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Photoorganocatalysis. What for?

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In the reactions reviewed, an organic molecule under irradiation catalyzes a chemical reaction. The activation is based either on hydrogen or on electron transfer. Commonly used photoorganocatalysts are aromatic ketones, quinones, heterocycles, dyes; intermediates formed are radicals, radical ions and ions from precursors such as alkanes, alkenes, amines, ethers *etc.* Oxidation (mainly oxygenation) and reduction processes are obtained along with the α-functionalization of amines and ketones, conjugate additions, cycloadditions *etc.* The key characteristic of the method is the smooth generation of highly reactive intermediates under mild conditions.

1. Introduction

Transition-metal catalysis has become one of the most important tools in organic synthesis due to the variety of reactions accessible.[1] Some drawbacks remain, however, such as the high cost and toxicity of the catalyst employed and in some cases the problems related to the disposal of the catalyst at the end of the reaction. In the last few years, a metal-free approach emerged that makes use of organic compounds as catalysts and has been dubbed as "organocatalysis". The work in the field has rapidly progressed with application in reactions such as nucleophilic substitutions, Michael additions, cycloadditions and aldol reactions. The asymmetric version of such processes has been likewise successfully developed.[2] Organocatalysts can be divided into two main classes depending on the interaction, covalent or non-covalent (H-bonding, proton transfer, ion pair formation) with the organic substrate within the catalytic cycle.[2]

In the former case, an organocatalyst (OC, see Scheme 1) reacts with an organic molecule (the first reagent, R_1) to form a stable organic compound or an intermediate (OC–R_A). At this stage, the activation induced by OC makes possible the attack of the second reagent (R_2) to form a second adduct (OC–R_B) that releases the end product P with the concomitant regeneration of OC.

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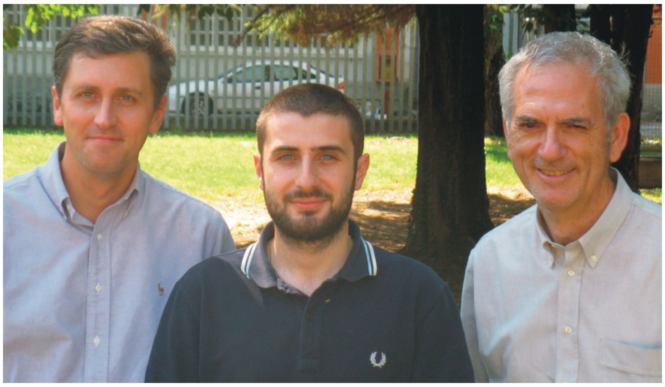
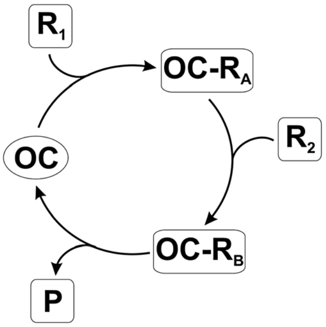


Maurizio Fagnoni, Davide Ravelli and Angelo Albini

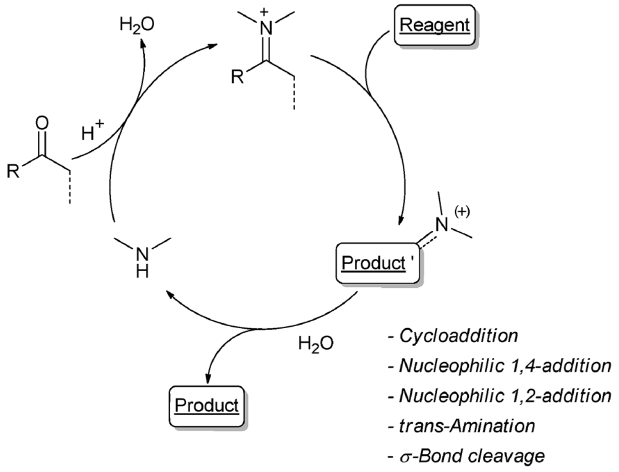
Davide Ravelli was born in 1984 and obtained his PhD from the University of Pavia in 2012 with a thesis on tetrabutylammonium decatungstate photocatalyzed C–C bond forming reactions (Prof. A. Albini as the supervisor). He is currently a post-doc student at the same University, pursuing the study on photocatalytic processes and evaluating the adoption of ionic liquids as electrolytes in lithium batteries. His research interests focus on radical mediated synthetic procedures and on the rationalization of organic reaction mechanisms by means of computational tools.

Maurizio Fagnoni graduated in Pavia in 1992 under the guidance of Prof. Angelo Albini. He is currently an Associate Professor of the Department of Chemistry at the University of Pavia. He is interested in the generation of reactive intermediates e.g. radicals, cations and radical ions by photochemical means. Particular attention has been given to eco-sustainable synthesis by using photocatalysis and photogenerated phenyl cations. In 2011 he was a recipient of the CINMPIS prize for "Innovation in organic synthesis" and of the "Exploration of new research frontiers Award" from Cariplo Foundation.

Angelo Albini completed his studies in Chemistry in 1972, did postdoctoral work at the Max-Planck Institute for Radiation Chemistry in Muelheim, Germany (1973–74) and joined the Faculty at Pavia in 1975, where he is currently a Professor of Organic Chemistry, after a period at the University of Torino and stays at the Universities of Western Ontario (Canada, 1976–77) and Odense (Denmark, 1983). He is active in the field of organic photochemistry, organic synthesis via radicals and ions, photoinitiated reactions, mild synthetic procedures in the frame of the increasing interest for sustainable/green chemistry and applied photochemistry.

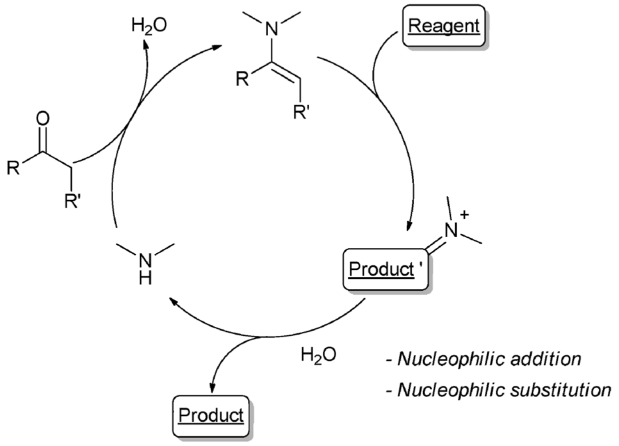


Scheme 1



Scheme 2

Most of the OCs used are (chiral) secondary amines and R_1 are electrophiles, typically aldehydes, ketones or α,β-unsaturated carbonyls. The OC promotes the generation of either an iminium ion (Scheme 2) or an enamine (Scheme 3). This causes, respectively, an increase in the electrophilicity of the starting carbonyl derivative – promoting nucleophiles addition or cycloaddition reactions – or the Umpolung of the starting carbonyl – leading to electrophilic addition onto the enamine intermediate.[2] Similarly, *N*-heterocyclic carbenes (NHCs), another class of widely used OCs, promote the Umpolung of an organic moiety (mainly aldehydes or Michael acceptors) for C–C bond formation reactions.[3] When chiral, the OC may make the process stereoselective.[2]



Scheme 3

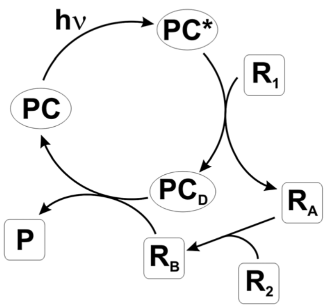
Photocatalysis, where an electronically excited species PC* acts as the catalyst, has been gaining interest and various organic transformations under such conditions have been reported recently, in most cases involving C–C bond formation (*via* activation of C–H bonds) or oxidations.[4] In many cases the catalyst is a transition metal complex,[4,5] as is *e.g.* the case of the use of coloured Ru and Ir complexes for the now rapidly developing visible light photocatalysis.[5] However, reactions where organic molecules play this role are known, indeed some of them are among the longest known photochemical reactions, and are also of interest for some peculiarities, which prompted activity in the field.[4a,6–7] As an example, their role in the photocatalyzed oxidation of pollutants has been recently reviewed.[8]

A photocatalytic cycle is depicted in Scheme 4. The excited catalyst activates a reagent R_1 that is transformed into R_A through a *chemical* reaction. The deactivated photocatalyst (PC_D) is then regenerated through a reverse process by an intermediate R_B, arising through a (series of) reaction(s) from R_A. PC re-enters the cycle and the final product P is obtained (Scheme 4).

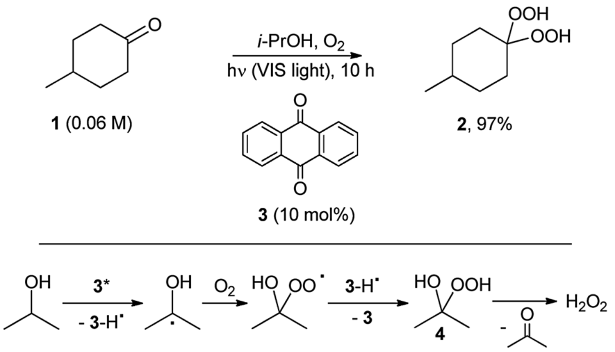
The present review refers to the case where the photocatalytic cycle involves only organic species, although this does not necessarily mean that a metal containing species does not participate in the follow-up steps.

Physical energy transfer (sensitization) is excluded from the definition,[9] as is the formation of a ground state complex,[10] and thus of a different species with a different absorption spectrum,[10,11] as well as the photochemical formation of a catalyst[4a] or of a thermally active reagent.[12] A representative example of the last case is shown in Scheme 5, where a cyclohexanone derivative (**1**) is converted into the corresponding *gem*-dihydroperoxide (**2**) by visible light irradiation in *i*-PrOH in the presence of oxygen and a catalytic amount of anthraquinone (**3**). Here the role of **3** is that of photogenerating the oxidant, be it the hydroxy hydroperoxide **4** or hydrogen peroxide from it (Scheme 5).[12]

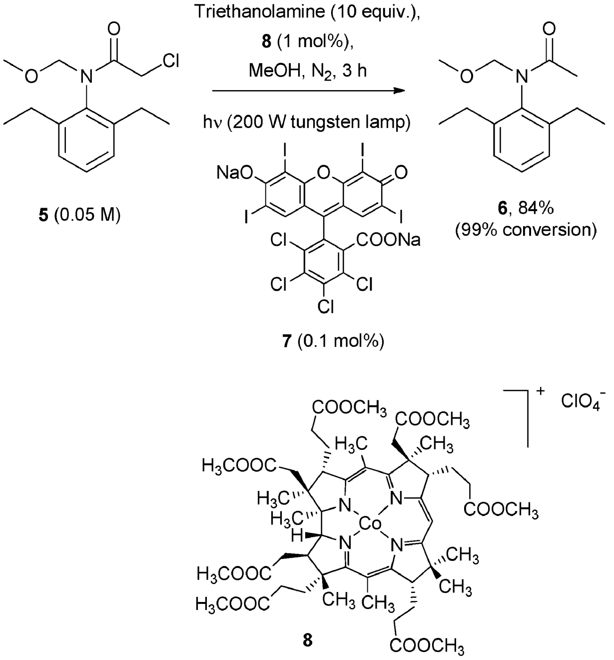
Likewise, a bio-inspired system was recently reported, where a dye (Rose Bengal, **7**, 0.1 mol%) was involved in the reduction



Scheme 4



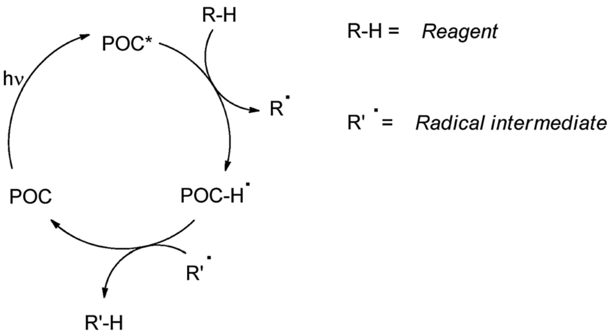
Scheme 5



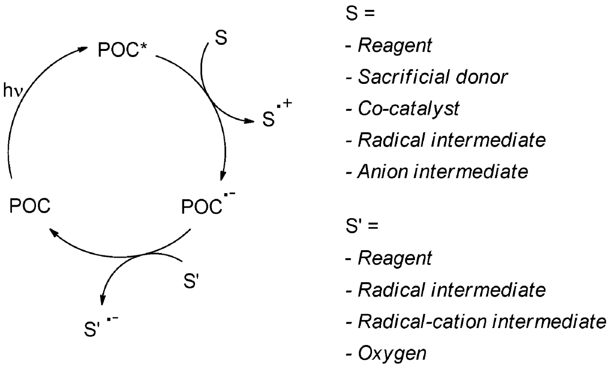
Scheme 6

of various alkyl chlorides including the toxic 1,1-bis(4-chlorophenyl)-2,2,2-trichloroethane (DDT) *via* a visible-light-driven process (Scheme 6).[13] This does not fit with the above definition because, although **7** absorbs light, the active species is the photogenerated reduced form of vitamin B12 derivative (**8**), a ground state compound present in small amounts (1 mol%).[13] Chloroamide **5** was efficiently dechlorinated to **6** in a satisfactory yield by irradiation with a 200 W tungsten lamp under these conditions (Scheme 6).

