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WEDNESDAY



THE DEVELOPMENT OF METAL-FREE TRANSFORMATIONS

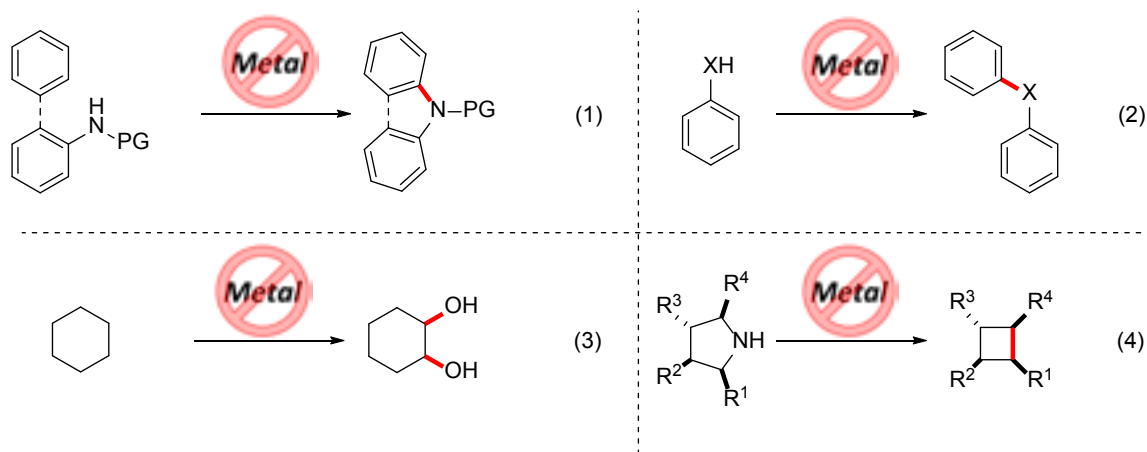
**Andrey Antonchick***

School of Science and Technology
 Nottingham Trent University
 Nottingham
 UK

andrey.antonchick@ntu.ac.uk

Contamination of chemical reaction products with trace amounts of impurities is a big problem. Especially small amounts of impurities of transition metals are a great problem, as there is no general method of purification, and these impurities could induce alterations in biological systems at low concentrations. The best way to avoid such problems is not to use transition metals for chemical transformations. The development of novel reactions without the use of transition metals is very challenging and the development of those transformations is highly desirable.

To address this problem, we have focused on developing new metal-free transformations. We developed metal-free organocatalytic electrophilic amination (eq. 1).¹ This process was later developed into electrocatalytic reactions.² We developed a set of oxidative aerobic transformations for the selective functionalisation of C-H bonds as a further development of these processes (eq. 2).³⁻⁶ Using the developed methods, we gained the knowledge to develop fundamentally new retrosynthetic disconnections. This resulted in the development of selective cis-vicinal dihydroxylation of alkanes under metal-free reaction conditions (eq. 3).⁷ Subsequently, we developed a selective method for the synthesis of cyclobutanes by pyrrolidine ring contraction (eq. 4).⁸

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CHEMOENZYMATIC TOTAL SYNTHESIS OF THE ANTIBIOTIC (-)-13-DEOXYTETRODECAMYCIN



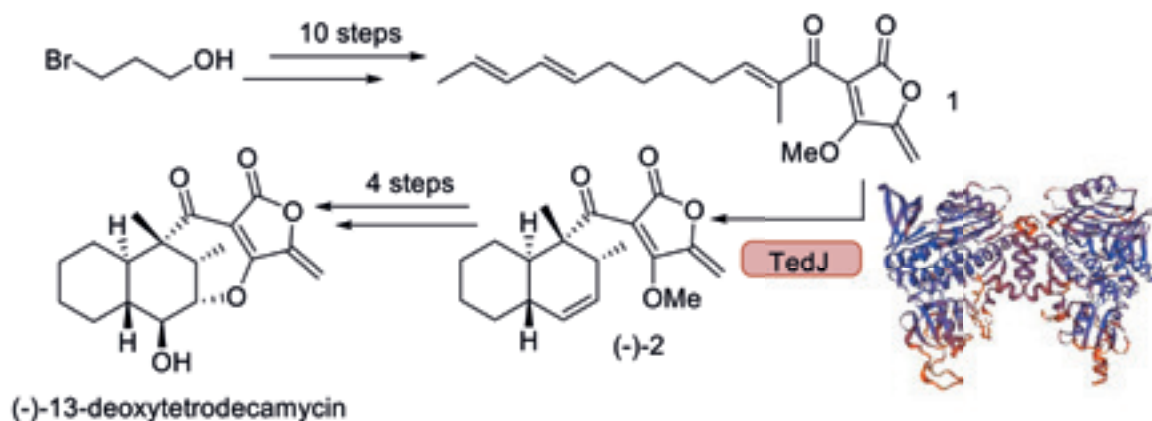
Joe Russell^a, Catherine Back,^b Chris Perry,^a Paul Raceb and Chris Willis^{a*}

