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Diastereo- and Enantioselective Intramolecular [2+2] Photocycloaddition Reactions of 3-(ω′-Alkenyl)- and 3-(ω′-Alkenyloxy)-Substituted 5,6-Dihydro-1*H*-pyridin-2-ones

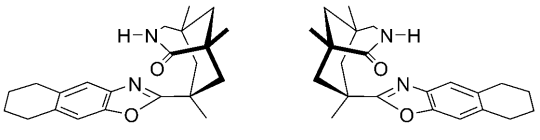
Dominik Albrecht, Florian Vogt, and Thorsten Bach*[a]

Abstract: 3-(ω′-Alkenyl)-substituted 5,6-dihydro-1*H*-pyridin-2-ones **2**–**4** were prepared as photocycloaddition precursors either by cross-coupling from 3-iodo-5,6-dihydro-1*H*-pyridin-2-one (**8**) or—more favorably—from the corresponding α-(ω′-alkenyl)-substituted δ-valerolactams **9**–**11** by a selenylation/elimination sequence (56–62% overall yield). 3-(ω′-Alkenyloxy)-substituted 5,6-dihydro-1*H*-pyridin-2-ones **5** and **6** were accessible in 43 and 37% overall yield from 3-diazopiperidin-2-one (**15**) by an α,α-chloroselenylation reaction at the 3-position followed by nucleophilic displacement of a chloride ion with an ω-alkenolate and oxidative elimination of selenoxide. Upon irradiation at $\lambda = 254$ nm, the precursor compounds underwent a clean intramolecular [2+2] photocycloaddition reaction. Substrates **2** and **5**, tethered by a two-atom chain, exclusively delivered the respective crossed products **19** and **20**, and substrates **3**, **5**, and **6**, tethered by longer chains, gave the straight products **21**–**23**. The completely regio- and diastereoselective photocycloaddition reactions proceeded in 63–83% yield. Irradiation in the presence of the chiral templates (−)-**1** and (+)-**31** at −75 °C in toluene rendered the reactions enantioselective with selectivities varying between 40 and 85% *ee*. Truncated template *rac*-**31** was prepared as a nor-analogue of the well-established template **1** in eight steps and 56% yield from the Kemp triacid (**24**). Subsequent resolution delivered the enantiomerically pure templates (−)-**31** and (+)-**31**. The outcome of the reactions is compared to the results achieved with 4-substituted 5,6-dihydro-1*H*-pyridin-2-ones and quinolones.

Keywords: asymmetric synthesis · cycloaddition · enantioselectivity · hydrogen bonds · photochemistry

Introduction

The template-based approach to chiral photocycloaddition products employing complexing agent (+)-**1** or its enantiomer (−)-**1** (Scheme 1) has emerged in recent years as a useful method to achieve enantioselective photochemical reactions in solution.[1] In this context, intra- and intermolecular [2+2] photocycloaddition reactions of 4-substituted quinolones have been particularly successful, frequently delivering the respective cyclobutane products in over 90% enantiomeric excess (*ee*).[2] The enantioselective intermolecular [2+2] photocycloaddition of a 4-alkylquinolone has been recently applied to the total synthesis of the melodinus alkaloid (+)-meloscine.[3] The mode of action of template **1** is based on the formation of a 1:1 complex of the substrate with the template, in which an efficient enantioface differentiation is possible. The driving force for this 1:1 association is the fact that the homochiral complexing agent **1** cannot dimerize in solution through hydrogen bonding due to the bulky tetrahydronaphthalene backbone.[2c,4] As a consequence, the formation of complexes with lactam substrates becomes favorable even though hydrogen-bound dimers of the substrates can be competitively formed.



(+)-**1** (−)-**1**

Scheme 1. Structure of the chiral complexing agent (+)-**1** and its enantiomer (−)-**1**.

[a] Dr. D. Albrecht, F. Vogt, Prof. Dr. T. Bach
Lehrstuhl für Organische Chemie I
Technische Universität München
Lichtenbergstrasse 4, 85747 Garching (Germany)
Fax: (+49) 89-289-13315
E-mail: thorsten.bach@ch.tum.de

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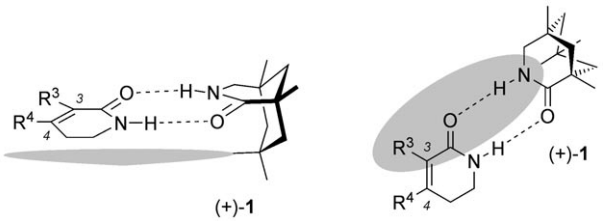
To extend the scope of substrates suitable for the enantioselective photocycloaddition concept, we recently studied the intramolecular [2+2] photocycloaddition of α,β-unsaturated lactams that bear a vinyl group linked by an appropriate spacer to the β-position of the lactam.[5] [2+2] Photocycloaddition reactions of this substrate class are rare and have not been explored comprehensively.[6] Work by us was directed towards the synthesis and [2+2] photocycloaddition reactions of the 4-substituted five-membered 1,5-dihydropyrrol-2-ones and six-membered 5,6-dihydro-1*H*-pyridin-2-ones (Scheme 2). Although the photocycloaddition



Scheme 2. A 1:1 complex of complexing agent (+)-**1** with a substituted δ-lactam in schematic side-view and top-view representations. The sterically demanding 5,6,7,8-tetrahydronaphtho[2,3-*d*]oxazole is depicted as a gray ellipsoid.

chemistry of these compounds was remarkably clean, it was disappointing to note that the enantiomeric excess of the resulting cyclobutanes was relatively low if the reactions were conducted in the presence of complexing agent (−)-**1** or (+)-**1**. Only the oxygen-substituted substrate (R^4 = 3′-butenyloxy) resulted in significant enantiomeric excess, but its reaction rate was very low at −60 °C (conversion of 45 % after 29 h). The fast-reacting carbon-substituted substrates (e.g., R^4 = 4′-pentenyl, 3′-butenyl) produced cyclobutanes in enantioselectivities below 40 % *ee*.[5] In a search for possible explanations for this lack of enantioface differentiation, we speculated that the substituent at the β-position, that is, C4 of a 5,6-dihydro-1*H*-pyridin-2-one compound, might not be fully within the reach of the bulky 5,6,7,8-tetrahydronaphtho[2,3-*d*]oxazole backbone attached to the hydrogen-bonding scaffold (Scheme 2). This explanation seems appropriate as the first step of an intramolecular photocycloaddition at such a lactam occurs likely by addition to C4. The chain R^4 attached to C4 can turn away from the shield because its conformation is - contrary to the substituent at C4 of quinolones (see below) - not restricted by 1,3-allylic strain.

