JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

ARTICLE

pubs.acs.org/JACS

Enantioselective Intramolecular [2 + 2]-Photocycloaddition Reactions of 4-Substituted Quinolones Catalyzed by a Chiral Sensitizer with a Hydrogen-Bonding Motif

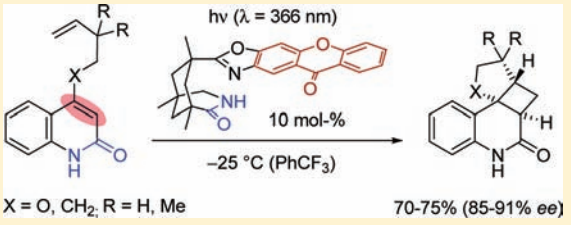
Christiane Müller,[†] Andreas Bauer,[†] Mark M. Maturi,[†] M. Consuelo Cuquerella,[‡] Miguel A. Miranda,*[,‡] and Thorsten Bach*[,†]

[†]Lehrstuhl für Organische Chemie I and Catalysis Research Center (CRC), Technische Universität München, D-85747 Garching, Germany

[‡]Instituto de Tecnología Química (UPV-CSIC), Universidad Politécnica de Valencia, 46022 Valencia, Spain

Supporting Information

ABSTRACT: Six 2-quinolones, which bear a terminal alkene linked by a three- or four-membered tether to carbon atom C4 of the quinolone, were synthesized and subjected to an intramolecular [2 + 2]-photocycloaddition. The reaction delivered the respective products in high yields (78−99%) and with good regioselectivity in favor of the straight isomer. If conducted in the presence of a chiral hydrogen-bonding template (2.5 equiv) at low temperature in toluene as the solvent, the reaction proceeded enantioselectively (83−94% ee). An organocatalytic reaction was achieved when employing a chiral hydrogen-bonding template with an attached sensitizing unit (benzophenone or xanthone). The xanthone-based organocatalyst proved to be superior as compared to the respective benzophenone. Closer inspection revealed that the reaction of 4-(pent-4-enyloxy)quinolone leading to a six-membered ring, annelated to the cyclobutane, was less enantioselective (up to 41% ee with 30 mol % catalyst) than the reaction of 4-(but-3-enyloxy)quinolone leading to a five-membered ring (90% ee with 5 mol % and 94% ee with 20 mol % catalyst). Photophysical data (emission spectra, laser flash photolysis experiments) proved that the latter photocycloaddition was significantly faster, supporting the idea that the dissociation of the substrate from the catalyst prior to the photocycloaddition is responsible for the decreased enantioselectivity. Under optimized conditions, employing 10 mol % of the xanthone-based organocatalyst at −25 °C in trifluorotoluene as the solvent, three of the other four substrates gave the intramolecular [2 + 2]-photocycloaddition products with high enantioselectivities (72−87% ee). In all catalyzed reactions, the yields based on conversion were moderate to good (40−93%).



INTRODUCTION

Chirality[1] is one of the most fascinating properties of matter. The quest to create chiral molecules enantioselectively and the desire to understand their interactions belong to the intellectually most challenging tasks of chemistry.[2] Photochemical, enantioselective approaches to chiral molecules have been pursued along different lines of research. Solid-state photochemistry offers access to enantioselective products by irradiation of homochiral crystals[3] or by employing chiral cavities.[4] In the liquid phase, chirality can be induced either by transforming a chiral solid-state conformation photochemically into a defined absolute configuration[5] or by irradiation with circularly polarized light.[6] An alternative approach is to employ noncovalent interactions to provide a chiral environment, in which a photochemical reaction takes place.[7] Apart from other supramolecular interactions,[8] hydrogen bonds have turned out to be a generally applicable means[9] to coordinate photochemical substrates in a spatially distinct three-dimensional fashion.[10] For use on a stoichiometric scale, template (+)-**1** (Figure 1) and its enantiomer[11] have proven to be useful complexing agents to induce high enantioselectivities in photochemical reactions of (dihydro)quinolones,[12] isoquinolones,[13] pyridones,[14] dihydropyridones,[15] imidazolidinones,[16] and aromatic amides.[17]

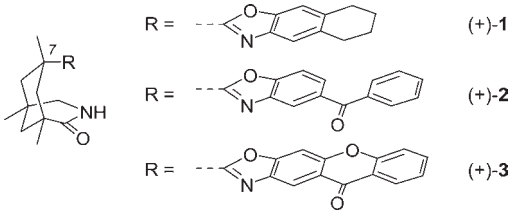


Figure 1. Chiral template (+)-**1** and chiral sensitizers (+)-**2** and (+)-**3**.

It was envisaged that it might be possible to combine the hydrogen-bonding ability of the 1,5,7-trimethyl-3-azabicyclo-[3.3.1]nonan-2-one skeleton with a catalytically active sensitizing[18] unit R attached to the 7-position of the scaffold. The distance dependence of triplet energy[19] or electron[20] transfer would allow for a sensitized intramolecular photochemical reaction to occur

Received: August 9, 2011
Published: September 28, 2011

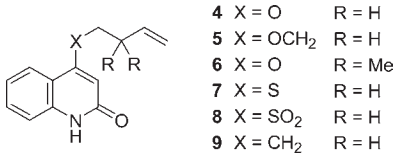
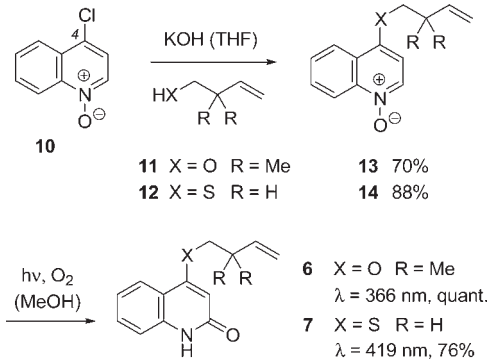


Figure 2. Substrates for the intramolecular [2 + 2]-photocycloaddition.

Scheme 1



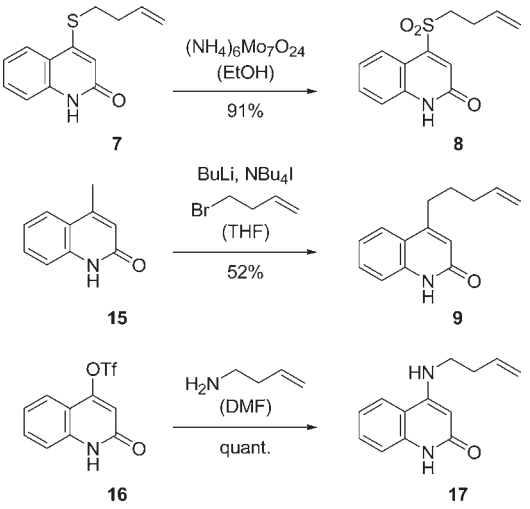
selectively in a 1:1 complex of substrate and catalyst. Our first successful experiment in this series was based on the use of catalyst (+)-**2** and its enantiomer, with which it was shown that a chirality multiplication is possible in an enantioselective radical cyclization initiated by a photoinduced electron transfer (70% ee with 30 mol % of catalyst).[21,22] In earlier work aiming at catalysis by triplet energy transfer, Krische !et al. had used a hydrogen-bonding template tethered to a benzophenone sensitizer to induce enantioselectivity in the intramolecular [2 + 2]-photocycloaddition[23] of 4-(but-3-enyloxy)quinolone (**4**, Figure 2)[24] (19% ee with 25 mol % of catalyst).[10a] When revisiting this photocycloaddition, we found that catalyst (+)-**3** can be employed to achieve very high enantioselectivities at low catalyst loadings (90% ee with 5 mol % catalyst).[25] Prerequisites for a high chemo- and enantioselectivity were the use of a nonpolar solvent (trifluorotoluene) at low temperature (−25 °C) and long wavelength irradiation (λ = 366 nm). This intriguing result led us to initiate a more extensive study on the enantioselective intramolecular [2 + 2]-photocycloaddition of 4-substituted quinolones. To this end, various substrates **4**−**9** (Figure 2) were synthesized and tested in photocycloaddition reactions mediated by either the stoichiometric template (+)-**1** or the catalyst (+)-**3**. For some substrates, it was found that they show an equally good performance as was previously observed for substrate **4**.

