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Photoredox Catalysis as an Efficient Tool for the Aerobic Oxidation of Amines and Alcohols: Bioinspired Demethylations and Condensations

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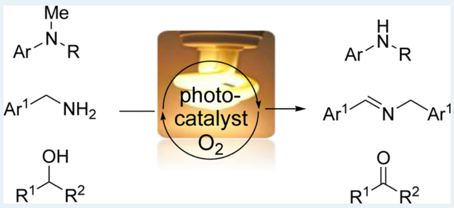
Supporting Information

ABSTRACT: Tertiary amines were readily converted into secondary amines through a photoredox-catalyzed N-demethylation, a bioinspired procedure that resembles nature's enzymatic pathways. Furthermore, the selective oxidation of primary amines as well as primary and secondary alcohols was achieved using photoredox catalysis. The protocols feature low catalyst loadings (1−2 mol %) and offer access to diverse imines and carbonyl compounds.



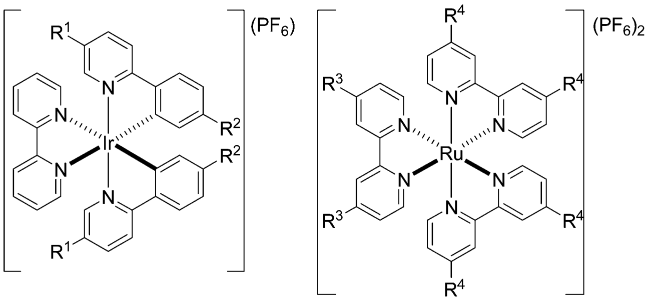
KEYWORDS: *visible light, N-demethylation, oxidation, oxygen, organic dye, cross dehydrogenative coupling*

INTRODUCTION

Recently, the application of visible light has attracted the interest of synthetic chemists, as it allows the construction of new carbon−carbon or carbon−heteroatom bonds in a highly efficient fashion.[1−15] The mild reaction conditions that typically feature low catalyst loadings, ambient reaction temperatures, and irradiation with either sunlight or standard household light render this approach attractive for the development of new, sustainable synthetic methods.

Although different photosensitizers are known to conduct photocatalytic transformations, inorganic ruthenium- and iridium-based polypyridyl complexes take up a unique role, as they possess well-known photochemical properties and can easily be tuned by the introduction of different ligands (Figure 1).[16−19]

In general, visible light photoredox catalysis has been established as an elegant method for the α-functionalization of tertiary amines and aldehydes, for promoting various intramolecular radical cyclizations, intra- and intermolecular cycloadditions, and reductive dehalogenation reactions.[11−15] Despite advances achieved in both bond-breaking and bond-forming reactions, the field of photoredox catalysis is still in its infancy. During the course of our research dedicated to the development of more sustainable chemical transformations, we were able to apply the photoredox catalysis concept to various reaction protocols that allow functionalization of tertiary amines and give access to valuable classes of compounds.[20−25]



$R^1 = R^2 = H$: **[1]**(PF_6)
$R^1 = CF_3$, $R^2 = F$: **[2]**(PF_6)

$R^3 = R^4 = H$: **[3]**$(PF_6)_2$
$R^3 = H$, $R^4 = t\text{-Bu}$: **[4]**$(PF_6)_2$
$R^3 = R^4 = t\text{-Bu}$: **[5]**$(PF_6)_2$

Figure 1. Investigated Ir and Ru complexes.

Herein, we report the application of photoredox catalysis to further useful transformations. On one hand, the deprotection of various tertiary amines leading to useful secondary amines was accomplished under visible light photoredox catalysis. On the other hand, the photochemical oxidation of different primary amines as well as primary and secondary alcohols, which form highly desirable imines and carbonyl compounds, was achieved under mild reaction conditions.

RESULTS AND DISCUSSION

Given the success of photoredox catalysis in the oxidation and functionalization of tertiary amines,[20−38] we envisioned now the synthesis of secondary amines from *N*-methyl tertiary amine through the hydrolysis of the hemiaminal generated in situ by trapping the iminium ion with water (Scheme 1). This photooxidation of *N*-methyl tertiary amines mimics the *N*-dealkylation by the cytochrome P-450 enzyme, which comprises three steps: 1 e^- oxidation, α-proton abstraction, and oxygen addition.[39−43]

Because of the stability of the *N*-methyl group, its cleavage constitutes a challenge for organic chemistry. Several N-demethylation methods are known; however, they are often unsatisfactory because of limited yields, chemoselectivity, and

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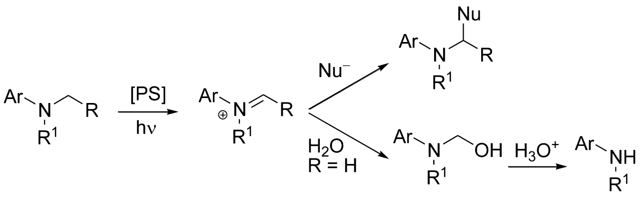
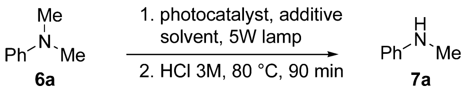
Scheme 1. Proposed Pathway for the Demethylation of *N*-Methyl Tertiary Amines



reagent toxicity.[44−49] Other approaches that are superior in terms of yield are often restricted to certain substrates only.[50−56] Hence, the development of new strategies for the *N*-demethylation seems to be important because of the impact and potential that its application would have in the synthesis of pharmaceuticals and agrochemical compounds.

