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Photocatalytic Systems with Flavinium Salts: From Photolyase Models to Synthetic Tool for Cyclobutane Ring Opening

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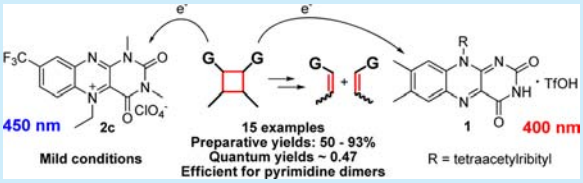
Supporting Information

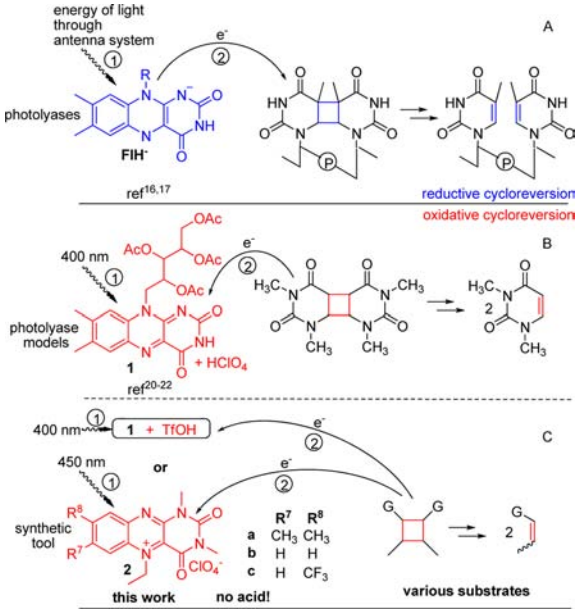
ABSTRACT: Two new photocatalytic systems based on flavinium species formed *in situ* by protonation of riboflavin-tetraacetate (**1**) with triflic acid or prepared in advance via alloxazine quaternization are presented as effective tools for oxidative cyclobutane ring [2 + 2] cycloreversion using visible light. The system with 1,3-dimethyl-8-trifluoromethylalloxazinium perchlorate (**2c**) was found to be superior allowing an acid-free mild procedure, which results in the opening of cyclobutanes with high oxidation potential (up to 2.14 V) and/or with sensitive groups (e.g., furan) without side reactions.



Cyclobutane cleavage reactions have been studied intensively because of their fundamental importance as well as their synthetic applications leading to both cyclic and acyclic systems.[1−3] Some cyclobutanes can be opened chemically,[1,2] or thermally (or by a mechanic impulse[4]), which is allowed by the strain energy of four-membered carbocycles (ca. 109 kJ/mol).[5] "Forbidden" thermal [2 + 2] cycloreversion leading to two alkenes was also demonstrated in a few cases;[1b,3e,6−8] however, considering the Woodward−Hoffmann rules, "allowed" [2 + 2] photocycloreversion represents the method of choice for this transformation.[9] In contrast to photochemical [2 + 2] cycloadditions, which have been accepted as a general synthetic tool toward four-membered carbocyclic rings,[10,11] their [2 + 2] photocycloreversions have still been the subject of theoretical or pioneering studies.[1b,12] One of the reasons is the need for a strong UV light of even shorter wavelength compared to those used in [2 + 2] photocycloaddition procedures. This might be overcome by visible light photocatalysis.[13]

To the best of our knowledge, with the exception of aromatic hydrocarbons and cyanoarenes used in the mechanistic studies of cyclobutane photocleavage using UV light,[14] only pyrylium and trityl salts have been proven as visible light absorbing photocatalysts/sensitizers for the [2 + 2] cycloreversion of a limited number of substrates.[15] With the aim of designing a versatile photocatalyst for this reaction, we turned our attention to the photorepair of UV-damaged DNA, which is provided by photolyases.[16,17] The nature of the repair reaction is the splitting of pyrimidine dimers to their original pyrimidine bases initiated by electron transfer from the reduced flavin cofactor $\mathbf{FlH^-}$ (Scheme 1a). Several DNA photolyase models based on this reductive process have been reported over the last three decades; however, most of the studies have been designed for intramolecular cycloreversion, i.e. with flavin species connected with dimer via a covalent or noncovalent bond.[18,19] There are a few oxidative photolyase models shown to be efficient in the intermolecular splitting of pyrimidine dimers that utilize electron transfer to excited riboflavin tetraacetate (**1**) or deazaflavin

