

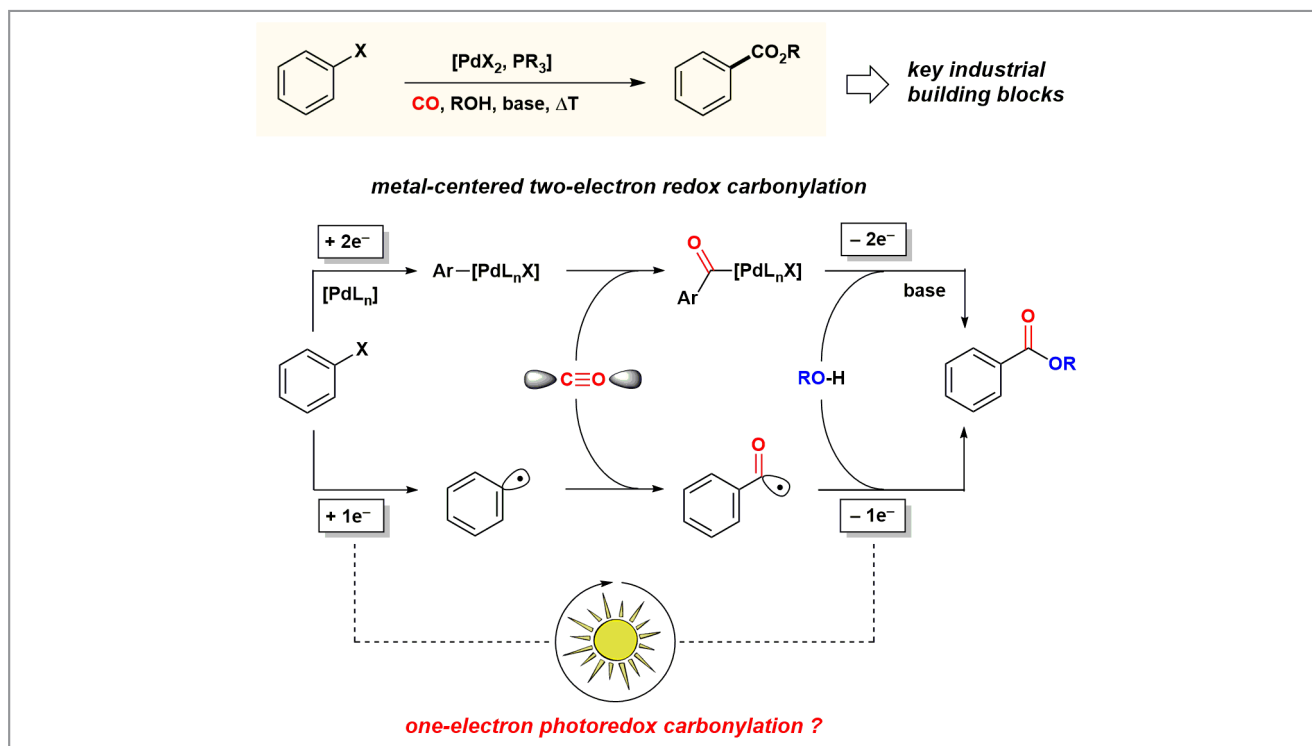
Organocatalysis Meets Visible Light Meets Carbon Monoxide

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"The formation of C–C bonds is at the very heart of organic synthesis," said Professor Axel Jacobi von Wangelin from the Institute of Organic Chemistry, University of Regensburg (Germany). "For example, the advent of transition-metal-catalyzed cross-coupling has probably changed the way we think about C–C bond formation like no other method in the last century. For good reason, this was acknowledged by the bestowal of the Nobel Prize in Chemistry 2010 to Heck, Suzuki, and Negishi," he continued. "An extension of such chemistry can be used to form various carbonyl compounds by application of a carbon monoxide atmosphere to similar reaction conditions." The CO molecule formally inserts between the two cross-coupling reagents, thus allowing for a modular assembly of ketones.¹ Professor Jacobi von Wangelin explained that only very recently, photocatalysis in the presence of visible light was introduced as a new reaction concept to C–C bond formations which commonly would have been forged by Pd-catalyzed Suzuki or Stille reactions. "Such visible-light-driven

