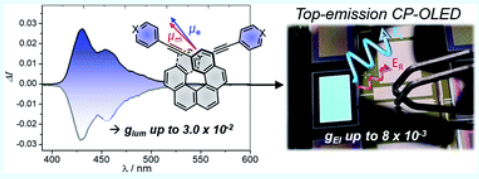


The nature of plasmon interaction with organic molecules is a subject of fierce discussion about thermal and non-thermal effects. Despite the abundance of physical methods for evaluating the plasmonic effects, chemical insight has not been reported yet. In this contribution, we propose a chemical insight into the plasmon effect on reaction kinetics using alkoxyamines as an organic probe through their homolysis, leading to the generation of nitroxide radicals. Alkoxyamines (TEMPO- and SG_1-substituted) with well-studied homolysis behavior are covalently attached to spherical Au nanoparticles. We evaluate the kinetic parameters of homolysis of alkoxyamines attached on a plasmon-active surface under heating and irradiation at a wavelength of plasmon resonance. The estimation of kinetic parameters from experiments with different probes (**Au–TEMPO**, **Au–SG_1**, **Au–SG_1–TEMPO**) allows revealing the apparent differences associated with the non-thermal contribution of plasmon activation. Moreover, our findings underline the dependency of kinetic parameters on the structure of organic molecules, which highlights the necessity to consider the nature of organic transformations and molecular structure in plasmon catalysis.

Achieving high circularly polarized luminescence with push–pull helicenic systems: from rationalized design to top-emission CP-OLED applications

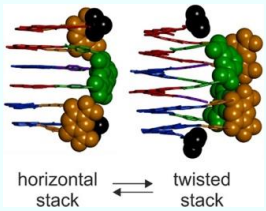
Kais Dhbaibi,ab Laura Abella, ORCID logo c Sylvia Meunier-Della-Gatta,d Thierry Roisnel, Nicolas Vanthuyne, Bassem Jamoussi, Grégory Pieters, Benoît Racine,Etienne Quesnel, Jochen Autschbach,*Jeanne Crassous*Ludovic Favereau* *Chem. Sci.* **2021**, *12*, 5522-5533

https://dx.doi.org/10.1039/D0SC06895K



While the development of chiral molecules displaying circularly polarized luminescence (CPL) has received considerable attention, the corresponding CPL intensity, g_{lum}, hardly exceeds 10^{-2} at the molecular level owing to the difficulty in optimizing the key parameters governing such a luminescence process. To address this challenge, we report here the synthesis and chiroptical properties of a new family of π-helical push–pull systems based on carbo[6]helicene, where the latter acts as either a chiral electron acceptor or a donor unit. This comprehensive experimental and theoretical investigation shows that the magnitude and relative orientation of the electric (μ_e) and magnetic (μ_m) dipole transition moments can be tuned efficiently with regard to the molecular chiroptical properties, which results in high g_{lum} values, *i.e.* up to 3–4 × 10^{-2}. Our investigations revealed that the optimized mutual orientation of the electric and magnetic dipoles in the excited state is a crucial parameter to achieve intense helicene-mediated exciton coupling, which is a major contributor to the obtained strong CPL. Finally, top-emission CP-OLEDs were fabricated through vapor deposition, which afforded a promising g_{EL} of around 8 × 10^{-3}. These results bring about further molecular design guidelines to reach high CPL intensity and offer new insights into the development of innovative CP-OLED architectures.

Large-Amplitude Conformational Changes in Self-Assembled Multi-Stranded Aromatic Sheets

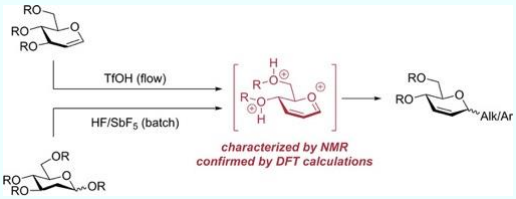


Joan Atcher, Pedro Mateus, Brice Kauffmann, Frédéric Rosu, Victor Maurizot, Ivan Huc* *Angew. Chem. Int. Ed.* **2021**, *60*, 2574

https://doi.org/10.1002/anie.202014670

The employment of the hexyl-substituted anion [HexCB11Cl11]− allowed the synthesis of a ZnII species, Zn[HexCB11Cl11]2, 3, in which the Zn2+ cation is only weakly coordinated to two carborate counterions and that is soluble in low polarity organic solvents such as bromobenzene. DOSY NMR studies show the facile displacement of at least one of the counterions, and this near nakedness of the cation results in high catalytic activity in the hydrosilylation of 1-hexene and 1-methyl-1cyclohexene. Fluoride ion affinity (FIA) calculations reveal a solution Lewis acidity of 3 (FIA=262.1 kJ mol−1) that is higher than that of the landmark Lewis acid B(C6F5)3 (FIA=220.5 kJ mol−1). This high Lewis acidity leads to a high activity in catalytic CO2 and Ph2CO reduction by Et3SiH and hydrogenation of 1,1-diphenylethylene using 1,4-cyclohexadiene as the hydrogen source. Compound 3 was characterized by multinuclear NMR spectroscopy, mass spectrometry, single crystal X-ray diffraction, and DFT studies.