Scheme 1. Design of [2 + 2] Cycloreversion Systems Considering the Function of Photolyases (a) and Oxidative Photolyase Models (b) Affording an Improved System with 1 + TfOH and an Unprecedented Acid-Free System with 2c (c)



protonated by perchloric acid,[20] coordinated to Mg^{2+},[21] or incorporated into SDS micelles,[22] which make the electron transfer exergonic (Scheme 1b). Here we report an improved system with **1** and triflic acid (TfOH), and an unprecedented system using alloxazinium salts **2** both being applicable as an efficient tool for the cycloreversion of various substrates with high oxidation potential (Scheme 1c).

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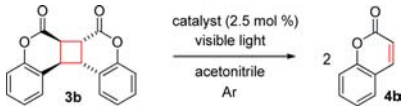
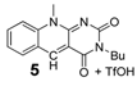
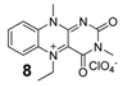
To find an efficient and versatile system for [2 + 2] cycloreversion, preliminary screening (Table 1) was performed

Table 1. Looking for Suitable Photocatalytic System for [2 + 2] Photocycloreversion[a]

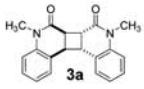
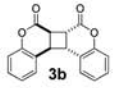
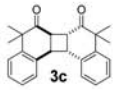
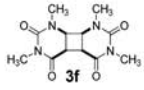
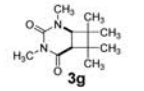
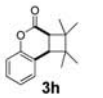
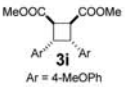
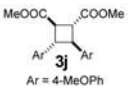
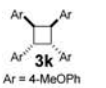
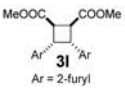


entry	catalyst	wavelength [nm]	conv 3 min [%]	conv 10 min [%]
1	-	400 or 450	-	0
2	**1**	450	-	0
3	**1**+Mg^{2+}	400	-	19[b]
4	**1**+Sc^{3+}	400	-	90[b]
5	**1**+$HClO_4$	400	-	18
6	**1**+TfOH	400	65	quant
7	**1**+TfOH(aq)	400	-	30
8		365	-	quant
9	Acr-Mes ClO_4 (**6**)	400	-	23
10	TPP BF_4 (**7**)	400	-	quant
11		400	-	2
12	**2a**	450	2	-
13	**2b**	450	12	-
14	**2c**	450	60	quant
15	**2c**	sunlight[c]	-	70[d]

[a]Reaction conditions: **3b** (0.02 mmol), photocatalyst (2.5 mol %), TfOH (0.01 mmol) only if mentioned, solvent (1 mL), visible light, rt, under Ar. [b]Polymeric side-product was formed. [c]Experiment performed under daylight at the window. GPS: N 50.101728, E 014.389929, 19th May 2016 at 9:30−9:45 a.m. [d]Quantitative conversion after 20 min.

using coumarin dimer **3b**, which has a substantially higher oxidation potential ($E^{0\prime}_{ox}$ = 2.05 V vs SCE) when compared to the previously studied pyrimidine dimers (e.g., **3f** in Table 2). The experiments were performed under an argon atmosphere to avoid side oxidation reactions. While excited riboflavin-tetraacetate (**1**, $E^{0\prime}_{red}$* = 1.67 V vs SCE, ref 23) was not strong enough for the oxidative cycloreversion of **3b** (Entry 2, Table 1), its coordination to Mg^{2+} and mainly to Sc^{3+} lead to systems with a higher oxidation power ($E^{0\prime}_{red}$* = 2.06 and 2.45 V vs SCE, respectively[24]) and provided coumarin (**4b**). Unfortunately, the reaction was accompanied by polymerization (entries 3 and 4). Protonation of **1** using aqueous $HClO_4$ (an alternative to coordination) has been previously shown as suitable for pyrimidine dimer splitting[20] but displayed low efficiency with **3b** (entry 5). Importantly the water-free alternative with TfOH was found to provide cycloreversion purely and quantitatively within 10 min of irradiation (entry 6). A further test of **1** + TfOH with a small amount of water equal to that being present in the experiment with $HClO_4$ (70%) showed that water decreased the efficiency of the system (cf. entries 5−7). As expected, 3-butyl-10-methyl-5-deazaflavin **5** with TfOH (entry 8) showed a high