Although the association behavior of the substrates is also relevant to enantioselectivity, we reasoned that substrate variation by using α-substituted α,β-unsaturated δ-lactams, that is, 3-substituted 5,6-dihydro-1*H*-pyridin-2-ones, as substrates in intramolecular [2+2] photocycloaddition reactions might be sensible. Initial intramolecular attack of an appropriately chosen alkenyl or alkenyloxy double bond to the photoexcited lactam should occur at C3 (Scheme 2) and should be in the range of the steric shield. Potential substrates **2**–**6** with which the hypothesis was to be tested are depicted in Scheme 3.

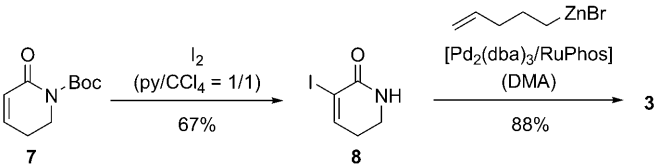
Herein, we report our work related to the photochemistry of 3-substituted 5,6-dihydro-1*H*-pyridin-2-ones. New synthetic routes to the precursor compounds **2**–**6** were devised, their photocycloaddition chemistry was studied, and the question of enantioselectivity was addressed. A noranalogue of the standard template **1** was prepared and employed in the [2+2] photocycloaddition reaction of the precursor compounds. The outcome of the reactions is compared with 4-substituted 5,6-dihydro-1*H*-pyridin-2-ones and the mechanistic differences are discussed.

2: *n* = 1; **3**: *n* = 2; **4**: *n* = 3 **5**: *n* = 1; **6**: *n* = 2

Scheme 3. The 3-substituted 5,6-dihydro-1*H*-pyridin-2-ones **2**–**6** as substrates for an intramolecular [2+2] photocycloaddition reaction.

Results and Discussion

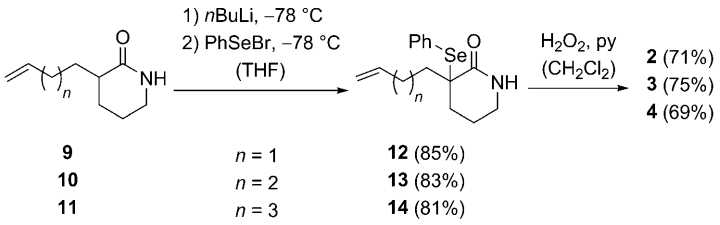
Synthesis of starting materials: The introduction of alkenyl substituents by cross-coupling reactions to the corresponding 3-halo-substituted 5,6-dihydro-1*H*-pyridin-2-ones struck us as the most straightforward entry to 3-substituted 5,6-dihydro-1*H*-pyridin-2-ones, such as **2**–**4**. Indeed, we recently reported the synthesis of 4-substituted 5,6-dihydro-1*H*-pyridin-2-ones by Negishi cross-coupling reactions of 4-bromo-substituted 5,6-dihydro-1*H*-pyridin-2-ones.[7] Moreover, Torisawa et al. had succeeded in the introduction of a new substituent at the 3-position of 3-iodo-substituted *N*-protected 5,6-dihydro-1*H*-pyridin-2-ones by a Negishi cross-coupling reaction.[8] There are further reports on the displacement of halogen substituents in α-halogenated α,β-unsaturated lactams by a cross-coupling reaction.[9] Thus, we identified iodide **8** as a suitable starting material for palladium-catalyzed cross-coupling reactions (Scheme 4). Given the relatively poor precedence for α-halogenation reactions of α,β-unsaturated lactams, we were delighted to observe a sufficient conversion into **8** by simply treating the known *N*-Boc-



Scheme 4. Synthesis of irradiation precursor **3** by a Negishi cross-coupling reaction. dba = dibenzylideneacetone, DMA = dimethylacetamide, RuPhos = 2-dicyclohexylphosphino-2″,6″-diisopropoxy-1,1″-biphenyl, py = pyridine.

protected lactam **7** [10] with iodine (2.5 equiv) in a 1:1 mixture of pyridine and carbon tetrachloride at ambient temperature.[11] The reaction was accompanied by *N*-Boc deprotection; the labile *N*-Boc-protected derivative of **8** could only be isolated in low amounts and in varying yields. The subsequent Negishi cross-coupling reaction of **8** in dimethylacetamide with pentenylzinc bromide (2 equiv), prepared from 5-bromo-1-pentene through reductive zincation,[12] proceeded at ambient temperature within 14 h using $[Pd_2(dba)_3]$ (5 mol%) as the catalyst and [RuPhos] (20 mol%)[13] as the ligand. The desired irradiation precursor **3** was obtained in 88% yield.

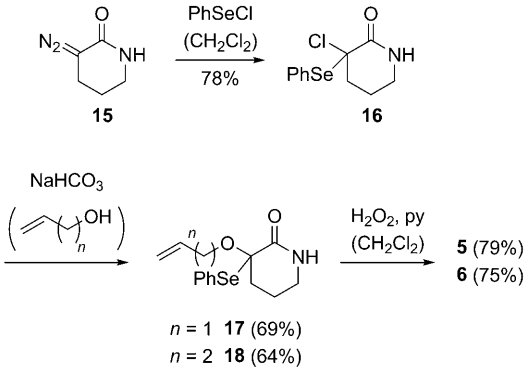
Although the introduction of further substituents at the 3-position of **8** (to the analogous lactams **2** and **4**) appeared feasible, the purification of the Negishi cross-coupling products was tedious. In addition, the synthesis of starting material **7** was lengthy[10] and was more time consuming than desirable. We, therefore, employed an alternative synthetic route to lactams **2**–**4**. The use of known α-alkenyl-substituted δ-valerolactams **9**–**11**, obtained by α-alkylation of the parent compound,[14] allowed short access to the desired compounds **2**–**4** within two steps (Scheme 5).



Scheme 5. Alternative approach to access irradiation precursors **2**–**4** starting from δ-lactams **9**–**11** via the intermediate selenides **12**–**14**.

