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Photochemistry of 4-(2′-Aminoethyl)quinolones: Enantioselective Synthesis of Tetracyclic Tetrahydro-1a*H*-pyrido[4′,3′:2,3]-cyclobuta[1,2-*c*] Quinoline-2,11(3*H*,8*H*)-diones by Intra- and Intermolecular [2 + 2]-Photocycloaddition Reactions in Solution

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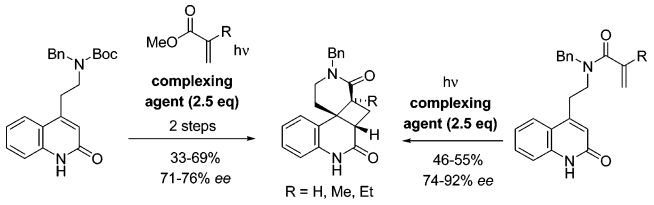
Received March 28, 2006



Enantioselective [2 + 2]-photocycloaddition reactions on 4-(2′-aminoethyl)quinolones in solution were studied using the enantiomerically pure complexing agent **1** as source of chirality. The intermolecular reactions of fully N-protected substrates **5a**−**5c** with different 2-alkyl-substituted acrylates **12**−**15** represent the first systematic study on the diastereoselectivity of their intermolecular [2 + 2]-photocycloadditions to unsymmetrically 1,1-disubstituted olefins (75−91% yield, d.r. = 58/42−95/5). *N*-Benzylic-protected photoproducts ***exo*-16a/b**−**19a/b** could easily be converted into lactams **20a/b**−**23a/b** by a sequence of Boc deprotection and thermal lactamization (74−98% yield). Identical products **20a**−**22a** were directly accessible by the intramolecular [2 + 2]-photocycloaddition of acrylic acid amides **2**−**4** (41−61% yield). The suitability of both pathways for an enantioselective reaction variant was proven (70−92% ee). Thus, tetracyclic lactams possessing the carbon framework **C** were obtained with good yields and enantioselectivities of up to 92% ee in intramolecular reactions. Comparative investigation of both routes showed that quinolone dimerization was the single most decisive factor preventing a complete chirality transfer. Functional group manipulations were successfully conducted with the primary photoproduct ***exo*-17a**. Finally, a new and unexpected type of benzylic hydrogen abstraction−radical cyclization reaction was discovered for substrate **5a**, which explains the photochemical instability of substrates **2**−**5** under short wavelength irradiation (λ = 300 nm).

Introduction

The incorporation of a quinoline moiety within a monoterpenoid alkaloid skeleton represents a very rare structural feature in the world of natural products, uniquely found in a small group of alkaloids from the Apocynacea species *Melodinus spp.*[1] Following its close structural relationship with indole alkaloids of the *Aspidospermine*[2] and *Leuconolam* type, several biomimetic syntheses of the pentacyclic *Melodinus* ring system **A** have been accomplished.[3] However, only a single racemic total synthesis of the prototypical compound (±)-meloscine[4] has been reported to date,[5] and attempts at an asymmetric synthesis have remained limited to the upper [5,6,5] tricyclic core structure.[6] All of the above-mentioned biomimetic and total synthetic methods rely on the formation of the quinoline moiety in a late or final step of the synthesis.

Following a fundamentally different approach and starting from intact 2-quinolones, we plan to access the lower part of the *Melodinus* ring system **B** using a 1,2-rearrangement of precursor structure **C** (Figure 1).[7] The envisioned diastereoselective 1,2-σ-bond shift should ideally conserve the stereogenic centers on the quinolone *c*-bond. Thus, complete stereocontrol

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10.1021/jo0606608 CCC: $33.50
Published on Web 06/28/2006

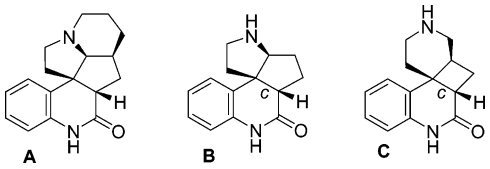

FIGURE 1. General structures of the *Melodius* alkaloid ring system **A** and the envisioned precursor structures **B** and **C**.

of the [3.3.0]-bicyclic structure **B** should be feasible via a stereoselective synthesis of the preceding [4.2.0]-bicyclic ring system **C**.

Cyclobuta[1,2-c]quinolones such as **C** are well-known to be accessible by the [2 + 2]-photocycloaddition reaction[8] of olefins and 2-quinolone.[9,10] This reaction has been thoroughly investigated for simple 4-alkoxyquinolones by Kaneko and Naito.[11] Preliminary investigations in our group suggested the applicability of this method also for bulky N-protected 4-(2′-aminoethyl)-quinolones.[12] As an important feature of the photochemical synthesis of structure **C**, the 2-quinolone substrates allow for the [2 + 2]-photocycloaddition to be conducted in an enantioselective fashion. Enantioselectivity arises from the efficient hydrogen bond-mediated complexation to the chiral complexing agent **1** (Figure 2). In such a complex, the bulky tetrahydronaphthalene shield effectively blocks one of the two enantiotopic faces of the prochiral, planar quinolone substrates and thus creates the necessary chiral environment for the enantioselective reaction to occur.[13]

Enantioselective photochemical reactions have long been and still are an especially challenging field of synthetic organic chemistry. Creation of a chiral environment around achiral substrates has been successfully achieved in the solid state, especially in homochiral crystals.[14] Alternative approaches

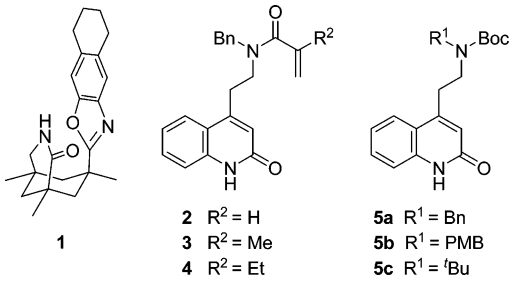

FIGURE 2. Structure of the chiral complexing agent **1** and the quinolone substrates for the intra- (**2**−**4**) and intermolecular (**5a**−**5c**) enantioselective [2 + 2]-photocycloadditions.

employ, for example, inclusion complexes,[15] ionic auxiliaries,[16] or chirally modified zeolites.[17] While these solid-state reactions are generally limited to intramolecular transformations,[18] reactions in solution naturally greatly expand the scope of suitable substrates.[19] However, these synthetically more useful enantioselective photoreactions in solution, achieved for example by means of chiral solvents[20] or circularly polarized light,[21] until recently gave only mediocre results with respect to both yields and enantioselectivities.[22,23] The advent of the chiral complexing

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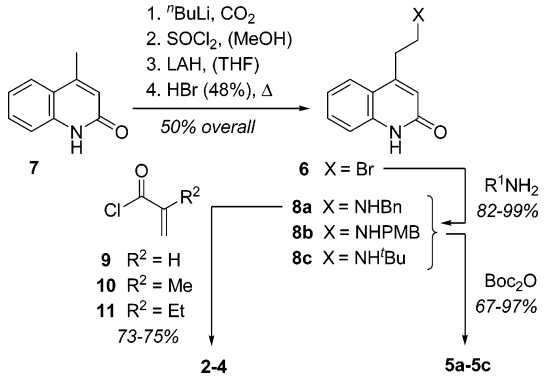
agent **1** has significantly changed this picture and enabled both intra- and intermolecular photochemical reactions in solution to be performed with unprecedented yields and enantiomeric purities.[24]

Compound **1** derived from Kemp's triacid[25] was originally designed in our laboratories to enable enantioselective [2 + 2]-photocycloadditions,[26,27] but additional applications for various types of photochemical transformations have been established.[28] Recently, the application of **1** has been successfully expanded to enantioselective radical cyclizations,[29] and it has been used as an NMR analytical tool.[30] To date, complexing agent **1** is the most efficient compound for enantioselective photoreactions mediated by hydrogen bonding to a chiral receptor,[31] although its use is naturally limited to sufficiently complexable substrate structures such as quinolones or pyridones.[32]

Following our preliminary studies on the synthesis of compounds possessing the carbon skeleton **C**,[12] we present here in detail our work on the intra- and intermolecular racemic and enantioselective [2 + 2]-photocycloadditions of quinolones **2**−**5** (Figure 2). Until now (with the single exception of diketene photocycloaddition[33]) no example of an intermolecular [2 + 2]-photocycloaddition between a quinolone and an unsymmetrically 1,1-substituted olefin has been reported, and only the simple 4-methoxyquinolone has been studied in the enantioselective intermolecular [2 + 2]-photocycloaddition using the chiral complexing agent **1**.[13,27] Thus, a first detailed study was conducted on the intermolecular [2 + 2]-photocycloaddition between N-protected quinolones **5a**−**5c** and different 2-alkyl-substituted acrylates, both under racemic and chiral reaction conditions. Leading to identical tetracyclic 1,9,10,11a-tetrahydro-1a*H*-pyrido[4′,3′:2,3]-cyclobuta[1,2-*c*]quinoline-2,11-(3*H*,8 *H*)-diones of structure **C**, a detailed comparison between inter- and intramolecular reaction pathways was possible. In addition to the anticipated [2 + 2]-photocycloaddition, benzyl-protected substrate **5a** was shown to undergo a new and unexpected type of photochemical hydrogen abstraction−radical cyclization reaction. Finally, different precursors for the desired 1,2-rearrangement were accessible from functional group manipulations on cyclobuta[*c*]quinolone carboxylates.

SCHEME 1



Results and Discussion

Preparation of Starting Materials. All starting materials **2**−**5** were synthesized starting from the common precursor 4-bromoethylquinolone (**6**), which was easily available using a literature-known four-step transformation of inexpensive 4-methylquinolone (**7**).[34] The synthesis of the chiral complexing agent **1** has been reported previously.[35]

As depicted in Scheme 1, reaction of **6** with neat primary amines gave the intermediate *N*-alkylamines **8a**−**8c** in high yields. For all following substances differing only in the *N*-alkyl protecting group, lower case letters **a**−**c** will be used to distinguish between the benzyl (**a**), *para*-methoxybenzyl (PMB, **b**), and *tert*-butyl (**c**) residue. Acylation of amine **8a** with acrylic acid chlorides **9**−**11** to the corresponding amides **2**−**4** proceeded surprisingly well, despite the methylenic α,β-unsaturation of the acid chlorides. The substrates for intramolecular reactions already incorporate an *N*-acyl protecting group necessary for successful [2 + 2]-photocycloadditions. Simple amines generally suffer from severe side reactions due to photoinduced electron transfer under irradiation.[36] Thus, amines **8a**−**8c** were *N*-Boc-protected to give the desired substrates **5a**−**5c** for the intermolecular reactions. The Boc protective group was chosen because of its high stability, a significant enhancement of substrate solubility in apolar solvents, and the possibility of mild cleavage orthogonal to the *N*-alkyl groups.[37] While **8a**,**8b** were easily protected in high yields (>90%) using di-*tert*-butyldicarboxylate (Boc_2O) in CH_2Cl_2, the attempted acylation of sterically hindered *tert*-butylamine **8c** either showed insufficient substrate conversion or lacked selectivity if more drastic reaction conditions were employed. Selective Boc protection to **5c** was finally achieved in acceptable yields (67%) under solvent-free conditions using an excess of Boc_2O at 100 °C.[38] All desired 4-(2′-aminoethyl)quinolones were thus obtained in high yields and multigram quantities by simple and robust two-step sequences.