With these considerations in mind, we decided to study the oxidation of *N*,*N*-dimethylaniline by the photoredox catalyst [**3**]$(PF_6)_2$ using different solvents (Table 1, entries 1−6).

Table 1. Optimization of Reaction Conditions



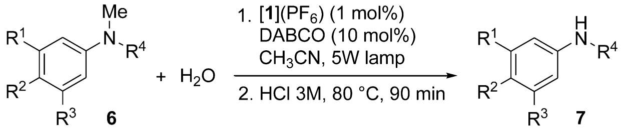
entry[a]	catalyst	additive (mol %)	solvent	conversion (%)[b]
1	[**3**]$(PF_6)_2$		toluene	
2	[**3**]$(PF_6)_2$		MeOH	
3	[**3**]$(PF_6)_2$		acetone	30
4	[**3**]$(PF_6)_2$		DMF	40
5	[**3**]$(PF_6)_2$		CH_3CN	45
6[c]	[**3**]$(PF_6)_2$		CH_3CN	45
7	[**3**]$(PF_6)_2$	H_2O (100)	CH_3CN	70
8	[**3**]Cl_2	H_2O (100)	CH_3CN	30
9	[**1**](PF_6)	H_2O (100)	CH_3CN	72
10	[**3**]$(PF_6)_2$	H_2O (100)/DABCO (10)	CH_3CN	83
11	[**3**]$(PF_6)_2$	H_2O (100)/PPh_3 (10)	CH_3CN	90
12	[**3**]$(PF_6)_2$	H_2O (100)/Py (10)	CH_3CN	67
13	[**1**](PF_6)	H_2O (100)/DABCO (10)	CH_3CN	98
14	[**1**](PF_6)	H_2O (100)/PPh_3 (10)	CH_3CN	90
15[d]	[**1**](PF_6)	H_2O (100)/DABCO (10)	CH_3CN	95

[a]Reaction conditions: **6a** (0.25 mmol), catalyst (1 mol %), 2 mL of solvent, 5 W fluorescent bulb, under air, 48 h. [b]Conversion determined by crude ^1H NMR analysis. [c]2 mol % of [**1**](PF_6) was used. [d]Reaction performed with an 11 W lamp.

Acetonitrile proved to be the best solvent, resulting in 45% conversion after 2 days. To improve the conversion, we explored the addition of water, which turned out to be more effective, leading to an improved conversion of 70% (Table 1, entry 7). Subsequently, different photocatalysts and various coadditives were evaluated (DABCO, PPh_3, and pyridine) (Table 1, entries 8−14). Optimization of the reaction conditions led to the establishment of 1 mol % [**1**](PF_6), 10 mol % DABCO, and 1 equiv of H_2O in acetonitrile as the optimum conditions.

With the optimal conditions in hand, we investigated the scope of the N-demethylation reaction (Table 2). In general, a variety of different *N*,*N*-dimethylanilines bearing substituents at the para or meta position provided the desired secondary amines in moderate to good yields. The presence of a PhCO electron-withdrawing group in the aromatic ring lowered the yield of the product (Table 2, entry 8). Finally, the methyl group was removed chemoselectively in the presence of different alkyl groups (Table 2, entries 11−13).[57,58]

Table 2. Scope of the N-Demethylation Reaction

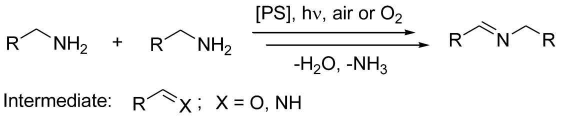


entry[a]	R^1	R^2	R^3	R^4	product	yield (%)[b]
1	H	H	H	Me	**7a**	82
2	H	Me	H	Me	**7b**	80
3	H	*t*-Bu	H	Me	**7c**	55
4	H	OMe	H	Me	**7d**	60
5	H	F	H	Me	**7e**	59
6	H	Cl	H	Me	**7f**	68
7	H	Br	H	Me	**7g**	65
8	H	PhCO	H	Me	**7h**	35
9	Me	H	H	Me	**7i**	64
10	Me	H	Me	Me	**7j**	57
11[c]	H	H	H	Et	**7k**	63
12[c]	H	H	H	Pr	**7l**	48
13[c]	H	H	H	$-(CH_2)_3Ph$	**7m**	40

[a]Reaction conditions: amine (0.25 mmol), [**1**](PF_6) 1 mol %, DABCO 10 mol %, H_2O (1 equiv), 2 mL of CH_3CN, 5 W fluorescent bulb, under air, 24−72 h. [b]Yield of the isolated product after column chromatography. [c]No byproduct formation was observed.