The reactions of 4-(but-3-enyloxy)quinolone (**4**) and 4-(pent-4-enyloxy)quinolone (**5**) were closely compared regarding the different parameters, which influence the enantioselectivity. Laser flash spectroscopic studies revealed that there are distinct differences in the photocycloaddition kinetics of **4** and **5**, which nicely explain the difference in enantioselectivity observed in the catalytic version of their enantioselective [2 + 2]-photocycloaddition reactions. A mechanistic picture was developed, which comprises the experimental facts so far obtained.

RESULTS AND DISCUSSION

Preparation of Starting Materials. Among the different possible approaches to 4-substituted quinolones, two major synthetic routes were used in this study. One route is based on easily accessible 4-chloroquinoline-*N*-oxide (**10**)[26] as starting material (Scheme 1). Nucleophilic displacement of the chlorine substituent is facilitated by the electron withdrawing power of the *N*-oxide and occurs readily either by an oxygen or by a sulfur nucleophile. Alcohols **11**[27] and **12**[28] were accessible by known procedures. Following the substitution pathway, ether **13** and thioether **14** were directly obtained from *N*-oxide **10** in very good yields.

Scheme 2



The key transformation in the *N*-oxide route to 4-substituted quinolones is the subsequent rearrangement, which is advantageously conducted photochemically.[29] A major improvement in this reaction step was made recently[12d] by performing the rearrangement in oxygen-purged methanol employing a continuous flow system. The photochemical rearrangement occurs on the singlet hypersurface and is consequently not sensitive to the presence of oxygen, while the potentially possible, but at this stage undesired intramolecular [2 + 2]-photocycloaddition of the quinolone products occurs on the triplet hypersurface (vide infra). The latter reaction is almost completely suppressed in the presence of oxygen, which allows for the isolation of the quinolones in high yields. Starting from *N*-oxide **13**, quinolone **6** was obtained in quantitative yield at an irradiation wavelength of λ = 366 nm. The thiosubstituted *N*-oxide **14** could be irradiated at longer wavelength (λ = 419 nm) and delivered the desired quinolone **7** in a yield of 76%.

A second route to quinolones relies on the synthetic modification of preformed quinolones by functional group manipulation and substitution. Oxidation[30] of sulfide **7** (Scheme 2) proceeded cleanly and furnished sulfone **8** in high yield.

Known 4-methylquinolone (**15**)[31] was transformed into the pent-4-enyl substituted quinolone **9** by deprotonation and subsequent electrophilic attack by but-3-enyl bromide as an alkylating agent. Amine **17** was prepared by nucleophilic displacement of the triflate group in quinolone **16** with *N*-but-3-enylamine.[32] The resulting product **17** was moisture sensitive, however, and hydrolyzed quickly to 4-hydroxyquinolone. As discussed in the next paragraph, its intramolecular [2 + 2]-photocycloaddition turned out to be capricious.

Preliminary Studies and Template-Induced Enantioselectivity. Intramolecular [2 + 2]-photocycloaddition reactions of

Scheme 3

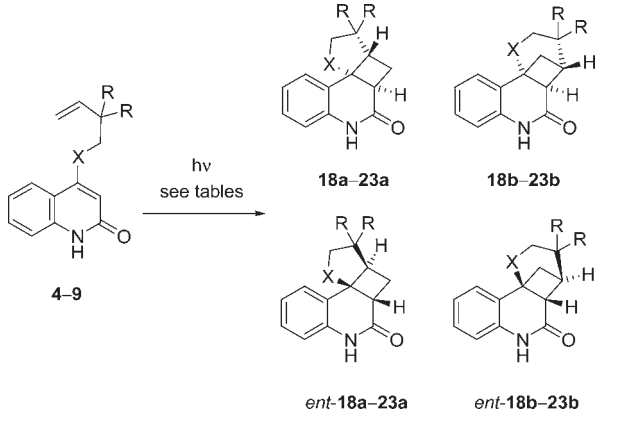


Table 1. Reaction Conditions, Regioselectivities, and Yields in the Intramolecular [2 + 2]-Photocycloaddition of Quinolones 4−9 (See Scheme 3)

entry	substrate[a]	X	R	product	t^b [h]	r.r.[c]	yield[d] [%]
1	**4**	O	H	*rac*-**18**	9[e]	86/14	78
2	**5**	OCH_2	H	*rac*-**19**	9	90/10	99
3	**6**	O	Me	*rac*-**20**	7	91/9	95
4	**7**	S	H	*rac*-**21**	2	>95/5	99
5	**8**	SO_2	H	*rac*-**22**	2	>95/5	92
6	**9**	CH_2	H	*rac*-**23**	0.5	>95/5	99

[a] All reactions were conducted at a substrate concentration of 5 mM at λ = 366 nm and ambient temperature in trifluorotoluene as the solvent. [b] Time required for complete conversion. [c] The regioisomeric ratio (r.r.) refers to the ratio of straight (**a**) to crossed (**b**) photocycloaddition product and was determined by ^{1}H NMR spectroscopy. [d] Yield of isolated product. [e] The reaction remained incomplete after 9 h (83% conversion).

quinolones[33] can lead to a multitude of isomers with up to four stereogenic centers being formed in a single reaction step. Because of the steric constraints exerted by the cyclobutane ring, the diastereoselectivity of the reactions is generally high. Consequently, there are only four major isomers to be taken into account (Scheme 3). Apart from one set of regioisomers, straight (**a**) and crossed (**b**), a set of enantiomers is to be expected. In the absence of any chiral information, the photocycloaddition proceeds racemically and the enantiomers are formed in equal amounts. Indeed, the first set of experiments performed with substrates **4**−**9** was to prove the general feasibility of the [2 + 2]-photocycloaddition and to obtain racemic material for comparison with enantiomerically enriched products (Table 1). Reactions were performed at conditions later used for the catalyzed reactions; that is, the solvent was trifluorotoluene at a relatively long wavelength (λ = 366 nm). Given the spectroscopic properties of the substrates (for UV−vis data, see page S17 in the Supporting Information), the long wavelength irradiation conditions were the reason why the previously reported facile [2 + 2]-photocycloaddition reactions[24] of substrates **4** and **5** proceeded slowly. In all cases (entries 1−6), yields and diastereoselectivities were high. The regioselectivity was clearly in favor of the straight products with the crossed photocycloaddition products resulting from **7**−**9** (entries 4−6) being not detectable at all. Because