To grant a maximum of comparability with the intramolecular [2 + 2]-photocycloadditions of acrylic acid amides **2**−**4**, 2-alkyl-substituted acrylates were chosen as olefin components in the intermolecular reactions. Methyl acrylate (**12**), methyl meth-

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SCHEME 2

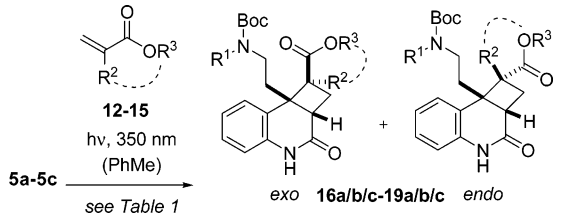

TABLE 1. Intermolecular [2 + 2]-Photocycloaddition Reactions between Quinolones 5a−5c (5−30 mM) and Acrylates 12−15 (5−20 Equiv) in Toluene at λ = 350 nm (RPR 3500 Å, 35 °C)

entry	substrate	acrylate	R^1	R^2	R^3	product	yield[a] (%)	d.r.[b] (exo/endo)
1	**5a**	**12**	Bn	H	CH_3	**16a**	80	92/8
2	**5a**	**13**	Bn	CH_3	CH_3	**17a**	89	73/27
3	**5a**	**14**	Bn	CH_2CH_3	CH_3	**18a**	75	58/42
4	**5a**	**15**	Bn	$-CH_2CH_{2-}$		**19a**	82	72/28[c]
5	**5b**	**12**	PMB	H	CH_3	**16b**	87	>90/10
6	**5b**	**13**	PMB	CH_3	CH_3	**17b**	84	71/29
7	**5b**	**14**	PMB	CH_2CH_3	CH_3	**18b**	91	60/40
8	**5b**	**15**	PMB	$-CH_2CH_{2-}$		**19b**	74	71/29[c]
9	**5c**	**12**	^{t}Bu	H	CH_3	**16c**	91	>95/5
10	**5c**	**13**	^{t}Bu	CH_3	CH_3	**17c**	77	83/17
11	**5c**	**14**	^{t}Bu	CH_2CH_3	CH_3	**18c**	76	69/31
12	**5c**	**15**	^{t}Bu	$-CH_2CH_{2-}$		**19c**	83	80/20[c]

[a] Yield of isolated products (sum of both diastereoisomers). [b] d.r. determined by HPLC and NMR analysis of the crude product mixture. [c] Diastereoisomers were completely separated. The given d.r.'s correspond to isolated, pure exo- and endo-diastereoisomers.

acrylate (**13**), and its cyclic analogue tulipaline (**15**) were commercially available. Methyl-2-ethyl acrylate (**14**) was prepared according to established procedures[39] and converted to its acyl chloride **11** by straightforward reaction with $SOCl_2$.[40]

Racemic [2 + 2]-Photocycloaddition Experiments. For intermolecular [2 + 2]-photocycloadditions, the N-protected quinolones **5a−5c** were irradiated with a moderate excess of acrylates **12−15** to give an array of 12 (3 × 4) photoproducts (Scheme 2). In contrast to our previous experiments on similar aminoethylquinolones, irradiation at λ = 300 nm proceeded sluggishly and gave complex mixtures without defined cycloaddition products (vide infra). Hence, irradiations were conducted in toluene solution in a Rayonet photoreactor with a wavelength of λ = 350 nm (RPR 3500 Å) at 35 °C. These irradiations proceeded smoothly in the concentration range of 5−30 mM of quinolone and with 5−20 equiv of acrylate to give the desired photoproducts **16a/b/c−19a/b/c** in high yields. In addition to a linear correlation between quinolone concentration and the reaction time until complete conversion (5−30 mM ↔ 0.5−3.0 h), variations of substrate concentration were without significant influence on the outcome of the reactions. The results of the racemic intermolecular [2 + 2]-photocycloaddition reactions are summarized in Table 1.

All [2 + 2]-photocycloadditions resulted exclusively in the formation of cis-annelated *head-to-tail* (HT) products. The observed regioselectivity is in clear contrast to the so-called Corey−De Mayo rules,[41] predicting a favored formation of *head-to-head* (HH) products for acceptor-substituted olefins.[42,43] The exclusive formation of cis-fused cyclobuta[*c*]quinolones is most conveniently explained by the steric rigidity of the quinolone ring.[9] As with simple 4-methoxyquinolone, the reaction with 2-unsubstituted methyl acrylate (**12**) additionally displayed a high degree of simple diastereoselectivity,[44] with the exo-HT products **16a−16c** formed almost exclusively (entries 1, 5, and 9). With R^2 = Et only a slight preference for the exo-products was preserved. Fortunately, the diastereoisomeric mixtures were at least partly separable using simple flash chromatography, with the separation becoming increasingly difficult for unpolar, especially ^{t}Bu-protected photoproducts. In contrast, the most polar diastereomeric tulipaline cycloadducts **19a−19c** were separable without problem. Sufficiently pure samples of all exo-diastereoisomers **16a/b/c−19a/b/c** could thus be obtained, yet isolation of pure endo-diastereoisomers of **17c**, **18b**, and **18c** was not achieved. While the diastereoselectivity of the reactions was profoundly dependent on the nature of acrylate substituents R^2, sterically constraining the acrylate ester moiety in a cyclic system exhibited no significant effect. The spirocyclic lactones **19a−19c** displayed nearly identical diastereomeric ratios (d.r.) as their open-chain analogues **17a−17c**. While the strong influence of the acrylate substitution was not unexpected, the observed effect of the *N*-alkyl protecting groups on the diastereomeric ratios came as a surprise. These groups are both electronically separated and sterically distant from the reacting quinolone double bond. However, *N*-^{t}Bu-protected quinolone **5c** repeatedly exhibited a degree of exo-diastereoselectivity (entries 9−12) higher than that of the benzylic-protected substrates **5a** and **5b** (entries 1−8). The surplus of exo-isomers generally consisted of 15−20%. In contrast, only a slight electronic modification of the benzyl protective group (Bn vs PMB) left the obtained diastereomeric ratios unaffected. The influence of the ^{t}Bu group can therefore best be explained by its steric influence on the intermediate 1,4-diradical species formed in the course of the [2 + 2]-photocycloaddition. The competition between diradical cleavage and ring closure is well-known to decisively affect both the regio- and the diastereoselectivity of [2 + 2]-photocycloadditions.[42,45] A steric effect of the ^{t}Bu group on the corresponding relative rate constants does not seem unlikely.[46]

Intramolecular racemic [2 + 2]-photocycloaddition reactions of acrylic acid amides **2−4** were carried out under the same conditions established for intermolecular irradiations (toluene solution, RPR 3500 Å, λ = 350 nm, 35 °C). However, in contrast to the high yields of photoproducts obtained in the intermolecular reactions, the six-membered lactams **20a−22a** could only be isolated in moderate yields (Scheme 3, upper section). Due to steric constraints, cis-cis-annelated tetracyclic products with a *straight* cyclobutane and a six-membered lactam

(39) (a) Iwakura, Y.; Sato, M.; Matsuo, Y. *Chem. Abstr.* **1961**, 3427−3228. (b) Attu-Ur-Rahman; Beisler, J. A.; Harley-Mason, J. *Tetrahedron* **1979**, *36*, 1063−1070.

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(42) Erickson, J. A.; Kahn, S. D. *Tetrahedron* **1993**, *49*, 9699−9712.

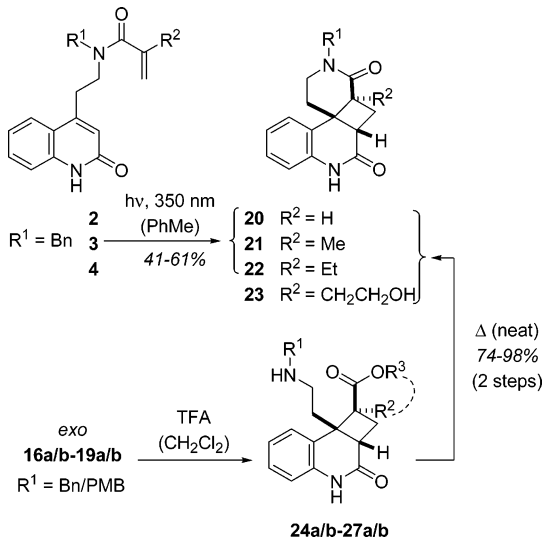
(43) For alternative mechanistic explanations of the regioselectivity of intermolecular [2 + 2]-photocycloaddtions, see: (a) Schuster, D. I.; Lem, G.; Kaprinidis, N. A. *Chem. Rev.* **1993**, *93*, 3−22. (b) Bauslaugh, P. G. *Synthesis* **1970**, *2*, 287−300.

(44) Kaneko, C.; Naito, T. *Chem. Pharm. Bull.* **1979**, *27*, 2254−2256.

(45) Andrew, D.; Hastings, D. J.; Weedon, A. C. *J. Am. Chem. Soc.* **1994**, *116*, 10870−10882.

(46) For studies about the importance of intermediate diradicals in Paterno−Büchi photocycloaddition, see: Abe, M.; Kawakami, T.; Ohata, S.; Nozaki, K.; Nojima, M. *J. Am. Chem. Soc.* **2004**, *126*, 2838−2846.

SCHEME 3



ring were formed exclusively.[47] *Crossed* products or transannelation could not be detected in any case. Even at substrate concentrations as low as 5 mM, formation of polar side products was evident, indicated by the occurrence of insoluble, yellow precipitates. The effect was most pronounced for α-unsubstituted substrate **2**, yielding only 41% of the desired product **20a**, but yields did not exceed 61% for α-methyl and α-ethyl lactams **21a** and **22a**, either. Since the *N*-benzyl aminoethylquinolones have already shown a high reactivity in intermolecular reactions even with a comparably low amount of olefinic reaction partner, these precipitates most probably originate from intermolecular oligomerization of the substrate molecules. However, further reduction of the substrate concentration to values as low as 0.5 mM did not significantly drive back these undesired reactions. A strong tendency toward the formation of associates even in very dilute solutions was therefore assumed, which was confirmed in consecutive experiments (vide infra).

Tetracyclic lactams **20a/b**−**23a/b** could also be synthesized from the products of the intermolecular [2 + 2]-photocycloaddition using a two-step sequence of Boc deprotection and thermal lactamization (Scheme 3, lower section). Thus, lactams **20a**−**22a** were accessible by both inter- and intramolecular [2 + 2]-photocycloaddition and proved identical in both physical and spectroscopic properties regardless of the synthetic method applied. Cleavage of the *N*-Boc-group with 10% v/v trifluoroacetic acid (TFA) in CH_2Cl_2 proceeded smoothly with yields generally >80% for all photoproducts. Due to the steric constraints mentioned before, only photoproducts with the carboxyl group exo relative to the bicyclic cyclobutane system were suitable for lactamization. The endo substituents R^2 showed a remarkably strong influence on the reactivity of the free secondary amines **24a/b**−**27a/b**. Spirocyclic lactones **27a** and **27b** already cyclized to a large extent under the standard workup conditions of the Boc deprotection due to relief of ring strain. Conversion could be completed by short heating of the product to 70 °C in toluene. Crude amines **24a** and **24b** with no endo substituent (R^2 = H) also showed a moderate amount of condensation products **20a** and **20b** after *N*-Boc deprotection, yet completion of the reaction required longer heating in toluene

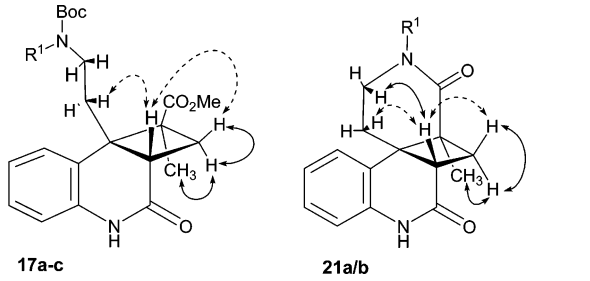


FIGURE 3. Significant NOE contacts in cyclobuta[*c*]quinolones **17a**−**17c** and tetracyclic lactams **21a**,**21b** (solid line: strong; broken line: weak).

to 110 °C. In contrast, α-alkyl-substituted aminoesters **25a**,**25b** and **26a**,**26b** were stable substances, indicating a profound influence of the alkyl substituent on the preferred relative conformation of the carboxylic ester. Even prolonged refluxing in toluene resulted only in traces of the desired product **22a**,**22b** for R^2 = Me, and free amines **26a**,**26b** (R^2 = Et) remained completely unchanged under these conditions. Lactamization of these hindered substrates could eventually be achieved by simple heating of the crude aminoesters above their respective melting points under Ar.[48] The condensation was clearly apparent by the evolution of gaseous methanol at 170−220 °C, and yields were high to excellent in all cases. Neat heating in an inert atmosphere generally proved to be the quickest and highest-yielding method of lactamization for all intermediates **24a/b**−**27a/b** regardless of their residues R^2. All *N*-Bn and *N*-PMB-protected amines were thus easily converted to the corresponding eight tetracyclic lactams **20a/b**−**23a/b** in high overall yields. As expected, *t*Bu-protected amines were completely unreactive toward lactamization, due to the steric bulk of the N-substituent. Even prolonged heating of model compound **24c** (R^2 = H) to 220 °C only resulted in a slow decomposition with no cyclization product being observable.

