Angewandte Chemie International Edition

Photocatalysis Hot Paper

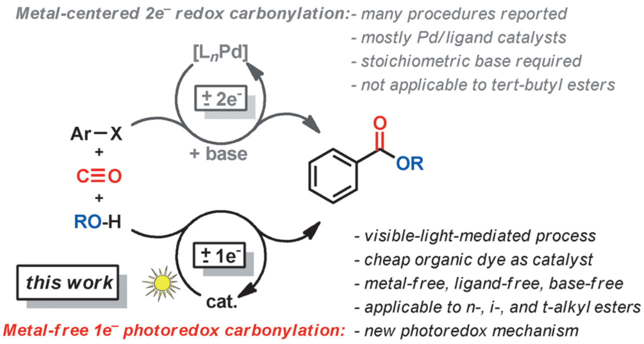
DOI: 10.1002/anie.201408516

Metal-Free Carbonylations by Photoredox Catalysis**

*Michal Majek and Axel Jacobi von Wangelin**

Abstract: *The synthesis of benzoates from aryl electrophiles and carbon monoxide is a prime example of a transition-metal-catalyzed carbonylation reaction which is widely applied in research and industrial processes. Such reactions proceed in the presence of Pd or Ni catalysts, suitable ligands, and stoichiometric bases. We have developed an alternative procedure that is free of any metal, ligand, and base. The method involves a redox reaction driven by visible light and catalyzed by eosin Y which affords alkyl benzoates from arene diazonium salts, carbon monoxide, and alcohols under mild conditions. Tertiary esters can also be prepared in high yields. DFT calculations and radical trapping experiments support a catalytic photoredox pathway without the requirement for sacrificial redox partners.*

Aromatic esters are key building blocks in the synthesis of fine chemicals, agrochemicals, pharmaceuticals, and materials.[1] They can be prepared by various methods,[2] most importantly by the esterification of benzoic acids with alcohols under Brønsted or Lewis acid catalysis at elevated temperatures, or alternatively by the trimodular reaction of an aromatic electrophile bearing a suitable leaving group, gaseous carbon monoxide, and the alcohol in the presence of transition-metal catalysts (mostly combinations of Pd or Ni complexes with phosphine ligands).[3] Several metal-catalyzed carbonylation reactions are being applied in industrial and academic syntheses of carbonyl compounds.[4] Carbon monoxide (CO) is abundantly available as a primary product from the gasification of all carbon-based raw materials (oil, natural gas, coal, biomass). The reaction mechanism of metal-catalyzed carbonylations bears a close relationship to cross-coupling reactions.[3] Although aryl halides are the most prominent class of electrophilic reagents in such reactions, arene diazonium salts offer specific advantages because of their ionic character, halogen-free preparation from anilines, and incorporation of a very potent leaving group, dinitrogen (N_2). Arene diazonium salts have been used in numerous cross-coupling procedures,[5] although there are only isolated reports of carbonylations to generate benzoates.[6] The generally accepted mechanism of metal-catalyzed carbonylations involves reductive activation of the electrophilic aryl-X species followed by CO insertion and nucleophilic displacement by the alcohol in the presence of stoichiometric amounts of a base.[7] The first and last step can be viewed as formal metal-centered two-electron redox reactions which result in an overall redox-neutral process (Scheme 1).[3]



Scheme 1. Pd-catalyzed versus photocatalyzed redox carbonylation.

Here, we report an alternative metal-free and base-free process which involves a hitherto unknown one-electron redox mechanism that is driven by visible light in the presence of an organic dye (Scheme 1, bottom). The following criteria provided further stimuli for our explorations of such redox carbonylations: 1) Reductive single electron transfer (SET) processes with arene diazonium salts proceed even with mild, nonmetallic, reducing agents because of their low redox potentials (ca. 0 V versus SCE).[8,9] 2) The availability of low lying σ- and π-orbitals makes CO a good radical trap. 3) The intermediate aryl radical can react with CO, while being unreactive toward the alcohol.