Table 2. Reaction Conditions, Enantioselectivities, and Yields in the Enantioselective Intramolecular [2 + 2]-Photocycloaddition of Quinolones 4−9 in the Presence of Chiral Template (+)-1 (See Scheme 3)

entry	substrate[a]	X	R	product	λ [nm]	t^b [h]	ee[c] [%]	yield[d] [%]
1	**4**	O	H	**18a**	300	3	89	43
2[e]	**5**	OCH_2	H	**19a**	300	1	>90	87
3	**6**	O	Me	**20a**	300	6	83	66
4	**7**	S	H	**21a**	366	1	89	89
5	**8**	SO_2	H	**22a**	366	1	90	99
6	**9**	CH_2	H	**23a**	366	2	94	99

[a] All reactions were conducted at a substrate concentration of 5 mM with 2.5 equiv of template (+)-**1** at −78 °C in toluene as the solvent. [b] Irradiation time. [c] The enantiomeric excess of the straight photocycloaddition products was determined by chiral HPLC analysis (see the Supporting Information). [d] Yield of isolated product. [e] The reaction has been studied in earlier work at −60 °C. The enantiomeric excess was determined by chemical shift experiments, which have a relatively high detection limit. The other enantiomer could not be detected.[12a]

there was no chiral information present, all products were racemic (*rac*-**18** to *rac*-**23**).

Although 4-(but-3-enylamino)quinolone (**17**) exhibits an absorption band, which is significantly shifted to longer wavelengths (λ > 350 nm) as compared to the corresponding 4-alkenyloxyquinolones **4** and **5**, its photocycloaddition proceeded sluggishly. There was a precipitate observed shortly after the irradiation was initiated, and even after 10 h the reaction had not gone to completion. The resulting product showed typical NMR data of the expected straight photocycloaddition product but was impossible to purify. Given these difficulties, the reaction was not further studied.

The enantioselectivity in intramolecular reactions of lactams in the presence of template (+)-**1** depends mainly on two parameters. The first parameter is the efficiency, with which binding to the substrate occurs. The second parameter is the intrinsic selectivity of the reaction in the bound substrate/template complex. This selectivity depends on conformational preferences for the ring-closing step and on the steric bias exerted by the substituent R (Figure 1) in this step. On the basis of previous studies with 4-substituted quinolones,[12d] it can be safely assumed that they bind at low temperature (<0 °C) in a nonpolar solvent quantitatively to template (+)-**1** provided that the template is present in superstoichiometric (2.5 equiv) amounts. The enantioselectivity in the intramolecular [2 + 2]-photocycloaddition of 4-substituted quinolones **4**−**9** in the presence of template (+)-**1** can consequently be considered a reliable way to investigate the feasibility of a highly enantioselective catalytic reaction assuming that the steric bias exerted by the substituents R (Figure 1) in (+)-**2** and (+)-**3** is similar to the steric bias of the 1′-oxa-3′-azacyclopenta[*b*]naphthalene shield in (+)-**1**. Reactions (Table 2) were performed in toluene at −60 °C at wavelengths that guarantee rapid conversion. Although the picture is only semiquantitative, it became evident that, for example, alkenyloxyquinolone **6** (entry 3) exhibits a lower intrinsic enantioselectivity. The regioselectivity was somewhat influenced by the template with an increased preference for the straight product in the previously less selective cases (entries 1−3). The absolute configuration of product **19a**[12a] and of the noranalogue of compound **18b**[34] had been earlier proven. Both compounds were

Scheme 4

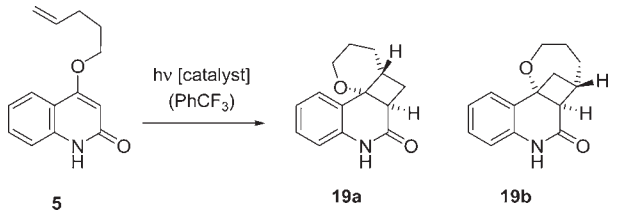


Table 3. Intramolecular [2 + 2]-Photocycloaddition of 4-(Pent-4-enyloxy)quinolone (5) in the Absence and Presence of an Achiral Catalyst (See Scheme 4)

entry	catalyst[a]	t^b [h]	product	r.r.[c]	conv.[d] [%]	yield[e] [%]
1		4	*rac*-**19**	91/9	46	22
2	benzophenone	4	*rac*-**19**	91/9	96	89
3	xanthone	4	*rac*-**19**	91/9	94	93

[a] Reactions were conducted at a substrate concentration of 10 mM and at λ = 366 nm with 20 mol % of the respective catalyst at −25 °C in trifluorotoluene as the solvent. [b] Irradiation time. [c] The regioisomeric ratio (r.r.) refers to the ratio of straight (*rac*-**19a**) to crossed (*rac*-**19b**) photocycloaddition product and was determined by ^{1}H NMR spectroscopy. [d] The conversion is based on reisolated starting material. [e] Yield of isolated product.

obtained by intramolecular [2 + 2]-photocycloaddition in the presence of template (+)-**1**, and both products are levorotatory. The absolute configuration of products **18a**, **20a**−**23a** was assigned on the basis of an analogy and on the basis of comparison of the chiroptical product data with known data. Indeed, dihydroquinolone products are expected to be levorotatory if the dihedral angle along the nitrogen-aryl axis (atoms C2−N1−C8a−C4a) has a negative sign.[21] According to molecular models, the twist resulting from the cyclobutane annelated to carbon atoms C3 and C4 of a dihydroquinolone should lead in compounds **18**−**23** to negative dihedral angles (and to a negative specific rotation) and for compounds *ent*-**18**−**23** to positive dihedral angles (and to a positive specific rotation). The specific rotations measured for all products **18a**−**23a** were indeed found to be negative.

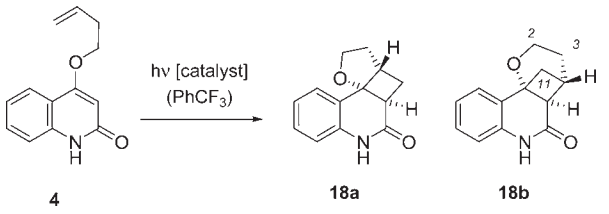
Catalytic Reactions with Substrates 4 and 5. Initial studies regarding a potential catalysis of the intramolecular [2 + 2]-photocycloaddition were performed with 4-(pent-4-enyloxy)quinolone (**5**). The choice for this substrate, as opposed to **4**, was based on the fact that a single straight regioisomer (compound *rac*-**19a**) was expected from its reaction. Indeed, Kaneko et al. had reported that substrate **4** delivered a 7:1 mixture of regioisomers (in MeOH as the solvent), whereas **5** gave a single product.[24] Our previous experiments[12a] also supported the notion that the reaction of **5** was highly regioselective (in particular in the presence of template (+)-**1**) and hence easier to analyze. Concerning catalysis, it was conceived that energy transfer from photoexcited aromatic ketones might be possible upon long wavelength (λ = 366 nm) irradiation. The electrophilic nature of the triplet nπ^*-state involved in the sensitization led us to use trifluorotoluene instead of toluene as the solvent in these and all subsequent studies. The absence of labile CH-bonds in trifluorotoluene makes hydrogen abstraction reactions from the solvent inefficient. A catalytic effect was detectable (Scheme 4, Table 3) when using benzophenone or xanthone as a sensitizer. In comparison to the uncatalyzed reaction, product formation was significantly increased after 4 h of irradiation time. Benzophenone and xanthone (entries 2 and 3) showed a similar rate enhancement, which could also be quantified in more extensive kinetic experiments (see page S20 in the Supporting Information). The catalyzed reaction was not only faster than the uncatalyzed reaction (entry 1) but led also to less byproduct and delivered higher yields of the respective cycloaddition product. The regioselectivity was in the expected range (r.r. = 91/9).