The synthesis of the desired lactams was generally higher yielding by the intermolecular than by the intramolecular [2 + 2]-photocycloaddition route. The efficiency of the intermolecular route was, however, somewhat limited by the diastereomeric ratios of the photocycloaddition step. Thermal lactamization was not significantly impaired when the reaction was carried out in a diastereoisomeric mixture. However, the decomposition of endo-diastereoisomers to various polar side products made the separation of pure lactams much more difficult. In summary, synthesis of the desired lactams was most efficient via the intermolecular route for R^2 = H and R^2 = CH_2CH_2OH (**20a**,**20b** and **23a**,**23b**). Unfavorable diastereoselectivities in intermolecular [2 + 2]-photocycloadditions with R^2 = Me and R^2 = Et rendered the intramolecular route more favorable for lactams **21a** and **22a.** Unfortunately, this alternative route showed inferior yields in both the acylation and the cycloaddition steps.

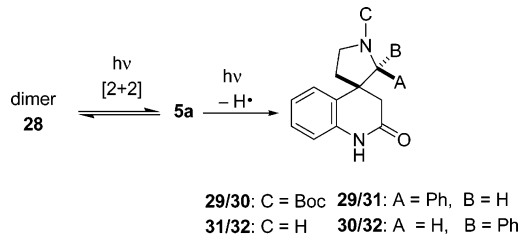
Lactamization finally served as an ultimate proof of the assignment of relative configurations to exo- and endo-diastereoisomers, which was previously conducted on the basis of observable NOE contacts in photocycloaddition products **16**−**19** (Figure 3).

Kinetic Studies, H-Abstraction, and Intramolecular Radical Cyclization of Substrate 5a. As discussed earlier, *N*-benzyl-protected aminoethylquinolones **2**−**4** and **5a** were nicely suited

(47) For the regioselectivity of intramolecular [2 + 2]-photocycloadditions, see: Liu, R. S. H.; Hammond, J. S. *J. Am. Chem. Soc.* **1967**, *89*, 4936−4944.

(48) Schnell, H.; Nentwig, J. In *Methoden der Organischen Chemie (Houben-Weyl)*; Thieme: Stuttgart, 1958; Vol. XI/2, p 529.

SCHEME 4



for [2 + 2]-photocycloaddition reactions using an irradiation wavelengths of $\lambda = 350$ nm. To elucidate the unexplained side reactions arising from irradiations at $\lambda = 300$ nm, model compound **5a** was irradiated without an olefinic reaction partner at both wavelengths. Detailed HPLC studies of the reaction mixtures unexpectedly indicated the formation of three new substances, all of which could be isolated in pure form (Scheme 4).

Product **28** arose from a reversible [2 + 2]-photocycloaddition of two molecules of **5a** and could clearly be identified as a substrate dimer by means of NMR and ESI-MS spectroscopy. As even small substituents in the 4-position of 2-quinolones have been reported to severely hinder quinolone dimerization,[49] the occurrence of up to 36% yield of isolated substrate dimer came as a surprise. Spectroscopic methods remained futile in the assignment of dimer stereochemistry, and thus an HH-cis-anti-cis connection can only be assumed following earlier studies.[50] The two remaining products were identified as the diastereoisomeric *spiro*-pyrrolidines **29** and **30**. These products possibly resulted from an initial hydrogen abstraction at the *N*-benzylic position via a seven-membered transition state and a subsequent radical process. An alternative mechanism involving a photoelectron transfer (PET) from the *N*-Boc-protected nitrogen atom to the excited quinolone and subsequent benzylic H-abstraction seems unlikely due to the high oxidation potential of amides and especially carbamates.[51] While PET-promoted photocyclization reactions are well-known for alkylamines,[52] corresponding reactions of alkylcarbamates have not been reported, and the only carbamates successfully employed in PET-promoted radical cyclization reactions thus far were additionally stabilized by α-silyl substituents.[53,54] As NOE spectroscopy again could give no clear configuration assignment for either **29** and **30** or their respective *N*-Boc-deprotected derivatives **31** and **32**, the attribution of relative configuration was based on the strong anisotropic effect of the aromatic phenyl ring on ^{1}H chemical shifts of different parts of the quinolone residue. While the two spirocyclic products were always obtained in a ratio of roughly 50/50, the relative ratios of pyrrolidines vs dimerization product were strongly dependent on the reaction time (Figure 4). Irradiation of isolated dimer **28** resulted in the formation of both products **29** and **30** and the substrate **5a**, the former two being unreactive toward further irradiation in pure form.

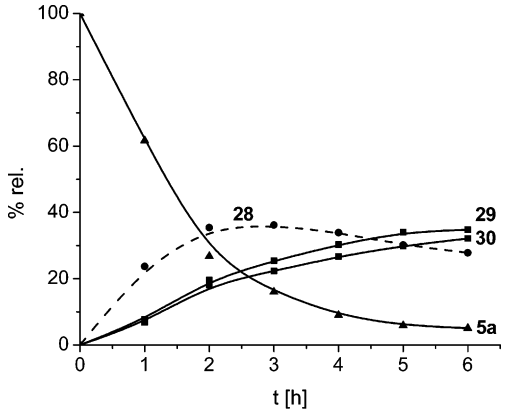


FIGURE 4. Time profile of the irradiation of pure quinolone **5a** (10 mM, toluene) at $\lambda = 350$ nm. The relative amounts of substrate and products were determined by HPLC analysis of the reaction mixture.

At first glance, Figure 4 seems to indicate a consecutive reaction with dimer **28** serving as an intermediate. This could be disproved by the following observations. First, reduction of the substrate concentration to 2.5 mM did markedly lower the amount of dimer **28** but was without any effect on the rate of formation of **29** and **30**. Second, in all irradiation experiments substrate **5a** was never entirely consumed but remained present in different, albeit small, equilibrium amounts. Hydrogen abstraction and [2 + 2]-dimerization therefore most likely constitute two independent types of reaction. Upon switching the irradiation wavelength from $\lambda = 350$ nm to $\lambda = 300$ nm, only minimal amounts of [2 + 2]-photodimer **28** could be observed and the formation of radical cyclization products was accelerated. A total of 66% of analytically pure *spiro*-pyrrolidines **29**/**30** (d.r. = 50/50) could be isolated. Thus, irradiation at $\lambda = 300$ nm seems to favor H-abstraction, while $\lambda = 350$ nm favors [2 + 2]-photocycloaddition. The pronounced influence of the excitation wavelength on the type of dominant photoreaction suggests that different types of excited states give rise to photocycloaddition and H-abstraction. [2 + 2]-Photocycloadditions on 2-quinolones are thought to originate from the lowest-lying triplet state,[10] resulting primarily in 1,4-diradicals after reaction with the olefin component. In contrast, the observed type of H-abstraction could be the result of electronically different intermediates formed by higher-energy excitation. ^{t}Bu-substituted quinolone **5c** was irradiated to measure the efficiency of the [2 + 2]-photocycloaddition without the concurrence of H-abstraction. As expected, only an equilibrium between substrate and dimer was observed. The amount of dimer was 6.5% at $\lambda = 300$ nm and 69% at $\lambda = 350$ nm. Contrary to benzylic amine **5a**, addition of 5 equiv of methyl acrylate (**12**) gave high yields of the [2 + 2]-product **16c** for both 350 *and* 300 nm. The reaction of **5c** at $\lambda = 300$ nm proceeded approximately 2−3 times more slowly than at $\lambda = 350$ nm. This can conveniently be explained by the overall smaller integral overlap of the long wavelength absorption spectrum of quinolone **5c** and the emission spectrum of RPR 3000 Å compared to RPR 3500 Å lamps.

The competition of hydrogen abstraction from the *N*-benzylic position and subsequent radical reactions was therefore undoubtedly the decisive reason for futile [2 + 2]-photocycloaddition attempts of substrates **5a** and **5b** at $\lambda = 300$ nm. This undesired reaction is considerably slowed at $\lambda = 350$ nm in favor of [2 + 2]-cycloaddition and can be completely suppressed

(49) Buchardt, O. *Acta Chem. Scand.* **1964**, *18*, 1389−1396.
(50) Taylor, E. C.; Paudler, W. W. *Tetrahedron Lett.* **1960**, *25*, 1−3.
(51) Yoshida, J.-I.; Isoe, S. *Tetrahedron Lett.* **1987**, *28*, 6621−6624.
(52) Example: Xu, W.; Zhang, X.-M.; Mariano, P. S. *J. Am. Chem. Soc.* **1991**, *113*, 8863−8878.
(53) Example: Jeon, Y. T.; Lee, C.-P.; Mariano, P. S. *J. Am. Chem. Soc.* **1991**, *113*, 8847−8863.
(54) For the lowering effect of α-silyl substituents on oxidation potentials, see: (a) Cooper, B. E.; Owen, W. J. *J. Organomet. Chem.* **1971**, *29*, 33−40. (b) Yoshida, J.-I.; Maekawa, T.; Murata, T.; Matsunaga, S.-I.; Isoe, S. *J. Am. Chem. Soc.* **1990**, *112*, 1962−1970.

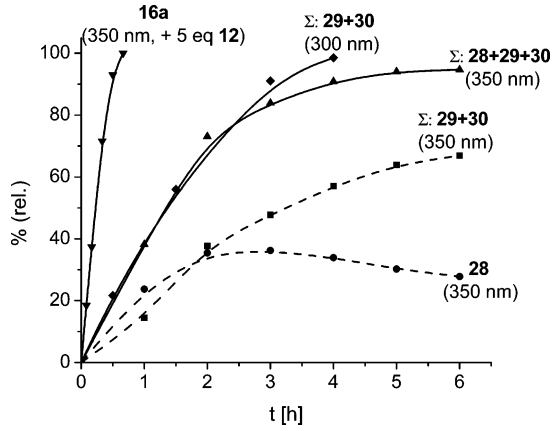


FIGURE 5. Photochemical product formation via [2 + 2]-photocycloaddition and/or hydrogen abstraction from substrate **5a** ($c = 10$ mM) using different excitation wavelengths.

with a slight excess of a suitable olefinic reaction partner. A comparison of reaction kinetics is depicted in Figure 5. Remarkably, both types of photoreactions displayed zero-order kinetics. It was therefore concluded that the reaction rates were mainly limited by the photon flux over a broad concentration range. Substrate limitation was a crucial factor only at the end of the reaction, that is, at substrate concentrations <10% (rel.) or <1 mM, respectively.