The utilization of visible light as an abundant source of energy to enable chemical transformations has recently experienced a renaissance, which is largely driven by new developments in the field of photoredox catalysis.[10] Significant effort has been devoted to visible-light-driven aromatic substitutions of arene diazonium salts in the presence of various photosensitizers.[11] Tris(bipyridine)ruthenium(II) and other metal complexes (Ir, Cu) have emerged as very powerful photocatalysts.[12] However, the good coordinating ability of CO ligands and the existence of numerous stable carbonyl complexes of Ru (and other metals) discourage the use of such organometallic catalysts for the proposed aromatic carbonylation process.[13] Organic dyes, for example, the cheap fluoresceins, display similar photocatalytic activity in some reactions[14] and seemed more appropriate as no interference by the presence of carbon monoxide is known.[15] Furthermore, CO only exhibits absorptions in the vacuum-UV range below 180 nm.[16]

Our initial studies on the proposed photocatalytic carbonylation with 4-methoxybenzenediazonium tetrafluoroborate (**1a**) in methanol were carried out under reaction conditions

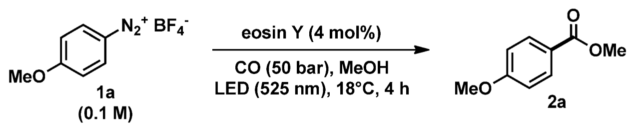
---

[*] Ing. M. Majek, Prof. Dr. A. Jacobi von Wangelin
Institute of Organic Chemistry, University of Regensburg
Universitaetsstrasse 31, 93040 Regensburg (Germany)
E-mail: axel.jacobi@ur.de

[**] This work was supported by the Graduate Program "Photokatalyse" of the DFG (GRK 1626).

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201408516.

Table 1: Selected optimization experiments.[a]

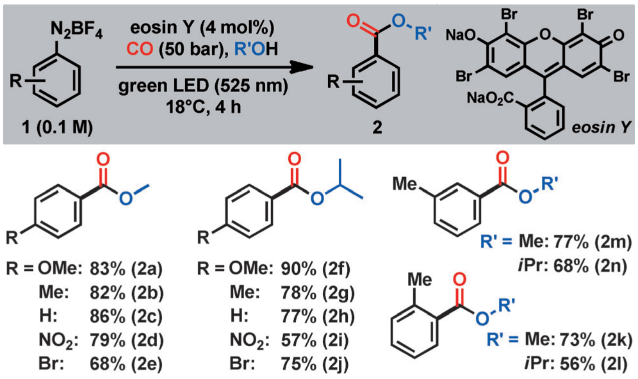


Entry	Deviation from the optimized conditions	Yield of **2a** [%]
1	–	83
2[b]	Rose bengal	8
3[b]	eosin B	29
4[b]	fluorescein	24
5[b]	$[Ru(bpy)_3]Cl_2$	30
6	without dye	2
7	dark reaction at 60 °C	<1

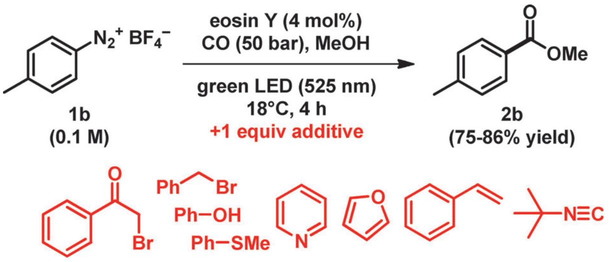
[a] Conditions: **1a** (0.1 mmol), eosin Y (0.04 mmol), methanol (1 mL), CO (50 bar), irradiation(LEDs, $\lambda_{max} = 525$ nm, 3.8 W), 18 °C, 4 h. [b] In methanol/acetonitrile (1/1). bpy = bypyridine.

that were reported for related photoredox Meerwein reactions.[17] Under irradiation with green light (LED, $\lambda_{max} = 525$ nm, 3.8 W), solutions of **1a** in methanol were treated under an atmosphere of CO at room temperature to give methyl 4-methoxybenzoate (**2a**, Table 1).[18]