Table 4. Reaction Conditions, Enantioselectivities, and Yields in the Enantioselective Intramolecular [2 + 2]-Photocycloaddition of Quinolone 5 in the Presence of Chiral Catalysts (+)-2 and (+)-3 (See Scheme 4)

entry[a]	catalyst	mol %	r.r.[b]	conv.[c] [%]	ee[d] [%]	yield[e] [%]
1	(+)-**2**	10	82/18	60	12	45
2	(+)-**3**	5	80/20	55	21	39
3	(+)-**3**	10	76/24	58	27	42
4	(+)-**3**	20	80/20	65	35	48
5	(+)-**3**	30	70/30	69	41	62

[a] All reactions were conducted at a substrate concentration of 10 mM by irradiation at λ = 366 nm for 4 h at −25 °C in trifluorotoluene as the solvent. [b] The regioisomeric ratio (r.r.) refers to the ratio of straight (**19a**) to crossed (**19b**) photocycloaddition product and was determined by ^{1}H NMR spectroscopy. [c] The conversion is based on reisolated starting material. [d] The enantiomeric excess of the straight photocycloaddition product **19a** was determined by chiral HPLC analysis. [e] Yield of isolated product.

Scheme 5



Reactions with the chiral benzophenone (+)-**2** and the xanthone (+)-**3** confirmed that both chromophores are similarly well suited to induce the desired rate acceleration (Table 4). However, benzophenone (+)-**2** was less effective in the chirality transfer from the catalyst to the product (entries 1 and 3). In general, the enantioselectivities were lower than was hoped based on the high enantioselectivities achieved with the superstoichiometrically used template (+)-**1** (vide supra). An increasing amount of catalyst (+)-**3** gave expectedly a higher selectivity (entries 2−5), but the result (41% ee at best) was not satisfactory. There were some additional observations. Catalyst decomposition was still severe despite the use of trifluorotoluene as the solvent. Hydrogen abstraction cannot occur from the solvent but rather occurs from the reaction products. As a consequence of the product chirality, different decomposition rates were observed for different enantiomers. After 1 h of irradiation time (40% conversion), both regioisomers **19a** and **19b** were formed with similar enantiomeric excess (37% ee and 38% ee). The ee of the major regioisomer **19a**, however, decreased as the reaction progressed, resulting in 27% ee after 4 h (58% conversion, entry

Table 5. Reaction Conditions, Enantioselectivities, and Yields in the Enantioselective Intramolecular [2 + 2]-Photocycloaddition of Quinolone 4 in the Presence of Chiral Catalysts (+)-2 and (+)-3 (See Scheme 5)

entry[a]	catalyst	mol %	t^b [h]	r.r.[c]	conv.[d] [%]	ee[e] [%]	yield[f] [%]
1			1	n.d.	19		5
2	(+)-**2**	10	1	84/16	57	39	51
3	(+)-**3**	10	1	78/22	64	92	58
4	(+)-**3**	10	2	77/23	81	90	75
5	(+)-**3**	10	4	>99/1	90	91	50
6	(+)-**3**	10	10	>99/1	100	89	46
7	(+)-**3**	5	1	78/22	50	90	48
8	(+)-**3**	20	1	79/21	73	94	53

[a] All reactions were conducted at a substrate concentration of 5 mM and at a temperature of −25 °C by irradiation at λ = 366 nm in trifluorotoluene as the solvent. [b] Irradiation time. [c] The regioisomeric ratio (r.r.) refers to the ratio of straight (**18a**) to crossed (**18b**) photocycloaddition product and was determined by ^{1}H NMR spectroscopy. [d] The conversion is based on reisolated starting material. [e] The enantiomeric excess of the straight photocycloaddition products was determined by chiral HPLC analysis. [f] Yield of isolated product.

3, Table 4). The crossed regioisomer **19b** showed after the same period of time an ee of 50%. The result is in line with a preferred decomposition of **19a** (as compared to its enantiomer *ent*-**19a**) in the case of the major regioisomer and of *ent*-**19b** (as compared to its enantiomer **19b**) for the minor regioisomer. From a practical point of view, the reactions slowed in all cases significantly after 4 h, indicating a significant decomposition of the sensitizer. The sensitizer could not be recovered.

When the same series of experiments conducted with substrate **5** and catalysts (+)-**2** and (+)-**3** were performed with 4-(but-3-enyloxy)quinolone (**4**), a much higher enantioselectivity was found (Scheme 5, Table 5). In particular, xanthone (+)-**3** showed a performance previously not encountered for a chiral triplet sensitizer. In the absence of a catalyst, only 19% of the starting material had reacted after 1 h of irradiation (Table 5, entry 1). With 10 mol % of xanthone (+)-**3**, the conversion was 64% after the same time period with the major regioisomer **18a** being formed in 92% ee (entry 3). Benzophenone (+)-**2** was inferior (entry 2) to xanthone (+)-**3** both in catalytic activity (57% conversion) and in enantioselectivity (39% ee). The instability of catalyst (+)-**3** became again evident from the decreased reaction rates at prolonged reaction times (entries 3−6). Byproducts were formed after 2 h, and the enantioselectivity dropped if complete conversion was to be achieved (entry 6). Remarkably, the decomposition of the sensitizer appears in this case to go hand in hand with the decomposition of the minor regioisomer **18b**. While the regioisomeric ratio **18a**/**18b** was 77/23 after 2 h (entry 4), the minor regioisomer had almost completely vanished after 4 h (entry 5). As already mentioned previously, hydrogen abstraction is likely to be the major reason for the decomposition, and one could speculate the exposed CH_2 protons at C2, C3, or C11 are readily abstracted. The catalytic activity of xanthone (+)-**3** was remarkable. Even if used in only 5 mol % (entry 7), significant conversion and high enantioselectivity (90% ee) were observed. Expectedly, a higher amount of catalyst (entry 8) resulted in higher conversion and an increase in enantioselectivity.

The minor regioisomer **18b** was not in all cases isolated in sufficient quantities to determine its enantiomeric excess. If the determination was possible and if the ee was measured, it never exceeded the ee of the straight product **18a** but was typically lower. Representative values, as determined, for example, for entry 3 of Table 5, were 90% ee for **18b** versus 92% ee for **18a**. In contrary to the reaction **5** → **19a**/**19b**, the enantiomeric excess of the major product did not change in the course of the photocycloaddition. Rather, the regioisomeric ratio changed as already discussed.

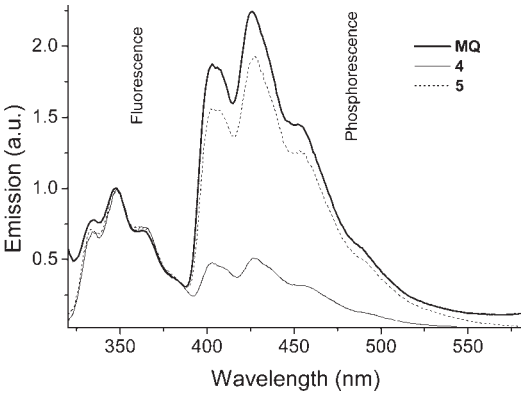


Figure 3. Emission spectra of **4**, **5**, and **MQ** registered at low temperature (−190 °C) in an ethanol matrix.