Enantioselective [2 + 2]-Photocycloaddition Experiments. Enantioselective intra- and intermolecular [2 + 2]-photocycloadditions with the chiral complexing agent **1** were performed using conditions previously established to grant a maximum of substrate complexation.[27] Most importantly, an excess of 2.5 equiv of **1** was necessary to override self-association of the 2-quinolones. It is important to note here that self-association of enantiopure **1** itself is effectively zero (see Supporting Information), due to the steric bulk of the tetrahydronaphthalene shield.[13] To further diminish impairment of hydrogen bond formation by solvent molecules or thermal movement, the reactions were conducted in the aprotic, non-polar solvent toluene at −60 °C, using a slightly modified Rayonet reactor RPR 3500 Å with a low-temperature immersion well. As concentration effects were expected to influence host−guest association to a considerable degree, the enantioselective intermolecular [2 + 2]-photocycloaddition was extensively investigated with respect to both quinolone and acrylate concentrations (Table 2). In general, neither cooling nor the presence of 2.5 equiv of complexing agent **1** had any noticeable influence on the reaction times, on the diastereomeric ratios obtained, or on the product yields in comparison with the corresponding racemic reactions at room temperature. Unfortunately, endo-diastereoisomers could not be completely separated from the complexing agent **1** due to similar polarities (Scheme 5). However, compound **1** could be recovered in 70−90% yield after the reactions, thus lowering the amount of actually used receptor to 25−75 mol %. Complexing agent **1** can therefore reasonably be considered a "quasi-catalyst" in the enantioselective reactions.

All exo-products **(+)-16a,16c** and **(−)-17a−19a** could be obtained with good enantioselectivities of 70−81% ee if the reactions were conducted at low temperature. **(+)-16a** was chosen as a model compound for further studies because of its high d.r. and thus most facile product isolation. Interestingly, **(+)-16a** showed the opposite sign of optical rotation as compared to the alkyl-substituted products **(−)-17a−19a**. This might be a further hint for a different, more lactam-like conformation of the carboxylic ester moiety, as was already indicated by the very facile ring closure in the thermal lactamization. As expected, conducting the reaction at higher temperatures lowered the obtained enantiomeric excesses dramatically (entry 1). However, variation of both quinolone and acrylate concentration left the observed ee's virtually unchanged (entries 2−5). Only at very low quinolone concentrations of $c = 0.5$ mM, reactions proceeded slowly and uncleanly because of an apparent substrate limitation. Possible side reactions due to hydrogen abstraction were completely undetectable at −60 °C. Consequently, the type of the *N*-alkyl protecting group R^1 was expected to be without significant influence. This was confirmed by the reaction of methyl acrylate (**12**) with the ^{t}Bu-protected quinolone **5c**, which gave basically identical results compared to its *N*-Bn counterpart **5a** (entries 5 and 6). 2-Substitution in the acrylate component showed to be without any effect on the enantioselectivity for R^2 = Et (entry 8). Interestingly, a somewhat higher enantioselectivity was obtained in the reaction with methyl methacrylate (**13**), and ee's were further increased with its cyclic analogue **14**. Thus, spirocyclic product **(−)-19a** showed the highest obtained enantiomeric excess with 81% ee. In comparison with the previously reported intermolecular [2 + 2]-photocycloadditions on 4-methoxyquinolone (81−98% ee),[13] however, all observed enantioselectivities were slightly reduced.

Formation of the undesired, minor enantiomers can theoretically arise from both incomplete complexation of the quinolone itself and from incomplete chiral shielding of the complexed quinolone. Acrylates might thus attack through a gap between the quinolone and the tetrahydronaphthalene shield of **1**. This gap attack should be hindered by increasing the steric bulk of R^2. Such a limitation of enantioselectivity by incomplete shielding is obviously contradicted by the comparably low ee in the reaction with bulky methyl-2-ethyl acrylate (**14**). Consequently, insufficient H-bonding between quinolones **5a/c** and the chiral complexing agent **1**, probably due to competing strong self-association of the quinolone, seems to be the dominant cause for the incomplete chirality transfer from complexing agent to photoproduct. NMR titration studies showed no weakening of the quinolone complexation by the addition of up to 1000 mM of methyl acrylate (**13**). A simple polar solvent effect of the excess acrylates is therefore also unlikely. The nature of the influence of R^2 and R^3 on the enantioselectivity of the reaction thus remains unclear until now.

The obtained cycloaddition products **(+)-16a** and **(−)-17a−19a** were further converted to the corresponding enantioenriched lactams **(+)-20a−23a** using established thermal conditions (Scheme 3.) Not surprisingly, these transformations fully conserved the enantiomeric excesses of the photoproducts within the margin of error of chiral HPLC. **(+)-20a−23a** were thus isolated with 71% ee (R^2 = H, Et) to 81% ee (R^2 = CH_2CH_2OH).

As in the racemic reactions at room temperature, yields of intramolecular [2 + 2]-photocycloadditions using enantioselective standard conditions were noticeably reduced by undesired intermolecular oligomerization. Amazingly, enantioselectivities of these intramolecular reactions were uniformly higher or at least equal to their intermolecular counterparts (Scheme 6).

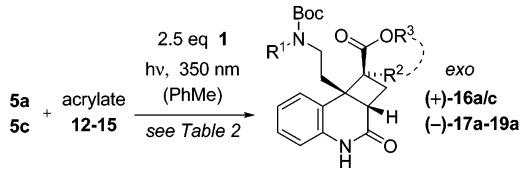
The observed yields and ee's can consistently be explained by the competition between quinolone self-association and complexation to the chiral receptor **1**. While quinolone dimers

TABLE 2. Enantioselective [2 + 2]-Photocycloaddition Reactions: 2.5 Equiv 1, RPR 3500 Å (Toluene)

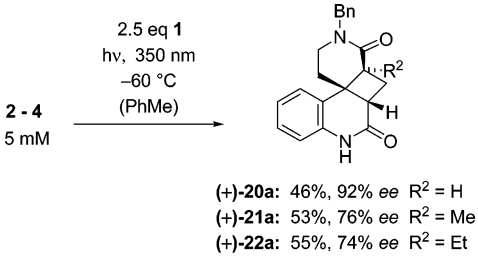
entry	quinolone	c_{quin} (mM)	acrylate	c_{acr} (mM)	product	R^1	R^2	R^3	*T* (°C)	yield[a] (%)	ee[b](%)
1	**5a**	20	**12**	200	**(+)-16a**	Bn	H	CH_3	+35	76	32
2	**5a**	5	**12**	25	**(+)-16a**	Bn	H	CH_3	−50	77	70
3	**5a**	20	**12**	100	**(+)-16a**	Bn	H	CH_3	−60	86	71
4	**5a**	20	**12**	55	**(+)-16a**	Bn	H	CH_3	−60	74	73
5	**5a**	5	**12**	25	**(+)-16a**	Bn	H	CH_3	−60	86	72
6	**5c**	5	**12**	25	**(+)-16c**	^{t}Bu	H	CH_3	−60	80	70
7	**5a**	5	**13**	25	**(−)-17a**	Bn	CH_3	CH_3	−60	63	76
8	**5a**	5	**14**	25	**(−)-18a**	Bn	CH_2CH_3	CH_3	−60	44	71
9	**5a**	5	**15**	25	**(−)-19a**[c]	Bn	$-CH_2CH_2-$		−60	45[c]	81

[a] Yield of isolated exo-diastereoisomer. [b] ee determined by chiral HPLC. (Chiralpak, AD/AD-H). [c] Additional purification by chromatography on Alox (neutral) was necessary.

SCHEME 5



SCHEME 6



exclusively lead to the formation of racemic product in the intermolecular case, association of amides **2**−**4** predominantly results in the formation of intermolecular oligomerization products. This difference in reactivity is further emphasized by the fact that, in contrast to the intermolecular case, intramolecular [2 + 2]-photocycloadditions are markedly slowed by cooling to −60 °C. The difference in temperature dependence is easily explained by the obvious requirement of close proximity between the quinolone ring and the acrylate C,C-double bonds for intramolecular reactions to occur. This is only likely in strongly bent, comparably high-energy conformations of the aminoethyl side chain. With these conformations being less populated at low temperatures, the efficiency of intramolecular reactions is markedly reduced. Lactams **(+)-20a**−**22a** produced by intramolecular [2 + 2]-photocycloaddition are therefore chiefly the product of monomeric and complexed substrates. Hence, a widespread intermolecular oligomerization, although lowering the yields, results in higher ee values of the lactam products by reducing racemic intramolecular reactions. This connection was confirmed by the irradiation of α-unsubstituted quinolone **2**, which gave both the lowest yield and the highest ee, according to the most pronounced and visible formation of insoluble, oligomeric precipitates.

The assignment of the absolute configuration of products **(+)-16a**, **(−)-17a**−**19a**, and **(+)-20a**−**23a** is based mainly on logical considerations about the geometry of H-bond mediated complexes of the quinolones **2**−**5** and the chiral complexing agent **1**. These should most certainly result in a selective shielding of the *re*-side with respect to C-3. Diastereomeric (−)-menthyl derivatives of lactam **21a** could be synthesized. Unfortunately, these compounds proved unexpectedly unstable, and no suitable single crystals for X-ray analysis could be obtained. However, the absolute stereochemistry depicted in Schemes 5 and 6 is very strongly supported by previous X-ray crystallographic results on the [2 + 2]-photocycloaddition products of similar 2-methoxyquinolones which employed the very same complexing agent **1**.[13]

All experimental results indicated a pronounced tendency of the employed aminoethylquinolones (**2**−**5**) toward self-association. This was finally confirmed by means of NMR titration experiments at room temperature in toluene-d_6 (see Supporting Information). Quantification of the obtained data was achieved using the HOSTEST computer program.[55] As expected, a 1:1 binding stoichiometry between **5a** and **1** was evident. The association constant of $K_A \cong 390\ M^{-1}$ was comparable with the value obtained for the complexation of 4-unsubstituted 2-quinolone and **1** ($K_A \cong 580\ M^{-1}$).[13] Thus, the bulky 4-substituent entails no hindering of host−guest complexation. However, optimal curve-fit of the binding isotherm **5a/1** required the assumption of an unusually large dimerization constant of **5a** ($K_{Dim} \cong 900\ M^{-1}$). This high value was also confirmed by a separate dilution experiment of pure **5a**. Although a high dimerization constant was indeed expected from the previous observations, the fact that dimerization is even stronger than host complexation came as a surprise. A casual role of secondary π-stacking interactions in *N*-benzyl-protected quinolone **5a** could be ruled out by the fact that *N*-^{t}Bu-substituted **5c** showed an even larger dimerization constant.[56] Substrate self-association thus clearly represents the single most decisive factor for incomplete complexation and chirality transfer from compound **1**. Considering that dimerization is about twice as strong as complexation, the ee values of >70% corresponding to a substrate complexation of >85% might seem illogically high. However, host−guest complexation is clearly enthalpically favored over guest dimerization as self-association of complexing agent **1** ($K_{Dim} \cong 0\ M^{-1}$) is completely suppressed by the bulky tetrahydronaphthalene shield. Consequently, with an excess of complexing agent **1**, complexation of **5a** and **1** gives rise to two hydrogen bonds per quinolone molecule, while dimerization of the substrate only results in two hydrogen bonds per *two* quinolone molecules. Uncomplexed or excess **1** remains uninvolved in hydrogen bonding. With the breaking of quinolone dimers and the formation of host−guest complexes effectively doubling the number of hydrogen bonds, enthalpy of complexation is expected to override dimerization, despite the adverse complexation constants $K_A \ll K_{Dim}$. In addition to the mere

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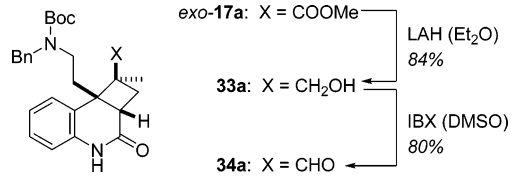
(56) For the importance of π-stacking in molecular recognition, see: Hunter, C. A. *Chem. Soc. Rev.* **1994**, *23*, 101−109.