Table 2. Substrate Scope of [2 + 2] Photocycloreversion Mediated by 1 + TfOH or by 2c and Visible Light[a,b]

entry	substrate	$E^{0\prime}_{ox}$ [V][c]	product	catalyst	conv[d] [%]	yield[e] [%]
1	 **3a**	1.34	 **4a**	**1**	quant	93[f]
				2c	quant	88
2	 **3b**	2.05	 **4b**	**1**+TfOH	quant	90[f]
				2c	quant	92
3	 **3c**	2.14	 **4c**	**1**+TfOH	30[g]	-
				2c	39[g]	52[i]
4	 **3d** Ar = Ph	>2.3	 **4d** Ar = Ph	**1**+TfOH	0	-
				2c	0	-
5	 **3e** Ar = 4-MeOPh	1.71	 **4e** Ar = 4-MeOPh	**1**+TfOH	quant	78
				2c	quant	86
6	 **3f**	1.77	 **4f**	**1**+TfOH	quant	94[f]
				2c	quant	91
7	 **3g**	1.55	**4f** + 	**1**+TfOH	quant[g]	62[h]
				2c	quant[g]	75[h]
8	 **3h**	2.02	**4b** + 	**1**+TfOH	77	68[i]
				2c	47	50
9	 **3i** Ar = 4-MeOPh	1.57	 **4h** Ar = 4-MeOPh	**1**+TfOH	quant	86
				2c	70	94
10	 **3j** Ar = 4-MeOPh	1.73	 **4h** Ar = 4-MeOPh	**1**+TfOH	20[g]	-
				2c	7[g]	-
11	 **3k** Ar = 4-MeOPh	1.35	 **4i** Ar = 4-MeOPh	**1**+TfOH	93	89[j]
				2c	78	88[j]
12	 **3l** Ar = 2-furyl	1.69	 **4j** Ar = furyl	**1**+TfOH	0	-
				2c	quant	86

[a]For experiments on analytical scale: **3** (0.02 mmol), **1** or **2c** (2.5 mol %), TfOH (0.01 mmol) only with **1**, solvent (1 mL), visible light (400 nm for **1** + TfOH and 450 nm for **2c**), rt, Ar, 10 min. [b]For preparative experiments: **3** (0.4 mmol), **1** or **2c** (5 mol %), TfOH (0.2 mmol) only with **1**, solvent (20 mL), visible light (400 nm for **1** + TfOH and 450 nm for **2c**), rt, Ar, 30 min. [c]Values vs SCE. [d]Conversion of analytical experiments. [e]From experiments on preparative scale. [f]10 min. [g]60 min with 10 mol % of the catalyst. [h]120 min. [i]240 min. [j]Contains 10% of *Z*-isomer.

efficiency but this system was excluded from further studies due to its absorption out of the visible region (λ_{max} = 325 nm). 9-Mesityl-10-methylacridinium perchlorate (**6**; Acr-Mes ClO_4; $E^{0\prime}_{red}$* = 2.06 V, ref 25), a typical representative for oxidative photocatalysis was not effective enough (entry 9); however,

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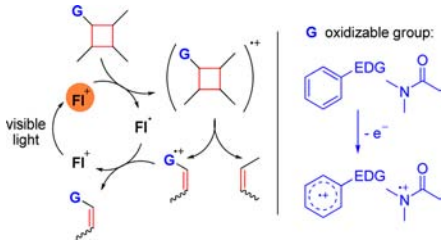
2,4,6-triphenylpyrylium tetrafluoroborate (**7**; TPP BF_4; $E^{0\prime}_{red}$* = 2.28 V vs SCE, ref 26) passed the test with **3b** (Entry 10), but its efficiency toward **3c** with higher oxidation potential (see Table 2) was relatively poor (conversion ~10% after 60 min with 10 mol % catalyst).