In the first step, the dianion generated from **9**–**11** by the addition of *n*-butyllithium (2 equiv) was trapped with phenylselenyl bromide (3 equiv) as the electrophile, thus furnishing α-phenylselenylated lactams **12**–**14** in yields of 81–85%. Subsequent treatment of **12**–**14** with aqueous hydrogen peroxide (9 equiv, 30% v/v) and pyridine (2.5 equiv) in dichloromethane afforded the desired irradiation precursors **2**–**4** in yields of 69–75%. This synthetic path was a more viable alternative to the Negishi cross-coupling approach shown in Scheme 4 and delivered pure compounds in three steps starting from commercially available δ-valerolactam.

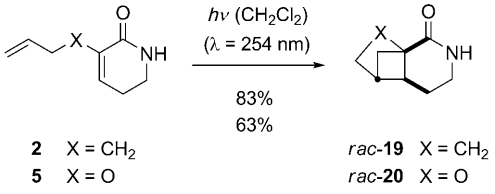
The α-alkenyloxy-substituted 5,6-dihydro-1*H*-pyridin-2-ones **5** and **6** were prepared to compare their behavior in the [2+2] photocycloaddition reactions to the alkenyl-substituted 5,6-dihydro-1*H*-pyridin-2-ones **2** and **3** with identical side-chain lengths at the 3-position. Intensive studies by Buckley and McKervey on reactions of α-diazoketones with selenium-based reagents[15] served as a guideline for a short access to compounds **5** and **6**. Additionally, the work of Bari and co-workers on the behavior of seleno β-lactams[16] encouraged us to attempt the synthetic route outlined in Scheme 6, for which the easily accessible α-diazolactam **15** proved to be a valuable starting material.[17] The addition of phenylselenyl chloride to a solution of **15** in dichloromethane delivered the α,α-adduct **16** in 78% yield through the loss of a nitrogen molecule. Attempts to prepare the analogous α-bromo adduct by the use of phenylselenyl bromide failed due to subsequent spontaneous elimination of hydrogen bromide in the desired product. The addition of a Lewis acid was not required to induce the α,α-chloroselenylation reaction. Substitution of the chloride ion by the corresponding alkenyloxy group was achieved by treatment of α,α-adduct **16** with sodium bicarbonate in a solution of allylic alcohol or 3-buten-1-ol. By this means, α-selenolactams **17** and **18** could be obtained in yields of 69 and 64%.



Scheme 6. Synthesis of irradiation precursors **5** and **6** starting from diazo compound **15** via the α,α-adduct **16** and selenides **17** and **18**.

As expected, the phenylseleno group in **17** and **18** was susceptible to elimination under mild oxidative conditions, as reported for **12**–**14** (see above). Thus, elimination of selenoxide occurred very efficiently at room temperature when the compounds were exposed to aqueous hydrogen peroxide (9 equiv, 30% v/v) and pyridine (2.5 equiv) in dichloromethane, whereupon 3-(allyloxy)-5,6-dihydro-1*H*-pyridin-2-one (**5**) and 3-(3′-butenyloxy)-5,6-dihydro-1*H*-pyridin-2-one (**6**) were obtained after purification in 79 and 75% yield.

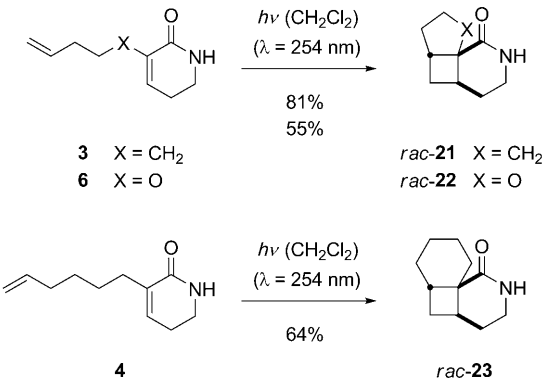
[2+2] Photocycloaddition reactions: Upon direct irradiation ($\lambda = 254$ nm, light source: Rayonet RPR-2537 Å; quartz vessel) of lactams **2**–**6** (Schemes 7 and 8), an efficient [2+2]



Scheme 7. Intramolecular [2+2] photocycloaddition reactions of substrates **2** and **5** to form the diastereomerically pure crossed products *rac*-**19** and *rac*-**20**.

photocycloadditition reaction was observed to provide the desired tricyclic products *rac*-**19**–*rac*-**23** in good yields. The optimized reaction conditions were identical to conditions previously reported.[5] The best results were achieved at room temperature by employing dichloromethane as the solvent at a substrate concentration of 5 mM. As expected from previous reports of related reactions,[18] the photocycloaddition reactions proceeded either to the crossed or straight photocycloaddition product, depending on the length of the spacer. Starting from amides **2** and **5**, the formation of the straight photocycloaddition products was unlikely. The short chain that connected the reactive centers would, in this reaction mode, only result in a highly strained bicyclo[2.2.0]hexane skeleton. In contrast, the formation of the crossed cycloaddition product with the concomitant formation of a bicyclo[2.1.1]hexane core was more likely and indeed occurred readily. Irradiation of amides **2** and **5** delivered the anticipated diastereomerically pure products *rac*-**19** and *rac*-**20** in good yields with reaction times of one hour or less (Scheme 7).

The [2+2] photocycloaddition reactions of amides **3**, **4**, and **6** (Scheme 8) were also rapid and high yielding. The



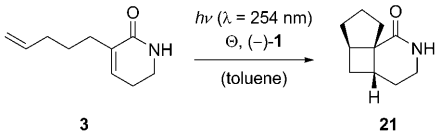
Scheme 8. Intramolecular [2+2] photocycloaddition reactions of substrates **3**, **6**, and **4** to form the diastereomerically pure straight products *rac*-**21**, *rac*-**22**, and *rac*-**23**.

length of the spacer between the reacting vinyl group and the β-position of the lactam allowed for exclusive formation of the straight products *rac*-**21**, *rac*-**22**, and *rac*-**23** in yields of 81, 65, and 64%, respectively. The reaction times for full conversion varied depending on the length of the side chain. The formation of the five-membered rings in the photocycloaddition products *rac*-**21** and *rac*-**22** was complete after one hour, whereas the transformation into the annelated six-membered ring in *rac*-**23** required two hours. Furthermore, the irradiation reactions of 5,6-dihydro-1*H*-pyridin-2-ones bearing a methylene group (X=CH_2) but no oxygen atom (X=O) at the 3-position led to higher yields if all the other parameters were unchanged (*rac*-**19** versus *rac*-**20** and *rac*-**21** versus *rac*-**22**).