Photophysical Experiments. A possible explanation for the striking substrate-dependent enantioselectivity was suspected to be found in the kinetics of the reactions. To gain insight into this aspect, the photophysics of **4** and **5** was studied and compared to that of 4-methoxyquinolone (**MQ**), which shares the same heterocyclic nucleus, but possesses a methoxy (instead of an alkenoxy) substituent at position C4. Fluorescence spectra of the three quinolones displayed a maximum at ca. 360 nm with quantum yields (ϕ_F) of 0.10, 0.11, and 0.12 for **4**, **5**, and **MQ**, respectively (Figure SI-3 in the Supporting Information). The singlet excited-state energies were determined from the intersection between the excitation and the emission spectra (Figure SI-4 in the Supporting Information) and were found to be the same for the three compounds: 358 kJ/mol (86 kcal/mol). This clearly indicates that the intramolecular [2 + 2]-photocycloaddition does not take place from the singlet excited state.

When emission was recorded at low temperature (−190 °C) in an ethanol matrix, a small fluorescence component was still observed. The position of the band was the same as in solution, but the spectra were better resolved. Moreover, the fluorescence intensity was comparable for the three quinolones (Figure 3). Conversely, large intensity differences in the long-wavelength phosphorescence band were observed. In particular, the phosphorescence of **4** was significantly lower than that of **5** (Figure 3). The relative quantum yields (ϕ_{Ph}) were determined by comparing the areas of the phosphorescence spectra. Taking into account that $\phi_{Ph} = \phi_{ISC} \times \tau_{Ph} \times k_{Ph}$, where k_{Ph} is the intrinsic emission rate constant, and assuming that ϕ_{ISC} (the intersystem crossing quantum yield) is the same for the quinolones, the ratio between the phosphorescence lifetimes and quantum yields of **4** and **5** is given by eq 1.

$$\frac{\phi_{Ph}(\mathbf{4})}{\phi_{Ph}(\mathbf{5})} = \frac{\tau_{Ph}(\mathbf{4})}{\tau_{Ph}(\mathbf{5})} = 0.38 \quad (1)$$

The reduced phosphorescence of quinolones **4** and **5** is consistent with the intramolecular [2 + 2]-photocycloaddition

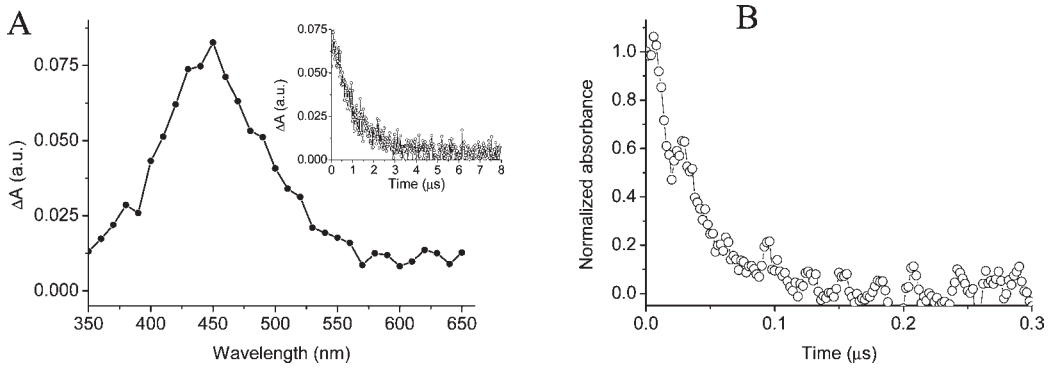
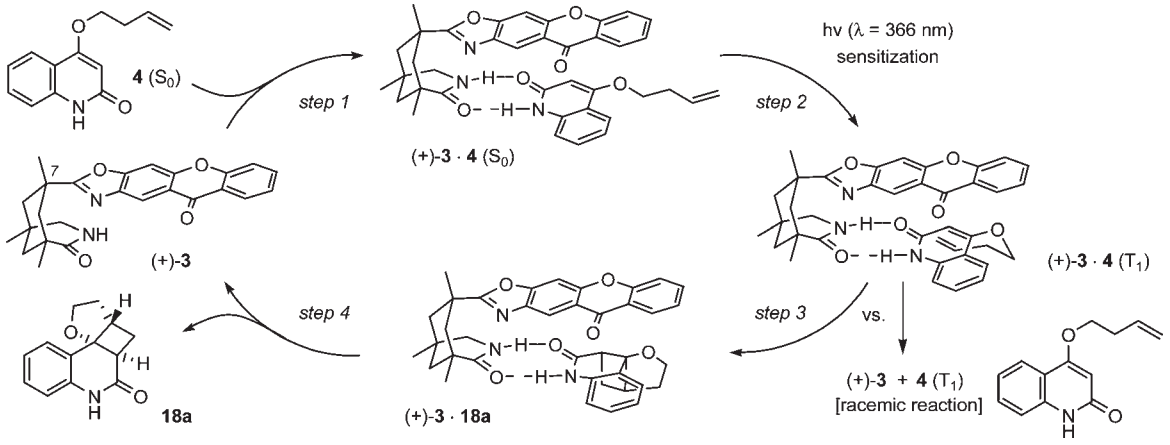


Figure 4. (A) Transient absorption spectra of a deaerated solution of **MQ**, 270 ns after laser excitation, and (B) decay profile of a deaerated solution of **5**, in trifluorotoluene upon laser excitation.

Scheme 6



reaction taking place from the triplet excited state. Besides, the remarkable differences between the phosphorescence intensities of **4** and **5** point to a higher reaction rate constant in the intramolecular [2 + 2]-photocycloaddition of the former substrate. Laser flash photolysis experiments performed at room temperature supported this conclusion. The transient absorption spectra of these quinolones showed a broad maximum centered at 460 nm after laser excitation (λ_{exc} = 308 nm). This is shown in Figure 4A for **MQ**; the spectra obtained with the other two quinolones were poor, due to partial decomposition. The 460 nm band was assigned to the triplet excited states, which was confirmed by means of sensitization experiments, using xanthone as triplet energy donor, and by oxygen quenching (Figure SI-6 in the Supporting Information). In trifluorotoluene, **MQ** and **5** triplet excited state lifetimes (τ_T) were 1 μs and 57 ns, respectively (Figure 4A, inset, and B). The triplet lifetime of **4** was too close to the detection limit of our laser setup to be accurately determined by direct measurement. Its value could be estimated, however, by assuming that the $\tau_{Ph}(\mathbf{4})/\tau_{Ph}(\mathbf{5})$ ratio is roughly the same as that of $\tau_T(\mathbf{4})/\tau_T(\mathbf{5})$. Hence, eqs 1 and 2 apply:

$$\tau_T(\mathbf{4}) = \tau_T(\mathbf{5}) \times 0.38 = 57\ \text{ns} \times 0.38 = 22\ \text{ns} \qquad (2)$$

The obtained value (22 ns) is actually feasible and could explain the dispersity of the experimental decay measurements (not shown).