The system with protonated riboflavin−tetraacetate (**1** + TfOH) seemed to be very promising. Nevertheless, one should bear in mind that acidic conditions are not compatible with all substrates. Thus, we wondered if flavin could be activated by quaternization (instead of protonation) to provide the flavinium species.[27] Notably 5-ethylisoalloxazinium salt **8** was not efficient (entry 11) because of the low excitation energy[28] but replacing it with the isomeric 5-ethylalloxazinium salt **2** (see Scheme 1c for the structure and ref 29 for the synthesis), in the best case one with electron-withdrawing CF_3 group, was shown to be a breakthrough because **2c** quickly provided full conversion (entries 12−14). The exceptionally high oxidation force of **2c** ensues from the fact that this salt utilizes an approximately as high excitation energy[30] as that observed with **1** (E^{0-0}(**1**) = 2.48 V[23]), and additionally, it is a much stronger oxidant in the ground state ($E^{0\prime}_{red}$ = +0.275 V[29] and −0.81 V[23] for **2c** and **1**, respectively).[31] The quantum yield of **3b**-cycloreversion catalyzed by **2c** was found to be 0.47. The high efficiency of the system was also demonstrated by a very fast reaction under sunlight (entry 15). It should be noted that **3b** opening was not observed in the blank experiments in the absence of the photocatalyst or light.

Furthermore, the substrate scope of our new photocatalytic systems, i.e., **1** + TfOH and **2c** was investigated in acetonitrile, which was proven to be the best solvent (for solvent screening, see the Supporting Information). As expected, substrate **3a** bearing an amide function was readily opened via both methods due to the low oxidation potential (Table 2, entry 1). We even observed opening of **3a** via **1** without acid, which was in accordance with the negative free Gibbs energy expected for electron transfer (eT) from **1*** to **3a** (ΔG_{eT} = −0.33 eV). Ester **3b** was opened smoothly using both methods (entry 2), while the cycloreversion of ketone **3c**, which has a 90 mV higher oxidation potential, needed a longer reaction time and higher catalyst loading (entry 3). Nevertheless, this could be also a result of the steric hindrance provided by the adjacent methyl groups on the sp^3 carbon atoms. The negative result with cyclic anhydride **3d** with a potential over 2.3 V shows the limit for substrates undergoing the cycloreversion reaction under our conditions (entry 4). Formal introduction of a methoxy group to **3d** makes the substrate readily cleavable as the oxidation potential was dropped significantly (entry 5). Derivatives **3g** and **3h** with an incorporated large tetramethylethylene group can also be opened (entries 7 and 8) but again need more catalyst and longer time. Notably quantitative conversion was not achieved by only reaction time prolongation keeping original loading of the catalyst because of its bleaching. Interestingly a significant *cis*-effect[1b,32] was observed for **3i** and **3j** cycloreversion, i.e., their opening was significantly dependent on the relative configuration of the phenyl and ethoxycarbonyl groups (entries 9 and 10) with a faster cleavage of C−C bonds between the *cis*-oriented substituents. Accordingly, derivative **3k** was readily opened (entry 11). Uracil dimers (e.g., **3f**, entry 6) can be also cleaved irrespective of their configuration and relative position of the rings (see the Supporting Information for isomers), which demonstrated the possible application of **2c** in preventing possible DNA damage by UV radiation. Very fast cycloreversion of furan containing cyclobutane **3l** (entry 12) shows the real advantage of an acid-free mild system with **2c** as the method with **1** + TfOH failed in this case providing only decomposition of the substrate. Analogously, darkening of the reaction mixture caused by product decomposition was observed in **3c** opening catalyzed by **1** + TfOH.