Insight into the Ferrier Rearrangement by Combining Flash Chemistry and Superacids

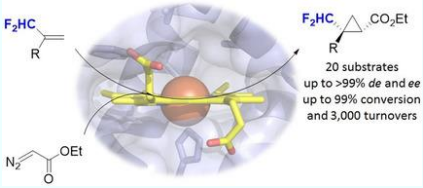


Naresh Bhuma, Ludivine Lebedel, Hiroki Yamashita, Yutaka Shimizu, Zahra Abada, Ana Ardá, Jérôme Désiré, Bastien Michelet, Agnès Martin-Mingot, Ali Abou-Hassan, Masahiro Takumi, Jérôme Marrot, Jesús Jiménez-Barbero, Aiichiro Nagaki, Yves Blériot, Sébastien Thibaudeau* *Angew. Chem. Int. Ed.* **2021**, *60*, 2036

https://doi.org/10.1002/anie.202010175

The transformation of glycals into 2,3-unsaturated glycosyl derivatives, reported by Ferrier in 1962, is supposed to involve an α,β unsaturated glycosyl cation, an elusive ionic species that has still to be observed experimentally. Herein, while combination of TfOH and flow conditions failed to observe this ionic species, its extended lifetime in superacid solutions allowed its characterization by NMR-based structural analysis supported by DFT calculations. This allyloxycarbenium ion was further exploited in the Ferrier rearrangement to afford unsaturated nitrogen-containing C-aryl glycosides and C-alkyl glycosides under superacid and flow conditions, respectively.

Biocatalytic Strategy for the Highly Stereoselective Synthesis of CHF2-Containing Trisubstituted Cyclopropanes

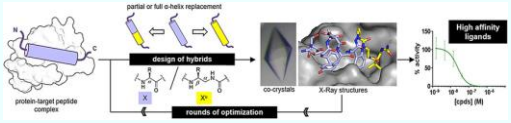


Daniela M. Carminati, Jonathan Decaens, Samuel Couve-Bonnaire, Philippe Jubault,* Rudi Fasan* *Angew. Chem. Int. Ed.* **2021**, *60*, 7072

https://doi.org/10.1002/anie.202015895

The difluoromethyl (CHF2) group has attracted significant attention in drug discovery and development efforts, owing to its ability to serve as fluorinated bioisostere of methyl, hydroxyl, and thiol groups. Herein, we report an efficient biocatalytic method for the highly diastereo- and enantioselective synthesis of CHF2-containing trisubstituted cyclopropanes. Using engineered myoglobin catalysts, a broad range of α-difluoromethyl alkenes are cyclopropanated in the presence of ethyl diazoacetate to give CHF2-containing cyclopropanes in high yield (up to >99 %, up to 3000 TON) and with excellent stereoselectivity (up to >99 % de and ee). Enantiodivergent selectivity and extension of the method to the stereoselective cyclopropanation of mono- and trifluoromethylated olefins was also achieved. This methodology represents a powerful strategy for the stereoselective synthesis of high-value fluorinated building blocks for medicinal chemistry, as exemplified by the formal total synthesis of a CHF2 isostere of a TRPV1 inhibitor.

Structural Basis for α-Helix Mimicry and Inhibition of Protein–Protein Interactions with Oligourea Foldamers

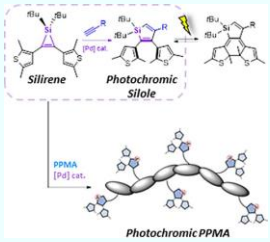


Léonie Cussol, Laura Mauran-Ambrosino, Jérémie Buratto, Anna Y Belorusova, Maxime Neuville, Judit Osz, Sébastien Fribourg, Juliette Fremaux, Christel Dolain, Sébastien R. Goudreau, Natacha Rochel, Gilles Guichard* *Angew. Chem. Int. Ed.* **2021**, *60*, 2296-2303

https://doi.org/10.1002/anie.202008992

Efficient optimization of a peptide lead into a drug candidate frequently needs further transformation to augment properties such as bioavailability. Among the different options, foldamers, which are sequence-based oligomers with precise folded conformation, have emerged as a promising technology. We introduce oligourea foldamers to reduce the peptide character of inhibitors of protein–protein interactions (PPI). However, the precise design of such mimics is currently limited by the lack of structural information on how these foldamers adapt to protein surfaces. We report a collection of X-ray structures of peptide–oligourea hybrids in complex with ubiquitin ligase MDM2 and vitamin D receptor and show how such hybrid oligomers can be designed to bind with high affinity to protein targets. This work should enable the generation of more effective foldamer-based disruptors of PPIs in the context of peptide lead optimization.

Dithienylethene-Based Photochromic Siloles: A Straightforward and Divergent Synthetic Strategy.

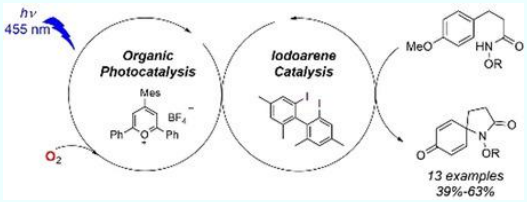


Marc Devillard,* Nour Nour Eddine, Marie Cordier, Gilles Alcaraz* *Angew. Chem. Int. Ed.* **2021**, *60*, 12356-12359

https://doi.org/10.1002/anie.202102540

A straightforward synthetic methodology for the preparation of photochromic siloles based on the dithienylethene motif is developed. It relies upon an efficient palladium-catalyzed annulation reaction of a 2,3-bis(3-thienyl)-silirene with terminal alkynes in mild conditions. The reaction is functional group-tolerant and can be performed in high yields with a variety of functional terminal alkynes. It can even be extended to a polymeric polypropargylmethacrylamide (PPMA) substrate affording the corresponding photochromic polymer with different degree of photochromic unit incorporation by simply adjusting the polymer/ silirene stoichiometric ratio.