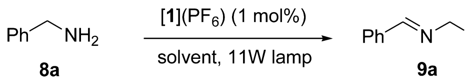
Next, on the basis of our previous work[20−25] on the photochemical oxidation of tertiary amines,[26−38,59−63] we became interested in extending the applicability of metal-based organic photosensitizers toward the photochemical oxidation of primary amines, which would yield versatile imine building blocks. Imines represent important and versatile intermediates for the synthesis of various fine chemicals, agrochemicals, and pharmaceuticals; hence, a variety of different methods for their synthesis has been developed in the past years. Apart from the classical approach of mixing an aldehyde and a primary amine, the catalytic oxidation of secondary amines was established as an attractive alternative approach.[64−76] In contrast, the oxidation of primary amines to imines (Scheme 2) has only very recently attracted considerable interest. To date, prominent examples of the photocatalytic oxidation of primary amines to yield aldehydes[77] or imines,[78−87] are utilizing either metal-free (organic dyes, g-C_3N_4) or metal-based (metal oxides) photosensitizers.

Scheme 2. Photochemical Oxidation of Primary Amines (PS = photosensitizer)



We initiated our studies on the photochemical oxidation of primary amines by evaluating the catalytic activity of [**1**](PF_6) in the oxidation of benzylamine (**8a**) in various solvents using different additives (Table 3). To our delight, the desired benzylideneimine **9a** was obtained in high yields under irradiation with a standard 11 W household fluorescent bulb

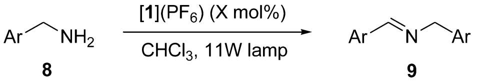
Table 3. Evaluation of Different Solvents and Additives in the Photochemical Oxidation of Benzylic Amines



entry^a	solvent	MS	time (h)	yield^b (%)
1	MeCN		20	80
2	chloroform		20	96
3	DMSO		30	98
4	methanol		20	74
5	benzene		20	9
6	toluene		20	7
7	MeCN	3 Å	20	98
8	chloroform	3 Å	20	96
9	chloroform	4 Å	20	>99
10	chloroform	5 Å	20	51
11	DMSO	3 Å	30	61
12	DMSO	4 Å	30	82
13	DMSO	5 Å	30	44

[a] Reaction conditions: 0.2 mmol **8a**, 1 mol % [**1**](PF_6), 2 mL of solvent, under air. [b] Calculated from ^1H NMR using 1,3,5-trimethoxybenzene as internal standard.

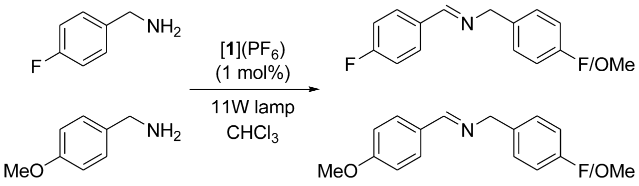
Table 4. Photochemical Oxidation of Benzylic Amines



entry^a	aryl	X mol % [**1**](PF_6)	**9**	yield (%)^b
1	Ph	1	**9a**	>99
2	4-Me-Ph	1	**9b**	>99
3	4-t-Bu-Ph	2	**9c**	97
4	4-MeO-Ph	1	**9d**	78
5	4-F-Ph	2	**9e**	>99
6	4-Cl-Ph	1	**9f**	87
7	4-Br-Ph	2	**9g**	98
8	2,4-Cl_2−Ph	2	**9h**	>99
9	2-Br-Ph	2	**9i**	95
10	2-MeO-Ph	1	**9j**	73
11	3-MeO-Ph	1	**9k**	80
12	2-Pyridinyl	1	**9l**	65

[a] Reaction conditions: 0.2 mmol **8**, 1 or 2 mol % [**1**](PF_6), 4 Å MS, 2 mL $CHCl_3$, under air. [b] Determined by ^1H NMR spectra using 1,3,5-trimethoxybenzene as internal standard.

Scheme 3. Photochemical Oxidation of Primary Amines



if polar solvents were utilized. Apolar solvents, such as benzene and toluene, proved to give only very low yields, most probably because of the low solubility of the photosensitizer (Table 3, entries 5 and 6). Of all solvents investigated, chloroform and acetonitrile proved best, as the desired oxidation product was formed in significantly shorter reaction times when compared to DMSO. Interestingly, only very low amounts of the undesired aldehydes were obtained, yet to suppress this unwanted side reaction, we further investigated the influence of molecular sieves. Because equimolar amounts of ammonia are liberated in the reaction mixture, the effect of different molecular sieves was investigated to trap both water and ammonia.[88] Gratifyingly, in the presence of molecular sieves, comparable or slightly better yields were observed in the case of acetonitrile and chloroform as solvents (Table 3, entries 7−9).