Previously, photosensitized cycloreversion was shown to occur via electron-transfer from the cyclobutane by $HClO_4$-protonated riboflavin−tetraacetate (**1**) both in the excited singlet and triplet states with possible participation of the chain reaction in aerated solutions.[20] Electron transfer was expected to take place on readily oxidizable groups, i.e., an amide nitrogen[33] or electron-rich aromatic ring,[34] which was followed by clean cyclobutane splitting (Scheme 2). The same process can be expected for the system with TfOH. For the alloxazinium salts-based photocatalytic cycloreversion reaction we also propose electron transfer on the basis of the observed fluorescence quenching of **2** by **3b** with a Stern−Volmer constant K_s = 8, 16, and 29 for **2a**, **2b**, and **2c**, respectively. A K_s value of 65 was observed for quenching the fluorescence of **2c** by **3a** with a low oxidation potential thereby demonstrating the limiting value. Electron transfer is also supported by significant quenching of photocycloreversion by anisole and 1,3-dimethoxybenzene with lower E_{ox} values compared to that for substrate **3b**, while quenching with benzene with higher E_{ox} was not effective (see the Supporting Information for details). The effect of oxygen on the cycloreversion reaction catalyzed by **2c** was negligible thus showing the reactions could be performed under air without loss of efficiency.

Scheme 2. Proposed Mechanism of the Oxidative [2 + 2] Cycloreversion of Cyclobutanes Bearing an Oxidizable Group G Using Flavinium Salt 2c or Protonated Flavin 1



In conclusion, we have described two versatile systems for [2 + 2] cycloreversion based on flavinium species. That with **1** and TfOH is analogous to the previously described system[20] **1** + $HClO_4$, but it is characterized by a broader substrate scope and higher efficiency. The method using alloxazinium salt **2c** is original and really represents new efficient and versatile tool for cycloreversion reactions. This mild procedure, which does not need any other additive, tolerates acid-sensitive groups and provides efficient opening of various cyclobutanes via an oxidative mechanism. Moreover, it represents an unprecedented application of flavinium salts in photocatalysis because, to date, they have only been used in organocatalysis.[27] Importantly, finding that excited alloxazinium salts are very strong oxidizing agents, whose oxidizing ability could even be potentially increased by another electron-withdrawing group, opens up a new area for flavin-based photoredox catalysis.[35]

■ ASSOCIATED CONTENT

Supporting Information

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General experimental section; synthesis and characterization of cyclobutanes; details on [2 + 2] cycloreversions; details on solvent screening and the effect of oxygen; UV−vis and fluorescence spectra of the catalytic systems; quenching experiments; hardcopy of NMR data for **2c**, **3** and **4** (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Namyslo, J. C.; Kaufmann, D. E. *Chem. Rev.* **2003**, *103*, 1485. (b) Schaumann, E.; Ketcham, R. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 225.

(2) (a) Marek, I.; Masarwa, A.; Delaye, P.-O.; Leibeling, M. *Angew. Chem., Int. Ed.* **2015**, *54*, 414. (b) Lee-Ruff, E.; Mladenova, G. *Chem. Rev.* **2003**, *103*, 1449. (c) Oppolzer, W. *Acc. Chem. Res.* **1982**, *15*, 135.

(3) (a) White, J. D.; Li, Y.; Kim, J.; Terinek, M. *J. Org. Chem.* **2015**, *80*, 11806. (b) White, J. D.; Li, Y.; Kim, J.; Terinek, M. *Org. Lett.* **2013**, *15*, 882. (c) Davis, D.; Vysotskiy, V. P.; Sajeev, Y.; Cederbaum, L. S. *Angew. Chem., Int. Ed.* **2011**, *50*, 4119. (d) Shipe, W. D.; Sorensen, E. J. *J. Am. Chem. Soc.* **2006**, *128*, 7025. (e) White, J. D.; Kim, J.; Drapela, N. E. *J. Am. Chem. Soc.* **2000**, *122*, 8665. (f) Crimmins, M. T.; Pace, J. M.; Nantermet, P. G.; Kim-Meade, A. S.; Thomas, J. B.; Watterson, S. H.; Wagman, A. S. *J. Am. Chem. Soc.* **2000**, *122*, 8453.

(4) Kean, Z. S.; Niu, Z.; Hewage, G. B.; Rheingold, A. L.; Craig, S. L. *J. Am. Chem. Soc.* **2013**, *135*, 13598.

(5) Schleyer, P. v. R.; Williams, J. E.; Blanchard, K. R. *J. Am. Chem. Soc.* **1970**, *92*, 2377.