Photoinduced Aerobic Iodoarene-Catalyzed Spirocyclization of N-Oxy-amides to N-Fused Spirolactams

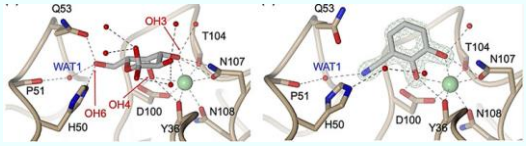


Loïc Habert, Kevin Cariou* *Angew. Chem. Int. Ed.* **2021**, *60*, 171-175

https://doi.org/10.1002/anie.202009175

Iodoarene catalysis is a powerful methodology that usually requires an excess of oxidant, or of redox mediator if the terminal oxidant is dioxygen, to generate the key hypervalent iodine intermediate to proceed efficiently. We report that, using the spiro-cyclization of amides as a benchmark reaction, aerobic iodoarene catalysis can be enabled by relying on a pyrylium photocatalyst under blue light irradiation. This unprecedented dual organocatalytic system allows the use of low catalytic loading of both catalysts under very mild operating conditions.

Non-Carbohydrate Glycomimetics as Inhibitors of Calcium(II)-Binding Lectins.

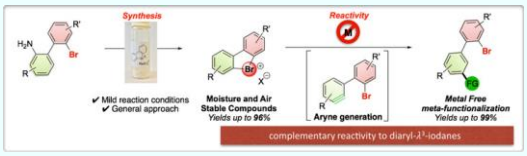


Sakonwan Kuhaudomlarp, Eike Siebs, Elena Shanina, Jérémie Topin, Ines Joachim, Priscila da Silva Figueiredo Celestino Gomes, Annabelle Varrot, Didier Rognan, Christoph Rademacher, Anne Imberty,* Alexander Titz * *Angew. Chem. Int. Ed.* **2021**, *60*, 8104-8114

https://doi.org/10.1002/anie.202013217

Because of the antimicrobial resistance crisis, lectins are considered novel drug targets. Pseudomonas aeruginosa utilizes LecA and LecB in the infection process. Inhibition of both lectins with carbohydrate-derived molecules can reduce biofilm formation to restore antimicrobial susceptibility. Here, we focused on non-carbohydrate inhibitors for LecA to explore new avenues for lectin inhibition. From a screening cascade we obtained one experimentally confirmed hit, a catechol, belonging to the well-known PAINS compounds. Rigorous analyses validated electron-deficient catechols as millimolar LecA inhibitors. The first co-crystal structure of a non-carbohydrate inhibitor in complex with a bacterial lectin clearly demonstrates the catechol mimicking the binding of natural glycosides with LecA. Importantly, catechol 3 is the first non-carbohydrate lectin ligand that binds bacterial and mammalian calcium(II)-binding lectins, giving rise to this fundamentally new class of glycomimetics.

Cyclic Diaryl λ3-Bromanes as Original Aryne Precursors.

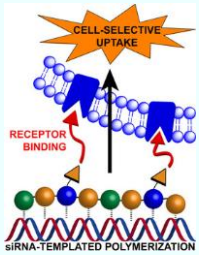


Matteo Lanzi, Quentin Dherbassy, Joanna Wencel-Delord* *Angew. Chem. Int. Ed.* **2021**, *60*, 14852-14857

https://doi.org/10.1002/anie.202103625

Despite the widespread application of hypervalent iodines, the corresponding lambda(3)-bromanes are less explored. Herein we report a general, safe, and high-yielding strategy to access cyclic diaryl lambda(3)-bromanes. These unique compounds feature reactivity that is appealing and complementary to that of lambda(3)-iodanes, generating arynes under mild reaction conditions and in the presence of a weak base. Accordingly, formal meta-selective transition-metal-free C-O and C-N couplings may be achieved. Mechanistic studies unambiguously support the aryne generation mechanism.

Cell-Selective siRNA Delivery Using Glycosylated Dynamic Covalent Polymers Self-Assembled In Situ by RNA Templating.



Nabila Laroui, Maëva Coste, Dandan Su, Lamiaa M. A. Ali, Yannick Bessin, Mihail Barboiu, Magali Gary-Bobo, Nadir Bettache,* Sébastien Ulrich * *Angew. Chem. Int. Ed.* **2021**, *60*, 5783-5787

https://doi.org/10.1002/anie.202014066

Dynamic covalent libraries enable exploring complex chemical systems from which bioactive assemblies can adaptively emerge through template effects. In this work, we studied dynamic covalent libraries made of complementary bifunctional cationic peptides, yielding a diversity of species from macrocycles to polymers. Although polymers are typically expressed only at high concentration, we found that siRNA acts as a template in the formation of dynamic covalent polymers at low concentration in a process guided by electrostatic binding. Using a glycosylated building block, we were able to show that this templated polymerization further translates into the multivalent presentation of carbohydrate ligands, which subsequently promotes cell uptake and even cell-selective siRNA delivery.