^a School of Chemistry, University of Bristol, Cantock's Close, Bristol, BS8 1TS

^b School of Biochemistry, Biomedical Sciences Building, University of Bristol, University Walk, Bristol, BS8 1TD

ktc19727@bristol.ac.uk@bristol.ac.uk

(-)-13-Deoxytetrodecamycin was isolated from cultures of *Streptomyces* WAC04657 and shown to exhibit antibiotic activity.^{1,2,3} We have developed a chemoenzymatic approach to the first total synthesis of (-)-13-deoxytetrodecamycin. Tetronate 1 was synthesised but did not undergo a Diels-Alder reaction under either thermal or Lewis acid conditions. However, using the the Diels-Alderase TedJ, *trans*-decalin (-)-2 was produced as a single diastereomer. The total synthesis was completed in four additional steps, confirming the structure of the natural product. Further studies on the enzyme TedJ are currently underway.



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VISIBLE LIGHT PHOTOREDOX CATALYSIS AS A TOOL FOR FUNCTIONALIZATION AND PREPARATION OF COMPLEX ORGANIC MOLECULES



Géraldine Masson

CNRS Research Director
Director ICSN-CNRS Institut de Chimie des Substances Naturelles
Université Paris-Saclay

geraldine.masson@cnrs.fr

Visible light photoredox catalysis has emerged as a powerful strategy for the selective formation of new C-H, C-C and C-heteroatom bonds.¹ Indeed, this useful synthetic tool allows chemists to make reactions which cannot be done with already known processes (or under harsh conditions) under mild and eco-friendly conditions. For the past five years, we have been interested in the development of novel photoredox-catalyzed transformations: (1) activation of sulfidic C-S bonds, and (2) tandem difunctionalization of olefins. This lecture will detail our contribution to this field by presenting the synthesis of a wide variety of complex organic molecules. Learning and understanding the catalytic processes and mechanism involved in our transformations are an important part of our research program and lead us to new developments.

VISIBLE-LIGHT-INDUCED AND IODINE-MEDIATED TUNABLE DIFUNCTIONALIZATION OF ALKYNES WITH SODIUM ARYLSULFINATES



Mandapati Bhargava Reddy,^a Eoghan M. McGarrigle^{a*}

^a Centre for Synthesis & Chemical Biology, UCD School of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland

bhargava.bhargavareddy@ucd.ie

Organosulfur compounds are attractive scaffolds because of their numerous applications in medicinal chemistry, agrochemicals, material science and organic chemistry. Among them, vinyl sulfones are important class of organosulfur molecules and versatile synthons in organic chemistry.¹ Due to their importance in various fields, many synthetic strategies were developed to synthesise sulfone-containing molecules. Among them, radical difunctionalization of alkynes is one of the most efficient approaches to access functionalized vinylsulfones with high step- and atom- economy.² In recent years visible-light-initiated iodine-mediated reactions are attractive because these avoid external photocatalysts and access desired products by addition elimination mechanism.³ In the present study, we wish to report the iodine-mediated tunable synthesis of 1,2-bissulfonylenes (30 examples) and β -sulfinyl alkenylsulfones (9 examples) under photochemical conditions. In this protocol, both terminal and internal alkynes successfully afforded bissulfonylene compounds without transition-metals and external photocatalysts under mild reaction conditions.