SCHEME 7



number of formed hydrogen bonds, hydrogen bonding between **5a** and **1** might further be favored energetically over quinolone dimerization by secondary interactions. However, as both complexation and dimerization result from the interaction of two six-membered lactams, simple models based on secondary electrostatic interactions[57] or empirical rules derived thereof[58] show no significant energetic difference between these two possibilities.[59] Preliminary microcalorimetric titration experiments between unsubstituted 2-quinolone and **1** indicated a highly positive association entropy.[13] A crucial role of additional solvent interactions with both host and guest molecules thus seems also possible,[60] although no reliable microcalorimetric data of the complexation of **5a** to **1** could yet be obtained due to the problematic solubility and dimerization behavior of quinolone **5a**.

Further Transformations of Photocycloaddition Product *exo*-17a. With the successful syntheses of enantioenriched lactams **(+)-20a−23a**, we proved the general accessibility of the desired tetracyclic carbon skeleton **C**. However, the *N*-benzyl-protected lactams were remarkably stable substances, and therefore only of limited use in the planned 1,2-rearrangement to [3.3.1]-bicyclic systems of structure **B**. Thus, functional group transformations of the open-chain methyl ester ***exo*-17a** were examined. To our delight, both the corresponding alcohol **33a** and the aldehyde **34a** were easily accessible in high yields using standard LAH reduction and subsequent IBX oxidation reactions (Scheme 7). The variability of functional groups certainly broadens the scope of possible rearrangement routes.

Similar to ester **17a**, alcohol **33a** was easily *N*-Boc deprotected with 10% TFA in CH_2Cl_2 to give the corresponding free amine (**35a**) in high yields. Contrary to all hitherto synthesized cyclobuta[*c*]quinolones, aldehyde **34a** was a comparably unstable substance. Even under mild acidic conditions (1% TFA, CH_2Cl_2), which left the *N*-Boc group completely untouched, **34a** exhibited a very fast, cycloreversive [2 + 2]-fragmentation of the cyclobutane ring to the parent quinolone **5a**.[61] Boc deprotection of aldehyde **34a** was therefore impossible, and the intriguing intramolecular condensation of an N-deprotected aldehyde could not be achieved.

Alcohol **33a** is currently being investigated as a substrate for an oxidation ring closure sequence to imines and iminium ions possessing a tetracyclic ring system **C** more prone to the planned rearrangement. First results seem promising and will be reported in due course.

Conclusion

In summary, we have achieved the first enantioselective syntheses of complex, tetracyclic, cyclobutane annelated lactams **(+)-20a−23a**. Products **(+)-20a−22a** were comparatively synthesized by both inter- and intramolecular [2 + 2]-photocycloaddition reactions employing the chiral complexing agent **1**. The 2-quinolone substrates exhibited an unexpectedly strong self-association, as was shown by NMR titration studies of model compound **5a**. The enantioselective [2 + 2]-photocycloaddition reactions gave good to very good enantiomeric excesses (70−92% ee) in intermolecular and intramolecular reactions. The methodology of enantioselective [2 + 2]-photocycloadditions in solution by hydrogen bond mediated complexation to **1** thus proved to be very robust and well-suited even for bulky substrates of problematic complexation behavior. In addition to these enantioselective syntheses, a detailed study on intermolecular [2 + 2]-photocycloadditions of unsymmetrically 1,1-disubstituted quinolones was conducted by the synthesis of a (3 × 4)-matrix of photoproducts. Model compound ***exo*-17a** proved to be suitable for selective functional group transformations, thus greatly widening the scope of obtainable cyclobutanes. Finally, an unexpected hydrogen abstraction−radical cyclization reaction was discovered for *N*-benzyl quinolone **5a**. Studies concerning its kinetics and selectivity were conducted, as were for [2 + 2]-photocycloadditions in comparison. The results indicated different modes of photochemical excitation for both reactions. The possibility of an envisioned 1,2-rearrangement reaction of compounds possessing the tetracyclic carbon skeleton **C** and their use for an enantioselective synthesis of *Melodinus* alkaloids is currently being investigated in our laboratories.

Experimental Section

Preparation of Starting Materials. Acryloyl chloride (**9**), methacryloyl chloride (**10**), methyl acrylate (**12**), methyl methacrylate (**13**), tulipaline (**15**), and 4-methyl-2(1*H*)-quinolone (**7**) are commercially available. Methyl-2-ethyl acrylate (**14**),[39] 2-ethyl acryloyl chloride (**11**),[40,62] 4-bromoethyl-2(1*H*)-quinolone (**6**),[34,63] and the chiral complexing agent **1**[35] were synthesized according to reported procedures. Alternative literature-known syntheses for high-priced tulipaline (**15**)[64] and 4-methyl-2(1*H*)-quinolone (**7**)[65] were employed to obtain larger quantities from inexpensive starting materials.

General Procedure for the Amination of Bromide 6. Bromide **6** was suspended in an excess (5−20 equiv) of the respective neat amine, and the suspension was stirred at the given temperature until complete conversion of the starting material was observed by TLC. After cooling to room temperature, crystallization from ether solutions and washing with H_2O and Et_2O gave the desired products as white crystalline solids.

4-[2-(Benzylamino)ethyl]-2(1*H*)-quinolone (8a). 6 (3.00 g, 11.9 mmol) and $BnNH_2$ (25.0 mL, 24.5 g, 229 mmol, 19 equiv) were stirred for 4 h at 65 °C to give 3.26 g (11.7 mmol, 99%) of **8a**. R_f = 0.24 (CH_2Cl_2/MeOH = 10/1); mp 132−133 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.60 (br, 1 H), 7.65 (d, ^3J = 7.0 Hz, 1 H), 7.42−7.35 (m, 2 H), 7.30−7.10 (m, 6 H), 6.55 (s, 1 H), 3.81 (s, 2 H), 3.10−2.90 (m, 4 H), 1.93 (br, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$)

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(61) For a similar fragmentation under drastic thermal conditions, see: Lange, G. L.; Lee, M. *Synthesis* **1986**, 117−120.

(62) Borszeky, K.; Mallat, T.; Baiker, A. *Tetrahedron: Asymmetry* **1997**, *8*, 3745−3753.

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δ 164.2 (C), 150.9 (C), 139.7 (C), 138.6 (C), 130.5 (CH), 128.4 (CH), 128.0 (CH), 127.1 (CH), 124.1 (CH), 122.5 (CH), 120.0 (CH), 119.7 (C), 116.9 (CH), 53.8 (CH_2), 48.0 (CH_2), 32.7 (CH_2); HRMS (EI) calcd for $C_{18}H_{18}N_2O$ 278.1419, found 278.1419; Anal. Calcd for $C_{18}H_{18}N_2O$ (278.35): C, 77.67; H, 6.52; N, 10.06. Found: C, 77.35; H, 6.70; N, 10.01.

General Procedure for Boc Protection of Amines 8a/b. The respective amine was suspended in CH_2Cl_2, 1.15 equiv of NEt_3 and 1.15 equiv Boc_2O were added, and the solution was stirred at room temperature until complete conversion of the starting material was observed by TLC. Water (30−50 mL) was added, the aqueous phase was extracted with 3 × 20 mL of CH_2Cl_2, and the combined organic layers were dried over Na_2SO_4 and filtered. Evaporation of the solvent and purification by column chromatography (CH_2Cl_2/MeOH = 20/1 as eluent) gave the desired Boc-protected amines.

***tert*-Butyl-*N*-benzyl-*N*-[2-(2-oxo-1,2-dihydro-4-quinolinyl)ethyl]carbamate (5a). 8a** (4.77 g, 17.1 mmol) was Boc-protected to give 6.28 g (16.6 mmol, 97%) of **5a** as a white solid. R_f = 0.60 (CH_2Cl_2/MeOH = 10/1); mp 149−151 °C; ^{1}H NMR (360 MHz, DMSO-d_6, 80 °C) δ 11.39 (br, 1 H), 7.70 (d, ^3J = 8.2 Hz, 1 H), 7.46 (virt t, ^3J = 7.6 Hz, 1 H), 7.35−7.15 (m, 6 H), 7.15 (virt t, ^3J = 7.6 Hz, 1 H), 6.30 (s, 1 H), 4.45 (s, 2 H), 3.47 (t, ^3J = 6.8 Hz, 2 H), 3.04 (t, ^3J = 6.8 Hz, 2 H), 1.52 (s, 9 H); ^{13}C NMR (90 MHz, DMSO-d_6, 80 °C) δ 161.0 (C), 155.4 (C), 148.3 (C) 138.7 (C), 138.0 (C), 129.6 (CH), 127.9 (CH), 127.0 (CH), 126.6 (CH), 123.8 (CH), 121.0 (C), 121.0 (CH), 118.5 (CH), 115.3 (CH) 78.6 (C), 49.4 (CH_2), 45.9 (CH_2), 30.0 (CH_2), 27.5 (CH_3); HRMS (EI) calcd for $C_{23}H_{26}N_2O_3$ 378.1943, found 378.1948; Anal. Calcd for $C_{23}H_{26}N_2O_3$ (378.46): C, 72.99; H, 6.92; N, 7.40. Found: C, 72.86; H, 6.94; N, 7.37.

General Procedure for the Acylation of Amine 8a. Amine **8a** was suspended in CH_2Cl_2 and cooled to 0 °C, 1.1 equiv of NEt_3 and 1.1 equiv of the corresponding freshly distilled acrylic acid chloride were added, and the mixture was stirred at room temperature for 1 h. The reaction was quenched with saturated $NaHCO_3$, and the aqueous phase was extracted with 3 × 20 mL of CH_2Cl_2. The organic phase was dried over Na_2SO_4, filtered, and evaporated to dryness. Column chromatography (CH_2Cl_2/MeOH = 20/1 as eluent) of the crude product gave the desired acrylic acid amides as white solids or foams.

***N*-Benzyl-*N*-[2-(2-oxo-1,2-dihydro-4-quinolinyl)ethyl]acrylamide (2).** Amine **8a** (209 mg, 751 μmol) was reacted with 70 μL (77.7 mg, 0.86 mmol, 1.1 equiv) of acryloyl chloride (**9**) to give 185 mg (557 μmol, 74%) of **2** as a white solid. R_f = 0.38 (CH_2Cl_2/MeOH = 10/1); mp 57/168 °C; ^{1}H NMR (360 MHz, DMSO-d_6) δ 11.38 (br, 1 H), 7.90−7.60 (br, 1 H), 7.47 (t, ^3J = 7.6 Hz, 1 H), 7.38−7.23 (m, 6 H), 7.16 (t, ^3J = 7.6 Hz, 1 H), 6.71 (dd, ^3J = 16.4 Hz, ^3J = 10.1 Hz, 1 H), 6.34 (s, 1 H), 6.17 (d, ^3J = 16.4 Hz, 1 H), 5.64 (d, ^3J = 10.1 Hz, 1 H), 4.69 (s, 2 H), 3.63 (t, ^3J = 7.5 Hz, 2 H), 3.02 (t, ^3J = 7.5 Hz, 2 H); ^{13}C NMR (90 MHz, DMSO-d_6) δ 165.7/165.5 (C), 161.4/161.3 (C), 148.7/147.9 (C), 138.9 (C), 137.8 (C), 130.3/130.2 (CH), 128.6/ 128.4 (CH), 128.2/128.1 (CH), 128.0/127.5 (CH_2), 127.8/127.3 (CH), 127.1/126.7 (CH), 124.4/ 124.1 (CH), 121.7/121.5 (CH), 121.6/121.0 (CH), 118.7/118.4 (C), 115.7/115.6 (CH), 50.6/47.9 (CH_2), 46.4/46.0 (CH_2), 30.8/29.8 (CH_2) (broad signals and/or doubled set of signals due to Boc coalescence); HRMS (EI) calcd for $C_{21}H_{20}N_2O_2$ 332.1525, found 332.1524.