With the optimum conditions in hand, a variety of different primary amines was investigated in this photocatalytic aerobic oxidation reaction (Table 4). In general, the photochemical oxidation of benzylic amines **8** could be performed with high efficiency using 1−2 mol % of photocatalyst. The amines are readily oxidized, providing the desired benzylidene imines **9** in high yields. In addition, only trace amounts of the undesired benzaldehydes were observed.

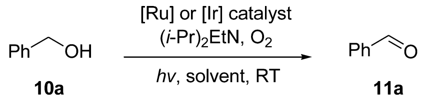
To gain further insight into the kinetics of the benzylamine oxidation, we conducted experiments in which equimolar amounts of electron-poor and electron-rich benzylic amines are present. For this purpose, we performed the oxidation of *p*-methoxybenzylamine in the presence of electron-poor *p*-fluorobenzylamine, yet all four possible benzylidene imines were obtained in comparable quantities (Scheme 3). This indicates that the influence of the substitution pattern of the benzylamine on the rate of single electron transfer from amine to the photoexcited state of the catalyst is almost negligible.[89]

In addition to the oxidation of benzylic amines, we became interested in extending the photochemical oxidative method toward the oxidation of alcohols,[90−95] allowing an operationally simple and environmentally benign access to valuable aldehydes and ketones. To achieve our goal, we began to investigate the reaction of benzyl alcohol (**10a**) with ruthenium and iridium-based photocatalytic systems (Figure 1). Under argon, only traces of the desired product **11a** were obtained in all cases. Changing from oxygen-free conditions to air atmosphere resulted in a slight improvement in conversion. On the basis of these initial results, we realized that another source of oxygen is strongly demanded. Looking for an ideal oxidizing agent, we considered the use of pure molecular oxygen under photocatalytic conditions for both economical and environmental reasons (Table 5).[96−99] Accordingly, the conversion increased when the reactions were performed under an O_2 atmosphere (Table 5, entries 3−7). Regarding the influence of the solvent, only DMF and acetonitrile allowed formation of the desired product **11a**. Moreover, we noticed much faster rates of oxidation in DMF. Notably, by increasing the amount of the catalyst [**5**](PF_6)$_2$ to 2 mol %, full conversion for the oxidation was observed (Table 5, entry 13).[100] Moreover, no reaction was observed in the presence of sunlight or blue LED light only (Table 5, entries 14, 15).

With the optimized conditions in hand, we explored the scope of the examined alcohols, and the results are summarized in Table 6. Basically, very good conversions (>99%) were observed in most of the tested reactions.

In the case of primary alcohols, product **11c** bearing a strong electron-withdrawing group in the meta position was obtained with 75% conversion (Table 6, entry 3). For the monosubstituted benzophenone derivatives, we observed the influence of electronic effect, as products **11g** and **11h** were obtained with 70 and 90% conversion, respectively. Notably, all disubstituted benzophenones **11j−k** and mixed alkyl−aryl ketones **11l−n** were obtained with quantitative conversions (Table 6, entries 10−14). Furthermore, in all cases, the reaction

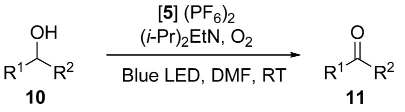
Table 5. Evaluation of Parameters in the Oxidation of Benzylalcohol 10a



entry[a]	photocatalyst	lamp	solvent	conversion (%)[b]
1	[**2**](PF_6)	11 W	DMF	traces
2	[**4**]$(PF_6)_2$	11 W	DMF	traces
3	[**5**]$(PF_6)_2$	11 W	DMF	40[c]
4	[**2**](PF_6)	blue LED	DMF	45
5	[**4**]$(PF_6)_2$	blue LED	DMF	45
6	[**5**]$(PF_6)_2$	blue LED	DMF	50
7[c]	[**5**]$(PF_6)_2$	blue LED	MeCN	40
8	[**5**]$(PF_6)_2$	blue LED	CH_2Cl_2	
9	[**5**]$(PF_6)_2$	blue LED	toluene	
10	[**5**]$(PF_6)_2$	blue LED	toluene/water (1:1)	traces
11	[**5**]$(PF_6)_2$	blue LED	EtOAc	
12	[**5**]$(PF_6)_2$	blue LED	MeOH	traces
13[d]	[**5**]$(PF_6)_2$	blue LED	DMF	>99
14		sunlight	DMF	
15		blue LED	DMF	

[a] Reaction conditions: **10a**, $(i\text{-}Pr)_2EtN$ (1.2 equiv), photocatalyst (1 mol %), solvent (0.5 M), lamp, rt, O_2 atmosphere, 48 h. [b] ^1H NMR conversion. [c] Reaction time: 72 h. [d] 2 mol % catalyst.