On the basis of the above data, the intramolecular photoreaction rate constant can be calculated as given by eq 3:

$$k(i) = \frac{1}{\tau_T(i)} - \frac{1}{\tau_T(\mathbf{MQ})} \qquad (3)$$

Thus, the reaction constants, $k(\mathbf{4})$ and $k(\mathbf{5})$, can be estimated at 4.5×10^7 and $1.7 \times 10^7\ s^{-1}$, respectively. Hence, at room temperature, the butenyloxy derivative **4** is markedly more reactive than the pentenyloxy analogue **5**. The photophysical studies corroborate the results obtained in the enantioselective reactions of substrates **4** and **5**. In the template-mediated enantioselective reaction (Table 2), the degree of enantioselectivities is only dependent on the thermodynamic parameters (association constant K_a and dimerization constant K_{dim}), which are expected to be identical for quinolones **4** and **5**. In the catalytic reactions, however, the rate of the [2 + 2]-photocycloaddition has an essential impact on the enantioselectivity. An excited substrate, which dissociates from the catalyst prior to [2 + 2]-photocycloaddition, will not react enantioselectively because, due to the low catalyst loading, it will not find a chiral template for reassociation. Apparently, the rate of the intramolecular [2 + 2]-photocycloaddition reactions of substrates **4** and **5** (or rather of their first C−C bond step) is in the order of the dissociation rate constant. The lower rate for cyclization to the six-membered ring causes the lower enantioselectivity observed for quinolone **5**.

Table 6. Reaction Conditions, Enantioselectivities, and Yields in the Enantioselective Intramolecular [2 + 2]-Photocycloaddition of Quinolones 4−9 in the Presence of 10 mol % of Chiral Catalyst (+)-3 (See Scheme 3)

entry[a]	substrate	t[b] [h]	product	r.r.[c]	conv.[d] [%]	ee[e] [%]	yield[f] [%]
1	**4**	2	**18**	77/23	81	90	75
2	**5**	1	**19**	78/22	41	38	34
3	**6**	1	**20**	82/18	79	85	73
4[g]	7	0.5	**21**	>95/5	53	72	21
5[g]	**8**	0.5	**22**	>95/5	31	6	28
6[g]	**9**	0.5	**23**	>95/5	84	87	70

[a] The reactions were conducted at a substrate concentration of 5 mM and at a temperature of −25 °C by irradiation at λ = 366 nm (16 lamps) in trifluorotoluene as the solvent. [b] Irradiation time. [c] The regioisomeric ratio (r.r.) refers to the ratio of straight (**a**) to crossed (**b**) photocycloaddition product and was determined by ^{1}H NMR spectroscopy. [d] The conversion is based on reisolated starting material. [e] The enantiomeric excess of the straight photocycloaddition products was determined by chiral HPLC analysis. [f] Yield of isolated product. [g] The photon flux was reduced by reducing the number of light sources (2 lamps instead of 16 lamps).

Excitation and Turnover. If one sums up the previous results on the catalytic cycle, a picture as drawn in Scheme 6 for the reaction of quinolone **4** evolves. The enantioselectivity depends on the association (step 1), on an efficient sensitization (step 2), and on the rate of the subsequent cyclization (step 3). Association data have been collected for substrate/template combination related to **4** and (+)-**3**,[12d] suggesting that the catalyst is at the outset of the reaction completely bound to the substrate (vide supra). In addition, from the data we have gathered by the spectroscopic studies mentioned above, there is a lower rate limit, at which the cyclization (step 3) competes effectively with dissociation from the catalyst. Dissociation of product **18a** from the template (step 4) is important to guarantee efficient turnover. Given that the product is considerably bulkier than the planar substrate, it is expected that a disfavorable interaction between the oxazolo[4,5-*b*]xanthone shield in catalyst (+)-**3** and the product facilitates an exchange from product to new substrate. A similar scenario has been previously observed in enantioselective reactions[12b] mediated by template (+)-**1**.

Regarding the sensitization (step 2), the question why this process is so effective and how it proceeds has not yet been addressed. Looking at the absorption data (see page S17 in the Supporting Information), it is apparent that xanthone (+)-**3** virtually absorbs all photons at long wavelength (λ = 350−370 nm). Its molar absorption coefficient ε is ≥3000 at 360 nm, whereas ε_{360} for the substrate is only 144; that is, it is by a factor of 20 smaller than ε_{360} of (+)-**3**. The significantly higher absorption of xanthone (+)-**3** seems to be important for the enantioselectivity. In the absence of the xanthone, 19% of starting material **4** (Table 5, entry 1) is converted after 1 h of irradiation into racemic product. If this reaction, which occurs by direct excitation of quinolone, was not suppressed, only a maximum ee of 81% could have been achieved. In other words, by harvesting all available photons, xanthone (+)-**3** channels the excitation of ground state (S_0) quinolone **4** into one possible mode occurring in the complex (+)-**3**·**4** (S_0). We have speculated earlier[25] that the sensitization occurs by energy transfer in this complex, thus generating the corresponding complex (+)-**3**·**4** (T_1), from which the photocycloaddition occurs. The question of whether xanthone (+)-**3** acts as an independent compound in the excitation step or whether the complex (+)-**3**·**4** (S_0) represents an absorption complex[35] needs to be further studied. In any case, intramolecular [2 + 2]-photocycloaddition (step 3) within the complex (+)-**3**·**4** (T_1) occurs highly enantioselectively from the bottom face of substrate **4**, while the top face is shielded by the oxazolo[4,5-*b*]xanthone part of catalyst (+)-**3**. Dissociation of the photoexcited quinolone **4** (T_1) is a competing pathway leading to racemic products **18**. In the case of substrate **5**, the lower photocycloaddition rate (relative to **4**) favors the dissociation, and this fact has been identified as a major reason for the low enantioselectivity observed in the conversion **5** → **19**.

Enantioselective Reactions of Substrates 6−9. From the mechanistic discussion in the previous section, it is apparent that the major issue regarding an enantioselective [2 + 2]-photocycloaddition of substrates **6**−**9** in the presence of xanthone (+)-**3** is the selective excitation (step 2). The rate of the [2 + 2]-photocycloaddition (step 3) was of less concern as the formation of five-membered rings was expected to be rapid. This is particularly true for substrate **6**, which bears a geminal dimethyl substitution (Thorpe−Ingold effect[36]). The outcome of the reactions is summarized in Table 6, with the previously discussed reactions of quinolones **4** and **5** included for comparison. Indeed, the xanthone-catalyzed reaction of the dimethyl-substituted compound **6** was more rapid (Table 6, entry 3) than the reaction of the parent substrate **4** (entry 1). After 1 h, the same conversion was observed for **6** as for **4** after 2 h. The enantioselectivity was high (85% ee) but did not completely match the selectivity achieved with quinolone **4**. The reason for the diminished selectivity appears to be the intrinsically lower enantiotopic face differentiation of the catalyst backbone as was already indicated by the reaction with stoichiometric amounts of template (+)-**1** (Table 2, entry 3).