Commercial eosin Y (4 mol %, employed as the disodium salt) was used as the metal-free photoredox catalyst. Unwanted dimerization (Ar_2) and reduction (Ar-H) was suppressed at higher dilutions by the higher relative concentrations of CO and the alcohol. Other dyes were less active (entries 2–5). Lower pressures of CO resulted in low conversion and competing hydrodediazotation (10–25 %) and biaryl coupling (ca. 5 %). Eosin-free (entry 6) as well as dark and thermal reactions (entry 7) produced only minimal amounts of **2a**. The optimized conditions were applied to the synthesis of various alkyl benzoates (Scheme 2). Several functional groups and electron-poor and -rich substituents (nitro, chloro, bromo, esters, benzylic protons) were tolerated in the substrates. A screening of various additives (Scheme 3) showed significant tolerance of halogen-containing electrophiles, acidic protons, π-nucleophiles, and electron-deficient arenes, without erosion of the ester yield or consumption of the additive.[18] The presence of 1 equiv phenol ($pK_a \approx 9$) was tolerated well, which is in contrast to the employment of phenol (in large excess) as a reaction partner under otherwise identical conditions, where complex product mixtures were formed. Methylthio-bearing compounds did not affect the ester formation, in agreement with a previous report,[19] where *S*-alkylated compounds were produced under similar conditions. Interestingly, *tert*-butylisonitrile—a competent radical trap in some reactions[20]—was tolerated. Iodobenzene only resulted in little interference, presumably by radical cleavage of the weak Ar–I bond. The addition of thiophenol led to a large decrease in the yield, which is known from reports of diazosulfide formation/photocatalytic cleavage under similar conditions.[21] Biaryl sulfide (Ar-S-Ar) coupling was observed in this case. The presence of aniline or *N*,*N*-dimethylaniline resulted in the quenching of the excited state of the dye. Azobenzenes were detected in small amounts. The addition of triphenylphosphine led to inhibition as a result of quenching of the excited dye. Accordingly, triphenylphosphine oxide was formed.[18]

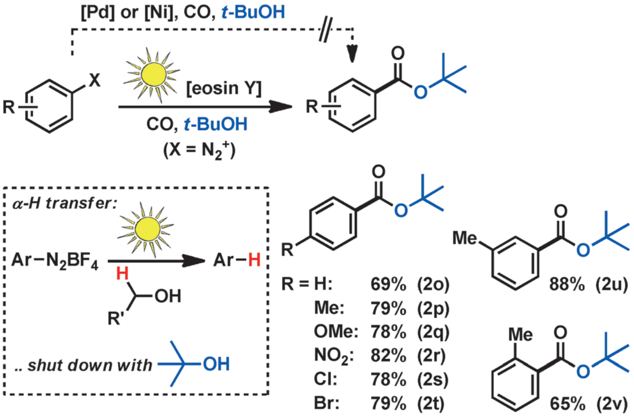


Scheme 2. General conditions and scope of the photoredox carbonylation.



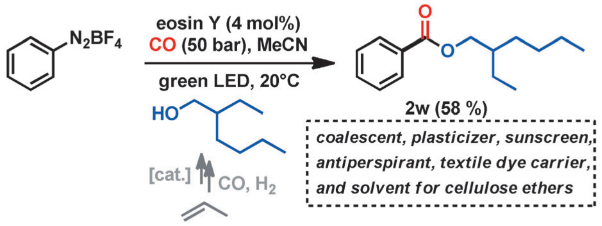
Scheme 3. Compatibility with various functionalized additives that resulted in unaffected ester formation without competing conversion of the additive.

tert-Butyl esters are notoriously difficult to obtain by conventional esterification procedures because of their steric bulk.[1,2,22] Palladium-catalyzed carbonylation procedures also fail to generate *tert*-butyl esters. The photocatalytic carbonylation, however, produced *tert*-butyl benzoates in very good yields, exceeding those of the less hindered methyl and isopropyl esters. This is due to the lack of α-hydrogen atoms within *tert*-butanol, which excludes undesired radical hydrogen abstraction and subsequent reductive reactions (Scheme 4).