Table 6. Scope of Various Alcohols under Photoirradiation Conditions



entry[a]	R^1	R^2	**11**	conversion (%)[b,c]
1	Ph	H	**11a**	>99
2	4-F-Ph	H	**11b**	>99
3	3-CF_3-Ph	H	**11c**	75
4	4-Me_2N-Ph	H	**11d**	>99
5	Ph	Ph	**11e**	>99
6	4-F-Ph	Ph	**11f**	>99
7	4-NO_2-Ph	Ph	**11g**	70
8	4-Me_2N-Ph	Ph	**11h**	90
9	Ph	$PhCH_2$	**11i**	>99
10	4-F-Ph	4-F-Ph	**11j**	>99
11	4-Me_2N-Ph	4-Me_2N-Ph	**11k**	>99
12	Ph	Et	**11l**	>99
13	4-CF_3-Ph	Me	**11m**	>99
14	4-MeO-Ph	Me	**11n**	>99

[a] Reaction conditions: **10**, $(i\text{-}Pr)_2EtN$ (1.2 equiv), photocatalyst (2 mol %), DMF (0.5 M), blue LED lamp, rt, O_2 atmosphere, 48 h. [b] Conversions are based on ^1H NMR analysis. [c] In all cases, the selectivity is >99%.

time was considerably shortened (24 h) by performing the reactions in a 1:1 DMF/water mixture.

■ CONCLUSION

In summary, we succeeded in expanding the repertoire of photoredox catalysis with protocols that allow the synthesis of valuable compounds under mild reaction conditions. A visible light photoredox catalytic process for the deprotection of various tertiary amines leading to secondary amines was presented. The photoredox *N*-deprotection method mimics the cytochrome P-450 oxidation of tertiary amines. Further studies expanding the scope of this N-deprotection using more reactive catalysts are currently underway. In addition, a convenient procedure was developed for the synthesis of various imines starting from readily available primary amines. A synthetically useful protocol for the photoredox catalyzed oxidation of primary and secondary alcohols with low catalyst loadings is also provided. A wide range of substrates is tolerated under these conditions, yielding the corresponding carbonyl compounds with full conversion in most cases. The use of inexpensive household light and the easy of handling make the developed methods particularly attractive for applications in synthesis.

■ EXPERIMENTAL SECTION

General Procedure for the Photoredox N-Demethylation Reaction. In a vial were placed the photoredox catalyst [**1**](PF_6) (2.0 mg, 0.0025 mmol), DABCO (2.8 mg, 0.025 mmol), H_2O (4.5 μL, 0.25 mmol), and amine (0.25 mmol) in acetonitrile. The reaction mixture was stirred for the time indicated under irradiation with the 5 W fluorescent bulb (distance ~5 cm). The reaction was monitored via TLC (hexanes/ethyl acetate, 9:1). Upon consumption of starting material, 1 mL of HCl 3 M solution was added, and the mixture was stirred at 80 °C for 90 min. NaOH 1 M (10 mL) was added, and the mixture was extracted with DCM (3 × 15 mL). The organic layers were dried over Na_2SO_4 and filtered, and the solvent was removed under reduced pressure. The corresponding secondary amine was obtained pure after column chromatography.

General Procedure for the Photoredox Oxidation of Primary Amines. In a screw-capped vial, amine (0.2 mmol, 1 equiv) and $[Ir(ppy)_2bpy]PF_6$ ([**1**](PF_6), 0.002 mmol, 1.4 mg, 0.01 equiv) were dissolved in the appropriate solvent (1 mL), then 90 mg of the appropriate molecular sieves was added, and the reaction mixture was stirred under irradiation with an 11 W fluorescent bulb from ~5 cm distance. 1,3,5-Trimethoxybenzene was used as internal standard, and the reaction mixture was analyzed by NMR spectroscopy. Yields are related to the internal standard.

General Procedure for the Photoredox Catalyzed Oxidation of Alcohols. In a tube, the appropriate photoredox catalyst (2 mol %, 0.004 mmol), and a substrate (0.20 mmol) were dissolved in the appropriate solvents (DMF or the mixture of DMF/water 1:1, 1 mL). Subsequently, 1.2 equiv of the *N*-ethyldiisopropylamine (0.24 mmol) was added, and the reaction mixture was stirred for the time indicated under irradiation with the light source (blue LED lamp, 455 nm, distance ~0.5 cm) in an oxygen atmosphere. The reaction was monitored via TLC (*c*-hexanes/ethyl acetate). Upon consumption of starting material, solvents were removed under reduced pressure to yield the desired product.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Characterization results for analines **7**, amines **9**, and aldehydes and phenones **11**. This material is available free of charge via the Internet at http://pubs.acs.org