The optimized reaction conditions delivered products of high analytical purity after flash chromatography. In all the cases, the use of anhydrous and degassed dichloromethane was of decisive importance for the success of the [2+2] photocycloaddition reactions. In oxygen-containing solvents, lower yields were observed due to decomposition reactions, which were visible by coloration of the reaction mixture. All the [2+2] photocycloaddition reactions mentioned so far proceeded with perfect regio- and simple diastereoselectivity. The products *rac*-**19**–*rac*-**23** were not contaminated with other regioisomers nor with other diastereoisomers. The regioselective formation of the straight versus crossed photocycloaddition products was unequivocally established by the NMR coupling pattern (^1H–^1H COSY) exhibited by the individual products. The [2+2] photocycloaddition reactions gave access to new ring systems, which are difficult to prepare by other methods. In addition, further reactions through ring opening of the lactam, for example, could lead to bicyclo[2.1.1]hexanes, bicyclo[3.2.0]heptanes, or a bicyclo[4.2.0]octane with an oxygen atom as a heteroatom in the 2-position for *rac*-**20** and *rac*-**22**. Additionally, one can consider ring-opening reactions that occurred at the cyclobutane[19] ring, thus providing access to spiro compounds in a highly diastereoselective fashion.

Enantioselectivity–temperature and concentration variation: Due to its easy accessibility, 5,6-dihydro-1*H*-pyridin-2-one **3** was selected for optimization of the reaction conditions in the enantioselective [2+2] photocycloaddition experiments (Table 1). According to the mode of action of the template (see above), the stereocontrol increases by increasing the amount of complexing agent (−)-**1** (Table 1, entries 2 and 3 as well as 4 and 5) and by lowering the reaction temperature, presumably due to the more extensive formation of the template–substrate complex. Toluene was the solvent of choice for the reaction because it had previously been optimal for the highly enantioselective [2+2] photocycloaddi-

Table 1. Variation in the amount of complexing agent (−)-**1**, temperature, and substrate concentration in the [2+2] photocycloaddition reaction of **3**→**21** and the influence on enantioselectivity.



Entry[a]	(−)-**1** [equiv]	Θ [°C]	*c* [mM]	*t* [h][b]	*ee* [%][c]
1	4.0	−75	5.0	4.0	84
2	2.6	−75	5.0	4.0	84
3	2.0	−75	5.0	4.0	81
4	2.0	−60	5.0	3.5	79
5	2.6	−60	5.0	3.5	82
6	2.6	−75	10.0	4.0	83

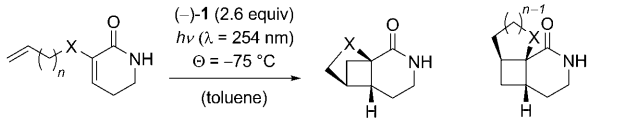
[a] All the reactions were conducted with Rayonet RPR-2537-Å lamps as the irradiation source and in toluene as the solvent. [b] Elapsed reaction times to achieve 100% conversion of the starting material. [c] The *ee* values were calculated from the enantiomeric ratios, which were determined by chiral GC analysis.

tion reactions of quinolones with complexing agents (+)-**1** or (−)-**1**.[2,20]

It can be inferred that an application of chiral template (−)-**1** in 2.6 equivalents is sufficient for a maximal induction of chirality at −75 °C (Table 1, entries 1–3). A comparison of entries 2 and 5 reveals that lower temperatures expectedly led to higher enantioselectivities with a slight decrease in the reaction rate (Table 1, entries 3 and 4). An increase in the substrate concentration, however, did not have a positive effect on the *ee* values (Table 1, entry 6). Therefore, the reaction conditions as described in entry 2 were employed for all subsequent enantioselective reactions in this study. It is noteworthy that for the reaction outlined in entry 2 87 % *ee* was observed after 53 % conversion, which then decreased to 84 % *ee* following complete conversion. This observation is consistent with the fact that the template slowly decomposes at an irradiation wavelength of $\lambda = 254$ nm.[5]

In a subsequent series of irradiation experiments, we investigated the substrate scope for the enantioselective [2+2] photocycloaddition reaction (Table 2). The [2+2] photocycloaddition precursors were subjected to the optimized irradiation conditions (see above), and the substrates containing an all-carbon tether generally provided products in higher yields and enantioselectivities relative to those with an oxygen atom in the tether. Additionally, the optimized conditions for the enantioselective [2+2] photocycloaddition reactions allowed for slightly higher yields in the formation of the crossed products relative to the straight counterparts (Table 2). This trend was not observed for irradiation experiments at room temperature in the absence of chiral agent (−)-**1**. Interestingly, the side-chain elongation of **4** ($n = 3$) versus **3** ($n = 2$) resulted in a dramatic decrease in the reaction rate and after four hours of irradiation of **4**, no conversion into the desired product was observed. Although the chiral template (−)-**1** potentially suffers from decomposition under the applied reaction conditions, substantial amounts of the template could be easily recovered by column chromatography in all cases (76–91 % recovery yield) except for **4** (Table 2, entry 3).

Table 2. Enantioselective [2+2] photocycloaddition reactions of substrates **2**–**6** in the presence of chiral template (−)-**1**.



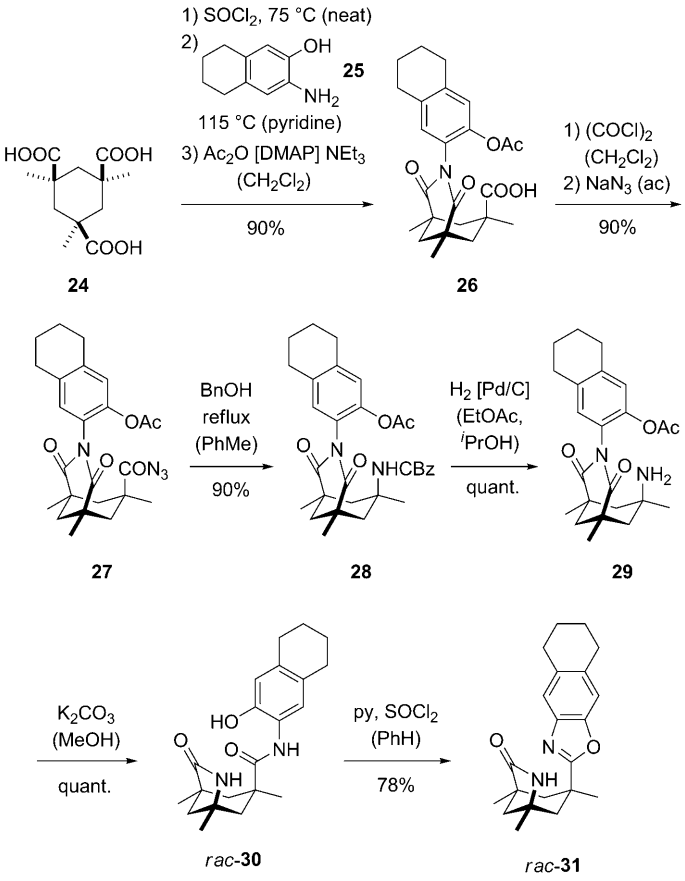
Entry[a]	Product	*t* [h]	Yield [%][b]	*ee* [%][c]	Recovery of (−)-**1** [%][d]
1	**19**	7.0	83	69	76
2	**21**	4.0	80	84	90
3	**23**	4.0	–[e]	n.d.[f]	n.d.[f]
4	**20**	5.5	61	40	88
5	**22**	4.0	53	60	91