Precise Alkoxyamine Design to Enable Automated Tandem Mass Spectrometry Sequencing of Digital Poly(phosphodiester)s.

Kévin Launay, Jean-Arthur Amalian, Eline Laurent, Laurence Oswald, Dr. Abdelaziz Al Ouahabi, Alexandre Burel, Florent Dufour, Christine Carapito, Jean-Louis Clément, Jean-François Lutz,* Laurence Charles,* Didier Gigmes * *Angew. Chem. Int. Ed.* **2021**, *60*, 917-926

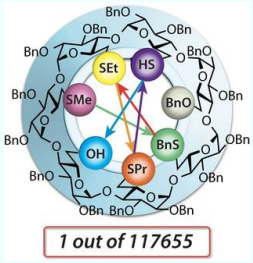
https://doi.org/10.1002/anie.202010171

A major step towards reliable reading of information coded in the sequence of long poly(phosphodiester)s was previously achieved by introducing an alkoxyamine spacer between information sub-segments. However, MS/MS decoding had to be performed manually to safely identify useful fragments of low abundance compared to side-products from the amide-based alkoxyamine used. Here, alternative alkoxyamines were designed to prevent side-reactions and enable automated MS/MS sequencing. Different styryl-TEMPO spacers were prepared to increase radical delocalization and stiffness of the structure. Their dissociation behavior was investigated by EPR and best results were obtained with spacers containing in-chain benzyl ring, with no side-reaction during synthesis or sequencing. Automated decoding of these polymers was performed using the MS-DECODER software, which interprets fragmentation data recorded for each sub-segment and re-align them in their original order based on location tags.

Programmed synthesis of Hepta-Differentiated beta-Cyclodextrin: 1 out of 117655 Arrangements.

Jiang Liu, Bo Wang, Cédric Przybylski, Olivia Bistri-Aslanoff, Mickaël Ménand, Yongmin Zhang, Matthieu Sollogoub* *Angew. Chem. Int. Ed.* **2021**, *60*, 12090-12096

https://doi.org/10.1002/anie.202102182

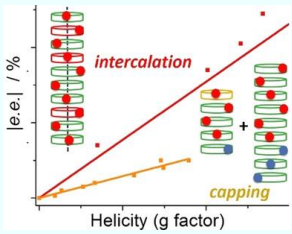


Cyclodextrin poly-functionalization has fueled progress in their use in multiple applications such as enzyme mimicry, but also in the polymer sciences, luminescence, as sensors or for biomedical applications. However, regioselective access to a given pattern of functions on beta-cyclodextrin is still very limited. We uncover a new orienting group, the thioacetate, that expands the toolbox available for cyclodextrin poly-hetero-functionalization using diisobutylaluminum hydride (DIBAL-H) promoted debenzylation. The usefulness of this group is illustrated in the first synthesis of a precisely hepta-hetero-functionalized beta-cyclodextrin. By way of comparison, a random hepta-functionalization would give 117655 different molecules. This synthesis is not simply the vain quest for the Holy Grail of CD hetero-functionalization, but it illustrates the versatility of the DIBAL-H oriented hetero-functionalization strategy, opening the way to a multitude of useful functionalization patterns for new practical applications.

Dissecting the Role of the Sergeants in Supramolecular Helical Catalysts: From Chain Capping to Intercalation.

Mayte A. Martínez-Aguirre, Yan Li, Nicolas Vanthuyne, Laurent Bouteiller, Matthieu Raynal* *Angew. Chem. Int. Ed.* **2021**, *60*, 4183-4191

https://doi.org/10.1002/anie.202012457

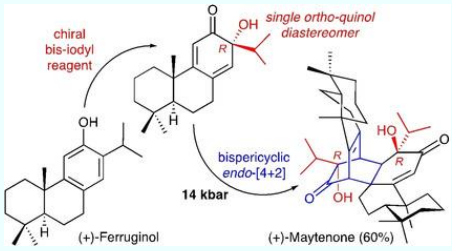


Controlling the properties of supramolecular assemblies requires unveiling the specific interactions between their components. In the present work, the catalytic properties and structure of co-assemblies composed of a benzene-1,3,5-tricarboxamide (BTA) ligand coordinated to copper (the soldier) and seven enantiopure BTAs (the sergeants) have been determined. Whatever the sergeant, the enantioselectivity of the reaction is directly proportional to the optical purity of the supramolecular helices. More strikingly, the role played by the sergeant in the co-assembly process differs significantly: from almost pure intercalator (when it is incorporated in the stacks of the soldier and generates long homochiral helices) to pure chain capper (when it leads to the formation of partly helically biased and short assemblies). The former situation leads to optimal enantioselectivity for the catalytic system under study (58 % ee) while the latter situation leads to very low selectivity (8 % ee). The successful rationalization of this high and unexpected difference is crucial for the development of more efficient catalysts and more elaborate supramolecular systems.

Bispericyclic Diels-Alder Dimerization of ortho-Quinols in Natural Product (Bio)Synthesis: Bioinspired Chemical 6-Step Synthesis of (+)-Maytenone.