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Roth, H. D. *Angew. Chem., Int. Ed.* **1989**, *28*, 1193−1207.
(2) Balzani, V.; Credi, A.; Venturi, M. *ChemSusChem* **2008**, *1*, 26−58.
(3) Fagnoni, M.; Dondi, D.; Ravelli, D.; Albini, A. *Chem. Rev.* **2007**, *107*, 2725−2756.
(4) Oelgemöller, M.; Jung, C.; Mattay, J. *Pure Appl. Chem.* **2007**, *79*, 1939−1974.
(5) Hoffmann, N. *Chem. Rev.* **2008**, *108*, 1052−1103.
(6) Albini, A.; Dichiarante, V. *Photochem. Photobiol. Sci.* **2009**, *8*, 248−254.
(7) Ravelli, D.; Dondi, D.; Fagnoni, M.; Albini, A. *Chem. Soc. Rev.* **2009**, *38*, 1999−2011.
(8) Albini, A.; Fagnoni, M., Eds.; *Handbook of Synthetic Photochemistry*; Wiley-VCH: Weinheim, 2010.
(9) Griesbeck, A.; Oelgemöller, M.; Ghetti, F., Eds.; *CRC Handbook of Organic Photochemistry and Photobiology*, 3rd ed.; CRC Press, Boca Raton, 2012.
(10) Hoffmann, N. *ChemSusChem* **2012**, *5*, 352−371.
(11) Zeitler, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9785−9789.
(12) Yoon, T. P.; Ischay, M. A.; Du, J. N. *Nat. Chem.* **2010**, *2*, 527−532.
(13) Narayanam, J. M. R.; Stephenson, C. R. J. *Chem. Soc. Rev.* **2011**, *40*, 102−113.
(14) Telpy, F. *Collect. Czech. Chem. Commun.* **2011**, *76*, 859−917.
(15) Xuan, J.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2012**, *51*, 6828−6838.
(16) Balzani, V.; Bergamini, G.; Campagna, S.; Puntoriero, F. *Top. Curr. Chem.* **2007**, *280*, 1−36.
(17) Campagna, S.; Puntoriero, F.; Nastasi, F.; Bergamini, G.; Balzani, V. *Top. Curr. Chem.* **2007**, *280*, 117−214.
(18) Flamigni, L.; Barbieri, A.; Sabatini, C.; Ventura, B.; Barigelletti, F. *Top. Curr. Chem.* **2007**, *281*, 143−203.
(19) Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, *77*, 1617−1622.
(20) Rueping, M.; Vila, C.; Koenigs, R. M.; Poscharny, K.; Fabry, D. C. *Chem. Commun.* **2011**, *47*, 2360−2362.
(21) Rueping, M.; Zhu, S.; Koenigs, R. M. *Chem. Commun.* **2011**, *47*, 8679−8681.
(22) Rueping, M.; Zhu, S.; Koenigs, R. M. *Chem. Commun.* **2011**, *47*, 12709−12711.
(23) Rueping, M.; Leonori, D.; Poisson, T. *Chem. Commun.* **2011**, *47*, 9615−9617.
(24) Rueping, M.; Zoller, J.; Fabry, D. C.; Poscharny, K.; Koenigs, R. M.; Weirich, T. E.; Mayer, J. *Chem.—Eur. J.* **2012**, *18*, 3478−3481.
(25) Rueping, M.; Koenigs, R. M.; Poscharny, K.; Fabry, D. C.; Leonori, D.; Vila, C. *Chem.—Eur. J.* **2012**, *18*, 5170−5174.
(26) Condie, A. G.; Gonzalez-Gomez, J. C.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2010**, *132*, 1464−1465.
(27) Xie, Z.; Wang, C.; deKrafft, K. E.; Lin, W. *J. Am. Chem. Soc.* **2011**, *133*, 2056−2059.
(28) Zhu, M.; Zheng, N. *Synthesis* **2011**, 2223−2236.
(29) Xuan, J.; Cheng, Y.; An, J.; Lu, L.-Q.; Zhang, X.-X.; Xiao, W.-J. *Chem. Commun.* **2011**, *47*, 8337−8339.
(30) Hari, D. P.; König, B. *Org. Lett.* **2011**, *13*, 3852−3855.
(31) Zou, Y.-Q.; Lu, L.-Q.; Fu, L.; Chang, N.-J.; Rong, J.; Chen, J.-R.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2011**, *50*, 7171−7175.
(32) Wang, C.; Xie, Z.; deKrafft, K. E.; Lin, W. *J. Am. Chem. Soc.* **2011**, *133*, 13445−13454.
(33) Freeman, D. B.; Furst, L.; Condie, A. G.; Stephenson, C. R. J. *Org. Lett.* **2012**, *14*, 94−97.
(34) Maity, S.; Theng, N. *Synlett* **2012**, *23*, 1851−1856.