General Procedure for Intermolecular Racemic [2 + 2]-Photocycloadditions. The respective quinolone and the corresponding acrylic acid esters were dissolved in toluene, and the solution was irradiated (light source: RPR 3500 Å, 35 °C, Duran filter) until complete conversion of the starting material was observed by TLC. The solution was evaporated to dryness, and the residue was purified by column chromatography (P/EtOAc = 50/50 → EtOAc as eluent) to give the exo-photocycloaddition products as unpolar and the endo-products as polar fractions.

***rac*-(1*S*,2a*S*,8b*R*)-8b-{2-[Benzyl(*tert*-butoxycarbonyl)amino]ethyl}-1-methyl-3-oxo-1,2,2a,3,4,8b-hexahydrocyclobuta[*c*]quinoline-1-methylcarboxylate (*exo*-17a). 5a** (767 mg, 2.04 mmol) and methyl methacrylate (**13**) (4.30 mL, 4.05 g, 40.5 mmol, 20 equiv) in 67.5 mL of PhMe were irradiated to give 500 mg (1.04 mmol, 51%) of ***exo*-17a**, 234 mg (489 μmol, 12%) of a mixture of diastereoisomers, and 132 mg (276 μmol, 14%) of ***endo*-17a** as white foams. d.r. (exo/endo) = 73/27, 89% overall, 51% ***exo*-17a**. R_f = 0.35 (P/EtOAc = 1/1); mp 77−78 °C; ^{1}H NMR (360 MHz, DMSO-d_6, 80 °C) δ 9.85 (br, 1 H), 7.35−7.20 (m, 3 H), 7.20−7.10 (m, 3 H), 7.00−6.95 (m, 2 H), 6.88 (d, ^3J = 7.8 Hz, 1 H), 4.31 (d, ^2J = 15.2 Hz, 1 H), 4.24 (d, ^2J = 15.2 Hz, 1 H), 3.64 (s, 3 H), 3.03 (dd, ^2J = 12.1 Hz, ^3J = 11.0 Hz, 1 H), 3.05−2.90 (m, 1 H), 2.90−2.85 (m, 1 H), 2.70−2.60 (m, 1 H), 2.15−2.05 (m, 1 H), 1.86 (dd, ^2J = 12.1 Hz, ^3J = 5.0 Hz, 1 H), 1.80−1.65 (m, 1H), 1.42 (s, 9 H), 0.92 (s, 3 H); ^{13}C NMR (90 MHz, DMSO-d_6, 80 °C) δ 173.8 (C), 169.7 (C), 154.3 (C), 138.5 (C), 138.1 (C), 127.9 (CH), 127.8 (CH), 127.1 (CH), 126.6 (CH), 126.4 (CH), 121.9 (CH), 120.0 (C), 115.2 (CH), 78.7 (C), 51.0 (CH_3), 49.9 (CH_2), 49.9 (C), 47.6 (C), 42.6 (CH_2), 36.6 (CH), 34.4 (CH_2), 32.5 (CH_2), 27.7 $(CH_3)_3$, 21.4 (CH_3); HRMS (EI) calcd for $C_{28}H_{34}N_2O_5$ 478.2468, found 478.2463. Anal. Calcd for $C_{28}H_{34}N_2O_5$ (478.58): C, 70.27; H, 7.16; N, 5.85. Found: C, 69.93; H, 7.21; N, 5.62 (Anal. of diastereoisomeric mixture).

***rac*-(1*R*,2a*S*,8b*R*)-8b-{2-[Benzyl(*tert*-butoxycarbonyl)amino]ethyl}-1-methyl-3-oxo-1,2,2a,3,4,8b-hexahydrocyclobuta[*c*]quinoline-1-methylcarboxylate (*endo*-17a).** R_f = 0.25 (P/EtOAc = 1/1); ^{1}H NMR (360 MHz, DMSO-d_6, 80 °C) δ 9.73 (br, 1 H), 7.30−7.15 (m, 3 H), 7.15−7.00 (m, 3 H), 6.95−6.85 (m, 2 H), 6.82 (d, ^3J = 7.8 Hz, 1 H), 4.32 (d, ^2J = 15.0 Hz, 1 H), 4.24 (d, ^2J = 15.0 Hz, 1 H), 3.27 (s, 3 H), 2.95 (virt t, ^3J = 9.0 Hz, 1 H), 2.90−2.85 (m, 1 H), 2.67 (virt t, ^3J = 11.0 Hz, 1 H), 2.60−2.50 (m, 1 H), 2.10−1.95 (m, 3 H), 1.42 (s, 3 H), 1.39 (s, 9 H); ^{13}C NMR (90 MHz, DMSO-d_6, 80 °C) δ 173.1 (C), 168.5 (C), 154.3 (C), 138.0 (C), 137.8 (C), 127.9 (CH), 127.6 (CH), 127.0 (CH), 126.6 (CH), 121.7 (CH), 115.1 (CH), 78.6 (C), 51.7 (C), 50.7 (CH_3), 49.3 (CH_2), 48.2 (C), 41.5 (CH_2), 38.0 (CH), 34.2 (CH_2), 31.6 (CH_2), 27.7 (CH_3), 18.8 (CH_3). (One C and CH signal were not resolved due to superimposition.); HRMS (EI) calcd for $C_{28}H_{34}N_2O_5$ 478.2468, found 478.2462. Anal. Calcd for $C_{28}H_{34}N_2O_5$ (478.58): C, 70.27; H, 7.16; N, 5.85. Found: C, 69.93; H, 7.21; N, 5.62 (Anal. of diastereoisomeric mixture).

General Procedure for Intramolecular Racemic [2 + 2]-Photocycloadditions. The respective acrylic acid amide (5 mM) was dissolved in toluene, and the solution was irradiated (light source: RPR 3500 Å, 35 °C, Duran filter) until complete conversion of the starting material was observed by TLC. The solution was evaporated to dryness, and the residue was purified by column chromatography (P/EtOAc = 50/50 as eluent) to give the desired lactams as white solids or foams.

***rac*-(1a*S*,7b*S*,11a*S*)-10-Benzyl-11a-methyl-1,9,10,11a-tetrahydro-1a*H*-pyrido-[4′,3′:2,3] cyclobuta[1,2-*c*]quinoline-2,11(3*H*,8*H*)-dione (21a). 3** (125 mg, 361 μmol) was irradiated to give 76 mg (219 μmol, 61%) of **21a**. R_f = 0.35 (EtOAc); mp 208−210 °C; ^{1}H NMR (360 MHz, $CDCl_3$) δ 9.32 (br, 1 H), 7.40−7.27 (m, 5 H), 7.19 (virt t, ^3J = 7.4 Hz, 1 H), 7.08 (virt t, ^3J = 7.0 Hz, 1 H), 7.04 (virt t, ^3J = 7.0 Hz, 1 H), 6.83 (d, ^3J = 7.9 Hz, 1 H), 4.83 (d, ^2J = 14.5 Hz, 1 H), 4.61 (d, ^2J = 14.5 Hz, 1 H), 3.67 (ddd, ^2J = 13.0 Hz, ^3J = 12.5 Hz, ^3J = 3.1 Hz, 1 H), 3.39 (ddd, ^2J = 13.0 Hz, ^3J = 5.0 Hz, ^3J = 3.0 Hz, 1 H), 3.22 (dd, ^3J = 11.0 Hz, ^3J = 7.9 Hz, 1 H), 2.78 (dd, ^2J = 12.6 Hz, ^3J = 11.0 Hz, 1 H), 2.27 (dd, ^2J = 12.6 Hz, ^3J = 7.9 Hz, 1 H), 2.21 (ddd, ^2J = 14.5 Hz, ^3J = 12.5 Hz, ^3J = 5.0 Hz, 1 H), 1.92 (ddd, ^2J = 14.5 Hz, ^3J = 3.1 Hz, ^3J = 3.0 Hz, 1 H), 1.15 (s, 3 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 174.0 (C), 171.0 (C), 137.0 (C), 136.0 (C), 128.8 (CH), 128.5 (CH), 128.1 (CH), 127.6 (CH), 123.4 (CH), 123.3 (C), 116.2 (CH), 51.2 (CH_2), 46.6 (C), 46.4 (C), 43.3 (CH_2), 37.6 (CH_2), 37.1 (CH), 34.3 (CH_2), 22.4 (CH_3). (One C signal was not resolved due to superimposition); HRMS (EI) calcd for $C_{22}H_{22}N_2O_2$ 346.1681, found 346.1676. Anal.

Calcd for $C_{22}H_{22}N_2O_2$ (346.42): C, 76.28; H, 6.40. Found: C, 76.13; H, 6.52.

General Procedure for *N*-Boc Deprotection. The respective *N*-Boc-protected substrate was stirred in 10% v/v TFA in CH_2Cl_2 for 2 h and then quenched with 25 mL of saturated $NaHCO_3$. The aqueous phase was extracted with 3 × 20 mL of CH_2Cl_2. The organic phase was dried over Na_2SO_4, filtered, and evaporated to dryness to give the crude free amines which were sufficiently pure for further reactions.

***rac*-(1*S*,2a*S*,8b*R*)-8b-[2-(Benzylamino)ethyl]-1-methyl-3-oxo-1,2,2a,3,4,8b-hexahydrocyclobuta[*c*]quinoline-1-methylcarboxylate (25a). *exo*-17a** (355 mg, 742 μmol) was *N*-Boc-deprotected to give 227 mg (600 μmol, 81%) of **25a** as slightly yellow solid. R_f = 0.35 (CH_2Cl_2/MeOH = 10/1); mp 152−153 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.22 (br, 1 H), 7.20−7.15 (m, 2 H), 7.15−7.10 (m, 4 H), 7.07 (d, ^3J = 7.6 Hz, 1 H), 6.97 (virt t, ^3J = 6.5 Hz, 1 H), 6.77 (d, ^3J = 7.9 Hz, 1 H), 3.69 (s, 3 H), 3.56 (s, 2 H), 3.19 (dd, ^2J = 12.0 Hz, ^3J = 11.0 Hz, 1 H), 3.05 (dd, ^3J = 11.0 Hz, ^3J = 5.0 Hz, 1 H), 2.42 (ddd, ^2J = 10.7 Hz, ^3J = 10.2 Hz, ^3J = 5.0 Hz, 1 H), 2.27 (ddd, ^2J = 10.7 Hz, ^3J = 10.0 Hz, ^3J = 5.0 Hz, 1 H), 2.21 (ddd, ^2J = 11.5 Hz, ^3J = 10.2 Hz, ^3J = 5.0 Hz, 1 H), 1.98 (dd, ^2J = 12.0 Hz, ^3J = 5.0 Hz, 1 H), 1.81 (ddd, ^2J = 11.5 Hz, ^3J = 10.0 Hz, ^3J = 5.0 Hz, 1 H), 0.98 (s, 3 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 175.1 (C), 172.5 (C), 138.7 (C), 137.7 (C), 128.4 (CH), 128.4 (CH), 128.1 (CH), 127.4 (CH), 127.1 (CH), 123.5 (CH), 121.3 (C), 116.1 (CH), 53.6 (CH_2), 51.9 (CH_3), 51.3 (C), 48.8 (C), 45.0 (CH_2), 38.2 (CH), 37.2 (CH_2), 33.5 (t, CH_2), 22.5 (CH_3); HRMS (EI) calcd for $C_{23}H_{26}N_2O_3$ 378.1943, found 378.1946.