(6) (a) Kammermeier, S.; Herges, R. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 417. (b) Ioannou, S.; Krassos, H.; Nicolaides, A. V. *Tetrahedron* **2013**, *69*, 8064.

(7) Doering, W. v. E.; Roth, W. R.; Breuckmann, R.; Figge, L.; Lennartz, H.-W.; Fessner, W.-D.; Prinzbach, H. *Chem. Ber.* **1988**, *121*, 1.

(8) Liese, J.; Hampp, N. *J. Phys. Chem. A* **2011**, *115*, 2927.

(9) (a) Hoffmann, R.; Woodward, R. B. *J. Am. Chem. Soc.* **1965**, *87*, 2046. (b) Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781.

(10) (a) Hehn, J. P.; Müller, C.; Bach, T. *Handbook of Synthetic Photochemistry*; Wiley-VCH Verlag GmbH & Co. KGaA, 2010; p 171. (b) Crimmins, M. T.; Reinhold, T. L. *Organic Reactions*; John Wiley & Sons, Inc., 2004.

(11) (a) Poplata, S.; Tröster, A.; Zou, Y.-Q.; Bach, T. *Chem. Rev.* **2016**, DOI: 10.1021/acs.chemrev.5b00723. (b) Xu, Y.; Conner, M. L.; Brown, M. K. *Angew. Chem., Int. Ed.* **2015**, *54*, 11918. (c) Liu, Y.; Song, R.; Li, J. *Sci. China: Chem.* **2016**, *59*, 161.

(12) (a) Mizuno, K.; Pac, C. *Cyclobutane Photochemistry*; CRC Press, 1995; p 358. (b) Pac, C. *Trends Phys. Chem.* **1990**, *1*, 15. (c) Pac, C.; Goan, K.; Yanagida, S. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 1951. (d) Lewis, F. D.; Kojima, M. *J. Am. Chem. Soc.* **1988**, *110*, 8664. (e) Pac, C.; Fukunaga, T.; Go-An, Y.; Sakae, T.; Yanagida, S. *J. Photochem. Photobiol., A* **1987**, *41*, 37. (f) Yonezawa, N.; Yoshida, T.; Hasegawa, M. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1083.

(13) (a) Ravelli, D.; Fagnoni, M.; Albini, A. *Chem. Soc. Rev.* **2013**, *42*, 97. (b) Schultz, D. M.; Yoon, T. P. *Science* **2014**, *343*, 1239176. (c) Xuan, J.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2012**, *51*, 6828. (d) Narayanam, J. M. R.; Stephenson, C. R. J. *Chem. Soc. Rev.* **2011**, *40*, 102.

(14) Pac, C.; Ohtsuki, T.; Shiota, Y.; Yanagida, S.; Sakurai, H. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1133.

(15) (a) Okada, K.; Hisamitsu, K.; Mukai, T. *Tetrahedron Lett.* **1981**, *22*, 1251. (b) Miranda, M. A.; Izquierdo, M. A.; Galindo, F. *J. Org. Chem.* **2002**, *67*, 4138.

(16) A. Sancar received the Nobel prize in 2015 for mechanistic studies of DNA-repair; for details see (a) https://www.nobelprize.org/nobel_prizes/chemistry/laureates/2015/sancar-facts.html. (b) For a review see: Sancar, A. *Chem. Rev.* **2003**, *103*, 2203.

(17) Brettel, K.; Byrdin, M. *Curr. Opin. Struct. Biol.* **2010**, *20*, 693.

(18) Carell, T.; Burgdorf, L.; Butenandt, J.; Epple, R.; Schwogler, A. *DNA Repair: from Model Compounds to Artificial Enzymes*; Wiley-VCH Verlag GmbH, 1999; p 242.

(19) (a) Friedel, M. G.; Cichon, M. K.; Carell, T. *Org. Biomol. Chem.* **2005**, *3*, 1937. (b) Butenandt, J.; Epple, R.; Wallenborn, E.-U.; Eker, A. P. M.; Gramlich, V.; Carell, T. *Chem. - Eur. J.* **2000**, *6*, 62. (c) Carell, T.; Epple, R. *Eur. J. Org. Chem.* **1998**, *1998*, 1245. (d) Wiest, O.; Harrison, C. B.; Saettel, N. J.; Cibulka, R.; Sax, M.; König, B. *J. Org. Chem.* **2004**, *69*, 8183.