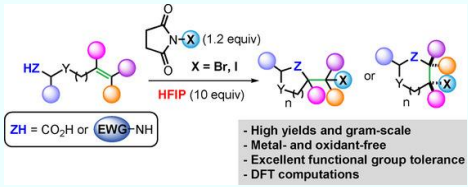
Philippe A. Peixoto, Mourad El Assal, Isabelle Chataigner, Frédéric Castet, Anaëlle Cornu, Romain Coffinier, Cyril Bosset, Denis Deffieux, Laurent Pouységu,* Stéphane Quideau* *Angew. Chem. Int. Ed.* **2021**, *60*, 14967-14974

https://doi.org/10.1002/anie.202103410



Many natural products of plant or microbial origins are derived from enzymatic dearomative oxygenation of 2-alkylphenolic precursors into 6-alkyl-6-hydroxycyclohexa-2,4-dienones. These so-called ortho-quinols cyclodimerize via a remarkably selective bispericyclic Diels-Alder reaction. Whether or not the intervention of catalytic or dirigent proteins is involved during this final step of the biosynthesis of these natural products, this cyclodimerization of ortho-quinols can be chemically reproduced in the laboratory with the same strict level of site-specific regioselectivity and stereoselectivity. This unique yet unified process, which finds its rationale in the inherent chemical reactivity of those ortho-quinols, is illustrated herein by an efficient and bioinspired first chemical synthesis of one of the most structurally complex and synthetically challenging examples of such natural cyclodimers, the bisditerpenoid (+)-maytenone.

Hexafluoroisopropanol-Promoted Haloamidation and Halolactonization of Unactivated Alkenes.

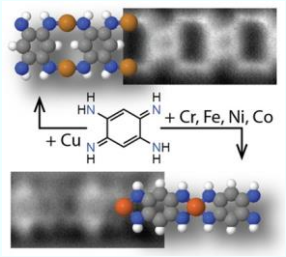


Chenxiao Qi, Guillaume Force, Vincent Gandon,* David Lebœuf*
Angew. Chem. Int. Ed. **2021**, *60*, 946-953

https://doi.org/10.1002/anie.202010846

Pyrrolidine and piperidine derivatives bearing halide functional groups are prevalent building blocks in drug discovery as halides can serve as an anchor for post-modifications. In principle, one of the simplest ways to build these frameworks is the haloamination of alkenes. While progress has been made in this field, notably with the development of enantioselective versions, this reaction is still fraught with limitations in terms of reactivity. Besides, a major question remaining is to understand the mechanism at work. The formation of a haliranium intermediate is typically mentioned, but limited mechanistic evidence supports it. Reported here is an efficient metal- and oxidant-free protocol to achieve the haloamidation of olefins, promoted by hexafluoroisopropanol, along with a DFT investigation of the mechanism. These findings should guide the future development of more complex transformations in the field of halofunctionalization.

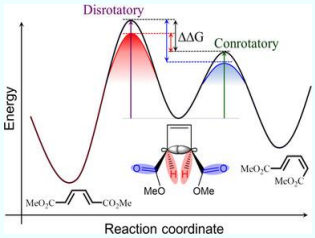
1D Coordination pi-d Conjugated Polymers with Distinct Structures Defined by the Choice of the Transition Metal: Towards a New Class of Antiaromatic Macrocycles.



Vijai M. Santhini, Christian Wäckerlin, Aleš Cahlík, Martin Ondráček, Simon Pascal, Adam Matěj, Oleksandr Stetsovych, Pingo Mutombo, Petr Lazar, Olivier Siri,* Pavel Jelínek* *Angew. Chem. Int. Ed.* **2021**, *60*, 439-445
https://doi.org/10.1002/anie.202011462

Recently pi-d conjugated coordination polymers have received a lot of attention owing to their unique material properties, although synthesis of long and defect-free polymers remains challenging. Herein we introduce a novel on-surface synthesis of coordination polymers with quinoidal ligands under ultra-high vacuum conditions, which enables formation of flexible coordination polymers with lengths up to hundreds of nanometers. Moreover, this procedure allows the incorporation of different transition-metal atoms with four- or two-fold coordination. Remarkably, the two-fold coordination mode revealed the formation of wires constituted by (electronically) independent 12-membered antiaromatic macrocycles linked together through two C-C single bonds.

Modifying Woodward-Hoffmann Stereoselectivity Under Vibrational Strong Coupling.

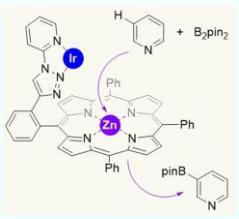


Abhijit Sau, Kalaivanan Nagarajan, Bianca Patrahau, Lucas Lethuillier-Karl, Robrecht M. A. Vergauwe, Anoop Thomas, Joseph Moran,* Cyriaque Genet,* Thomas W. Ebbesen* *Angew. Chem. Int. Ed.* **2021**, *60*, 5712-5717

https://doi.org/10.1002/anie.202013465

Vibrational strong coupling (VSC) has recently been shown to change the rate and chemoselectivity of ground-state chemical reactions via the formation of light-matter hybrid polaritonic states. However, the observation that vibrational-mode symmetry has a large influence on charge-transfer reactions under VSC suggests that symmetry considerations could be used to control other types of chemical selectivity through VSC. Here, we show that VSC influences the stereoselectivity of the thermal electrocyclic ring opening of a cyclobutene derivative, a reaction which follows the Woodward-Hoffmann rules. The direction of the change in stereoselectivity depends on the vibrational mode that is coupled, as do changes in rate and reaction thermodynamics. These results on pericyclic reactions confirm that symmetry plays a key role in chemistry under VSC.