[a] All the reactions were conducted at a substrate concentration of 5 mM with Rayonet RPR-2537-Å lamps as the irradiation source in toluene at −75 °C. [b] Yield of the isolated products. [c] The *ee* values were calculated from the enantiomeric ratios, which were determined by chiral GC analysis. [d] Yield of the recovered template (−)-**1**. [e] No conversion into the desired product was observed. [f] Value could not be determined.

The absolute product configuration can be deduced from the configuration of the respective 1:1 complex of the photocycloaddition precursor and template (−)-**1**. An approach from the less shielded *si* face (relative to C4) is favored, thus leading to the depicted products. For products **19** and **21**, the configuration was conclusively proven by comparison of measured and calculated CD spectral/optical rotation (OR) data (see the Supporting Information).[21] The major enantiomer exhibited a negative OR value at $\lambda = 589.3$ nm and showed a negative Cotton effect below $\lambda = 210$ nm in both cases. In addition, **21** showed a positive Cotton effect at $\lambda = 225$ nm. These data fit perfectly the calculated values. In addition, all the other major enantiomers **20**, **22**, and **23** obtained by reaction in the presence of (−)-**1** were levorotatory, thus supporting the observation that the chirality of the twisted lactam chromophore determines the optical properties of these compounds.

Enantioselectivity–template variation: The variable enantioselectivities achieved with carbon-tethered, relative to the oxygen-tethered, 3-substituted 5,6-dihydro-1*H*-pyridin-2-ones was considered to indicate a weaker template association of the oxygen-tethered substrates relative to the carbon-tethered substrates. Although the association constants for these bimolecular complexes can be obtained by various methods,[22] their determination is a very time-consuming exercise, the reliability of which is limited in cases with poorly soluble substrates. We, therefore, wanted to devise a slightly modified template as an alternative probe for template association. To this end, the noranalogue of template **1**, namely, template **31**, was prepared, which contains a γ-lactam unit as a recognition site as compared to the δ-lactam in the conventional template **1** (Scheme 9).

The synthesis commenced with the Kemp triacid (**24**), which was upon successive treatment with thionyl chloride and the known 3-amino-5,6,7,8-tetrahydronaphthalen-2-ol (**25**) converted into an *ortho*-imidophenol.[23,24] Because the free phenol turned out to be inseparable from impurities, it was protected to yield the acetate **26** in 90 % over three steps. The formation of the corresponding acid chloride was achieved with oxalyl chloride under DMF catalysis. Subsequent treatment with sodium azide yielded the corresponding acyl azide **27** in 90 % yield, which underwent a thermal Curtius degradation in refluxing toluene containing benzyl alcohol to trap the primary isocyanate as carbamate **28** (90 % yield).[25,26] Hydrogenolytic cleavage of the resulting benzyloxycarbonyl (Cbz) group quantitatively delivered amine **29** as the starting material for the planned imide/lactam rearrangement.[26] Potassium carbonate in methanol induced the ring contraction and the acetate deprotection to

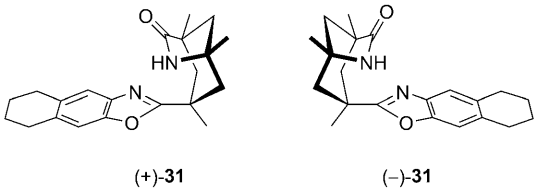


Scheme 9. Transformation of the Kemp triacid (**24**) into template **31** through a Curtius rearrangement of azide **27** and subsequent lactam ring formation of amine **29**. DMAP = 4-dimethylaminopyridine.

form the desired racemic five-memered γ-lactam *rac*-**30**, which underwent cyclization to form the benzoxazole *rac*-**31** under known conditions.[27]

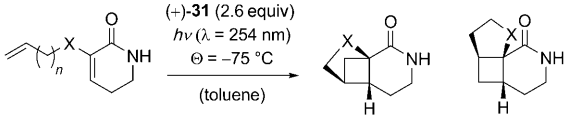
Separation of the enantiomers of **31** was possible either by semipreparative HPLC or by conventional resolution of the diastereoisomeric carbamates that resulted from the reaction of *rac*-**31** with (−)-menthyl chloroformate and subsequent hydrolysis (see the Supporting Information).[27] The absolute configuration was determined by NMR titration studies by employing a previously reported method.[4b] Notably, the (+)-enantiomer of **31** corresponds to (−)-**1** with regard to its stereodirecting groups, whereas (+)-**31** and (+)-**1** behave as if they were enantiomers (Scheme 10).

In a series of irradiation experiments with the four 3-substituted 5,6-dihydro-1*H*-pyridin-2-ones **2**, **3**, and the oxygen-containing analogues **5** and **6**, we investigated the influence of the truncated complexing agent (+)-**31** on their enantioselective [2+2] photocycloaddition reactions (Table 3) under the optimized irradiation conditions (see above). Upon irradiation in the presence of (+)-**31**, oxygen-containing substrates **5** and **6** delivered a remarkably higher enantiomeric excess in the products (Table 3, entries 3 and 4) than with (−)-**1** (Table 2, entries 4 and 5). The substrates



Scheme 10. Structure of the chiral complexing agent (+)-**31** and its enantiomer (−)-**31**.