(20) Pac, C.; Miyake, K.; Masaki, Y.; Yanagida, S.; Ohno, T.; Yoshimura, A. *J. Am. Chem. Soc.* **1992**, *114*, 10756.

(21) Miyake, K.; Masaki, Y.; Miyamoto, I.; Yanagida, S.; Ohno, T.; Yoshimura, A.; Pac, C. *Photochem. Photobiol.* **1993**, *58*, 631.

(22) Yasuda, M.; Nishinaka, Y.; Nakazono, T.; Hamasaki, T.; Nakamura, N.; Shiragami, T.; Pac, C.; Shima, K. *Photochem. Photobiol.* **1998**, *67*, 192.

(23) Mühldorf, B.; Wolf, R. *Chem. Commun.* **2015**, *51*, 8425.

(24) Fukuzumi, S.; Yasui, K.; Suenobu, T.; Ohkubo, K.; Fujitsuka, M.; Ito, O. *J. Phys. Chem. A* **2001**, *105*, 10501.

(25) Fukuzumi, S.; Ohkubo, K. *Org. Biomol. Chem.* **2014**, *12*, 6059.

(26) Martiny, M.; Steckhan, E.; Esch, T. *Chem. Ber.* **1993**, *126*, 1671.

(27) Flavinium salts have been widely used in organocatalytic redox reactions, see: (a) Iida, H.; Imada, Y.; Murahashi, S. I. *Org. Biomol. Chem.* **2015**, *13*, 7599. (b) Cibulka, R. *Eur. J. Org. Chem.* **2015**, *2015*, 915.

(28) (a) Sichula, V.; Hu, Y.; Mirzakulova, E.; Manzer, S. F.; Vyas, S.; Hadad, C. M.; Glusac, K. D. *J. Phys. Chem. B* **2010**, *114*, 9452. (b) Quick, M.; Weigel, A.; Ernsting, N. P. *J. Phys. Chem. B* **2013**, *117*, 5441.

(29) Ménová, P.; Dvořáková, H.; Eigner, V.; Ludvík, J.; Cibulka, R. *Adv. Synth. Catal.* **2013**, *355*, 3451.

(30) Similar excitation energy of **1** and **2c** can be expected when comparing absorption and excitation spectra: λ_{abs} = 442 nm, λ_{em} = 506 nm for **1** and λ_{abs} = 449 nm, λ_{em} = 529 nm for **2c** in acetonitrile; see the Supporting Information for details.

(31) Value $E^{0\prime}{}_{red}{}^{*}$ = 2.74 V vs SCE can be estimated for **2c** based on $E^{0\prime}{}_{red}$ = +0.275 V (ref 29) and excitation energy E^{0-0} = 2.46 eV calculated as the average of absorption (hc/λ_{abs}) and emission (hc/λ_{em}) energies.

(32) Kaupp, G. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 817.

(33) Krüger, O.; Wille, U. *Org. Lett.* **2001**, *3*, 1455.

(34) Ischay, M. A.; Ament, M. S.; Yoon, T. P. *Chem. Sci.* **2012**, *3*, 2807.

(35) Very recent applications of flavins in photocatalysis: (a) Neveselý, T.; Svobodová, E.; Chudoba, J.; Sikorski, M.; Cibulka, R. *Adv. Synth. Catal.* **2016**, *358*, 1654. (b) Metternich, J. B.; Gilmour, R. *J. Am. Chem. Soc.* **2016**, *138*, 1040. (c) Mühldorf, B.; Wolf, R. *Angew. Chem., Int. Ed.* **2016**, *55*, 427. (d) Mojr, V.; Svobodová, E.; Straková, K.; Neveselý, T.; Chudoba, J.; Dvořáková, H.; Cibulka, R. *Chem. Commun.* **2015**, *51*, 12036. (e) Metternich, J. B.; Gilmour, R. *J. Am. Chem. Soc.* **2015**, *137*, 11254.

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