(35) Shi, L.; Xia, W. *Chem. Soc. Rev.* **2012**, *41*, 7687−7697.
(36) DeLaive, P. J.; Lee, J. T.; Sprintschnik, H. W.; Abruna, H.; Meyer, T. J.; Whitten, D. G. *J. Am. Chem. Soc.* **1977**, *99*, 7094−7097.
(37) Delaive, P. J.; Sullivan, B. P.; Meyer, T. J.; Whitten, D. G. *J. Am. Chem. Soc.* **1979**, *101*, 4007−4008.
(38) Delaive, P. J.; Foreman, T. K.; Giannotti, C.; Whitten, D. G. *J. Am. Chem. Soc.* **1980**, *102*, 5627−5631.
(39) *Cytocrome P-450*; Sato, R., Omura, T., Eds.; Kodansha Ltd: Tokyo, 1978.
(40) Gorrod, J. W. *Biological Oxidation of Nitrogen*; Elsevier/North Holland Biomedical Press: New York, 1978.
(41) Guengerich, F. P. *J. Biochem. Mol. Toxicol.* **2007**, *21*, 163−168.
(42) Okazaki, O.; Guengerich, F. P. *J. Biol. Chem.* **1993**, *268*, 1546−1552.
(43) Seto, Y.; Guengerich, F. P. *J. Biol. Chem.* **1993**, *268*, 9986−9997.
(44) von Braun, J. *Chem. Ber.* **1900**, *33*, 1438−1452.
(45) Flynn, E. H.; Murphy, H. W.; McMahon, R. E. *J. Am. Chem. Soc.* **1955**, *77*, 3104−3106.
(46) Morimoto, S.; Misawa, Y.; Adachi, T.; Nagate, T.; Watanabe, Y.; Omura, S. *J. Antibiot.* **1990**, 286−294.
(47) Peat, A. J.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 1028−1030.
(48) Murahashi, S.-I.; Naota, T.; Yonemura, K. *J. Am. Chem. Soc.* **1988**, *110*, 8256−8258.
(49) Thavaneswaran, S.; McCamley, K.; Scammells, P. J. *Nat. Prod. Commun.* **2006**, *1*, 885−897.
(50) Stenmarck, H. G.; Brazzale, A.; Ma, Z. *J. Org. Chem.* **2000**, *65*, 3875−3876.
(51) McCamley, K.; Ripper, J. A.; Singer, R. D.; Scammells, P. J. *J. Org. Chem.* **2003**, *68*, 9847−9850.
(52) Thavaneswaran, S.; Scammells, P. J. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 2868−2871.
(53) Sako, M. M.; Shimada, K.; Hirota, K.; Maki, Y. *J. Am. Chem. Soc.* **1986**, *108*, 6039−6041.
(54) Ripper, J. A.; Tiekink, E. R. T.; Scammells, P. J. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 443−445.
(55) Dong, Z.; Scammells, P. J. *J. Org. Chem.* **2007**, *72*, 9881−9885.
(56) Rosenau, T.; Hofinger, A.; Potthast, A.; Kosma, P. *Org. Lett.* **2004**, *6*, 541−544.
(57) Miyake, Y.; Nakajima, K.; Nishibayashi, Y. *J. Am. Chem. Soc.* **2012**, *134*, 3338−3341.
(58) Zhang, X.; Yeh, S.-R.; Hong, S.; Freccero, M.; Albini, A.; Falvey, D. E.; Mariano, P. S. *J. Am. Chem. Soc.* **1994**, *116*, 4211−4220.
(59) Li, Z.; Bohle, D. S.; Li, C.-J. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 8928−8933.
(60) Li, C. J. *Acc. Chem. Res.* **2009**, *42*, 335−344.
(61) Yoo, W.-J.; Li, C.-J. *Top. Curr. Chem.* **2010**, *292*, 281−302.
(62) Lewis, F. D. *Acc. Chem. Res.* **1986**, *19*, 401−405.
(63) Yoon, U. C.; Mariano, P. S. *Acc. Chem. Res.* **1992**, *25*, 233−240.
(64) Murahashi, S.-I.; Naota, T.; Taki, H. *J. Chem. Soc., Chem. Commun.* **1985**, 613−614.
(65) Yamaguchi, K.; Mizuno, N. *Angew. Chem., Int. Ed.* **2003**, *42*, 1480−1483.
(66) Samec, J. S. M.; Éll, A. H.; Bäckvall, J.-E. *Chem.—Eur. J.* **2005**, *11*, 2327−2334.
(67) Ibrahem, I.; Samec, J. S. M.; Bäckvall, J. E.; Cordova, A. *Tetrahedron Lett.* **2005**, *46*, 3965−3968.
(68) Zhu, B.; Angelici, R. J. *Chem. Commun.* **2007**, 2157−2159.
(69) Murahashi, S.-I.; Okano, Y.; Sato, H.; Nakae, T.; Komiyaa, N. *Synlett* **2007**, 1675−1678.
(70) Zhu, B.; Lazar, M.; Trewyn, B. G.; Angelici, R. J. *J. Catal.* **2008**, *260*, 1−6.