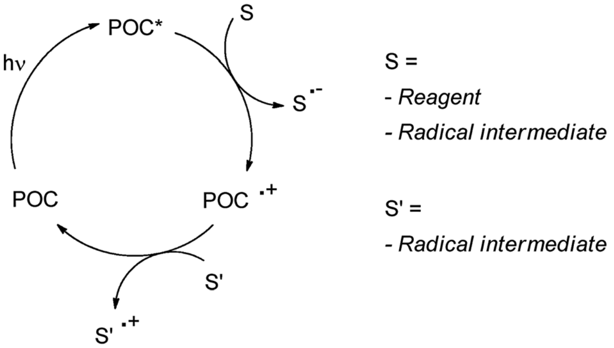
As mentioned above, photocatalytic reactions necessarily involve the activation of (one of) the reagent(s) (that is incorporated into the end product) by excited photoorganocatalysts (POC*, or by other short-lived intermediates directly generated from them, such as radical ions $POC^{\bullet+}$ or $POC^{\bullet-}$) and thus must be a fast process. Adopting the above conditions coupled with the requirement that the catalyst is regenerated in practice limits the viable modes of action of a photocatalyst to hydrogen atom transfer (HAT, Scheme 7) or electron transfer (ET, Schemes 8 and 9) as illustrated in previous reviews.[4]



Scheme 7



Scheme 8



Scheme 9

In the HAT mechanism, homolytic hydrogen abstraction from a C–H bond (*e.g.* in ethers, aldehydes, alcohols and alkanes) leads to the formation of a nucleophilic carbon-centered radical prone to react with Michael acceptors in conjugate addition reactions.[4a] The reaction is successful when the $POC\text{-}H^{\bullet}$ species is able to back-donate a hydrogen atom to a radical intermediate formed in the reaction (Scheme 7). Known POCs acting in this way are limited to aromatic ketones and quinones.[4a,14]

In the ET mechanism either an oxidative or a reductive activation is involved (see Schemes 8 and 9). The situation depicted in Scheme 8 is quite common. In that case, electron transfer from reagent S generates the radical cation $S^{\bullet+}$ that undergoes the chemistry. The POC is regenerated, often by the oxygen mediated oxidation of $POC^{\bullet-}$ from the first step (Scheme 8). In some instances, however, other donors are initially oxidized, such as a sacrificial donor (usually a tertiary amine), a co-catalyst (again another organic molecule) or radical or anionic intermediates in turn generated in the process. In a limited number of cases the reaction starts with the reduction of a reagent by photogenerated $POC^{\bullet-}$. Moreover, the regeneration of the POC can be accomplished by an ET reaction between $POC^{\bullet-}$ and radicals or radical cations (Scheme 8). On the other hand, the capability of POC* to reduce a reagent is less commonly exploited (Scheme 9).

In contrast to the HAT mechanism, there is a wide variety of POCs able to behave as oxidants or reductants when in the excited state. These include acridinium salts, (thia)pyrylium salts,[15] diazapyrenium salts, riboflavin tetraacetate, aromatic esters and nitriles, substituted benzophenones,[14] polycyclic aromatics (*e.g.* phenanthrene) and more recently dyes.[7] In a couple of cases the POC mimics the action of titanium dioxide as a microelectrode, namely the semiconductor mesoporous carbon nitride polymer (a heterogeneous POC),[16] and the 9-mesityl-10-methylacridinium ion.

Table 1 gathers the key electrochemical parameters for the ground and excited states of some organic photoredox catalysts in comparison with those of $Ru(bpy)_3^{2+}$, the most widely used metal complex in visible light photocatalysis, along with their absorption. It is apparent that POCs are excellent one electron oxidants in the excited states (E^*_{red} ranging between 1.0 and 3.0 V *vs.* SCE). In contrast, transition metal photocatalysts usually undergo an initial reduction or oxidation *via* the excited state (*e.g.* Ru^{2+*} to either Ru^+ or Ru^{3+}) and this leads to the species actually involved in the catalytic cycle, either a good reductant (E_{red} *ca.* −1.4 V *vs.* SCE for Ru^+) or a modest oxidant (E_{ox} *ca.* 1.3 V *vs.* SCE for Ru^{3+}).[5b]

Most POCs exhibit some activity even when exposed to solar light, since most of them absorb strongly in the UV-A region and a significant fraction is coloured (Table 1).

The aim of the present review is to highlight the emerging trends in the application of a photoorganocatalyst in organic synthesis. For most of the reported reactions, the amount of the organocatalyst used tends to be larger than that of the metal-based catalyst. The present discussion will be limited to reactions taking place with a <20% molar proportion of the photocatalyst, excluding reactions where the additive is used in a stoichiometric amount, although some of these are closely analogous to the catalytic proper reactions.

Table 1 Electrochemical parameters of the ground and excited states and absorption maxima of selected photoorganocatalysts in comparison with that of the metal photoredox catalyst $Ru(bpy)_3^{2+}$[a]

Photocatalysts (PC)	E_{red} (PC/$PC^{\bullet-}$)	E_{ox} ($PC^{\bullet+}$/PC)	E^*_{red} (PC*/$PC^{\bullet-}$)	E^*_{ox} ($PC^{\bullet+}$/PC*)	Absorption[b] (nm)
Rose Bengal (**7**)	−0.78	1.09	0.99	−0.68	559
10-Methylacridinium ion (**19**)	−0.43		2.32		320–470
Eosin Y (**23**)	−1.14	0.72	1.18	−1.60	539
9,10-Dicyano-anthracene (**46**)	−0.89		1.97		330–440
Benzophenone (**62**)	−1.68		1.55		320–380
Phenanthrene (**81**)	−2.49	1.83	1.10	−1.76	300–350
$Ru(bpy)_3^{2+}$	−1.33	1.29	0.84	−0.86	450

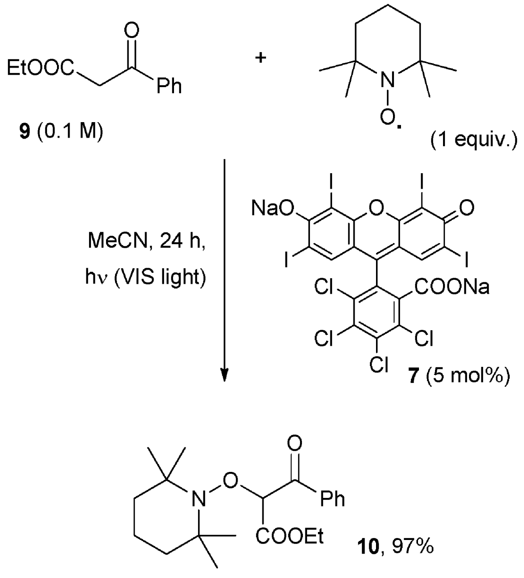
[a] Redox potentials are reported in V *vs.* SCE; bpy = 2,2′-bipyridine.
[b] Absorption maxima or the convenient absorption range for preparative irradiations.

2. Applications of photoorganocatalysts (POC) in synthesis

Known reactions that answer the above definition by using POC are limited in number, but quite varied. In this section these have been classified into oxidations, reductions, alkylations and other C–C bond forming reactions and arylations. The collection is not exhaustive and is biased toward the most recent applications. Further examples can be found in previously published reviews.[4a,b,6]

2.1. Oxidations

2.1.1. FORMATION OF C–X BONDS (X = O, P, N). In all of the reported cases, the formation of a single C–X bond involves an initial electron transfer reaction between the POC and the substrate. The reactions forming C–O bonds are appealing from the eco-sustainable point of view since in most such reactions atmospheric oxygen (O_2) is incorporated. A recent example is the α-oxyamination of aromatic β-ketoesters (**9**) by using Rose Bengal (**7**, 5 mol%) in the role of POC as indicated in Scheme 10.[17] Visible light was used to promote the reaction and a 11 W household fluorescent bulb was found convenient. The authors claimed that an ET between **7*** and the ketoester initiated the process and was followed by a thermal ET step. As a result, **7** was regenerated and a α-keto-α-carboxyethyl radical was formed, which in turn gave the final α-oxyaminated compound (**10**) by trapping by TEMPO (Scheme 10). Yields

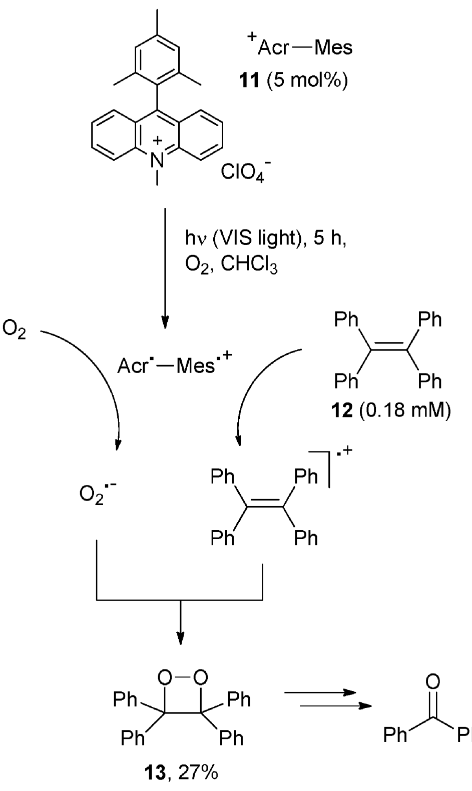


Scheme 10

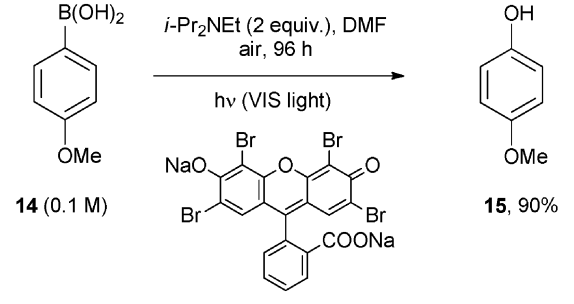
ranged from 64 to 97% provided that an aromatic β-ketoester was used. The oxidation was likewise applied to α-fluoro-β-ketoesters. The reaction was effective even under oxygen-free conditions.[17] Thus, singlet oxygen had no role in the reaction, while the involvement of TEMPO also as an oxidant could not be excluded.