General Procedure for Lactamization of *exo*-[2 + 2]-PCA Products. The respective crude *N*-Boc-deprotected amine was heated under Ar (Büchi Kugelrohr, GKR-50) to 200 °C for 20 min, cooled to room temperature, and purified by column chromatography (EtOAc or CH_2Cl_2/MeOH = 20:1 as eluent) to give the desired lactams as white solids or foams.

For example, 200 mg (418 μmol) of ***exo*-17a** were *N*-Boc-deprotected and thermally lactamized to give 116 mg (335 μmol, 80%) of **21a** (see above).

General Procedure for Enantioselective Intermolecular [2 + 2]-Photocycloadditions. The respective quinolone (5−20 mM), the chiral complexing agent **1** (2.5 equiv), and the corresponding acrylate (5 equiv) were dissolved in toluene, and the solution was irradiated at −60 °C (light source: RPR 3500 Å, Duran filter) until complete conversion of the starting material was observed by TLC (usually <1 h). The solution was evaporated to dryness, and the residue was purified by column chromatography (P/EtOAc = 50/50 as eluent) to give the enantioenriched exo-product as unpolar and recovered compound **1** as polar fraction. Isolation of pure endo-diastereoisomers was not attempted.

(+)-(1*S*,2a*S*,8b*S*)-8b-{2-[Benzyl(*tert*-butoxycarbonyl)amino]-ethyl}-3-oxo-1,2,2a,3,4,8b-hexahydrocyclobuta[*c*]quinoline-1-methylcarboxylate ((+)-*exo*-16a). 5a (19.1 mg, 50.4 μmol, 20 mM), 1 (52.9 mg, 150 μmol, 2.5 equiv), and **12** (11.5 μL, 10.8 mg, 137 μmol, 2.7 equiv) in 2.5 mL of PhMe were irradiated to give 17.3 mg (37.3 μmol, 74%) of **(+)-*exo*-16a** (73% ee) and 32.1 mg (89.8 μmol, 65%) of recovered **1**. $[\alpha]^{20}_D$ +4.0 (*c* 1.0, CH_2Cl_2); HPLC (Chiralpak AD, Hex/*i*-PrOH = 90/10, 1 mL/min) t_R = 22.4 min ((+), 86.5%), t_R = 26.4 min ((−), 13.5%).

(+)-(1*S*,2a*S*,8b*S*)-8b-[2-(*tert*-butoxycarbonyl)(*tert*-butylamino)-ethyl]-3-oxo-1,2,2a,3,4,8b-hexahydrocyclobuta[*c*]quinoline-1-methylcarboxylate ((+)-*exo*-16c). 5c (20.0 mg, 58.1 μmol, 5 mM), **1** (21.2 mg, 145 μmol, 2.5 equiv), and **12** (26.0 μL, 25.0 mg, 290 μmol, 5 equiv) in 2.5 mL of PhMe were irradiated to give 20.0 mg (46.5 μmol, 80%) of **(+)-*exo*-16c** (71% ee) and 43 mg (122 μmol, 84%) of recovered **1**. $[\alpha]^{20}_D$ +5.2 (*c* 1.0, CH_2Cl_2); HPLC (Chiralpak AD, Hex/*i*-PrOH = 97/3, 1 mL/ min) t_R = 29.9 min ((+), 85.5%), t_R = 35.0 min ((−), 14.5%).

(−)-(1*S*,2a*S*,8b*R*)-8b-{2-[Benzyl(*tert*-butoxycarbonyl)amino]-ethyl}-1-methyl-3-oxo-1,2,2a,3,4,8b-hexahydrocyclobuta[*c*]quinoline-1-methylcarboxylate ((−)-*exo*-17a). 5a (35.0 mg, 92.5 μmol, 5.0 mM), **1** (81.5 mg, 231 μmol, 2.5 equiv), and **13** (49.0 μL, 46.1 mg, 460 μmol, 5.0 equiv) in 18.5 mL of PhMe were irradiated to give 28.0 mg (58.5 μmol, 63%) of **(−)-*exo*-17a** (76% ee), 6.0 mg (12.5 μmol, 14%) of a mixture of diastereoisomers, and 69 mg (196 μmmol, 85%) of recovered **1**. $[\alpha]^{20}_D$ −20.4 (*c* 0.93, CH_2Cl_2); HPLC (Chiralpak AD, Hex/*i*-PrOH = 90/10, 1 mL/min) t_R = 15.5 min ((−), 88%), t_R = 28.4 min ((+), 12%).

(−)-(1*S*,2a*S*,8b*R*)-8b-2-[Benzyl(*tert*-butoxycarbonyl)amino]-ethyl-1-ethyl-3-oxo-1,2,2a,3,4,8b-hexahydrocyclobuta[*c*]quinoline-1-methylcarboxylate ((−)-*exo*-18a). 5a (35.0 mg, 92.5 μmol, 5.0 mM), **1** (81.5 mg, 231 μmol, 2.5 equiv), and **14** (57.1 μL, 52.5 mg, 460 μmol, 5.0 equiv) in 18.5 mL of PhMe were irradiated to give 20.0 mg (40.6 μmol, 44%) of **(−)-*exo*-17a** (71% ee), 11.0 mg (22.4 μmol, 24%) of a mixture of diastereoisomers, and 67 mg (190 μmol, 82%) of recovered **1**. $[\alpha]^{20}_D$ −14.4 (*c* 1.0, CH_2Cl_2); HPLC (Chiralpak AD, Hex/*i*-PrOH = 90/10, 1 mL/min) t_R = 15.5 min ((−), 85.5%), t_R = 29.4 min ((+), 14.5%).

(−)-(1*S*,2a*S*,8b*R*)-8b-{2-[Benzyl(*tert*-butoxycarbonyl)amino]-ethyl}-1-[*spiro*-(4-γ-butyrolactonyl)]-3-oxo-1,2,2a,3,4,8b-hexahydrocyclobuta[*c*]quinoline ((−)-*exo*-19a). 5a (35.0 mg, 92.5 μmol, 5.0 mM), **1** (81.5 mg, 231 μmol, 2.5 equiv), and **15** (40.3 μL, 45.1 mg, 460 μmol, 5.0 equiv) were irradiated in 18.5 mL of PhMe. Double column chromatography (1st: silica: 2.5 × 10 cm, P/EtOAc = 50/50 → EtOAc as eluent, 2nd: ALOX neutral: 2.5 × 10 cm, CH_2Cl_2 → CH_2Cl_2/MeOH = 98/2 as eluent) gave 20.0 mg (42.0 μmol, 45%) of **(−)-*exo*-19a** (81% ee) and 38 mg (108 μmmol, 45%) of recovered **1**. $[\alpha]^{20}_D$ −28.4 (*c* 0.89, CH_2Cl_2); HPLC (Chiralpak AD, Hex/(*i*-PrOH + 0.1% w/v NEt_3) = 60/40, 0.8 mL/min) t_R = 8.7 min ((−), 90.5%), t_R = 11.2 min ((+), 9.5%).

General Procedure for Enantioselective, Intramolecular [2 + 2]-Photocycloadditions. The respective acrylic acid amide (5 mM) and the chiral complexing agent **1** (2.5 equiv, 12.5 mM) were dissolved in toluene, and the solution was irradiated at −60 °C (light source: RPR 3500 Å, Duran filter) until complete conversion of the starting material was observed by TLC (2−3 h). The solution was evaporated to dryness, and the residue was purified by column chromatography (P/EtOAc = 1/1 → EtOAc as eluent) to give compound **1** as unpolar fraction and the desired lactam as polar fraction.

(+)-(1a*S*,7b*S*,11a*S*)-10-Benzyl-1,9,10,11a-tetrahydro-1a*H*-pyrido[4′,3′:2,3]-cyclobuta[1,2-*c*] quinoline-2,11(3*H*,8*H*)dione ((+)-20a). 19.9 mg (60.0 μmol, 5.0 mM) **2** and 52.9 mg (150 μmol, 2.5 eq) **1** were irradiated to give 40 mg (113 μmol, 75%) recovered **1** and 9.2 mg (27.7 μmol, 46%) **(+)-20a** (92% *ee*). $[\alpha]_D^{20}$ +57.0 (*c* = 0.5, CH_2Cl_2); HPLC (Chiralpak AD-H, Hex/(*i*-PrOH+0.1% w/v NEt_3) = 40/60, 0.8 mL/min) t_R = 9.6 min ((+), 96.0%), t_R = 12.5 min ((−), 4.0%).

(+)-(1a*S*,7b*S*,11a*S*)-10-Benzyl-11a-methyl-1,9,10,11a-tetrahydro-1a*H*-pyrid o-[4′,3′:2,3] cyclobuta[1,2-*c*]quinoline-2,11(3*H*,8*H*)-dione ((+)-21a). 3 (20.8 mg, 60.0 μmol, 5.0 mM) and **1** (52.9 mg, 150 μmol, 2.5 equiv) were irradiated to give 43 mg (122 μmol, 81%) of recovered **1** and 11.0 mg (31.8 μmol, 53%) of **(+)-20a** (76% ee). $[\alpha]^{20}_D$ +57.1 (*c* 0.69, CH_2Cl_2); HPLC (Chiralpak AD-H, Hex/(*i*-PrOH + 0.1% w/v NEt_3) = 40/60, 0.8 mL/min) t_R = 8.1 min ((−), 12%), t_R = 13.8 min ((+), 88%).

(+)-(1a*S*,7b*S*,11a*S*)-10-Benzyl-11a-ethyl-1,9,10,11a-tetrahydro-1a*H*-pyrido[4′,3′:2,3] cyclobuta[1,2-*c*]quinoline-2,11(3*H*,8*H*)-dione ((+)-22a). 4 (21.6 mg, 60.0 μmol, 5.0 mM) and **1** (52.9 mg, 150 μmol, 2.5 equiv) were irradiated to give 45 mg (128 μmol, 85%) of recovered **1** and 12.0 mg (33.3 μmol, 55%) of **(+)-20a** (74% ee). $[\alpha]^{20}_D$ +68.1 (*c* 0.75, CH_2Cl_2); HPLC (Chiralpak AD-H, Hex/(*i*-PrOH + 0.1% w/v NEt_3) = 40/60, 0.8 mL/min) t_R = 8.0 min ((−), 13%), t_R = 11.5 min ((+), 87%).

(+)-(1a*S*,7b*R*,11a*R*)-10-Benzyl-11a-(2-hydroxyethyl)-1,9,10,-11a-tetrahydro-1a*H*-pyrido [4′,3′:2,3]cyclobuta[1,2-*c*]quinoline-2,11(3*H*,8*H*)dione ((+)-23a). According to general procedures, 15 mg (30 μmol) of **(−)-*exo*-19a** (81% *ee*) were *N*-Boc-deprotected and thermally lactamized to give 8 mg (21 μmol, 73%) of **(+)-22a** (81% ee). $[\alpha]^{20}_D$ +55.4 (*c* 0.5, CH_2Cl_2); HPLC (Chiralpak AD-H,

Hex/(*i*-PrOH + 0.1% w/v NEt_3) = 40/60, 0.8 mL/min) t_R = 7.7 min ((−), 9.5%), t_R = 31.1 min ((+), 90.5%).

Hydrogen Abstraction−Radical Cyclization and Dimerization of 5a. 5a (500 mg, 1.32 mmol, 30 mM) in 44.0 mL of PhMe was irradiated (light source: RPR 3500 Å, 35 °C, Duran filter) for 6 h. After evaporation to dryness, the crude product mixture was separated by column chromatography (silica, 3.0 × 20 cm, P/EtOAc = 50/50 → 20/80 as eluent) to give 62 mg (164 μmol, 12%) of **29**, 80 mg (211 μmol, 16%) of a diastereomeric mixture, 58 mg (153 μmol, 12%) of **30**, and 180 mg (239 μmol, 36%) of the dimeric product **28**.