(71) Aschwanden, L.; Mallat, T.; Grunwaldt, J.-D.; Krumeich, F.; Baiker, A. *J. Mol. Catal. A: Chem.* **2009**, *300*, 111−115.
(72) Aschwanden, L.; Mallat, T.; Krumeich, F.; Baiker, A. *J. Mol. Catal. A: Chem.* **2009**, *309*, 57−62.
(73) Jiang, G.; Chen, J.; Huang, J.-S.; Che, C.-M. *Org. Lett.* **2009**, *11*, 4568−4571.
(74) So, M.-H.; Liu, Y.; Ho, C.-M.; Che, C.-M. *Chem.—Asian J.* **2009**, *4*, 1551−1561.
(75) Aschwanden, L.; Mallat, T.; Maciejewski, M.; Krumeich, F.; Baiker, A. *ChemCatChem* **2010**, *2*, 666−673.
(76) Miyamura, H.; Morita, M.; Inasaki, T.; Kobayashi, S. *Bull. Chem. Soc. Jpn.* **2011**, *84*, 588−599.
(77) Lechner, R.; König, B. *Synthesis* **2010**, 1712−1718.
(78) Lang, X.; Ji, H.; Chen, C.; Ma, W.; Zhao, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 3934−3937.
(79) Lang, X.; Ma, W.; Zhao, Y.; Chen, C.; Ji, H.; Zhao, J. *Chem.—Eur. J.* **2012**, *18*, 2624−2631.
(80) Su, F.; Mathew, S. C.; Möhlmann, L.; Antonietti, M.; Wang, X.; Blechert, S. *Angew. Chem., Int. Ed.* **2011**, *50*, 657−660.
(81) Furukawa, S.; Ohno, Y.; Shishido, T.; Teramura, K.; Tanaka. *ACS Catal.* **2011**, *1*, 1150−1153.
(82) Huang, H.; Huang, J.; Liu, Y.-M.; He, H.-Y.; Cao, Y.; Fan, K.-N. *Green Chem.* **2012**, *14*, 930−934.
(83) Liu, L.; Zhang, S.; Fu, X.; Yan, C.-H. *Chem. Commun.* **2011**, *47*, 10148−10150.
(84) Berlicka, A.; König, B. *Photochem. Photobiol. Sci.* **2010**, *9*, 1359−1366.
(85) Park, J. H.; Ko, K. C.; Kim, E.; Park, N.; Ko, J. H.; Ryu, D. P.; Ahn, T. K.; Lee, J. Y.; Son, S. U. *Org. Lett.* **2012**, *14*, 5502−5505.
(86) For the photoredox catalyzed generation of imines intermediates, see: Wang, Z.-Q.; Hu, M.; Huang, X.-C.; Gong, L.-B.; Xie, Y.-X.; Li, J.-H. *J. Org. Chem.*, **2012**, *77*, 8705-8711.
(87) Zhu, S.; Rueping, M. *Chem. Commun.*, **2012**, *48*, DOI: 10.1039/C2CC36995H.
(88) Due to the composition and pore size of 3, 4, and 5 Å molecular sieves, these can have a different impact on the reaction.
(89) However, an alternative mechanism involving the generation of singlet oxygen, as proposed in references 81 and 82 cannot be ruled out, and it is the subject of current investigations.
(90) Zhang, M.; Wang, Q.; Chen, C.; Zang, L.; Ma, W.; Zhao, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 6081−6084.
(91) Wang, Q.; Zhang, M.; Chen, C.; Ma, W.; Zhao, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 7976−7979.
(92) Su, F.; Mathew, S. C.; Lipner, G.; Fu, X.; Antonietti, M.; Blechert, S.; Wang, X. *J. Am. Chem. Soc.* **2010**, *132*, 16299−16301.
(93) Shishido, T.; Miyatake, T.; Teramura, K.; Hitomi, Y.; Yamashita, H.; Tanaka, T. *J. Phys. Chem. C* **2009**, *113*, 18713−18718.
(94) Cano-Yelo, H.; Deronzier, A. *Tetrahedron Lett.* **1984**, *25*, 5517−5520.
(95) For the oxidation of benzylic ethers, see: Tucker, J. W.; Narayanam, J. M. R.; Shah, P. S.; Stephenson, C. R. J. *Chem. Commun.* **2011**, *47*, 50404−5042.
(96) Trost, B. M. *Angew. Chem., Int. Ed.* **1995**, *34*, 259−281.
(97) Trost, B. M. *Science* **1991**, *254*, 1471−1477.
(98) ten Brink, G. J.; Ardens, I. W. C. E.; Sheldon, R. A. *Science* **2000**, *287*, 1636−1639.
(99) Yamaguchi, K.; Mizuno, N. *Chem.—Eur. J.* **2003**, *9*, 4353−4361.
(100) Amine is necessary to facilitate the deprotonation of the oxoniumion formed by oxidation with the Ru^{2+}/O_2 system. In the absence of amine, the conversion of the reaction is considerably lower.

■ NOTE ADDED AFTER ASAP PUBLICATION

After this paper was published online November 26, 2012, a spelling error was corrected in the name of author Anna Szadkowska. The corrected version was reposted November 27, 2012.