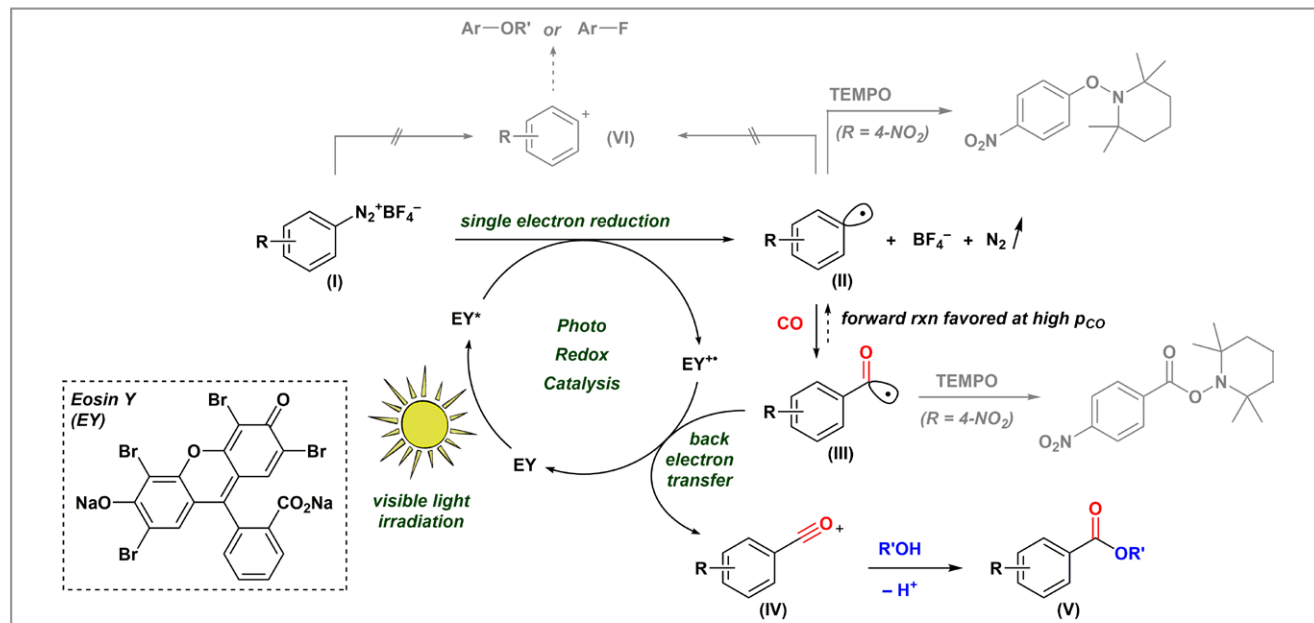
reactions with metal-free organic dye catalysts (such as eosin Y) use arenediazonium salts as good electrophiles and electron-rich arenes as nucleophilic coupling partners although the mechanism involves single-electron redox steps,"² he said. Professor Jacobi von Wangelin's group is embedded within the Graduate School on Photocatalysis at the University of Regensburg and is running a highly successful research program on cross-coupling reactions. Professor Jacobi van Wangelin said: "Our situation surely helped to breed the idea of adopting a photoredox mechanism for carbonylative coupling reactions. However, our initial efforts toward a carbonylative aryl–aryl coupling were not met with success. When we resorted to methanol as a solvent, we were delighted to observe the formation of the methyl ester instead. Et voilà!"

According to Professor Jacobi von Wangelin, there are isolated literature reports of Pd-catalyzed carbonylations of arenediazonium salts to esters³ but the group rapidly realized that their mechanism was very distinct and novel. In fact,



Scheme 1

DFT calculations, we firmly believed that a one-electron redox cycle is operating that does not require any sacrificial redox partners.” He acknowledged that the initial photocatalytic reduction of arenediazonium ion to the aryl radical was already postulated in related transformations. “Subsequent reaction with CO appeared to be the key step, probably being also rate-limiting. However, the ester can only be formed if the



cf. Pd catalysis: no metal, no ligand, no base!

eosin Y:

Yields for various R and R' groups:

<p>R = H: 86%</p> <p>Me: 82%</p> <p>OMe: 80%</p> <p>NO₂: 76%</p> <p>Br: 65%</p>	<p>R = H: 74%</p> <p>Me: 70%</p> <p>OMe: 89%</p> <p>NO₂: 51%</p> <p>Br: 72%</p>	<p>R = H: 65%</p> <p>Me: 79%</p> <p>OMe: 75%</p> <p>NO₂: 72%</p> <p>Cl: 68%</p> <p>Br: 76%</p>	<p>R' = Me: 71%</p> <p><i>i</i>-Pr: 52%</p> <p><i>t</i>-Bu: 56%</p>	<p>R' = Me: 77%</p> <p><i>i</i>-Pr: 65%</p> <p><i>t</i>-Bu: 85%</p>	<p>55%</p>
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tert-alkyl esters!

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resultant acyl radical can be oxidized to the acylium ion by the eosin radical cation since methanol is not a competent radical trap. Once this oxidation occurs, ionic reaction with the bulk solvent gives the desired methyl benzoate,” said Professor Jacobi von Wangelin. “The mechanistic beauty of this process resides within the operation of the two usually incompatible reduction and oxidation processes in the same system. The selectivity of the reaction is dictated by the matching redox potentials of the photocatalyst, the substrate, and the acyl radical intermediate. As our colleagues Armido Studer and Dennis P. Curran put it: the electron is the catalyst!”⁴

According to Professor Jacobi von Wangelin, this new carbonylation mechanism distinguishes itself from the conventional Pd catalysis in that it formally cycles around one electron driven by visible light rather than two electrons driven by the Pd/Pd²⁺ redox couple and stoichiometric base. “Furthermore, the intermediacy of the highly electrophilic and rather unhindered (planar) acylium ion engages in nucleophilic trappings with *n*-, *i*- and *t*-alkanols,” he said. “With *tert*-butanol, efficient synthesis of *tert*-butyl benzoates was achieved which is not possible under Pd or Ni catalysis.”

“We are aware – even more so after the more than half-year period from initial submission to publication – that the competition is keen in this research area but we hope to be able to make further contributions to the development of metal-free formal cross-coupling methodologies. Clearly, the conversion of less activated electrophiles is desirable, as is the application of optimized reactor types. The International Year of Light 2015 will certainly produce more exciting photochemistry and hopefully some transitions into manufacture,” concluded Professor Jacobi von Wangelin.

Matthias Fenske

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About the authors



Axel Jacobi von Wangelin (left) was born into the 1974 World Cup euphoria in Berlin (Germany) and spent a joyful boyhood in the backyards of Berlin-Friedrichshain. Axel abandoned capital city pace when he took up chemistry studies at the University of Erlangen (Germany). His Masters thesis and a subsequent research stay with John A. Gladysz allowed him to work at the University of Utah (USA) where he also advanced his mountaineering skills. Back in Germany, Axel joined Matthias Beller's group at the Leibniz-Institute of Catalysis in Rostock from where he obtained a Ph.D. in 2002. After a short industrial stay at De-

gussa AG in Frankfurt (Germany), he was a postdoctoral fellow with Kingsley J. Cavell at Cardiff University (UK) and Barry M. Trost at Stanford University (USA). In 2006, he started his independent career at the University of Cologne (Germany). Since 2011, Axel is Professor of Organic Chemistry at the University of Regensburg. His recent research achievements were recognized with the ORCHEM Award of the Liebig Association (2012), the Heisenberg fellowship (2011), and the Science Award of the Industrieclub (2009).

Michal Majek (right) is a native of the Slovak Republic where he attended a high school with maths and natural science focus in Bratislava. From 2006–2012, he studied at the Institute of Chemical Technology in Prague (Czech Republic) and enjoyed inspiring research stays at the Universities of Glasgow and St. Andrews (UK). In 2012, he joined the group of AJvW at the University of Regensburg where he was admitted to the Graduate College “Photocatalysis”. In his research, he combines theoretical, physical and chemical approaches to light-driven chemical transformations. He single-handedly initiated a research program with special emphasis on organocatalytic, visible-light-mediated aromatic substitutions. In his spare time, he travels and – when at home – coaches the Slovak Chemistry Olympic teams.