As is apparent from Table 1, the background reaction, that is, the reaction occurring by direct excitation at λ = 366 nm, was significant for substrates **7**−**9**. Attempts to conduct the catalyzed photocycloaddition of substrates **7**−**9** at longer wavelength (λ = 419 nm) were not successful. However, it was possible to reduce the photon flux by reducing the number of fluorescent lamps. A reduction by a factor of 8 (2 instead of 16 lamps) led to a low conversion in the absence of a catalyst after 30 min. The reaction of substrate **7**, for example, went to 33% conversion with the complete lamp set but only to 9% conversion with two lamps. As a consequence, the catalytic effect of 10 mol % of catalyst (+)-**3** was significant, leading to a more than 5-fold increase in conversion (Table 6, entry 4) and to 72% ee. This procedure was even more successful for substrate **9**, which had given complete conversion after 30 min if the complete lamp set was used at −25 °C. The conversion was lowered to 22% under the modified conditions, and the rate acceleration in the presence of catalyst (+)-**3** was notable, resulting in 84% conversion (70% of isolated product) and a remarkable enantioselectivity of 87% ee (Table 6, entry 6). Only with sulfone **8** was it impossible to reduce the conversion significantly. Even more importantly, a catalytic effect was not observed. Because of the electron-withdrawing nature of the sulfone group, it is likely that the triplet energy of substrate **8** is not appropriate for sensitization leading to a disappointingly low enantiomeric excess (Table 6, entry 5).

■ CONCLUSION

The present study represents a first step toward a deeper understanding of enantioselective photochemical reactions catalyzed

by hydrogen-bonding sensitizers such as compounds (+)-**2** and (+)-**3**. It revealed the importance of kinetic factors in designing an optimal catalytic cycle, and it showed the scope and limitations regarding different 4-substituted quinolones. The reactions are preparatively useful for oxygen-, carbon-, and sulfur-tethered alkenes, which can react by rapid five-membered ring closure to yield the respective cyclobutane products in the photocycloaddition step. Regarding the excitation, it remains to be elucidated which mechanism accounts for the excitation of the quinolone in its reactive triplet state. Regarding a potential extension of this work, other substrates have to be found, which show a relatively large singlet−triplet gap and which do not absorb at longer wavelengths ($\lambda \leq 350$ nm). In this respect, it will be revealing to study the influence of various substituents at the quinolone chromophore on the photophysical and photochemical behavior of these substrates.

■ ASSOCIATED CONTENT

Supporting Information. Detailed experimental procedures, characterization data for new compounds, and experimental details of the photophysical measurements. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
mmiranda@qim.upv.es; thorsten.bach@ch.tum.de

■ ACKNOWLEDGMENT

This work was supported by the Deutsche Forschungsgemeinschaft (DFG) in Germany (Schwerpunktprogramm Organokatalyse and Graduiertenkolleg GRK 1626 Chemical Photocatalyis). Financial support from the Spanish Government is also acknowledged (JAE-doc fellowship for M.C.C. and CTQ2009-13699).

■ REFERENCES

(1) Lord Kelvin, W. T. *Baltimore Lectures 1884*; C. J. Clay & Sons: London, 1904; p 436, p 619.

(2) (a) Riehl, J. P. *Mirror-Image Asymmetry: An Introduction to the Origin and Consequences of Chirality*; Wiley: Hoboken, 2010. (b) Wagnière, G. H. *On Chirality and the Universal Asymmetry*; Verlag Helvetica Chimica Acta: Zürich, 2007. (c) Lough, W. J., Wainer, I. W., Eds. *Chirality in Natural and Applied Science*; Blackwell: Oxford, 2002.

(3) (a) Sakamoto, M. *J. Photochem. Photobiol., C* **2006**, *7*, 183–196. (b) Sakamoto, M. In *Molecular and Supramolecular Photochemistry (Vol. 11): Chiral Photochemistry*; Inoue, Y., Ramamurthy, V., Eds.; Dekker: New York, 2004; pp 415−461.

(4) (a) Sivaguru, J.; Natarajan, A.; Kaanumalle, L. S.; Shailaja, J.; Uppili, S.; Joy, A.; Ramamurthy, V. *Acc. Chem. Res.* **2003**, *36*, 509–521. (b) Shailaja, J.; Kaanumalle, L. S.; Sivasubramanian, K.; Natarajan, A.; Ponchot, K. J.; Pradhan, A.; Ramamurthy, V. *Org. Biomol. Chem.* **2006**, *4*, 1561–1571. (c) Sivasubramanian, K.; Kaanumalle, L. S.; Uppili, S.; Ramamurthy, V. *Org. Biomol. Chem.* **2007**, *5*, 1569–1576.

(5) Sakamoto, M.; Kato, M.; Aida, Y.; Fujita, K.; Mino, T.; Fujita, T. *J. Am. Chem. Soc.* **2008**, *130*, 1132–1133 and references cited therein.

(6) (a) Rau, H. In *Molecular and Supramolecular Photochemistry (Vol. 11): Chiral Photochemistry*; Inoue, Y., Ramamurthy, V., Eds.; Dekker: New York, 2004; pp 1−44. (b) Rau, H. *Chem. Rev.* **1983**, *83*, 535–547.

(7) Review: Müller, C.; Bach, T. *Aust. J. Chem.* **2008**, *61*, 557–564.

(8) Recent examples: (a) Yang, C.; Mori, T.; Origane, Y.; Ko, Y. H.; Selvapalam, N.; Kim, K.; Inoue, Y. *J. Am. Chem. Soc.* **2008**, *130*, 8574–8575. (b) Ke, C. F.; Yang, C.; Mori, T.; Wada, T.; Liu, Y.; Inoue, Y. *Angew. Chem., Int. Ed.* **2009**, *48*, 6675–6677. (c) Fukuhara, G.; Chiappe, C.; Mele, A.; Melai, B.; Bellina, F.; Inoue, Y. *Chem. Commun.* **2010**, *46*, 3472–3474.

(9) For a key reference to the use of hydrogen bonds for supramolecular control of photochemical reactivity in the solid state, see: MacGillivray, L. R.; Papaefstathiou, G. S.; Friscic, T.; Hamilton, T. D.; Bucar, D.-K.; Chu, Q.; Varshney, D. B.; Georgiev, I. G. *Acc. Chem. Res.* **2008**, *41*, 280–291.

(10) Examples: (a) Cauble, D. F.; Lynch, V.; Krische, M. J. *J. Org. Chem.* **2003**, *68*, 15–21. (b) Tanaka, K.; Fujiwara, T. *Org. Lett.* **2005**, *7*, 1501–1503. (c) Gerard, B.; Sangji, S.; O'Leary, D. J.; Porco, J. A., Jr. *J. Am. Chem. Soc.* **2006**, *128*, 7754–7755. (d) Mizoguchi, J.; Kawanami, Y.; Wada, T.; Kodama, K.; Anzai, K.; Yanagi, T.; Inoue, Y. *Org. Lett.* **2006**, *8*, 6051–6054. (e) Kawanami, Y.; Pace, T. C. S.; Mizoguchi, J.; Yanagi, T.; Nishijima, M.; Mori, T.; Wada, T.; Bohne, C.; Inoue, Y. *J. Org. Chem.* **2009**, *74*, 7908–7921.

(11) Bach, T.; Bergmann, H.; Grosch, B.; Harms, K.; Herdtweck, E. *Synthesis* **2001**, 1395–1405.

(12) (a) Bach, T.; Bergmann, H.; Grosch, B.; Harms, K. *J. Am. Chem. Soc.* **2002**, *124*, 7982–7990. (b) Grosch, B.; Orlebar, C. N.; Herdtweck, E.; Kaneda, M.; Wada, T.; Inoue, Y.; Bach, T. *Chem.-Eur. J.* **2004**, *10*, 2179–2189. (c) Selig, P.; Herdtweck, E.; Bach, T. *Chem.-Eur. J.* **2009**, *15*, 3509–3525. (d) Bakowski, A.; Dressel, M.; Bauer, A.; Bach, T. *Org. Biomol. Chem.* **2011**, *9*, 3516–3529.