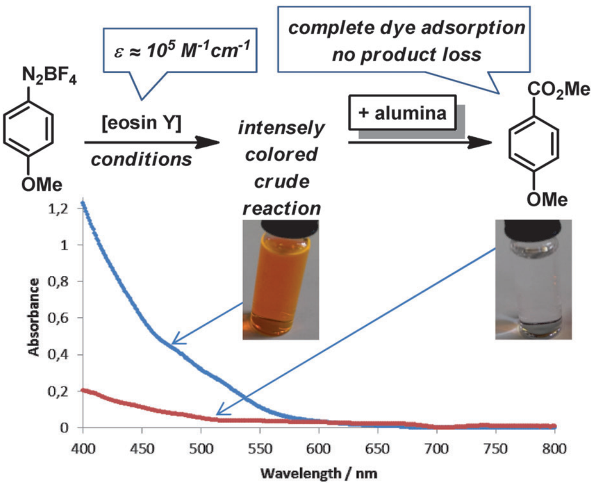
Scheme 4. Photocarbonylation to *tert*-butyl benzoates.

We have probed the effectiveness of the metal-free photocarbonylation in the context of the synthesis of **2w**, a low-odor, low-volatility, and low-viscosity ester produced on multiton scales for applications as a coalescent in the formulation of latex paints (Velate 368), a plasticizer in the manufacture of key polymers, as a sunscreen, and an antiperspirant ingredient in cosmetics (Finsolv EB), as a textile dye carrier for the treatment of synthetic fibers, and as a solvent for cellulose ethers.[23] Under standard conditions, 2-ethylhexyl benzoate (**2w**) was obtained in 58% yield from the reaction of PhN_2BF_4 with 2-ethylhexanol and CO under irradiation with green light (Scheme 5). Acetonitrile was used as a cosolvent to solubilize the diazonium salt in the fatty alcohol. Methyl 4-anisate (**2a**) is another technical product with applications as a food and flavor ingredient. Technical applications of catalytic reactions are always associated with the search for an effective technique for catalyst separation. The intensely colored eosin Y ($\varepsilon \approx 10^5\,M^{-1}cm^{-1}$, 530 nm, ethanol)[24] was removed from the reaction mixture by adsorption on basic alumina.[25] UV/Vis spectra documented the complete removal of the dye, while <1% of the product was lost in this operation (Scheme 6).

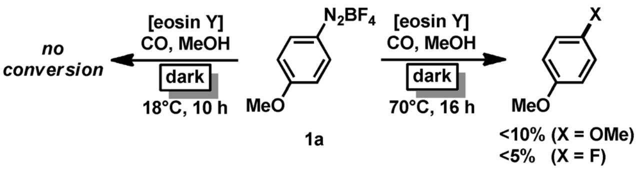


Scheme 5. Synthesis of the technical ester **2w**.

The mechanistic proposal of a visible-light-driven dye-catalyzed process was supported by the following experiments: The product yields severely dropped when no photocatalyst was present in the reaction and/or under dark conditions. Reactions in the dark and at increased temperature (up to 70 °C) gave no carbonylation product, which excludes homolytic bond cleavage of the starting material to an aryl radical under these conditions. Instead, the thermal dark reaction of **1a** in methanol at 70 °C produced small amounts of the corresponding methyl ether and aryl fluoride (Scheme 7). This observation is consistent with previous reports of unsuccessful attempts to thermolytically carbonylate diazonium salts.[26]

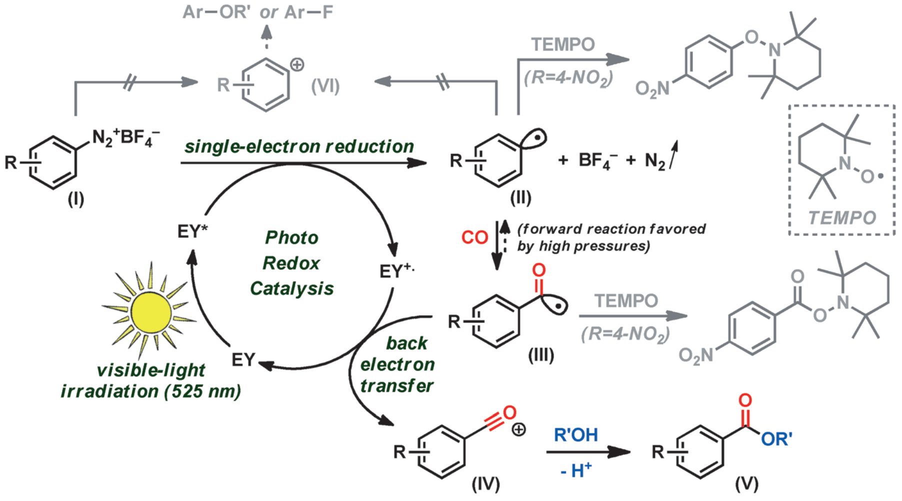


Scheme 6. Dye removal with basic alumina. Bottom: corresponding absorption spectra before (blue) and after (red) work-up.