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BIS(PYRIDYL)ALLENES AS VERSATILE LIGANDS FOR NOVEL METAL COMPLEXES



María Paz Muñoz,^{a,b} Hanna K. Maliszewska^b

^a Chemistry Department, Lancaster University, Bailrigg, Lancaster, LA1 4YB, UK

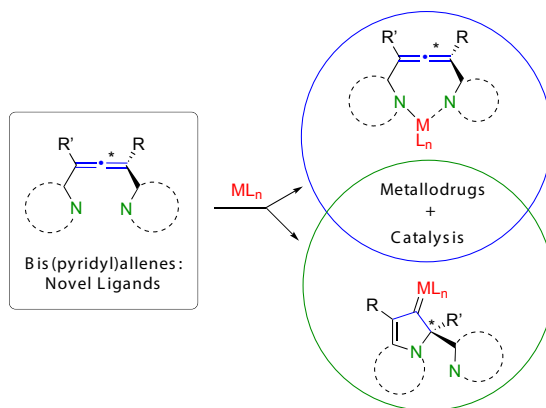
^b School of Chemistry, University of East Anglia, Norwich, NR4 7TJ, UK

m.munoz-herranz@lancaster.ac.uk

From being regarded as a chemical curiosity the allene functional moiety has now emerged as one of very useful synthetic tools of modern organic and organometallic chemistry.¹ The allene functional group is known to act as a ligand in transition metal complexes through its double bonds, but when decorated with two donor units on each of the terminal substituents, it becomes a new attractive ligand scaffold with increased coordination sites. Since 2008 only a handful of such structures have emerged, incorporating mainly phosphorus-based groups capable of complexation to various metal centres,² in which the allenic structure retains its chemical integrity. However, very few catalytic reactions have been reported with some of these allene-metal complexes and progress in this field is slow, probably due to the ability of metals to activate the allene towards nucleophilic attack, which disrupts the allene backbone.

In this talk the synthesis of complementary pyridine-based allenic structures,³ in the racemic version, followed by their complexation with various metallic centres (Pd(II), Pt(II and IV) and Au(I and III)) will be discussed. Depending on the nature of the metal used, the ligands retained their cumulene system in new organometallic compounds.⁴ While in the presence of others, cyclisation from nucleophilic attack of one of the pyridines into the metal-activated allene afforded carbene-type complexes.⁵

The complexes have shown promising activities as antimicrobial, antifungal⁶ and anticancer agents. Interestingly compounds of both classes have displayed unprecedented selective interaction with non canonical forms of DNA strands in FRET-based DNA melting studies (e.g. a stabilising interaction of i-motif by a gold carbene, and a destabilizing interaction between a Pd-bis(pyridyl)allene complex and i-motif). The complexes also exhibited high activity in initial testing of their catalytic capacity, in particular, performing well as catalysts in cyclisation of 1,6-enynes and Heck reactions.^{4,5} Further biological and catalytic screening, and the asymmetric version of these new organometallic systems are currently ongoing in our laboratory.



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NOVEL SYNTHETIC METHODS IN HALOGEN-ATOM TRANSFER AND NITROARENE REACTIVITY

**Daniele Leonori**

Institute of Organic Chemistry
RWTH Aachen University
Aachen
Germany

daniele.leonori@rtwh-aachen.de

In this presentation I will discuss two recent research lines from my group focused on the development and understanding of halogen-atom transfer and excited nitroarene reactivity.

- 1) **Halogen-atom transfer (XAT).** Organic halides are valuable building blocks for the generation of alkyl and aryl radicals. However, their applications in photoredox catalysis can be difficult owing to their very negative reduction potentials. I will present our recent work focused on the use of α -aminoalkyl radicals as XAT mediators for the homolytic activation of alkyl iodides and bromides and their application in synthesis.^{1,2} Furthermore, I will discuss a non-canonical activation mode in XAT that eludes both kinetic and thermodynamic control.³
- 2) **Photoexcited nitroarenes.** Nitroaromatics are widely available feedstocks that are routinely used for the preparation of anilines. I will present our most recent work that demonstrates how these species can be used, upon blue light irradiation, to promote the ozonolysis-style cleave of olefins⁴ and also, in a skeletal editing logic, to allow preparation of complex and highly functionalised azepanes.⁵

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