Enzyme-like Supramolecular Iridium Catalysis Enabling C-H Bond Borylation of Pyridines with meta-Selectivity



Jonathan Trouvé, Dr. Paolo Zardi, Shaymaa Al-Shehimy, Thierry Roisnel, Rafael Gramage-Doria * *Angew. Chem. Int. Ed.* **2021**, *60*, 18006-18013

https://doi.org/10.1002/anie.202101997

The use of secondary interactions between substrates and catalysts is a promising strategy to discover selective transition metal catalysts for atom-economy C-H bond functionalization. The most powerful catalysts are found via trial-and-error screening due to the low association constants between the substrate and the catalyst in which small stereo-electronic modifications within them can lead to very different reactivities. To circumvent these limitations and to increase the level of reactivity prediction in these important reactions, we report herein a supramolecular catalyst harnessing ZnN interactions that binds to pyridine-like substrates as tight as it can be found in some enzymes. The distance and spatial geometry between the active site and the substrate binding site is ideal to target unprecedented meta-selective iridium-catalyzed C-H bond borylations with enzymatic Michaelis-Menten kinetics, besides unique substrate selectivity and dormant reactivity patterns.

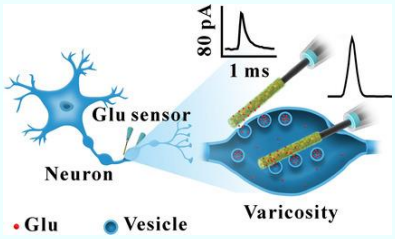
Alkylidene Meldrum's Acids as Platforms for the Vinylogous Synthesis of Dihydropyranones.

Stéphane Wittmann, Thomas Martzel, Cong Thanh Pham Truong, Martial Toffano, Sylvain Oudeyer, Régis Guillot, Chloée Bournaud, Vincent Gandon, Jean-François Brière,* Giang Vo-Thanh* *Angew. Chem. Int. Ed.* **2021**, *60*, 11110-11114

https://doi.org/10.1002/anie.202014489

Upon Bronsted base organocatalysis, ketone-derived alkylidene Meldrum's acids proved to be competent vinylogous platforms able to undergo a formal (4+2) cycloaddition reaction with dihydro-2,3-furandione, providing an unprecedented route to 3,6-dihydropyran-2-ones as spiro[4.5]decane derivatives with up to 98 % ee thanks to the commercially available Takemoto catalyst. Preliminary investigation showed that this reaction could be extended to other activated ketones, establishing these alkylidene Meldrum's acids as a novel C4-synthon in the vinylogous series.

Quantitative Nano-amperometric Measurement of Intravesicular Glutamate Content and its Sub-Quantal Release by Living Neurons.

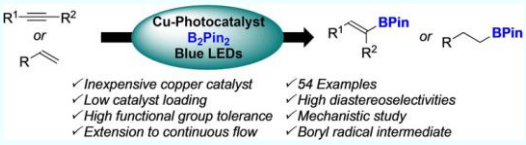


Xiao-Ke Yang, Fu-Li Zhang, Wen-Tao Wu, Yun Tang, Jing Yan, Yan-Ling Liu, Christian Amatore,* Wei-Hua Huang * *Angew. Chem. Int. Ed.* **2021**, *60*, 15803-15808

https://doi.org/10.1002/anie.202100882

Quantitative measurements of intravesicular glutamate (Glu) and of transient exocytotic release contents directly from individual living neurons are highly desired for understanding the mechanisms (full or sub-quantal release?) of synaptic transmission and plasticity. However, this could not be achieved so far due to the lack of adequate experimental strategies relying on selective and sensitive Glu nanosensors. Herein, we introduce a novel electrochemical Glu nanobiosensor based on a single SiC nanowire that can selectively measure in real-time Glu fluxes released via exocytosis by large Glu vesicles (ca. 125 nm diameter) present in single hippocampal axonal varicosities as well as their intravesicular content before exocytosis. These measurements revealed a sub-quantal release mode in living hippocampal neurons, viz., only ca. one third to one half of intravesicular Glu molecules are released by individual vesicles during exocytotic events. Importantly, this fraction remained practically the same when hippocampal neurons were pretreated with L-Glu-precursor L-glutamine, while it significantly increased after zinc treatment, although in both cases the intravesicular contents were drastically affected.

Copper-Photocatalyzed Hydroboration of Alkynes and Alkenes.

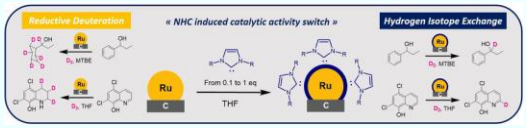


Mingbing Zhong, Yohann Gagné, Taylor O. Hope, Xavier Pannecoucke, Mathieu Frenette, Philippe Jubault, Thomas Poisson* *Angew. Chem. Int. Ed.* **2021**, *60*, 14498-14503

https://doi.org/10.1002/anie.202101874

The photocatalytic hydroboration of alkenes and alkynes is reported. The use of newly-designed copper photocatalysts with B(2)Pin(2) permits the formation a boryl radical, which is used for hydroboration of a large panel of alkenes and alkynes. The hydroborated products were isolated in high yields, with excellent diastereoselectivities and a high functional group tolerance under mild conditions. The hydroboration reactions were developed under continuous flow conditions to demonstrate their synthetic utility. The reaction mechanism was studied and suggested an oxidation reaction between an in situ formed borate and the Cu-photocatalyst in its excited state for the boryl radical formation.