In contrast, oxygen was required in the photocatalytic oxidation of anthracenes and olefins, where visible light (Xenon lamp) was likewise effective.[18] In this case a charge-separation dyad was used as a photocatalyst, such as the 9-mesityl-10-methylacridinium ion (**11**, Acr$^+$–Mes, 5 mol%) developed by Fukuzumi *et al.* Accordingly, irradiation of an oxygen saturated solution of 9,10-dimethylanthracene or tetraphenylethylene resulted in the formation of dimethylepidioxyanthracene and tetraphenylethylene dioxetane, respectively. The reaction was initiated by the photoexcitation of Acr$^+$–Mes that caused an intramolecular electron transfer reaction to form Acr$^\bullet$–Mes$^{\bullet+}$ that in turn was able to oxidize the organic substrate (to the corresponding radical cation) as well as to reduce oxygen to $O_2^{\bullet-}$. The coupling between the two last species gave rise to a dioxetane.[18] Scheme 11 illustrates the typical mode of action of Acr$^+$–Mes in the photooxidation of tetraphenylethylene (**12**) where the corresponding dioxetane **13** was isolated in 27% yield.[19] The oxidation potential of the dioxetane is quite low (*ca.* 1.56 V *vs.* SCE) and accordingly, further oxidation can occur upon prolonged irradiation and benzophenone is ultimately formed.[18,19]

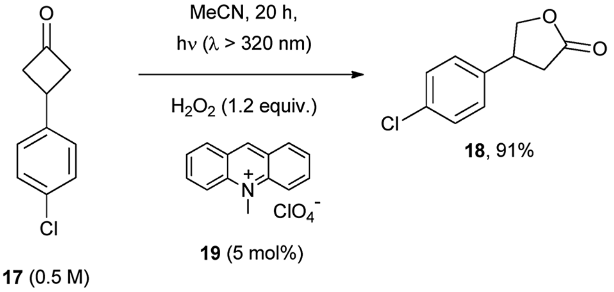
The direct aerobic oxidative hydroxylation of arylboronic acids to phenols is another interesting application of a dye photocatalyzed formation of a C–O bond by using air as the oxidant.[20] The process was usually carried out by using Ru or Ir based complexes, but in a single case (see Scheme 12) Acid Red 87 (Eosin Y) disodium salt (**16**) was successfully adopted. The reduced photocatalyst (formed by a photoinduced ET reaction with an amine such as *i*-Pr$_2$NEt) was able to reduce oxygen to the superoxide radical anion that in turn added to the boron atom of the arylboronic acids (*e.g.* **14**). This caused a series of rearrangements that upon final hydrolysis gave the corresponding phenol (**15**) in an excellent yield (Scheme 12).[20]



Scheme 11



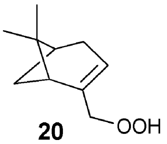
Scheme 12



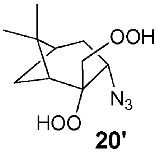
Scheme 13

Acridinium salts (**19**) are effective POCs also in the Baeyer–Villiger oxidation of cyclobutanones (**17**) to γ-lactones (**18**) that occurs from modest to good yields in the presence of 1.2 equiv. hydrogen peroxide (Scheme 13).[21]

Two dyes (Rhodamine B and Rhodamine 6G, *ca.* 0.1 mol%) were used for the azidohydroperoxidation of myrtenyl hydroperoxide (**20**) in the presence of the azide anion and oxygen. The photoinduced oxidation of the azide anion generated an azidyl radical prone to be added to the double bond of **20**. Trapping of the resulting radical by oxygen followed by a further ET step led to the azido bis-hydroperoxide **20′**.[22] Despite the modest yields (not exceeding 13%), the reaction was notable for the concomitant addition of the N$_3$ and OOH groups onto the double bond of **20**.

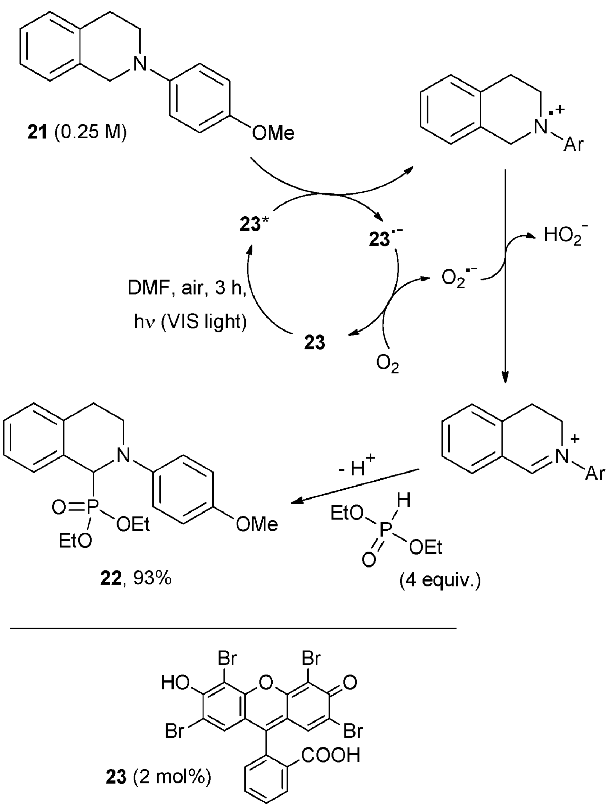


20

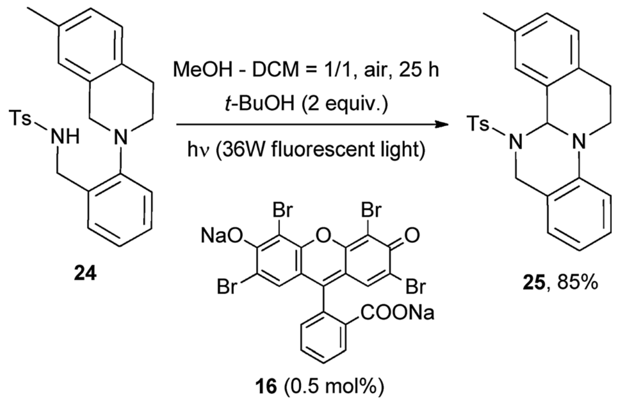


20'

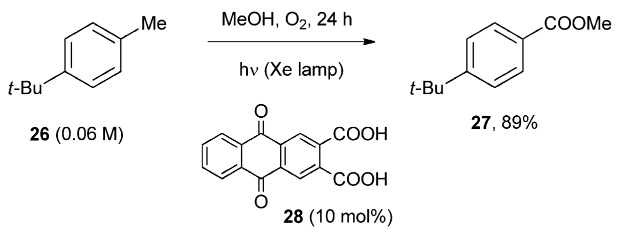
A case of C–P bond formation by photocatalysis was recently reported and involved the reaction of a number of *N*-aryl tetrahydroisoquinolines (**21**) in the presence of an excess of



Scheme 14



Scheme 15



Scheme 16

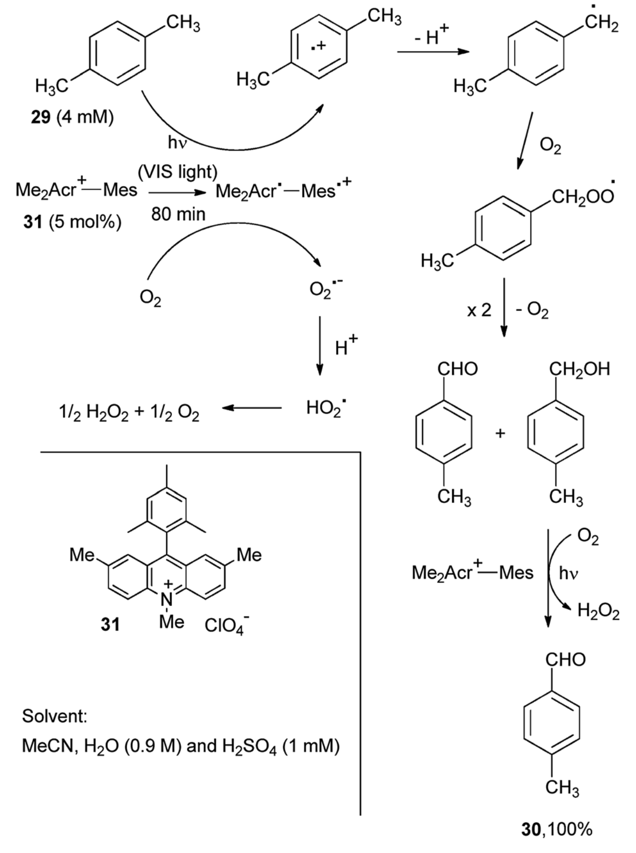
diethyl phosphite, resulting in an oxidative synthesis of α-amino phosphonates (**22**, Scheme 14).[23] Green LEDs were used as the light source and Eosin Y (**23**, 2 mol%) as POC, regenerated by the air dissolved. In common with other photocatalytic reactions of the easily oxidized tetrahydroisoquinolines, the mechanism involves oxidation by POC* and H transfer from the radical cation to $O_2^{\bullet -}$, in this case followed by trapping of the resulting iminium ion by the phosphorus nucleophile (yield of the phosphonate exceeding 80%, Scheme 14).[23]

Very recently, substituted *N*-aryl tetrahydroisoquinolines were used as the starting materials for the preparation of isoquino[2,1-*a*]pyrimidines *via* an intramolecular photocatalyzed formation of a C–N bond again by using Eosin Y disodium salt (**16**, 0.5 mol%) as POC.[24] The strategy was in this case based on the intramolecular addition of a pendant *N*-tosyl moiety onto the iminium ion formed. Thus, 4-methyl-*N*-(2-(7-methyl-3,4-dihydroisoquinolin-2(1*H*)-yl)benzyl)benzenesulfonamide (**24**) was functionalized under mild conditions to give 3-methyl-5-tosyl-5,6,12,13-tetrahydro-4b*H*-isoquinolino[2,1-*a*]quinazoline (**25**) in 85% yield upon 25 h irradiation by a 36 W fluorescent light (Scheme 15).[24]

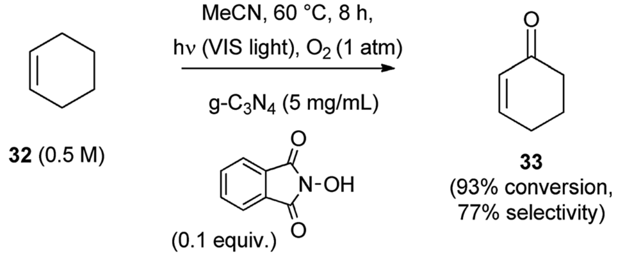
2.1.2. FORMATION OF X=O BONDS. Oxidation processes forming X=O bonds (X = C, S) have also been reported, and the largest part involved the conversion of methyl aromatics and of benzyl alcohols to the corresponding carbonyl or carboxyl derivatives. Again, molecular oxygen mostly is the oxygen source and the activation involves either hydrogen or electron transfer. With anthraquinone derivatives the first mechanism operates. Thus, excited anthraquinone-2,3-dicarboxylic acid (**28**) abstracted a benzylic hydrogen in 4-*t*-butyltoluene (**26**) and the resulting benzyl radical was trapped by oxygen. In methanol the corresponding hemiacetal was formed and a second hydrogen abstraction/oxygen addition sequence afforded the methyl ester **27** (Scheme 16).[25] The reaction was effective even with polymethylated benzenes, provided that a larger amount of POC was used. Under these conditions, *p*-xylene was oxidized to dimethyl terephthalate in 46% yield.[25]

Moreover, when the reaction was carried out in ethyl acetate and by using 2-chloroanthraquinone (8 mol%) as the POC, the corresponding benzoic acids were formed.[26] In this aerobic oxidation, improved yields were obtained in the presence of both bases (potassium carbonate) and acids (trifluoroacetic acid, TFA).