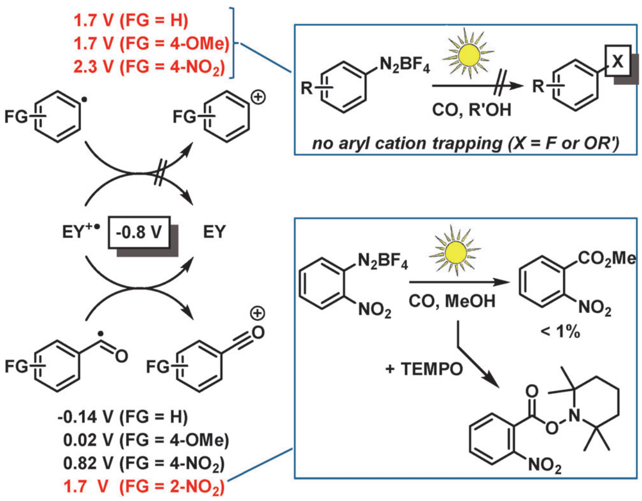


Scheme 7. Dark reactions of 4-anisyldiazonium salt (**1a**).

We have performed detailed mechanistic studies to prove the postulate of a light-driven reduction/oxidation cascade which is devoid of any sacrificial redox partner. On the basis of related literature reports[11,17,27] and our own findings we propose the following operating mechanism (Scheme 8): The electron-deficient arene diazonium salt (**I**) accepts one electron from the electron-rich, dianionic, photoexcited state of eosin Y (**EY***). This single-electron transfer (SET) results in the release of dinitrogen (N_2) and generation of aryl radical **II**. This initiation step is thermodynamically favored due to the more positive redox potential of the **I**→**II** reduction (ca. 0 V versus SCE)[9] compared with the $\mathbf{EY}^{\cdot+}\rightarrow$ **EY*** reduction (−1.1 V versus SCE). The aryl radical **II** then rapidly reacts with CO to afford acyl radical **III**.[28] The addition of the radical trap TEMPO (2,2,6,6-tetramethylpiperidinyloxyl) results in the formation of adducts with both radical species (**II**, **III**) being observed.[18] We further propose that **III** undergoes rapid one-electron oxidation to give the highly electrophilic acylium ion **IV**. Reaction thereof with the alcohol affords the benzoate ester **V**. The back electron transfer (BET) is presumed to be fast, as no adduct of acyl radical **III** with electron-rich π-donors (anisole, furan, styrene) was detected. This assumption can be instructively substantiated by thermodynamic data: The redox potential of the $\mathbf{EY}^{+}\rightarrow\mathbf{EY}$ reduction is −0.8 V (versus SCE). The potential of the **III**→**IV** redox couple is not available experimentally, since both species are short lived. However, an estimation of this redox potential could be derived from DFT calculations,[18,29] which provided values between −0.14 V and 0.82 V (versus SCE) depending on the substitution pattern on the aromatic ring (Scheme 9). Therefore, the BET step is thermodynamically feasible. Calculation of the redox potential of the back electron transfer for the 2-nitroaroyl radical species gave a prohibitive value of 1.7 V (versus SCE). Indeed, 2-nitrobenzenediazonium tetrafluoroborate did not afford the desired ester under carbonylation conditions. The addition of TEMPO to the reaction resulted in the formation of the benzoyl–TEMPO adduct. Both experiments provide further evidence of the postulated mechanism involving the carbonylation of the intermediate



Scheme 8. Mechanism of the visible-light-driven eosin-catalyzed carbonylation of arene diazonium salts.