Table 3. Enantioselective [2+2] photocycloaddition reactions of substrates **2**, **3**, **5**, and **6** in the presence of chiral template (+)-**31**.



2/**3** (*n* = 1/2)
5/**6** (*n* = 1/2)

19: X = CH_2
20: X = O
21: X = CH_2
22: X = O

Entry[a]	Product	*t* [h]	Yield [%][b]	*ee* [%][c]	Recovery of (+)-**31** [%][d]
1	**19**	5.5	74	50	95
2	**21**	4.0	76	85	93
3	**20**	5.5	70	56	100
4	**22**	6.0	76	79	92

[a] All the reactions were conducted at a substrate concentration of 5 mM with Rayonet RPR-2537-Å lamps as the irradiation source in toluene at −75 °C. [b] Yield of the isolated products. [c] The *ee* values were calculated from the enantiomeric ratios, which were determined by chiral GC analysis. [d] Yield of the recovered template (+)-**31**.

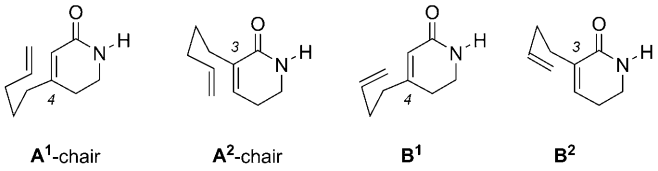
containing an all-carbon tether, however, gave lower (Table 3, entry 1) or only slightly higher (Table 3, entry 2) selectivities. The yields of the products were in the same range. Template (+)-**31** seems to be somewhat more stable under the irradiation conditions because recovery of the template was almost complete after column chromatography.

Discussion

Although the improvements achieved with template **31** relative to **1** are not ground-breaking, it is apparent from these results that the association behavior of the substrate with the template plays a role in the enantioface-differentiating process. It is also apparent, however, that the association of 5,6-dihydro-1*H*-pyridin-2-ones with another lactam based on two hydrogen bonds is limited and cannot be increased without significant electronic and structural changes. It can be concluded that an enantiomeric excess of 50–85 % *ee* can be achieved with 3-substituted 5,6-dihydro-1*H*-pyridin-2-ones in the presence of templates derived from the Kemp triacid. Higher selectivities are not feasible presumably because the substrate/template association is not perfect.

To understand the differences between 3- and 4-substituted 5,6-dihydro-1*H*-pyridin-2-ones, a closer look at the conformational aspects of the [2+2] photocycloaddition reac-

tion may be helpful. Indeed, a comparison of the enantioselective template-mediated [2+2] photocycloaddition reaction of 3-(4′-pentenyl)-5,6-dihydro-pyridin-1*H*-one (**3**; 84% *ee*, 80% yield) with its 4-substituted analogue[5] (34% *ee*, 80% yield) under low-temperature reaction conditions reveals that the initial hypothesis (Scheme 2), which concerned better substrate shielding of substrates with a substituent at the 3-position, seems to hold. Productive chair-type conformations "**A**^{1}-chair" and "**A**^{2}-chair" can be responsible for rapid and very effective photocycloaddition reactions (Scheme 11).

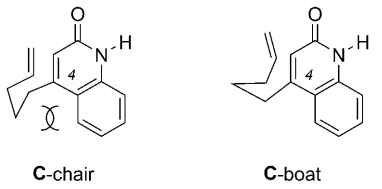


Scheme 11. Conformations **A**^{1}-chair, **A**^{2}-chair, **B**^{1}, and **B**^{2} that result in a productive intramolecular [2+2] photocycloaddition reaction to the straight and crossed products (via **A** and **B**, respectively).

From comparing Scheme 11 with Scheme 2, it is evident that the alkyl chain in the **A**^{1}-chair conformation folds away from the tetrahydronaphthalene shield of the template, whereas the steric interaction is more intense in the conformation of the **A**^{2}-chair substrate **3**. In an analogous fashion, the 3′-butenyl-substituted substrates react presumably through related envelope-type conformations **B**^{1} and **B**^{2} with the first C–C formed between C3 or C4 and the respective terminal carbon atom of the butenyl side chain. Indeed, the 4-substituted analogue of substrate **2** shows also a significantly poorer performance in its enantioselective intramolecular photocycloaddition reaction (37% *ee*)[5] than substrate **2** itself (69% *ee*). Six-membered ring formation that starts from substrate **4** is apparently not feasible at low temperature due to a disfavored trajectory of the reacting centers.

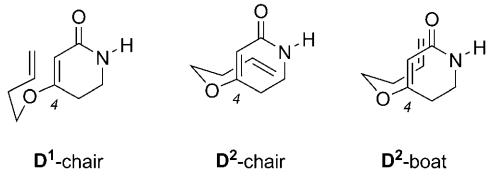
The relatively high enantioselectivities ($\geq$90% *ee*) observed in the template-induced enantioselective [2+2] photocycloaddition reaction of many 4-substituted quinolones appears at first sight to contradict the analysis provided for 4-substituted 5,6-dihydro-1*H*-pyridin-2-ones. As earlier mentioned, however, the situation in intramolecular quinolone photocycloaddition reactions (e.g., for 4-(4′-pentenyl)quinolone) is different as 1,3-allylic strain disfavors the chair conformation "**C**-chair" but favors the conformation "**C**-boat", in which the steric interaction of the chain with the template becomes significant (Scheme 12). In addition, higher association constants of quinolones to template **1** are expected relative to 5,6-dihydro-1*H*-pyridin-2-ones due to the entirely flat structure of the quinolone heterocycle.

Conformations similar to the **A**^{2}-chair and **B**^{2} should also be adopted preferentially by the oxygen analogues **5** and **6** of substrates **2** and **3**. The lower enantioselectivity achieved with these substrates in the presence of template **1** could be



Scheme 12. The preferred conformation **C**-boat in the intramolecular [2+2] photocycloaddition reactions of 4-substituted quinolones as opposed to the disfavored conformation **C**-chair.

associated at least partially with their lower association tendency. Indeed, the noranalogue of **1**, namely, template **31**, provided a significantly improved enantioselectivity (see above). The unusual behavior of 4-(4′-butenyloxy)-5,6-dihydro-1*H*-pyridin-2-one, the regioisomer of substrate **6**, which gave high enantioselectivities (75% *ee*) previously, albeit at an extremely slow conversion,[5] is not in line with the preferred conformation of the "**D**^{1}-chair", which would be expected to be highly productive but only moderately enantioselective. It is speculated that due to a dipole–dipole repulsion[28] the **D**^{2}-chair conformation is preferred to lead to a 1,4-biradical, which is, however, not competent to form a four-membered ring (the resulting product would be a *trans*-fused oxabicyclo[3.2.0]heptane). The productive **D**^{2}-boat conformation is less populated but delivers—if product formation occurs—a relatively high enantiomeric excess because the butenyloxy chain is directed into the proximity of the tetrahydronaphthalene backbone (Scheme 13).