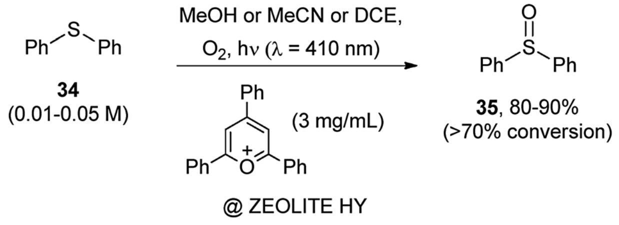
An example of the ET mechanism is the clean and chemoselective oxidation of methyl aromatics (*e.g.* *p*-xylene, **29**) by using the 9-mesityl-2,7,10-trimethylacridinium ion (**31**, Me_2Acr^+-Mes, 5 mol%) as the photocatalyst.[27] ET oxidation followed by deprotonation yielded benzyl radicals that could add oxygen leading to a mixture of *p*-tolualdehyde and *p*-methyl benzyl alcohol (Scheme 17). The oxidation conditions allowed the further oxidation of the alcohol to the aldehyde **30**, but the high oxidation potential of the latter prevented any further oxidation by the $Mes^{\bullet +}$ moiety. As shown in Scheme 17 an equivalent amount of hydrogen peroxide was likewise liberated in the reaction. Another example is the oxidation of β-methylnaphthalene to β-naphthaldehyde with 9-mesityl-10-methylacridinium perchlorate as the catalyst and again oxygen as the oxidant, albeit a non-negligible amount of 2-methyl-1,4-naphthoquinone was also formed. Notice that this catalyst acts



Scheme 17



Scheme 18



Scheme 19

as an oxygen sensitizer with less easily oxidized substrates, such as alkenes.[28]

The oxidation of primary and secondary benzyl alcohols to aromatic aldehydes and, respectively, ketones was likewise efficient with acridinium salts as POCs (λ > 310 nm).[29,30] Yields were good (>80%), independently of the presence of ring substituents. Various benzylic oxidations could be carried out by having recourse to riboflavin tetraacetate (10 mol%) that is another convenient POC for the benzylic oxidation of alkylbenzenes, as well as of *N*-acylbenzylamide to the corresponding imide (83% yield in aqueous acetonitrile, 30 min irradiation).[31]

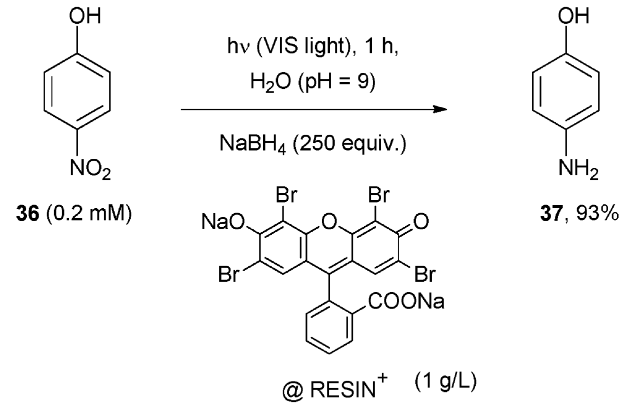
As hinted in the introduction, heterogeneous POCs are also available. Thus, mesoporous carbon nitride (mpg-C_3N_4)[16,32] is a solid-state semiconductor based on a polymeric melon (a slightly disordered precursor of graphitic carbon nitride having a band gap of 2.7 eV, which corresponds to an optical wavelength of 460 nm). This has some similarities with TiO_2, but absorbs in the visible region. The oxidation of benzyl alcohols with mpg-C_3N_4 (50 mg per mmol of alcohol) required the use of a stainless steel autoclave.[32] The selectivity was high, but the conversion not complete. Graphitic carbon nitride (g-C_3N_4)[16] in conjunction with *N*-hydroxyphthalimide acted as a metal-free photocatalytic system for the allylic oxidation of various alkenes,[33] as shown in Scheme 18 for the conversion of cyclohexene (**32**) into cyclohexenone (**33**). The actual C–H activating agent was the corresponding nitroxyl radical.

The same protocol was applied to the oxidation of styrene to benzaldehyde, of ethyl benzene to acetophenone and of cyclohexane to cyclohexanone (in the last case, however, the conversion was limited to *ca.* 6%).[33]

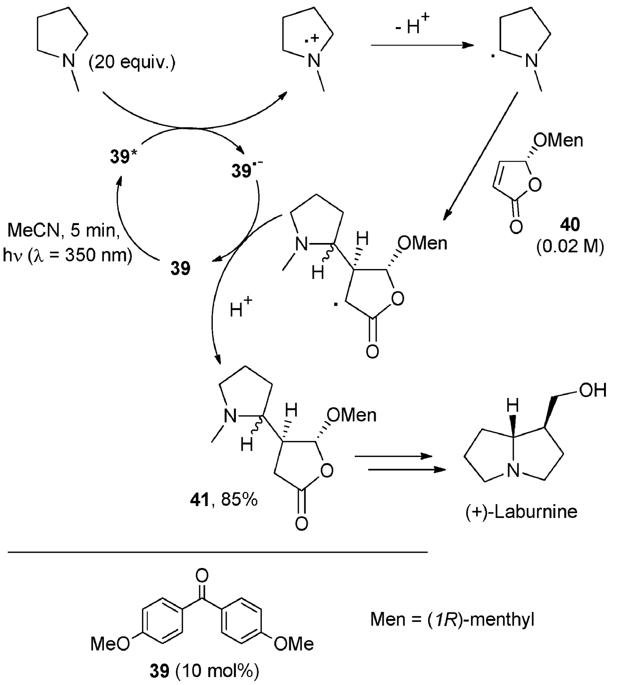
The formation of S=O bonds by oxidation of sulfides can be treated here. The use of 2,4,6-triphenylpyrylium salts[15] encapsulated within zeolite Y as an inert support[34] (Scheme 19) was found effective for the chemoselective oxidation of diphenyl sulfide **34**, whether in medium polar and in polar protic solvents. The encapsulation avoided the degradation of the photocatalyst generally observed in solution. In most cases the process gave mixtures of oxidized derivatives namely disulfides, sulfinic and sulfenic esters as well as sulfonic acids. However, in the case of aromatic sulfides the formation of the corresponding sulfoxides **35** was predominant and in some cases exclusive (see Scheme 19).[34]

Carbon nitride (mpg-C_3N_4) has been likewise used for the photocatalytic selective oxidation of sulfides to sulfoxides with O_2 as the oxidant at room temperature.[35]

2.2. REDUCTION. Reductive processes promoted by an organic photocatalyst have been less often applied. Reductive dehalogenation, *e.g.* of phenacyl bromide to acetophenone, was tested with various dyes as POCs (fluorescein, nile red, rhodamine B and others) and inexpensive Eosin Y (**23**, 2.5 mol%) gave the best results (quantitative conversion upon irradiation with green light from high-power LEDs, $\lambda \approx$ 530 nm). The reaction was carried out in the presence of excess *i*-Pr_2NEt and of an equimolar amount of the Hantzsch ester.[36] The latter compound was used as a hydride source to avoid potential side reactions. Noteworthily, in some cases, as in the reduction of 4-bromobenzyl 2-phenyl-2-chloroacetate to 4-bromobenzyl 2-phenylacetate, the yields were equal or better than those obtained under transition-metal photocatalyzed conditions. The use of a simple microreactor made of a fluorinated



Scheme 20



Scheme 21

ethylene propylene copolymer tubing coiled around the lamp considerably increased the rate of conversion.[37]

Resin-supported Eosin Y was used as the POC in the reduction of 4-nitrophenol (**36**) to 4-aminophenol (**37**) under visible light. The reaction gave good yields and occurred in the presence of $NaBH_4$ that reduced the excited state of the dye (Scheme 20). An important advantage of the method is that the catalyst can be reused at least three times with no significant loss in the rate constant of the reaction.[38]

2.3. Formation of C–C bonds

2.3.1. SYNTHESIS OF α-FUNCTIONALIZED AMINES. The α-functionalization of amines (actually limited to tertiary amines) is one of the most studied reactions involving photocatalysis by an organic molecule (see also Section 2.1.1. and Scheme 14). ET is efficient with such good donors and leads to either α-amino radicals or iminium ions. Dyes,[7] aromatic ketones[4a,14] and cyanoarenes[4a] are commonly used as POCs.

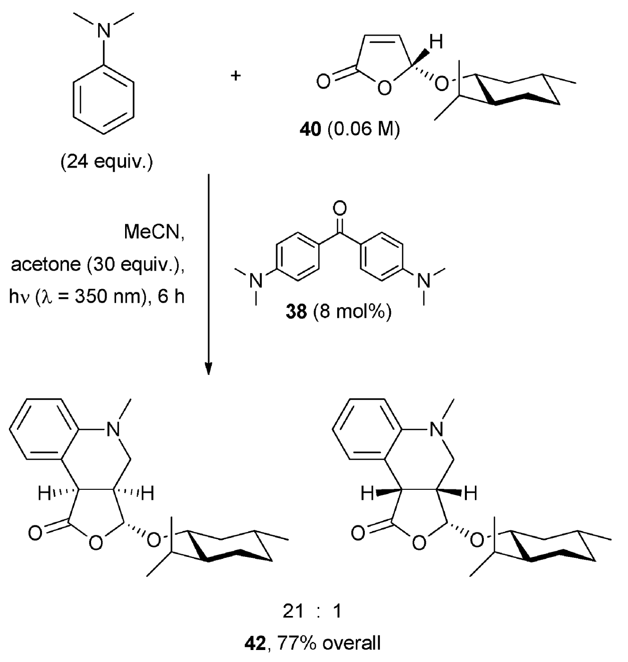
As an example, the one electron oxidation of *N*-methylpyrrolidine by excited 4,4′-dimethylaminobenzophenone (**38**) or 4,4′-dimethoxybenzophenone (**39**, Scheme 21) and selective deprotonation from a ring α-position gave a nucleophilic radical that was trapped by conjugate addition onto electron-poor olefins.[39] Photoaddition onto methyl acrylate, acrylonitrile and dimethyl maleate was obtained in good yields by using a 10 mol% amount of **39**.[39]

Interestingly, when using a chiral olefin such as (5*R*)-5-menthyloxy-2[5*H*]-furanone (**40**) the addition took place with facial diastereoselectivity (≥ 90%).[40] The adduct formed (**41**, 85% yield)[39] was later elaborated in a few steps for the preparation of pyrrolizidine and indolizidine alkaloids including (−)-isoretronecanol and (+)-laburnine (Scheme 21).[41]

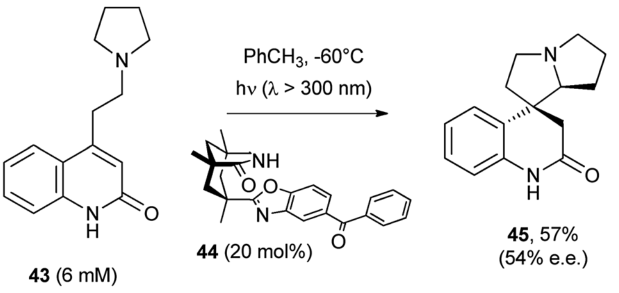
The addition of dithiocarbamate to the solution appeared to improve efficiency and selectivity of some of these reactions. In the extreme case the alkylation of *N*,*N*-dimethylacrylamide took place only in the presence of such an additive.[42]

A variation of this process led to the tetrahydroquinoline derivative **42** in a good yield and with excellent stereoselectivity by addition of the α-amino radical generated from *N*,*N*-dimethylaniline to furanone **40** (bearing a chiral menthyloxy group) and by cyclization (see Scheme 22).[43] The reaction was photocatalyzed by Michler's ketone (**38**) at λ = 350 nm.