Scheme 9. The back electron transfer (BET): DFT calculations on the prohibitive redox process to aryl cations (top left), the operating BET to give acylium ions (bottom left), and supportive preparative experiments (right).

2-nitroaryl radical, but the BET to **EY**$^{\bullet+}$ is thermodynamically prohibited.[21]

The reaction of aryl cations with CO is known from acid-catalyzed Gatterman-Koch carbonylations,[30] but can be excluded on the basis of DFT calculations. The carbonylation of aryl cations (**VI**, from thermal heterolysis of the arene diazonium) was already disproven (Scheme 7). A potential back electron transfer with **EY**$^{\bullet+}$ at the aryl radical stage (**II**) can likewise be refuted. The DFT-derived reduction potentials of the **VI/II** couples of our substrates are 1.7–2.3 V (versus SCE).[18] These values are prohibitively high in comparison with the oxidizing power of **EY**$^{\bullet+}$ (−0.8 V versus SCE) and thus exclude the intermediacy of aryl cations.

This new procedure enables metal-free and base-free carbonylations through an photoredox mechanism catalyzed by an organic dye. Alkyl benzoates can be prepared from arene diazonium salts, CO, and alcohols at room temperature under irradiation with visible light. The reaction uses catalytic eosin Y as a cheap photosensitizer. Mechanistic studies support the sequential operation of SET reduction, carbonylation, and back electron transfer to give aroylium cations, which undergo rapid addition to alcohols. Unlike with metal-catalyzed carbonylations, *tert*-butyl esters can be prepared in good yields. The general method has been applied to the synthesis of industrial intermediates.

Experimental Section

General procedure: A vial (3 mL) was charged with a magnetic stir bar, the arene diazonium salt (0.1 mmol), and eosin Y (0.04 mmol) under N_2, and capped with a rubber septum. Dry solvent (1 mL, alcohol or mixture with MeCN if the solubility of the diazonium salt was poor) was added. The vial was purged with N_2 (5 min) in the dark and transferred to a reactor containing a Quartz window bottom (Parr Instr.; Figure 1). The septum was punctured with a needle. The reactor was sealed, placed on a magnetic stirrer, and slowly filled with CO (50 bar). The reaction was irradiated with external LEDs (λ_{max} = 525 nm, 3.8 W). After 4 h at 18 °C, the gas was released and the vial retrieved. Water (5 mL) was added to give an emulsion, which was extracted with ethyl acetate (2×5 mL). The organic phases were washed (5 mL brine) and dried (Na_2SO_4). Volatiles were evaporated and the residues purified by chromatography on SiO_2 gel.

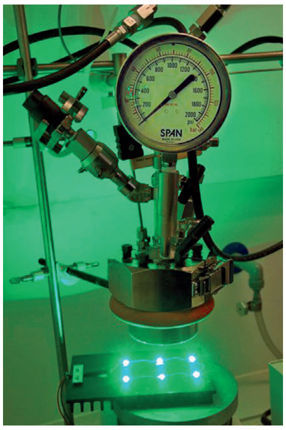


Figure 1. High-pressure photoreactor.

Received: August 28, 2014
Revised: September 23, 2014

Keywords: carbonylation · esters · organocatalysis · photoredox catalysis · redox reaction · visible light

[1] W. Riemenschneider, H. M. Bolt in *Ullmann's Encyclopedia of Industrial Chemistry*, *Vol. 13*, Wiley-VCH, Weinheim, **2005**, p. 245.

[2] J. Otera, J. Nishikido, *Esterification: Methods, Reactions, and Applications*, 2nd ed., Wiley-VCH, Weinheim, **2010**.

[3] A. Brennführer, H. Neumann, M. Beller, *Angew. Chem. Int. Ed.* **2009**, *48*, 4114; *Angew. Chem.* **2009**, *121*, 4176.

[4] a) J. Magano, J. R. Dunetz, *Chem. Rev.* **2011**, *111*, 2177; b) H. M. Colquhoun, D. J. Thompson, M. V. Twigg, *Carbonylation. Direct Synthesis of Carbonyl Compounds*, Plenum, New York, **1991**.

[5] A. Roglans, A. Pla-Quintana, M. Moreno-Manas, *Chem. Rev.* **2006**, *106*, 4622.