Scheme 13. Conformations **D** accessible to 4-(4′-butenyloxy)-5,6-dihydro-1*H*-pyridin-2-one. The unproductive conformation **D**^{2}-chair is believed to be preferred over the conformation **D**^{1}-chair due to dipole minimization, whereas the productive conformation **D**^{2}-boat accounts for a high enantioselectivity in a template-induced enantioselective intramolecular [2+2] photocycloaddition reaction.

Conclusion

In summary, the hypothesis that 3-substituted 5,6-dihydro-1*H*-pyridin-2-ones react in a template-directed [2+2] photocycloaddition reaction with higher enantioselectivity than their respective 4-substituted analogues could be verified. The intramolecular [2+2] photocycloaddition reactions of 3-(ω′-alkenyl)- and 3-(ω′-alkenyloxy)-substituted 5,6-dihydro-1*H*-pyridin-2-ones proceeded with excellent regio- and diastereoselectivites to the respective crossed or straight addition products. Enantioselectivities achieved in the presence of the chiral complexing agents (−)-**1** and (+)-**31** reached, in the best cases, 69% *ee* for **19** with **1**; 85% *ee* for

21 with **31**; 56% *ee* for **20** with **31**; and 79% *ee* for **22** with **31**. It is likely that a further improvement in the selectivities requires stronger template–substrate binding, which in turn requires tuning of the electronic properties of the template. Current studies along these lines are in progress.

Experimental Section

General: All commercially available chemicals were used as received without further purification. Reactions involving the water-sensitive chemical *n*-butyllithium were performed in dried glassware under argon using anhydrous solvents. Common solvents for chromatography (i.e., pentane, EtOAc, CH_2Cl_2, and MeOH) were distilled prior to use. Ceric ammonium molybdate (CAM) or potassium permanganate were used to visualize TLC spots, which could not be clearly detected by UV radiation. IR spectra were recorded from powders (for solids) or films (for liquids) in the attenuated total reflection (ATR) mode. ^{1}H and ^{13}C NMR spectra were recorded in the indicated solvent. Chemical shifts are reported relative to solvent residue signals as an internal standard. Apparent multiplets, which occur as a result of the accidental equality of coupling constants of magnetically nonequivalent protons are marked as virtual (virt.). The multiplicities of the ^{13}C NMR signals were determined by jmod experiments. The ^{13}C NMR spectra of all the new compounds are presented in the Supporting Information.

Preparation of starting materials: *tert*-Butyl-5,6-dihydro-2-oxopyridine-1(2*H*)-carboxylate (**7**),[10] 3-(3′-butenyl)piperidin-2-one (**9**),[14] 3-(4′-pentenyl)piperidin-2-one (**10**),[14] 3-(5′-hexenyl)piperidin-2-one (**11**),[14] 3-diazopiperidin-2-one (**15**),[17] and 3-amino-5,6,7,8-tetrahydronaphthalene-2-ol (**25**)[24] were synthesized according to reported procedures. 5-Bromo-1-pentene, 3-buten-1-ol, and the Kemp triacid (**24**) are commercially available.

3-Iodo-5,6-dihydro-1*H*-pyridin-2-one (8): Iodine (3.22 g, 12.7 mmol) was added to a solution of *tert*-butyl-2-oxo-5,6-dihydro-2*H*-pyridine-1-carboxylate (**7**;[10] 1.00 g, 5.07 mmol) in CCl_4/pyridine (50 mL, 1:1) at room temperature, and the mixture was stirred for 4 h. Saturated aqueous NH_4Cl (250 mL) was added to the reaction mixture, which was extracted with EtOAc (3×100 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography (EtOAc) to give iodide **8** as a pale-yellow solid (758 mg, 3.40 mmol, 67%). R_f=0.48 (EtOAc, 100%; CAM, UV); m.p. 85 °C; ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ=7.38 (t, ^3J=4.7 Hz, 1H), 6.98 (brs, 1H), 3.51–3.47 (AA′XX′, m, 2H), 2.41–2.35 ppm (AA′XX′, m, 2H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ=162.3 (s), 150.5 (d), 95.6 (s), 40.1 (t), 28.0 ppm (t); IR (powder): $\tilde{\nu}$=3205 (s), 2872 (s), 1677 (vs), 1594 (s), 1472 (s), 1416 (m), 1398 (m), 1347 (s), 1329 (m), 1275 (s), 1229 (m), 1192 (w), 1009 (s), 989 (m), 902 (w), 880 (m), 848 (m), 772 (s), 700 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 223 (100) [M^+], 194 (55), 166 (14), 152 (3), 127 (3), [I^+], 96 (21) [$M-I^+$], 53 (8), 39 (26); HRMS (70 eV): *m*/*z* calcd for C_5H_6INO: 222.9494 [M^+]; found: 222.9496.

3-(4′-Pentenyl)-5,6-dihydro-1*H*-pyridin-2-one (3): *Synthesis with 3-(4′-pentenyl)-3-(phenylselanyl)piperidin-2-one (**13**) as the starting material*: Aqueous hydrogen peroxide (848 μL, 8.38 mmol; 30% v/v) was added to a solution of 3-(4′-pentenyl)-3-(phenylselanyl)piperidin-2-one (**13**; 300 mg, 931 μmol) and pyridine (187 μL, 184 mg, 2.33 mmol) in CH_2Cl_2 (10 mL) at room temperature, and the mixture was stirred for 2 h. Saturated aqueous NH_4Cl (20 mL) was added to the reaction mixture, which was extracted with CH_2Cl_2 (3×20 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography (EtOAc) to give **3** as a colorless solid (115 mg, 698 μmol, 75%).