(13) Austin, K. A. B.; Herdtweck, E.; Bach, T. *Angew. Chem., Int. Ed.* **2011**, *50*, 8416–8419.

(14) Bach, T.; Bergmann, H.; Harms, K. *Org. Lett.* **2001**, *3*, 601–603.

(15) (a) Aechtner, T.; Dressel, M.; Bach, T. *Angew. Chem., Int. Ed.* **2004**, *43*, 5849–5851. (b) Albrecht, D.; Vogt, F.; Bach, T. *Chem.-Eur. J.***2010**, *16*, 4284–4296. (c) See also: Bach, T.; Bergmann, H.; Brummerhop, H.; Lewis, W.; Harms, K. *Chem.-Eur. J.* **2001**, *7*, 4512–4521.

(16) Bach, T.; Aechtner, T.; Neumüller, B. *Chem.-Eur. J.* **2002**, *8*, 2464–2475.

(17) Bach, T.; Grosch, B.; Strassner, T.; Herdtweck, E. *J. Org. Chem.* **2003**, *68*, 1107–1116.

(18) For initial, seminal contributions to the area of enantioselective photochemical synthesis by sensitization, see: (a) Hammond, G. S.; Cole, R. S. *J. Am. Chem. Soc.* **1965**, *87*, 3256–3257. (b) Ouannès, C.; Beugelmans, R.; Roussi, G. *J. Am. Chem. Soc.* **1973**, *95*, 8472–8474. (c) Inoue, Y.; Yokoyama, T.; Yamasaki, N.; Tai, A. *Nature* **1989**, *341*, 225–226. (d) Vondenhof, M.; Mattay, J. *Chem. Ber.* **1990**, *123*, 2457–2459. (e) Kim, J.-I.; Schuster, G. B. *J. Am. Chem. Soc.* **1992**, *114*, 9309–9317.

(19) Dexter., D. L. *J. Chem. Phys.* **1953**, *21*, 836–850.

(20) Oevering, H.; Paddon-Row, M. N.; Heppener, M.; Oliver, A. M.; Cotsaris, E.; Verhoeven, J. W.; Hush, N. S. *J. Am. Chem. Soc.* **1987**, *109*, 3258–3269.

(21) Bauer, A.; Westkämper, F.; Grimme, S.; Bach, T. *Nature* **2005**, *436*, 1139–1140.

(22) (a) Wessig, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 2168–2171. (b) Inoue, Y. *Nature* **2005**, *436*, 1099–1100.

(23) General reviews: (a) Hehn, J. P.; Müller, C.; Bach, T. In *Handbook of Synthetic Photochemistry*; Albini, A., Fagnoni, M., Eds.; Wiley-VCH: Weinheim, 2010; pp 171−215. (b) Iriondo-Alberdi, J.; Greaney, M. F. *Eur. J. Org. Chem.* **2007**, 4801–4815. (c) Fleming, S. A. In *Molecular and Supramolecular Photochemistry*; Griesbeck, A. G., Mattay, J., Eds.; M. Dekker: New York, 2005; Vol. 12, pp 141−160. (d) Margaretha, P. In *Molecular and Supramolecular Photochemistry*; Griesbeck, A. G., Mattay, J., Eds.; M. Dekker: New York, 2005; Vol. 12, pp 211−237. (e) Bach, T. *Synthesis* **1998**, 683–703. (f) Mattay, J.; Conrads, R.; Hoffmann, R. *Methoden Org. Chem.*; Houben-Weyl, 1995; Vol. E 21c, pp 3085−3132. (g) Crimmins, M. T.; Reinhold, T. L. *Org. React.* **1993**, *44*, 297–588. (h) Becker, D.; Haddad, N. *Org. Photochem.* **1989**, *10*, 1–162. (i) Crimmins, M. T. *Chem. Rev.* **1988**, *88*, 1453–1473. (j) Baldwin, S. V. *Org. Photochem.* **1981**, *5*, 123–225. (k) Bauslaugh, P. G. *Synthesis* **1970**, 287–300.

(24) Kaneko, C.; Suzuki, T.; Sato, M.; Naito, T. *Chem. Pharm. Bull.* **1987**, *35*, 112–123.

(25) Müller, C.; Bauer, A.; Bach, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 6640–6642.
(26) Ochiai, E. *J. Org. Chem.* **1953**, *18*, 534–551.
(27) (a) Eilbracht, P.; Acker, M.; Rosenstock, B. *Chem. Ber.* **1989**, *122*, 151–158. (b) Boyd, V. L.; Summers, M. F.; Ludeman, S. M.; Egan, W.; Zon, G.; Regan, J. B. *J. Med. Chem.* **1987**, *30*, 366–374.
(28) Minozzi, M.; Nanni, D.; Walton, J. C. *Org. Lett.* **2003**, *5*, 901–904.
(29) (a) Albini, A.; Fasani, E.; Dacrema, L. M. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2738–2742. (b) Albini, A.; Alpegiani, M. *Chem. Rev.* **1984**, *84*, 43–71.
(30) Sorg, A.; Brückner, R. *Synlett* **2005**, 289–293.
(31) (a) Wolfe, J. F.; Trimitsis, G. B.; Morris, D. R. *J. Org. Chem.* **1969**, *34*, 3263–3268. (b) Martin, O.; de la Cuesta, E.; Avendaño, C. *Tetrahedron* **1995**, *51*, 7547–7554.
(32) (a) Courtois, G.; Mesnard, D.; Dugue, B.; Miginiac, L. *Bull. Chim. Soc. Fr.* **1987**, 93–98. (b) Jacobson, M. A.; Williard, P. G. *J. Org. Chem.* **2002**, *67*, 3915–3918.
(33) For some key references on the [2 + 2]-photocycloaddition of quinolones, see: (a) Evanega, G. R.; Fabiny, D. L. *J. Org. Chem.* **1970**, *35*, 1757–1761. (b) Kaneko, C.; Naito, T. *Chem. Pharm. Bull.* **1979**, *27*, 2254–2256. (c) Naito, T.; Kaneko, C. *Chem. Pharm. Bull.* **1980**, *28*, 3150–3152. (d) Lewis, F. D.; Reddy, G. D.; Elbert, J. E.; Tillberg, B. E.; Meltzer, J. A.; Kojima, M. *J. Org. Chem.* **1991**, *56*, 5311–5318. (e) See also refs 12,24.
(34) (a) Bach, T.; Bergmann, H.; Harms, K. *Angew. Chem., Int. Ed.* **2000**, *39*, 2302–2304. (b) Bergmann, H. Ph.D. thesis, Universität Marburg, 2001.
(35) Turro, N. J.; Ramamurthy, V.; Scaiano, J. C. *Modern Molecular Photochemisty of Organic Compounds*; University Science Books: Sausalito, CA, 2010; pp 247−249.
(36) (a) Beesley, R. M.; Ingold, C. K.; Thorpe, J. F. *J. Chem. Soc., Trans.* **1915**, 1080–1106. (b) Jung, M. E.; Gervay, J. *J. Am. Chem. Soc.* **1991**, *113*, 224–232. (c) Bachrach, S. M. *J. Org. Chem.* **2008**, *73*, 2466–2468.