An intramolecular version of the reaction was developed by Bach and coworkers, where a catalytic enantioselective reaction was performed. Here the POC (a functionalized benzophenone) was tethered to a chiral complexing agent (**44**) able to embed the substrate **43** through hydrogen bonding.[44] The irradiation of the



Scheme 22

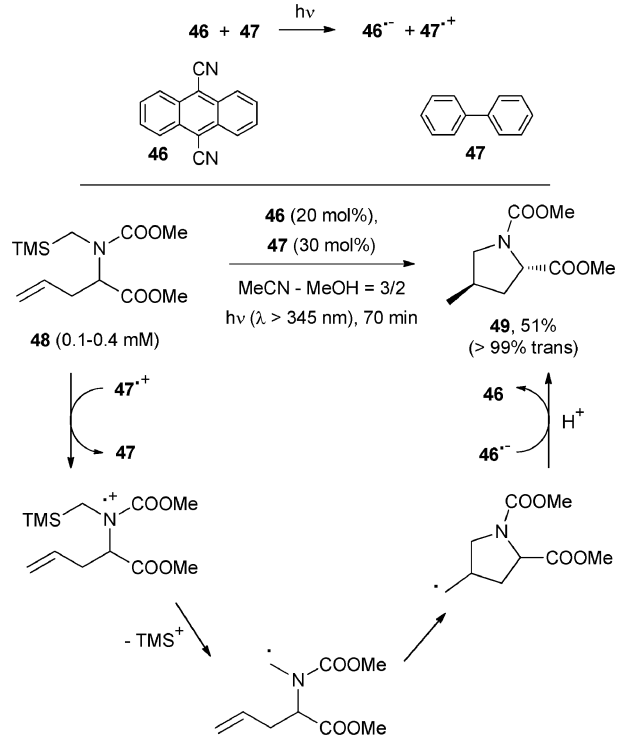


Scheme 23

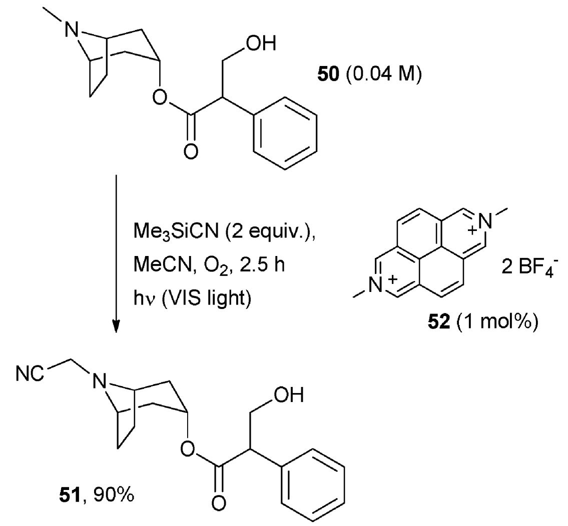
complex generated a α-amino radical prone to react intramolecularly in a chiral environment. As a result, the chiral pyrrolizidine **45** was formed in a good yield with a satisfactory ee (Scheme 23).[44]

On the other hand, using Eosin Y for the radical (from methyldiphenylamine) alkylation of diethyl ethylidenemalonate resulted in a poor yield (9%), compared with 90% when an Ir complex was chosen.[45]

α-Amino radicals can be likewise generated from α-silyl amines (**48**). The trimethylsilyl (TMS) group lowers the oxidation potential of the substrate, thus making a cyanoarene such as 9,10-dicyanoanthracene (**46**) able to cause photoinduced ET[46] in the presence of a co-catalyst (biphenyl, **47**, see Scheme 24). Desilylation of the radical cation (in a protic medium), intramolecular cyclization onto a double bond, reduction by $\mathbf{46}^{\bullet -}$ and protonation gave carbamate **49** in a decent yield and in high diastereomeric excess. Related cyclizations were used for inducing structural changes in oligopeptides by introducing the structural motif present in compound **48** into the peptide chain.



Scheme 24



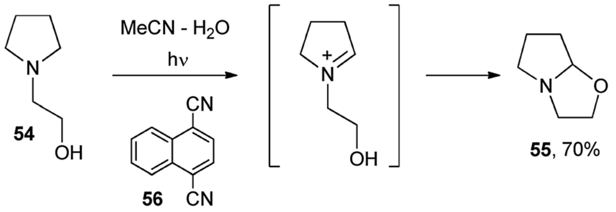
Scheme 25

An alternative way consisted of the homolytic hydrogen abstraction from the amine radical cation previously formed to generate an electrophilic iminium ion that could then be trapped by carbon nucleophiles. Oxygen was usually required as a hydrogen atom scavenger. In a pioneering work, the Santamaria group photocyanated a series of alkaloids by using the visible light absorbing POC *N*,*N*′-dimethyl-2,7-diazapyrenium-bis-(tetrafluoroborate) (**52**, DAP^{2+}, 2 BF_4^-, 1 mol%) and Me_3SiCN as the cyanide source.[47] Under these simple conditions, atropine **50** gave α-aminonitrile **51** in 90% yield. The success of the reaction was in part attributed to the stability of the radical cation generated by monoelectronic reduction of the diazapyrenium salt (Scheme 25).

Rose Bengal photocatalyzed the cyanation of the *N*-acetyl-2,16-dihydro derivative of the alkaloid tabersonine (33% yield, 2 h irradiation)[48] as well as that of *N*-aryl-tetrahydroisoquinolines (5 mol% catalyst, in combination with graphene oxide, **53**).[49] The mild conditions required allowed for the C–H functionalisation of these tertiary amines by using Me_3SiCN as the nucleophile. Using **53** improved the rate and the efficiency of the reaction. The process was likewise applied for the trifluoromethylation of the isoquinoline derivative by using $TMSCF_3$ as the nucleophile.[49] The reaction was considered 'green' because of the use of a cheap organic dye as POC and air as the oxidant.

Cyanoarenes (*e.g.* 1,4-dicyanonaphthalene, **56**) are again suitable for the regioselective generation of iminium ions by oxidation of unsymmetrical tertiary amines. In this case the cation could be formed by oxidation of the α-amino radical by the ground state cyanoarene. Substituted pyrrolidines (*e.g.* **54**) were then purposely employed for the complete regioselective synthesis of tetrahydro-1,3-oxazines such as **55** (Scheme 26).[50]

N-aryl-tetrahydroisoquinolines underwent smooth dehydrogenative coupling reaction in the presence of dyes (Rose Bengal and Eosin Y gave the best performance), thus offering a facile metal-free way of building sp^3–sp^3 C–C bonds.[23,51,52] The α-functionalisation of tertiary amines *via* Henry and Mannich



Scheme 26

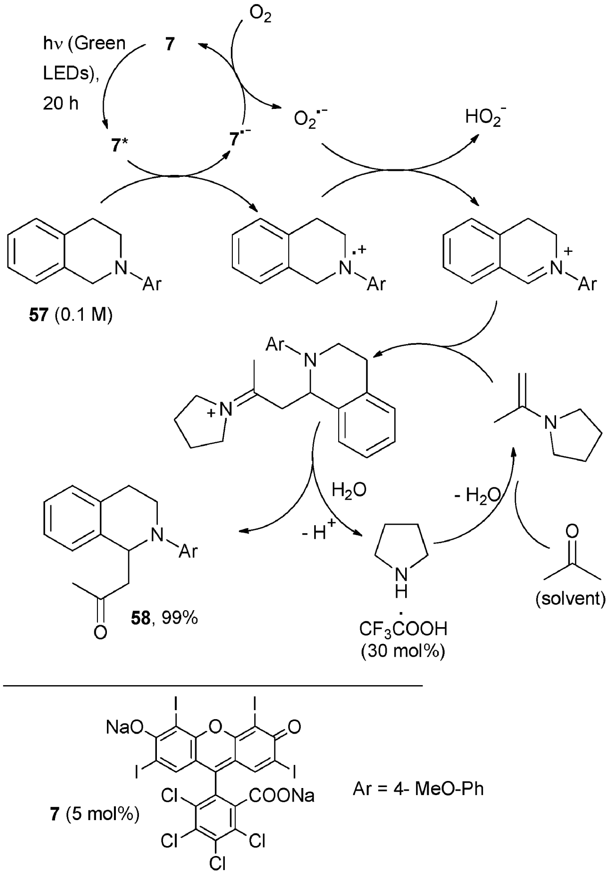
reactions was thus obtained. As an example, irradiation with green light LEDs of a mixture of the isoquinoline and nitromethane (or another nitroalkane) gave the corresponding Henry coupled product in a high yield (at least with benzylamines),[51] which was further improved when solar light was used. Henry adducts from *N*-aryl tetrahydroisoquinolines were likewise reported by using Eosin Y bis-(tetrabutylammonium salt) (2 mol%) as the POC.[52] In this work, further insights into the mechanism were obtained and the role of superoxide radical anion ($O_2^{\bullet-}$) was documented[52] (see further Scheme 14).

The dehydrogenative-Mannich reaction catalysed by Rose Bengal **7** was likewise reported as illustrated in Scheme 27. Here the nucleophile was an enamine generated *in situ* from acetone (the solvent of the reaction) and an organocatalyst (pyrrolidine), promoted by TFA.[51] Under these conditions, the substituted isoquinoline **57** smoothly gave aminoketone **58** after 20 h irradiation in almost quantitative yield (Scheme 27). When using cyclohexanone, substituting (L)-proline for pyrrolidine improved the yield and imparted a good diastereoselectivity.[51]

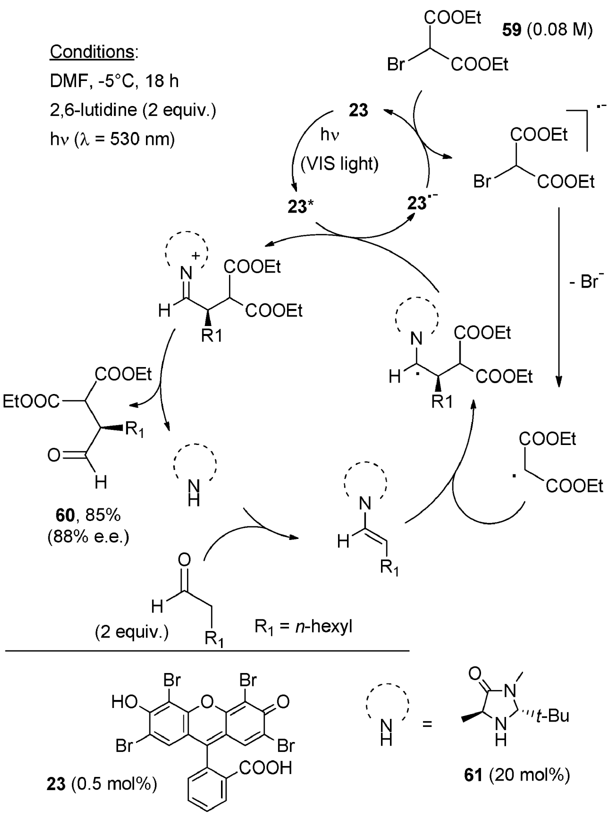
The oxidative coupling of tetrahydroisoquinolines with dialkyl malonates (used as the solvent) was similarly obtained by irradiation at 530 nm in the presence of 2 mol% Eosin Y. The products were isolated in excellent yields since the excess of dialkyl malonate was easily eliminated by Kugelrohr distillation.[23]