Dimeric Product (28), Presumably HH-cis-anti-cis. R_f = 0.50 (EtOAc); mp 193−196 °C (dec); ^{1}H NMR (360 MHz, DMSO-d_6, 80 °C) δ 9.55 (br, 1 H), 7.20 (br, 4 H), 7.00−6.85 (m, 5 H), 4.09 (s, 2 H), 2.97 (s, 1 H), 2.86 (br, 1 H), 2.37 (br, 1 H), 1.71 (br, 1 H), 1.30 (m, 10 H); ^{13}C NMR (90 MHz, DMSO-d_6, 80 °C) 166.8 (C), 154.1 (C), 138.0 (C), 137.7 (C), 127.8 (CH), 127.7 (CH), 127.1 (CH), 126.9 (CH), 126.6 (CH), 122.0 (CH), 120.5 (C), 115.4 (CH), 78.6 (C), 49.8 (C), 49.6 (CH_2), 45.1 (CH), 42.0 (CH_2), 37.9 (CH_2), 27.6 (CH_3); Anal. Calcd for $C_{46}H_{52}N_4O_6$ (756.43): C, 72.99; H, 6.92. Found: C, 72.88; H, 7.25.

***rac*-(4*R*,2′*S*)-3,4-Dihydroquinoline-2(1H)-on-4-*spiro*-3′-(2′-phenyl)pyrrolidine-1-*tert*-butylcarbamate (29).** R_f = 0.64 (EtOAc); mp 235 °C (dec); ^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 9.97 (s, 1 H), 7.37−7.32 (m, 2 H), 7.32−7.26 (m, 1 H), 7.22 (t, ^3J = 7.3 Hz, 1 H), 7.20−7.14 (m, 3 H), 7.05 (t, ^3J = 7.5 Hz, 1 H), 6.98 (d, ^3J = 7.7 Hz, 1 H), 4.95 (s, 1 H), 3.78 (virt t, ^3J = 9.2 Hz, 1 H), 3.36 (ddd, ^2J = 10.0 Hz, ^3J = 10.4 Hz, ^3J = 7.3 Hz, 1 H), 2.27 (d, ^2J = 15.8 Hz, 1 H), 2.07 (ddd, ^2J = 12.5 Hz, ^3J = 9.7 Hz, ^3J = 9.6 Hz, 1 H), 1.98−1.92 (m, 1 H), 1.50 (d, ^2J = 15.8 Hz, 1 H), 1.26 (br, 9 H); ^{13}C NMR (90 MHz, DMSO-d_6, 80 °C) δ 167.9 (C), 152.8 (C), 136.8 (C), 129.1 (C), 127.8 (C), 127.6 (CH), 127.3 (CH), 126.8 (CH), 126.4 (CH), 123.5 (CH), 122.0 (CH), 115.6 (CH), 78.3 (C), 67.8 (CH), 46.3 (C), 44.4 (CH_2), 39.5 (CH_2), 33.1 (CH_2), 27.6 (CH_3); HRMS (EI) calcd for $C_{23}H_{26}N_2O_3$ 378.1943, found 378.1944.

***rac*-(4*R*,2′*R*)-3,4-Dihydroquinoline-2(1*H*)-on-4-*spiro*-3′-(2′-phenyl)pyrrolidine-1-*tert*-butylcarbamate (30).** R_f = 0.60 (EtOAc); mp 225 °C (dec); ^{1}H NMR (500 MHz, DMSO-d_6, 80 °C) δ 10.09 (s, 1 H), 7.03−6.98 (m, 4 H), 6.88 (d, ^3J = 7.7 Hz, 1 H), 6.63−6.59 (m, 2 H), 6.51 (t, ^3J = 7.5 Hz, 1 H), 6.46−6.43 (m, 1 H), 4.68 (s, 1 H), 3.78 (dd, ^3J = 10.4 Hz, ^2J = 10.3 Hz, 1 H), 3.36 (ddd, ^3J = 10.7 Hz, ^2J = 10.3 Hz, ^3J = 7.1 Hz, 1 H), 2.76 (ddd, ^2J = 12.3 Hz, ^3J = 10.7 Hz, ^3J = 10.4 Hz, 1 H), 2.60 (s, 2 H), 1.77 (dd, ^2J = 12.3 Hz, ^3J = 7.1 Hz, 1 H), 1.23 (br, 9 H); ^{13}C NMR (90 MHz, DMSO-d_6, 80 °C) δ 170.5 (C), 154.7 (C), 140.8 (C), 136.9 (C), 128.3 (CH), 127.5 (CH), 126.7 (CH), 125.9 (CH), 125.7 (CH), 124.3 (C), 122.8 (CH), 115.6 (CH), 79.8 (C), 66.6 (CH), 49.0 (C), 43.9 (CH_2), 41.5 (CH_2), 30.2 (CH_2), 28.0 (CH_3); HRMS (EI) calcd for $C_{23}H_{26}N_2O_3$ 378.1943, found 378.1945.

Further Transformations of Photocycloaddition Product *exo*-17a. *rac*-*N*-2-[(1*S*,2a*S*,8b*R*)-1-(Hydroxymethyl)-1-methyl-3-oxo-1,2,2a,3,4,8b-hexahydrocyclo-buta[*c*]quinoline-8b-yl]ethyl-*N*-benzyl-*tert*-butylcarbamate (33a). Ester *exo*-**17a** (252 mg, 527 μmol) in 20 mL of dry Et_2O at 0 °C was treated dropwise with 0.66 mL of 1.0 M LAH in THF (659 μmol, 1.25 equiv), and the mixture was stirred for an additional 30 min. The excess hydride was destroyed by the addition of several drops of H_2O. The solution was filtered, washed with 3 × 20 mL of Et_2O, and evaporated. Purification by column chromatography (silica, 3.0 × 10 cm, P/EtOAc = 50/50 → EtOAc as eluent) of the residue afforded 191 mg (424 μmol, 80%) of alcohol **33a** as a white foam. R_f = 0.33 (EtOAc); mp 105 °C; ^{1}H NMR (360 MHz, DMSO-d_6, 80 °C) δ 9.65 (br, 1 H), 7.30−7.21 (m, 3 H), 7.10−7.00 (m, 3 H), 7.03 (d, ^3J = 7.6 Hz, 1 H), 6.92 (virt t, ^3J = 7.3 Hz, 1 H), 6.82 (d, ^3J = 7.8 Hz, 1 H), 4.78 (br, 1 H), 4.33 (d, ^2J = 15.3 Hz, 1 H), 4.20 (d, ^2J = 15.3 Hz, 1 H), 3.59 (d, ^2J = 10.8 Hz, 1 H), 3.38 (d, ^2J = 10.8 Hz, 1 H), 2.88−2.82 (m, 2 H), 2.57−2.50 (m, 1 H), 2.30−2.18 (m, 2 H), 2.13−2.08 (m, 1 H), 1.66−1.61 (dd, ^2J = 10.8 Hz, ^3J = 7.1 Hz, 1 H), 1.40 (s, 9 H), 0.73 (s, 3 H); ^{13}C NMR (90 MHz, DMSO-d_6, 80 °C) δ 169.9 (C), 154.4 (C), 138.1 (C), 129.9 (C), 127.9 (CH), 127.8 (CH), 127.0 (CH), 126.7 (CH), 126.6 (CH), 122.9 (C), 121.5 (CH), 114.9 (CH), 78.5 (C), 65.7 (CH_2), 49.3 (CH_2), 46.9 (C), 45.3 (C), 42.3 (CH_2), 37.7 (d, CH), 33.6 (CH_2), 33.3 (CH_2), 27.8 (CH_3), 22.1 (CH_3); Anal. Calcd for $C_{27}H_{34}N_2O_4$ (450.57): C, 71.97; H, 7.61. Found: C, 71.68; H, 7.71.

***rac*-*N*-2-[(1*S*,2a*S*,8b*R*)-1-Formyl-1-methyl-3-oxo-1,2,2a,3,4,8b-hexahydro-cyclobuta[*c*] quinoline-8b-yl]ethyl-*N*-benzyl-*tert*-butylcarbamate (34a).** Alcohol **33a** (50.0 mg, 111 μmol) and IBX (93.2 mg, 333 μmol, 3 equiv) in 3.0 mL of DMSO were stirred for 22 h. To this mixture were added 60 mL of H_2O and 10 mL of saturated $NaHCO_3$, phases were separated, and the aqueous layer was extracted with 3 × 30 mL of EtOAc. The combined organic phases were washed with 50 mL of H_2O and 50 mL of brine, dried over Na_2SO_4, and filtered. The solvent was removed in a vacuum. Purification of the residue by column chromatography (silica, 3.0 × 10 cm, P/EtOAc = 50/50 → EtOAc as eluent) afforded 40 mg (89 μmol, 80%) of aldehyde **34a** as a white foam. R_f = 0.65 (EtOAc); ^{1}H NMR (360 MHz, DMSO-d_6, 80 °C) δ 9.86 (s, 1 H), 9.76 (s, 1 H), 7.31−7.18 (m, 4 H), 7.18 (t, ^3J = 7.7 Hz, 1 H), 7.13−7.08 (m, 2 H), 7.00 (t, ^3J = 7.5 Hz, 1 H), 6.90 (d, ^3J = 7.9 Hz, 1 H), 4.30 (d, ^2J = 15.3 Hz, 1 H), 4.21 (d, ^2J = 15.3 Hz, 1 H), 2.97 (virt t, ^3J = 10.9 Hz, 1 H), 2.95−2.85 (m, 2 H), 2.63−2.56 (m, 1 H), 2.22 (ddd, ^2J = 12.1 Hz, ^3J = 10.7 Hz, ^3J = 4.9 Hz, 1 H), 1.87−1.79 (m, 1 H), 1.75 (dd, ^2J = 10.8 Hz, ^3J = 5.5 Hz, 1 H), 1.39 (s, 9 H), 0.86 (s, 3 H); ^{13}C NMR (90 MHz, DMSO-d_6, 80 °C) δ 204.1 (C), 169.1 (C), 154.3 (C), 138.3 (C), 137.9 (C), 127.9 (CH), 127.8 (CH), 127.3 (CH), 127.0 (CH), 126.6 (CH),121.9 (CH), 120.1 (C), 115.3 (CH), 78.7 (C), 53.4 (C), 49.4 (CH_2), 48.9 (C), 42.0 (CH_2), 37.6 (CH), 34.5 (CH_2), 29.7 (CH_2), 27.7 (CH_3) 18.3 (CH_3); HRMS (EI) calcd for $C_{27}H_{32}N_2O_4$ 448.23621, found 448.23637.

Acknowledgment. Support of this research by the Deutsche Forschungsgemeinschaft (SPP 1179 Organokatalyse) and by the Fonds der Chemischen Industrie is gratefully acknowledged. P.S. is grateful for a scholarship from the Studienstiftung des Deutschen Volkes. We cordially thank Craig S. Wilcox (University of Pittsburgh) for making his HOSTEST program available to us. We also thank Olaf Ackermann for assistance with HPLC experiments and Christine Schwarz for conducting high-temperature NMR experiments.

Supporting Information Available: General experimental methods. NOESY NMR, HPLC, and UV data for selected compounds. Fully assigned ^{1}H and ^{13}C NMR spectroscopic data for compounds **5b**, **5c, 8b**, **8c**, *exo*-**16a**−**16c**, *exo*-**17b**,**17c**, *exo*-**18a**−**18c**, *exo*-**19a**−**19c**, *endo*-**17b**, *endo*-**18a**, *endo*-**19a**−**19c**, **25a**, **25b**, **26a**, **26b**, **31**, **32**, and **35a**. ^{13}C NMR spectra, IR and MS data for all compounds. NMR titration data of compounds **1** and **5a**. UV−vis spectra of compounds **1**, **3**, **5a**−**5c**, ***exo*-17a**, **28**, and **29**. NOE charts of compounds **16c** and **21a**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0606608