Tuning the Reactivity of a Heterogeneous Catalyst using N-Heterocyclic Carbene Ligands for C–H Activation Reactions.



Alberto Palazzolo, Timothée Naret, Marion Daniel-Bertrand, David-Alexandre Buisson, Simon Tricard, Philippe Lesot, Yannick Coppel, Bruno Chaudret, Sophie Feuillastre, Grégory Pieters* *Angew. Chem. Int. Ed.* **2020**, *59*, 20879-20884

https://doi.org/10.1002/anie.202009258

We report the dramatic impact of the addition of N-heterocyclic carbenes (NHCs) on the reactivity and selectivity of heterogeneous Ru catalysts in the context of C–H activation reactions. Using a simple and robust method, we prepared a series of new air-stable catalysts starting from commercially available Ru on carbon (Ru/C) and differently substituted NHCs. Associated with C–H deuteration processes, depending on Ru/C-NHC ratios, the chemical outcome can be controlled to a large extent. Indeed, tuning the reactivity of the Ru catalyst with NHC enabled: 1) increased chemoselectivity and the regioselectivity for the deuteration of alcohols in organic media; 2) the synthesis of fragile pharmaceutically relevant deuterated heterocycles (azine, purine) that are otherwise completely reduced using unmodified commercial catalysts; 3) the discovery of a novel reactivity for such heterogeneous Ru catalysts, namely the selective C-1 deuteration of aldehydes.

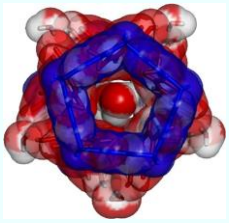
A Bis-Acridinium Macrocycle as Multi-Responsive Receptor and Selective Phase-Transfer Agent of Perylene.

Johnny Hu, Jas S. Ward, Alain Chaumont, Kari Rissanen, Jean-Marc Vincent,* Valérie Heitz,* Henri-Pierre Jacquot de Rouville* *Angew. Chem. Int. Ed.* **2020**, *59*, 23206-23212

https://doi.org/10.1002/anie.202009212

A bis-acridinium cyclophane incorporating switchable acridinium moieties linked by a 3,5-dipyridylanisole spacer was studied as a multi-responsive host for polycyclic aromatic hydrocarbon guests. Complexation of perylene was shown to be the most effective and was characterized in particular by a charge-transfer band as signal output. Effective catch and release of the guest was triggered by both chemical (proton/hydroxide) and redox stimuli. Moreover, the dicationic host was also easily switched between organic and perfluorocarbon phases for applications related to the enrichment of perylene from a mixture of polycyclic aromatic hydrocarbons.

Biomimetic Approach for Highly Selective Artificial Water Channels Based on Tubular Pillar[5]arene Dimers.



Dmytro Strilets, Shixin Fa, Arthur Hardiagon, Marc Baaden, Prof. Tomoki Ogoshi, Mihail Barboiu* *Angew. Chem. Int. Ed.* **2020**, *59*, 23213-23219

https://doi.org/10.1002/anie.202009219

Artificial water channels mimicking natural aquaporins (AQPs) can be used for selective and fast transport of water. Here, we quantify the transport performances of peralkyl-carboxylate-pillar[5]arenes dimers in bilayer membranes. They can transport ≈10^7 water molecules/channel/second, within one order of magnitude of the transport rates of AQPs, rejecting Na+ and K+ cations. The dimers have a tubular structure, superposing pillar[5]arene pores of 5 Å diameter with twisted carboxy-phenyl pores of 2.8 Å diameter. This biomimetic platform, with variable pore dimensions within the same structure, offers size restriction reminiscent of natural proteins. It allows water molecules to selectively transit and prevents bigger hydrated cations from passing through the 2.8 Å pore. Molecular simulations prove that dimeric or multimeric honeycomb aggregates are stable in the membrane and form water pathways through the bilayer. Over time, a significant shift of the upper vs. lower layer occurs initiating new unexpected water permeation events through toroidal pores.

Enzyme-Cleavable Linkers for Protein Chemical Synthesis through Solid-Phase Ligations.

Skander A. Abboud, Mehdi Amoura, Jean-Baptiste Madinier, Brigitte Renoux, Sébastien Papot, Véronique Piller, Vincent Aucagne* *Angew. Chem. Int. Ed.* **2021**, *60*, 18612-18618

https://doi.org/10.1002/anie.202103768

A chemoenzymatic approach was developed for the synthesis of proteins by solid-supported chemical ligation based on a tailor-made phosphatase-cleavable linker (see scheme). The size of the enzyme used directly correlates with the efficiency of the release of the synthesized protein. The method was applied to the synthesis of a 15 kDa polypeptide, the longest sequence ever synthesized through solid-phase native chemical ligation.

Chalcogen-Bonding Catalysis with Telluronium Cations.