2.3.2. SYNTHESIS OF α-FUNCTIONALIZED CARBONYL DERIVATIVES. Two approaches have been reported for the α-functionalization of carbonyl derivatives. The first one starts from an aldehyde and makes use of asymmetric cooperative photoredox organocatalysis (see Scheme 28),[36] by using Eosin Y (**23**, 0.5 mol%) as POC in conjunction with MacMillan's imidazolidinone organocatalyst (**61**, 20 mol%). The thermal organocatalyst generated a nucleophilic chiral enamine, whereas the photocatalyst had the role of reducing bromomalonate **59** to the corresponding radical anion. Loss of bromide ion then gave the malonyl radical that added to the enamine and afforded the α-functionalized aldehyde **60** in a high yield and enantiomeric excess under mild, metal-free conditions (Scheme 28).[36] This synergistic organocatalytic photoredox α-alkylation was later carried out in a microreactor, which reduced the time required for completing the reaction to 45 min rather than the 18 h needed for the same process in batch.[37]

A slight modification of the reaction described in Scheme 28 was recently reported and made use of Rose Bengal (0.5 mol%)



Scheme 27

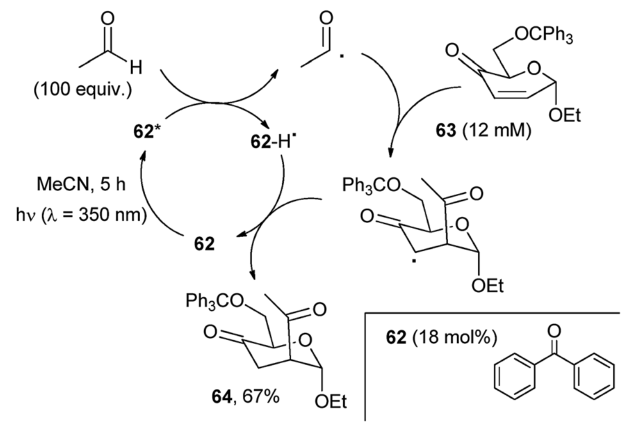


Scheme 28

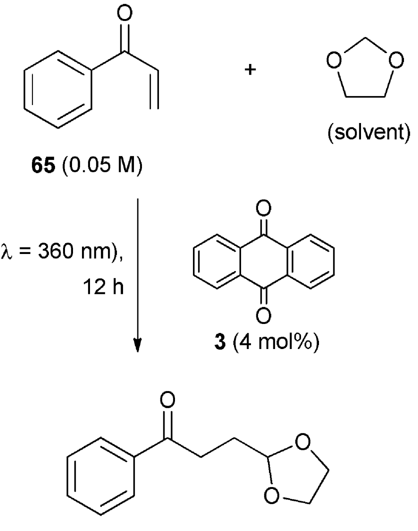
and of the same imidazolidinone organocatalyst, along with LiCl (10 mol%) and 2,6-lutidine (2 equiv.) as additives.[53]

The second approach exploits the ET activation of organoselenium compounds to build carbocation equivalents. Thus, oxidation of an alkyl phenyl selenide by excited 1,4-dicyanonaphthalene (10 mol%), addition to an enol silyl ether and PhSe radical loss gave a α-functionalized ketone in up to 80% yield. The reaction was completed in 8 to 10 hours in MeCN – H_2O (4/1) and equilibration with dissolved air was sufficient for reoxidizing the photocatalyst.[54]

2.3.3. CONJUGATE ADDITION ONTO ALKENES (SYNTHESIS OF β-FUNCTIONALIZED CARBONYL OR CARBOXYL DERIVATIVES). Many reactions pertaining to this category are based on the photocatalytic generation of a nucleophilic alkyl radical and ensuing addition onto Michael acceptors (*e.g.* α,β-unsaturated nitriles, esters, aldehydes and ketones), resulting in an easy preparation of β-functionalized carbonyl or carboxyl derivatives. Further examples are found in Section 2.3.1. The radicals can be obtained either by a hydrogen transfer reaction (*via* homolytic cleavage of a C–H bond) or by an electron transfer process (*via* loss of an electrofugal group from the first formed radical cation). In the former case the POCs were aromatic ketones[14] (mainly benzophenone **62**) or anthraquinones whereas in the latter case polycondensed aromatics, aromatic esters and nitriles were a convenient choice.[4a] The use of aromatic ketones for the photochemical activation of C–H bonds was born at the same time as photochemistry, but their application as POC (*viz.* the use in substoichiometric amounts) was inaugurated by Fraser-Reid.[55] Acetals, alcohols and aldehydes were used for the alkylation/acylation of carbohydrate derived α-enones (that reacted more readily than comparable carbocyclic α-enones), as is the case for the regioselective functionalisation of hex-2-enopyranosid-4-ulose **63** in the presence of excess acetaldehyde to give glycoside **64** in 67% yield (see Scheme 29).[55b] Compound **63** was chosen as a model electrophile and various alcohols (including ethylene glycol) and acetals such as 1,3-dioxolane derivatives gave satisfactory alkylations.[55a,b] The main drawback of the reaction was that the hydrogen donors had to be used as the reaction medium.



Scheme 29



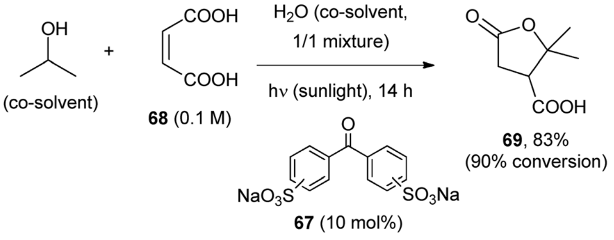
Scheme 30

1,3-Dioxolanes were studied in more detail for the introduction of a masked formyl (or acyl) group. In this case, benzophenone had to be used in a stoichiometric amount, but anthraquinone **3** worked at a lower concentration, as seen in the **3** photocatalyzed addition of 1,3-dioxolane onto phenyl vinyl ketone (**65**) to give the monoprotected 1,4-ketoaldehyde **66** in 65% yield (Scheme 30).[56]

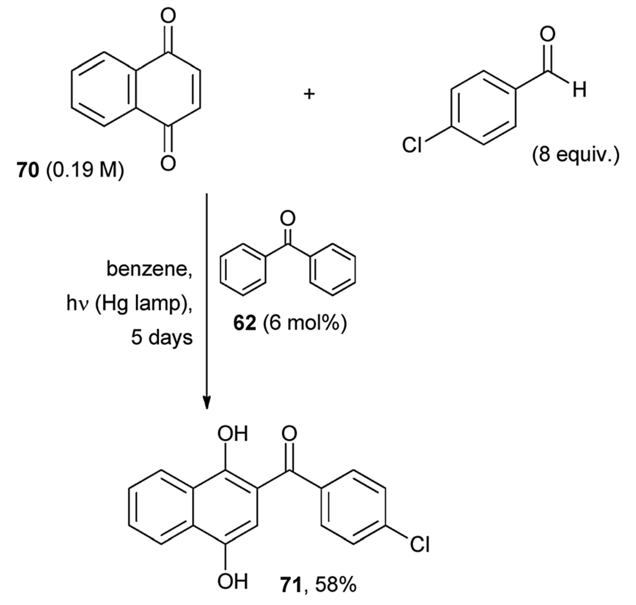
When using chiral enones such as 1,3-dioxin-4-one derivatives, the alkylation (benzophenone, 15 mol% as the POC) occurred from the a-side in both inter- and intramolecular reactions, leading to highly diastereoselective processes. As one may expect, the most efficient reaction occurred with the unsubstituted 1,3-dioxin-4-one.[57]

This mild reaction (and the analogous introduction of a protected ketone function by reaction with 2-alkyl-1,3-dioxolanes) was used for the functionalization of such sensitive substrates as α,β-unsaturated aldehydes for the preparation of 1,4-monoprotected dialdehydes and ketoaldehydes.[58]

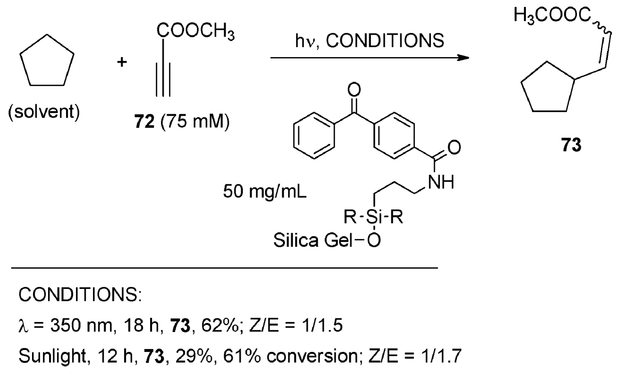
POCs such as benzophenone disodium disulfonate (**67**) or the sodium salt of 4-benzoylbenzoic acid (20 mol%) were used in a mixed aqueous solvent with good results and the additional advantage that the products could be recovered from the mixture containing the catalyst by a mere extraction.[58] Terebic acid (**69**) was obtained from isopropanol and maleic acid (**68**) by using **67**, a synthesis that was carried out on a 10 g scale by 10–15 hours (over three days) exposure to sunlight in a solar concentrator (SOLFIN apparatus, Scheme 31).[59]



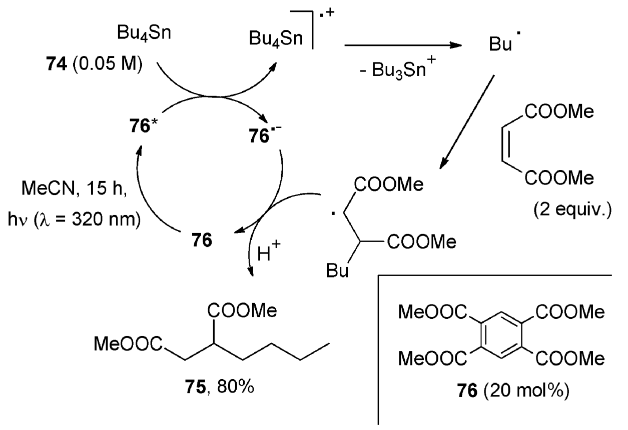
Scheme 31



Scheme 32



Scheme 33



Scheme 34

The labile formyl C–H bond in aldehydes (whether aliphatic or aromatic) was photocatalytically activated by benzophenone (6 mol%), a process that the authors dubbed as ''photo Friedel–Crafts acylation'' of 1,4-naphthoquinone (**70**, Scheme 32).[60] Naphthohydroquinones (*e.g.* **71**) were formed in moderate to good yields and were smoothly oxidized to valuable acylated naphthoquinones. In the absence of the POC some acylation occurred by direct irradiation, but required a long irradiation time and an excess of the aldehyde for completion.[60]

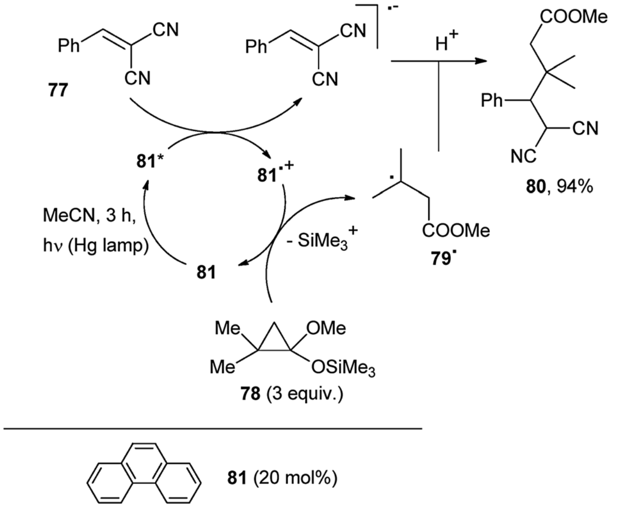
The activation of strong C–H bonds in alkanes could likewise be obtained by POCs.[4a,61–62] The reaction was usually carried out in neat cycloalkane under either homogeneous or heterogeneous conditions. Thus, vinyl cycloalkanes (usually *E*/*Z* mixtures) were obtained by benzophenone (14 mol%) photocatalyzed addition of cycloalkanes onto electron-poor alkynes.[61] Apparently, the aggressive vinyl radical formed abstracted hydrogen from the alkane, making the reaction efficient, even with a low POC concentration. Adoption of a (potentially recyclable) supported catalyst and of UV-A lamps or sunlight as the light source enhanced the clean/green chemistry character of this alkylation, as in the case of aminopropylsilica bound benzophenone in the synthesis of methyl 3-cyclopentyl-2-propenoate (**73**, *E*/*Z* mixture) starting from cyclopentane and methyl propiolate (**72**) (see Scheme 33).