[6] a) J. C. Clark, R. C. Cookson, *J. Chem. Soc.* **1962**, 686; b) K. Kikukawa, K. Kono, K. Nagira, F. Wada, T. Matsuda, *J. Org. Chem.* **1981**, *46*, 4413; c) S. Sengupta, S. K. Sadhukhan, S. Bhattacharyya, J. Guha, *J. Chem. Soc. Perkin Trans. 1* **1998**, 407.

[7] C. F. J. Barnard, *Organometallics* **2008**, *27*, 5402.

[8] A. N. Abeywickrema, A. L. J. Beckwith, *J. Org. Chem.* **1987**, *52*, 2568.

[9] a) P. Allongue, M. Delamar, B. Desbat, O. Fagebaume, R. Hitmi, J. Pinson, J.-M. Saveant, *J. Am. Chem. Soc.* **1997**, *119*, 201; b) C. Combellas, D.-E. Jiang, F. Kanoufi, J. Pinson, F. I. Podvorica, *Langmuir* **2009**, *25*, 286.

[10] a) J. M. R. Narayanam, C. R. J. Stephenson, *Chem. Soc. Rev.* **2011**, *40*, 102; b) K. Zeitler, *Angew. Chem. Int. Ed.* **2009**, *48*, 9785; *Angew. Chem.* **2009**, *121*, 9969; c) D. M. Schultz, T. P. Yoon, *Science* **2014**, *343*, 985; d) D. Ravelli, S. Protti, M. Fagnoni, A. Albini, *Curr. Org. Chem.* **2013**, *17*, 2366.

[11] Selected examples: a) D. Kalyani, K. B. McMurtrey, S. R. Neufeldt, M. S. Sanford, *J. Am. Chem. Soc.* **2011**, *133*, 18566; b) D. P. Hari, P. Schroll, B. König, *J. Am. Chem. Soc.* **2012**, *134*, 2958; c) B. Sahoo, M. N. Hopkinson, F. Glorius, *J. Am. Chem. Soc.* **2013**, *135*, 5505.

[12] Selected examples: Ru: a) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322; Ir: b) A. Noble, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2014**, *136*, 11602; c) M. T. Pirnot, D. A. Rankic, D. B. C. Martin, D. W. C. MacMillan, *Science* **2013**, *339*, 1593; d) S. Zhu, A. Das, L. Bui, H. Zhou, D. P. Curran, M. Rueping, *J. Am. Chem. Soc.* **2013**, *135*, 1823; Cu: e) M. Majek, A. Jacobi von Wangelin, *Angew. Chem. Int. Ed.* **2013**, *52*, 5919; *Angew. Chem.* **2013**, *125*, 6033; f) M. Pirtsch, S. Paria, T. Matsuno, H. Isobe, O. Reiser, *Chem. Eur. J.* **2012**, *18*, 7336.

[13] G. B. Deacon, J. M. Patrick, B. W. Skelton, N. C. Thomas, A. H. White, *Aust. J. Chem.* **1984**, *37*, 929.

[14] a) D. A. Nicewicz, T. M. Nguyen, *ACS Catal.* **2014**, *4*, 355; b) D. P. Hari, B. König, *Chem. Commun.* **2014**, *50*, 6688; c) D. Ravelli, M. Fagnoni, A. Albini, *Chem. Soc. Rev.* **2013**, *42*, 97.

[15] a) M. Okada, T. Fukuyama, K. Yamada, I. Ryu, D. Ravelli, M. Fagnoni, *Chem. Sci.* **2014**, *5*, 2893; b) I. Ryu, A. Tani, T. Fukuyama, D. Ravelli, M. Fagnoni, A. Albini, *Angew. Chem. Int. Ed.* **2011**, *50*, 1869; *Angew. Chem.* **2011**, *123*, 1909.

[16] H.-C. Lu, H.-K. Chen, B.-M. Cheng, Y.-P. Kuo, J. F. Ogilvie, *J. Phys. B* **2005**, *38*, 3693.

[17] D. P. Hari, B. König, *Angew. Chem. Int. Ed.* **2013**, *52*, 4734; *Angew. Chem.* **2013**, *125*, 4832.