Robin Weiss, Emmanuel Aubert, Patrick Pale,* Victor Mamane*
Angew. Chem. Int. Ed. **2021**, *60*, 19281-19286

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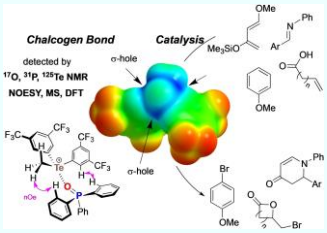
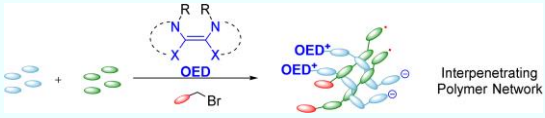


Chalcogen bonding results from non-covalent interactions occurring between electrodeficient chalcogen atoms and Lewis bases. Among the chalcogens, tellurium is the strongest Lewis acid, but Te-based compounds are scarcely used as organocatalysts. For the first time, telluronium cations demonstrated impressive catalytic properties at low loadings in three benchmark reactions: the Friedel–Crafts bromination of anisole, the bromolactonization of ω-unsaturated carboxylic acids and the aza-Diels–Alder between Danishefsky's diene and imines. The ability of telluronium cations to interact with a Lewis base through chalcogen bonding was demonstrated on the basis of multi-nuclear (^{17}O, ^{31}P, and ^{125}Te) NMR analysis and DFT calculations.

Switching from Single to Simultaneous Free-Radical and Anionic Polymerization with Enamine-Based Organic Electron Donors.

Yuxi Zhao, Marion Rollet, Laurence Charles, Gabriel Canard, Didier Gigmes, Patrice Vanelle, Julie Broggi* *Angew. Chem. Int. Ed.* **2021**, *60*, 19389-19396

https://doi.org/10.1002/anie.202106733

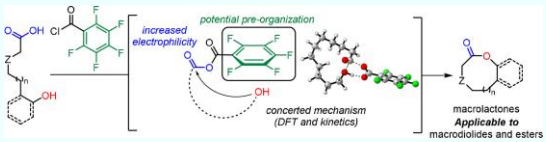


Although most monomers can polymerize through different propagation pathways, polymerization-initiating systems that can switch from one mode to another are rare. In this study, we demonstrate that enamine-based organic electron donors (OEDs) constitute the first systems able to initiate either free-radical or anionic polymerization under simple, mild, and safe conditions. While direct electron-transfer reduction of monomers by OEDs results in the initiation of anionic chain-growth polymerization, introduction of a competing oxidant with a higher reduction potential than the monomer switches the former anionic propagation to a clean radical-propagation process. The benefit of this dual-mode activator is highlighted in the synthesis of an interpenetrating polymer network through simultaneous initiation of radical and anionic propagation processes.

Macrolactonization Reactions Driven by a Pentafluorobenzoyl Group.

Guillaume Force, Anna Perfetto, Robert J. Mayer, Ilaria Ciofini, David Lebœuf* *Angew. Chem. Int. Ed.* **2021**, *60*, 19843-19851

https://doi.org/10.1002/anie.202105882

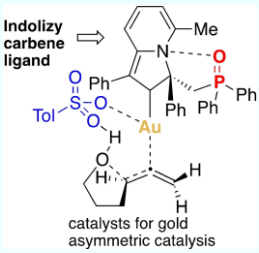


Macrolactones constitute a privileged class of natural and synthetic products with a broad range of applications in the fine chemicals and pharmaceutical industry. Despite all the progress made towards their synthesis, notably from seco-acids, a macrolactonization promoter system that is effective, selective, flexible, readily available, and, insofar as possible, compatible with manifold functional groups is still lacking. Herein, we describe a strategy that relies on the formation of a mixed anhydride incorporating a pentafluorophenyl group which, due to its high electronic activation enables a convenient access to macrolactones, macrodiolides and esters with a broad versatility. Kinetic studies and DFT computations were performed to rationalize the reactivity of the pentafluorophenyl group in macrolactonization reactions.

Indolizy Carbene Ligand. Evaluation of Electronic Properties and Applications in Asymmetric Gold(I) Catalysis.

Thibaut Martinez, Avassaya Vanitcha, Claire Troufflard, Nicolas Vanthuyne, Jérémy Forté, Geoffrey Gontard, Gilles Lemière,* Virginie Mouriès-Mansuy,* Louis Fensterbank* *Angew. Chem. Int. Ed.* **2021**, *60*, 19879-19888

https://doi.org/10.1002/anie.202106142



We report herein a new family of carbene ligands based on an indolizine-ylidene (Indolizy) moiety. The corresponding gold(I) complexes are easily obtained from the gold(I)-promoted cyclization of allenylpyridine precursors. Evaluation of the electronic properties by experimental methods and also by DFT calculations confirms strong σ-donating and π-accepting properties of these ligands. Cationization of the gold(I) complexes generates catalytic species that trigger diverse reactions of (poly)unsaturated precursors. When armed with a methylene phosphine oxide moiety on the stereogenic center adjacent to the nitrogen atom, the corresponding bifunctional carbene ligands give rise to highly enantioselective heterocyclizations. DFT calculations brought some rationalization and highlighted the critical roles played by the phosphine oxide group and the tosylate anion in the asymmetric cyclization of γ-allenols.