As for the ET generation of alkyl radicals from aliphatic donors, tetrasubstituted stannanes[63] were mainly used due to their low oxidation potential, with UV-B absorbing cyanoarenes or aromatic esters as POCs. As an example, Bu_4Sn (**74**) was used for the alkylation of dimethyl maleate in the presence of tetramethylpyromellitate (**76**, 20 mol%) to afford succinate **75** in 80% yield (Scheme 34).[63a] The high reduction potential of cyanoarenes in the excited state allows peculiar reactions, *e.g.* the use of acetals as electron donors. Thus, the alkylation of dialkyl maleates or acetylenedicarboxylates starting from 2-alkyl-2-phenyl-1,3-dioxolanes took place in the presence of 1,2,4,5-tetracyanobenzene (10 mol%).[63a] In the last reaction, the presence of a co-catalyst such as phenanthrene or biphenyl was often mandatory for obtaining a satisfactory alkylation yield.

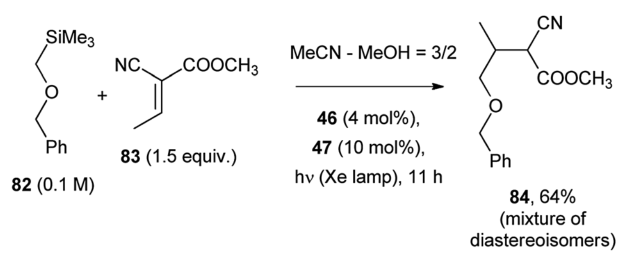
1,1-Disubstitued olefins such as vinylidene malononitrile or vinylidene cyanoacetate are powerful radical traps and are often used in photocatalyzed alkylation reactions.[64,65] Scheme 35 reports the functionalization of a 1,1-dicyanoethylene derivative (**77**) by addition of the $^\bullet CR_2CH_2CO_2Me$ radical, in turn arising *via* ring opening of a cyclopropanone silyl acetal, such as **78**, induced by oxidative photocatalysis by phenanthrene (**81**).[64a] More precisely, excited phenanthrene reduced **77** and $Phen^{\bullet+}$ thus formed oxidized **78** and radical $\mathbf{79}^\bullet$ from it by loss of the Me_3Si cation. Radical–radical anion coupling between $^\bullet CR_2CH_2CO_2Me$ and $\mathbf{77}^{\bullet-}$ gave dinitrile **80** in 94% yield.

A related reaction made use of β,β-dialkyl substituted ketene silyl acetals as electron donors, again in the regioselective introduction of $R'O_2CR_2C$ groups onto electron-poor olefins photocatalyzed by phenanthrene (20 mol%).[64b] Thus, irradiation of a MeCN solution containing 1-methoxy-2-methyl-1-trimethylsiloxypropene, 1,1-dicyano-2-phenylethene and phenanthrene gave the desired 4,4-dicyano-2,2-dimethyl-3-phenylbutyric acid methyl ester in 95% yield.[64b]

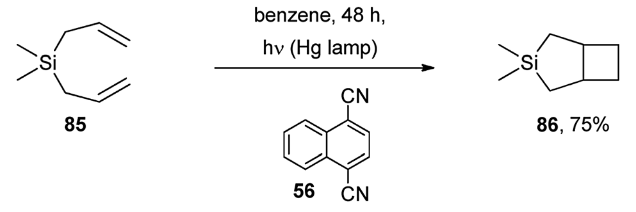
Higher oxidation potential derivatives such as α-silyl ethers (*e.g.* **82**), required a more powerful oxidant, such as 9,10-dicyanoanthracene (**46**; 4 mol%) with biphenyl (**47**; 10 mol%) as a



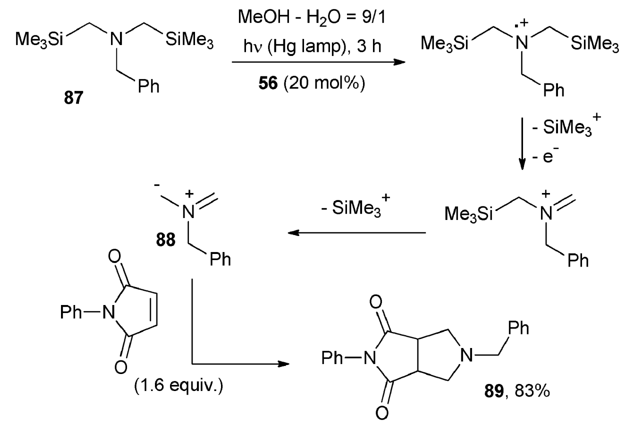
Scheme 35



Scheme 36



Scheme 37



Scheme 38

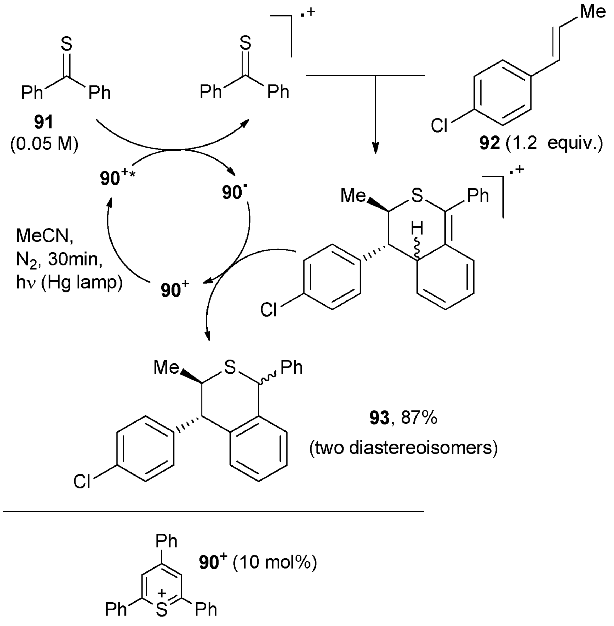
co-catalyst (Scheme 36). In this case, desilylation of the radical cation (requiring a nucleophilic cosolvent, such as methanol) gave a α-oxy radical that was trapped by an electron-withdrawing substituted olefin, *e.g.* by **83** to give cyanoester **84** (64% yield).[65]

2.3.4. Cycloaddition. The application of organic photocatalysis in cycloaddition reactions is limited at present, but suggests a potentially large and varied scope.[4a] The process relies on the Umpolung of one of the educts by POC oxidation (similarly to what happens in some metal catalyzed reactions). An intramolecular [2+2] cycloaddition is known for the conversion of diallyldimethylsilane (**85**) to 3,3-dimethyl-3-silabicyclo[3.2.0]-heptane (**86**) in 75% yield through a Pyrex filtered irradiation (1,4-dicyanonaphthalene **56** as POC, high pressure mercury lamp, $\lambda > 280$ nm, Scheme 37).[66] The reaction took place only in aromatic solvents and did not apply to allyltrimethylsilane, thus the intermediacy of triplexes between diene, POC and the solvent was postulated.[66]

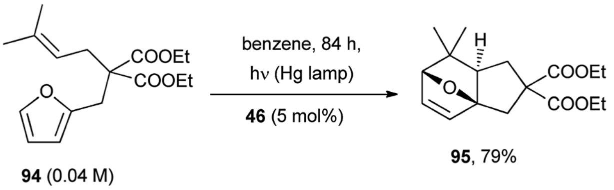
An elegant way for the construction of a five membered ring was developed by Pandey and coworkers by a photocatalyzed 1,3-dipolar cyclization, as shown in Scheme 38.[67] Here the 1,3-dipole (a non-stabilized azomethine ylide) was generated starting from *bis*-silyl amine **87** by two consecutive photooxidations. Again **56** (20 mol%) was used as the POC and initially an iminium cation was generated upon oxidation of **87**, TMS cation loss ensued by oxidation. In turn, the cation underwent a second desilylation and the resulting 1,3-dipole **88** was trapped by the dipolarophile *N*-phenylmaleimide yielding the bicyclic compound **89** in 83% yield.[67] Noteworthily, the POC was almost completely recovered at the end of the reaction.

Six-membered rings were obtained through a photocatalyzed Diels–Alder type reaction. Most of the work in this field is due to the group of Prof. Steckhan. A typical example involved exocyclic dienes and indoles for building highly functionalized tetrahydrocarbazole derivatives. The reaction was initiated by oxidation of the indole moiety to the corresponding radical cation followed by reaction with the diene. Triphenylpyrylium tetrafluoroborate and tris(4-methoxyphenyl)pyrylium tetrafluoroborate (5 mol%) were found suitable as POCs.[15,68] Analogously, (thia)pyrylium salt **90**$^+$ was used as a photoredox photocatalyst in the [4+2] cycloaddition between thiobenzophenone (**91**) and a 4-substituted-β-methylstyrene (*e.g.* **92**, Scheme 39).[69] Interestingly, in this case both reagents could be oxidized by the excited photocatalyst but only radical cation **91**$^{\bullet+}$ was reactive and added to the neutral arylalkene **92** to give the thia-1,2,3,4-tetrahydronaphthalene radical cation. Back electron transfer to this species from the pyranyl radical **90**$^\bullet$ led to the sulfur heterocycle **93**, along with the recovered photocatalyst.[69]

A recent application concerns with the intramolecular photocycloaddition between a furan moiety and a non-activated alkene in the diethyl malonate derivative **94**.[70] The photooxidation was catalyzed by 9,10-dicyanoanthracene (**46**, 5 mol%) and afforded oxabicyclo[2.2.1]heptane **95** (Scheme 40). With alkyl substituted furans, the cycloadducts were formed with a high stereoselectivity.