[18] For further details, see the Supporting Information.

[19] M. Majek, A. Jacobi von Wangelin, *Chem. Commun.* **2013**, *49*, 5507.

[20] L. Benati, R. Leardini, M. Minozzi, D. Nanni, R. Scialpi, P. Spagnolo, S. Strazzari, G. Zanardi, *Angew. Chem. Int. Ed.* **2004**, *43*, 3598; *Angew. Chem.* **2004**, *116*, 3682.

[21] X. Wang, G. D. Cuny, T. Noel, *Angew. Chem. Int. Ed.* **2013**, *52*, 7860; *Angew. Chem.* **2013**, *125*, 8014.

[22] a) T. W. Greene, P. G. M. Wuts, *Protective Groups in Organic Synthesis*, Wiley, New York, **1999**; b) a thermal radical carbonylation of Ar-I with KO*t*Bu: H. Zhang, R. Shi, A. Ding, L. Lu, B. Chen, A. Lei, *Angew. Chem. Int. Ed.* **2012**, *51*, 12542; *Angew. Chem.* **2012**, *124*, 12710.

[23] R. Stanley, *Paint Coat. Ind.* **2001**, *17*, 68.

[24] E. Zipfel, J.-R. Grezes, W. Seiffert, H. W. Zimmermann, *Histochemistry* **1982**, *75*, 539.

[25] E. Forgacs, T. Cserhati, G. Oros, *Environ. Int.* **2004**, *30*, 953.

[26] E. S. Lewis, J. M. Insole, *J. Am. Chem. Soc.* **1964**, *86*, 32.

[27] M. Majek, F. Filace, A. Jacobi von Wangelin, *Beilstein J. Org. Chem.* **2014**, *10*, 981.

[28] For acyl radicals in different mechanisms, see Refs. [15], [22b], and: a) C. Chatgilialoglu, D. Crich, M. Komatsu, I. Ryu, *Chem. Rev.* **1999**, *99*, 1992; b) I. Ryu, *Chem. Soc. Rev.* **2001**, *30*, 16; c) S. Sumino, A. Fusano, H. Okai, T. Fukuyama, I. Ryu, *Beilstein J. Org. Chem.* **2014**, *10*, 150; d) T. Kawamoto, T. Okada, D. P. Curran, I. Ryu, *Org. Lett.* **2013**, *15*, 2144; e) A. Fusano, S. Sumino, S. Nishitani, T. Inoue, K. Morimoto, T. Fukuyama, I. Ryu, *Chem. Eur. J.* **2012**, *18*, 9415.

[29] a) M.-H. Baik, R. A. Friesner, *J. Phys. Chem. A* **2002**, *106*, 7407; b) Y. Fu, L. Liu, H.-Z. Yu, Y.-M. Wang, Q.-X. Guo, *J. Am. Chem. Soc.* **2005**, *127*, 7227.

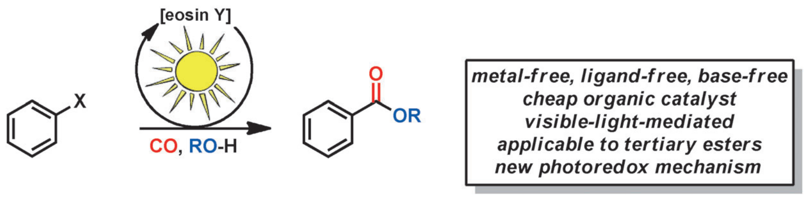
[30] M. Tanaka, M. Fujiwara, Q. Xu, Y. Souma, H. Ando, K. K. Laali, *J. Am. Chem. Soc.* **1997**, *119*, 5100.

Communications

Photocatalysis

M. Majek,
A. Jacobi von Wangelin* ____ ■■■■–■■■■

Metal-Free Carbonylations by Photoredox Catalysis



A metal-free and base-free carbonylation has been developed which affords primary, secondary, and tertiary alkyl benzoates under irradiation with visible light in the presence of eosin Y as a photocatalyst. The mechanism has been studied by spectroscopic, theoretical, and preparative methods, and appears to involve intermediate aryl and aroyl radical species as well as a light-driven one-electron redox cycle without any sacrificial redox partner.