Scheme 39



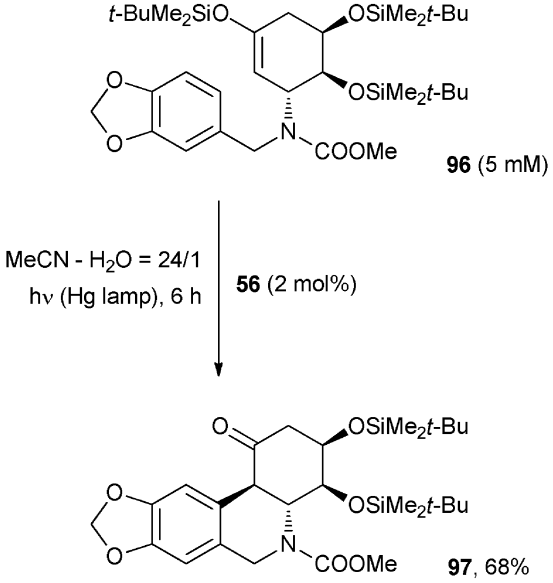
Scheme 40

2.4. Arylations

Photocatalyzed formation of Ar–X bonds (mainly Ar–C) has also been reported (see also Section 2.1.1). An interesting example deals with the synthesis of (+)-2,7-dideoxypancratistatin, a model compound for the preparation of phenanthridone alkaloids. One of the key steps of this synthesis was a 1,4-dicyanonaphthalene (**56**, 2 mol%) ET initiated carbocyclization (Scheme 41).[71] Thus, irradiation of enol silyl ether **96** in aqueous acetonitrile in the presence of **56** gave cyclized product **97** in 68% yield as a single diastereoisomer.[71]

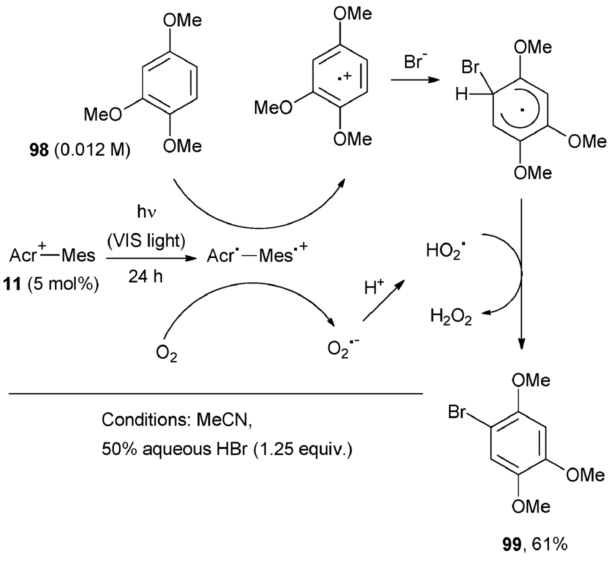
The same POC was employed in the PET oxidation of aromatics substituted with an enol silyl ether moiety. Depending on the structure of the starting aromatic, the reaction led to different benzannulated as well as benzospiroannulated benzyl ketones with the intermediacy of an arene radical cation.[72]

The high reducibility of aryl diazonium salts has been recently exploited for the transition-metal-free formation of aryl-heteroaryl or aryl-vinyl bonds.[73] The excited photocatalyst (Eosin Y, **23**, 1 mol%) was able to reduce the diazonium salt that upon nitrogen loss gave an aryl radical. This in turn added to furan in a regioselective fashion and the resulting radical adduct was oxidized by POC$^{\bullet+}$ and the desired 2-arylfuran was finally formed upon proton loss.[73a] The reaction conditions well tolerated the presence of several functional groups on the aromatic ring. Under the same visible light irradiation conditions, both *N*-Boc protected pyrroles and thiophenes were likewise smoothly arylated.[73a] Arylation of unsaturated compounds such as alkenes, alkynes and enones was later developed by the same group by photoredox catalysis (Eosin Y, 7.5 mol%, green LEDs as the light source) in an updated version of the Meerwein arylation.[73b] In particular, the coupling between an aromatic diazonium salt and styrene in DMSO allowed for the preparation of stilbene derivatives in what can be considered an actual metal-free photo-Heck reaction.



Scheme 41

A single case was reported where the formation of Ar–Br bonds occurred in place of Ar–C bonds. Aqueous HBr was used here as the bromine source and the 9-mesityl-10-methylacridinium ion (**11**, 5 mol%) as the photocatalyst.[74] Scheme 42 shows the photobromination of 1,2,4-trimethoxybenzene (**98**) by visible light



Scheme 42

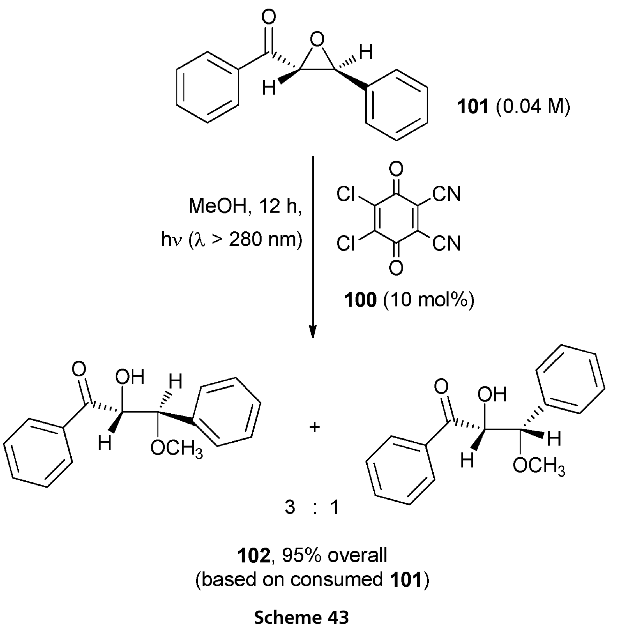
photolysis of an aerated acetonitrile mixture containing the photocatalyst and HBr to afford the brominated derivative **99** in 61% yield. The photocatalytic bromination started by an intramolecular photoinduced electron transfer from the mesitylene moiety to the singlet excited state of the acridinium ion. An electron transfer from aromatic compounds to the mesitylene radical cation moiety and from the acridinyl radical moiety to oxygen then ensued. The selective monobromination took place by bromide addition onto the resulting radical cation of the starting aromatic derivative (Scheme 42).[74] Other methoxysubstituted aromatics were likewise well suited for this reaction.

2.5. Miscellaneous

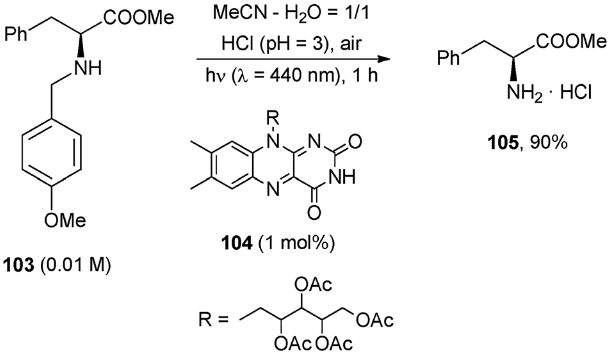
The ring opening of an epoxide by MeOH addition using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (**100**) as the POC has been likewise reported (Scheme 43).[75] An initial ET between **100*** and α-epoxyketone **101** was envisaged. The thus formed intermediate $\mathbf{101}^{+}$ added methanol and gave the corresponding α-hydroxy-β-methoxyketone **102** as a mixture of diastereoisomers through $C_β$–O bond cleavage in excellent yields.[75] Notice however that the same process took place, indeed in a higher yield, under microwave irradiation.

Photoorganocatalysis has also been found useful for the photodeprotection of the amine group, when protected as a methoxybenzyl derivative (Scheme 44).[76] The reaction is based on the flavin-mediated aerobic photooxidation of benzyl amines such as **103**. Thus, 1 h photolysis of an acidic acetonitrile–water solution containing **103** and riboflavin tetraacetate (**104**, 1 mol%) allowed for the isolation of the hydrochloride salt of phenylalanine methyl ester (**105**) in 90% yield.

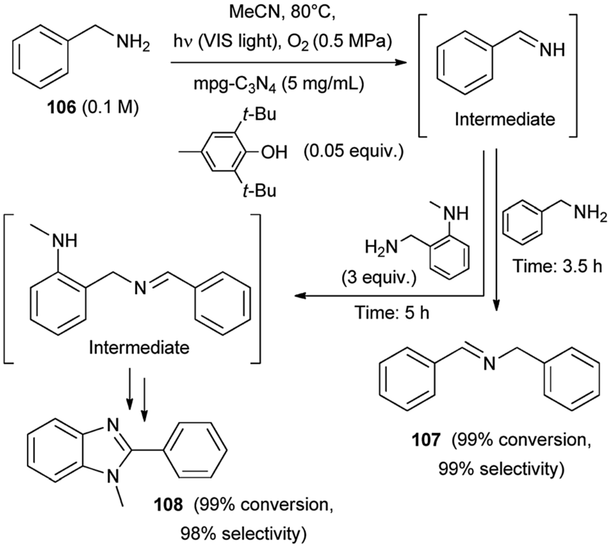
Aerobic oxidative coupling of benzyl amines (*e.g.* **106**) was carried out by mpg-C_3N_4 under visible light irradiation.[77] Thus, the corresponding imine was initially formed that upon reaction with the starting benzyl amine afforded the corresponding *N*-benzylidene benzylamine (**107**, a second imine), within 3.5 h irradiation (Scheme 45). When a substituted aromatic amine was added to the reaction mixture various heteroaromatics including benzoxazoles, benzimidazoles (**108**) and benzothiazoles were obtained *via* intramolecular cyclization and subsequent oxidation of the imine formed. (Scheme 45).[77]



Scheme 43



Scheme 44



Scheme 45

Another emerging application of photoorganocatalysts is their use in radical or cationic polymerizations through a photoredox process.[78] In this case, POCs are mainly polycyclic aromatics such as pyrene, anthracene, naphthacene, and pentacene derivatives[78a,b] albeit mesoporous graphitic carbon nitride was used as well.[78c] The process starts with an ET reaction between the POC* and an organic molecule under visible light irradiation. The radicals formed in the process (from an amine, an alkyl halide, a trialkylsilane) initiate the polymerization.

3. Conclusion and perspective

Photoorganocatalysis fundamentally differs from organocatalysis. The key idea of organocatalysis is that the substrate becomes covalently bound or at least complexed to a small organic molecule. This enhances the reactivity or changes it (frequently causing the Umpolung of the substrate) and quite often directs the stereochemistry of the ensuing attack, so that in the mind of synthesis practitioners organocatalysis is classified essentially as a method for asymmetric synthesis. This does not apply in any way to photoorganocatalysis (as defined here), because the short lifetime of electronically excited states makes possible only very fast reactions that are unlikely to be affected by a chiral moiety present in the catalyst. It is unlikely that during the ns to μs lifetime of the excited state a strong interaction develops, let alone arriving at a significant stereoselectivity. Rather, the field of action of POC involves, just as in the PC case, the activation of the substrate through a chemical reaction and the formation of a reactive intermediate, such as a radical, an ion or a radical ion. Thus, the two phenomena are essentially unrelated, but this will not hinder, in our opinion, that the two disciplines grow independently. In fact, POC takes advantage of the high energy of excited states of 'small' organic molecules for generating intermediates under otherwise unattainable mild conditions either *via* atom transfer or *via* a redox process. The high energy incorporated into the excited states makes accessible reaction paths that have no role in thermal reactions, catalytic or not, unless extremely aggressive reagents are used, whereas here these are generated in the neat solvent or in a medium conveniently devised for trapping them. Furthermore, the two actions may be combined. As an example, in the process shown in Scheme 28, the nucleophile is generated *in situ* through thermal organocatalysis and the electrophilic radical through independent POC. This is a promising way to profit from the characteristics of both phenomena. A case where a single photoorganocatalyst (**44**) complexes the reagent and is involved in the activation step (through the operation of two different moieties of the molecule) is illustrated in Scheme 23. This may be another development path (scarcely trodden at present). Whether the present POC definition should be widened to include the formation of a ground state complex may be an argument of debate.

Advancement in the area requires that robust photocatalysts are developed that rival inorganic complexes and semiconductor oxides in terms of light fastness and can thus exploit their high and varied reactivity for activating chemical processes much beyond the sparse examples present in the literature at this moment. New compounds and materials that could be tested as POCs may become available also from different fields, such as organic compounds applied in solar cells, for water splitting or photocatalytic depollution as well as from other photoresponsive materials and devices. In particular carbon based materials such as nanocarbons[79] or graphene-based derivatives[80] or other aromatic compounds such as acene-based derivatives, oligothiophenes, porphyrins and phthalocyanines[81] need to be considered as new POCs. Furthermore, as mentioned, it is possible that more general interactions between organocatalysis and photo(organo)catalysis develop in the future and exploit the opposite characteristics of the two methods.

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