*Synthesis with 3-iodo-5,6-dihydro-1H-pyridin-2-one (**8**) as the starting material*: A mixture of dry dimethylacetamide (2 mL), iodine (7.00 mg, 27.5 μmol), and zinc dust (55.2 mg, 844 μmol) was stirred at room temperature in a dry 10-mL Schlenk tube under argon until the yellow color of iodine had disappeared. 5-Bromo-1-pentene (67.3 μL, 568 μmol) was added to the reaction mixture, which was stirred at 80 °C for 3 h. The mixture was cooled to room temperature and stirring was stopped. The remaining zinc dust was allowed to settle (ca. 1 h). The supernatant liquid containing pentenylzinc bromide could be easily transferred in a syringe and was submitted to a Negishi cross-coupling reaction (see below).

Compound **8** (63.0 mg, 282 μmol) was added to a solution of [$Pd_2(dba)_3$] (13.0 mg, 14.2 μmol) and [RuPhos] (26.4 mg, 56.8 μmol) in dry dimethylacetamide (2 mL) at room temperature. After the mixture had been stirred for 10 min, the pre-prepared solution of pentenylzinc bromide was added immediately. After the reaction mixture had been stirred at room temperature for 14 h, the solvent was removed under reduced pressure. Purification by flash chromatography (EtOAc) yielded **3** as a colorless solid (41.0 mg, 248 μmol, 88%). R_f=0.50 (EtOAc, 100%; CAM, UV); m.p. 36–38 °C; ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ=6.46 (brs, 1H), 6.31 (t, ^3J=4.3 Hz, 1H), 5.79 (ddt, ^3J=16.6, ^3J=10.2, ^3J=6.6 Hz, 1H), 5.01–4.90 (m, 2H), 3.37–3.32 (AA′XX′, m, 2H), 2.42–2.22 (m, 4H), 2.09–2.02 (AA′XX′, m, 2H), 1.57–1.49 ppm (m, 2H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ=167.5 (s), 138.7 (d), 135.3 (s), 135.0 (d), 114.6 (t), 39.8 (t), 33.4 (t), 29.8 (t), 27.8 (t), 24.3 ppm (t); IR (powder): $\tilde{\nu}$=3188 (m), 3066 (m), 2931 (s), 1670 (vs), 1621 (vs), 1481 (m), 1427 (m), 1353 (m), 1289 (m), 1155 (m), 994 (m), 931 (m), 916 (m), 867 (m), 835 (m), 811 (m), 763 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 165 (47) [M^+], 150 (19), 136 (49), 124 (37) [$M-C_3H_5^+$], 111 (100) [$M-C_4H_6^+$], 95 (26), 82 (83), 67 (22), 53 (27), 41 (28) [$C_3H_5^+$]; HRMS (70 eV): *m*/*z* calcd for $C_{10}H_{15}NO$: 165.1154 [M^+]; found: 165.1156.

3-(3′-Butenyl)-5,6-dihydro-1*H*-pyridin-2-one (2): Aqueous hydrogen peroxide (1.48 mL, 14.6 mmol, 30% v/v) was added to a solution of 3-(3′-butenyl)-3-(phenylselanyl)piperidin-2-one (**12**; 500 mg, 1.62 mmol) and pyridine (325 μL, 320 mg, 4.05 mmol) in CH_2Cl_2 (15 mL) at room temperature, and the mixture was stirred for 2 h. Saturated aqueous NH_4Cl (30 mL) was added to the reaction mixture, which was extracted with CH_2Cl_2 (3×30 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography (EtOAc) to give **2** as a colorless oil (174 mg, 1.15 mmol, 71%). R_f=0.48 (EtOAc, 100%; CAM, UV); ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ=6.31 (t, ^3J=4.3 Hz, 1H), 6.39 (brs, 1H), 5.80 (ddt, ^3J=16.8, ^3J=10.2, ^3J=6.6 Hz, 1H), 5.03–4.94 (m, 2H), 3.38–3.31 (AA′XX′, m, 2H), 2.38–2.30 (m, 4H), 2.25–2.19 ppm (m, 2H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ=167.2 (s), 138.2 (d), 135.4 (d), 134.7 (s), 115.0 (t), 40.0 (t), 32.8 (t), 29.8 (t), 24.4 ppm (t); IR (film): $\tilde{\nu}$=3195 (m), 2926 (m), 2874 (s), 1664 (vs), 1614 (vs), 1578 (w), 1477 (m), 1453 (m), 1436 (m), 1416 (m), 1291 (m), 1279 (m), 1070 (m), 1021 (m), 737 (s), 691 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 151 (100) [M^+], 136 (92), 122 (22), 107 (21), 93 (19), 81 (31), 53 (39), 41 (26) [$C_3H_5^+$]; HRMS (70 eV): *m*/*z* calcd for $C_9H_{13}NO$: 151.0997 [M^+]; found: 151.0998.

3-(5′-Hexenyl)-5,6-dihydro-1*H*-pyridin-2-one (4): Aqueous hydrogen peroxide (1.09 mL, 10.7 mmol, 30% v/v) was added to a solution of 3-(5′-hexenyl)-3-(phenylselanyl)piperidin-2-one (**14**; 400 mg, 1.19 mmol) and pyridine (239 μL, 235 mg, 2.97 mmol) in CH_2Cl_2 (10 mL) at room temperature, and the mixture was stirred for 2 h. Saturated aqueous NH_4Cl (20 mL) was added to the reaction mixture, which was extracted with CH_2Cl_2 (3×20 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography (EtOAc) to give **4** as a colorless oil (147 mg, 821 μmol, 69%). R_f=0.51 (EtOAc, 100%; CAM, UV); ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ=6.33–6.32 (m, 1H), 5.96 (brs, 1H), 5.85 (ddt, ^3J=16.9, ^3J=10.1, ^3J=6.7 Hz, 1H), 5.01–4.90 (m, 2H), 3.40–3.36 (AA′XX′, m, 2H), 2.34–2.24 (m, 4H), 2.08–2.03 (m, 2H), 1.50–1.40 ppm (m, 4H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ=167.4 (s), 139.1 (d), 135.5 (s), 134.8 (d), 114.4 (t), 40.0 (t), 33.7 (t), 30.2 (t), 28.7 (t), 28.1 (t), 24.3 ppm (t); IR (film): $\tilde{\nu}$ = 3189 (m), 2928 (m), 2856 (s), 1672 (vs), 1624 (vs), 1479 (m), 1455 (m), 1428 (m), 1339 (m), 1291 (m), 1105 (m), 993 (m), 908 (m), 848 (m), 752 (m), 738 (m), 670 (m), 658 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 179 (48) [M^+], 164 (9), 150 (32), 138 (100) [$M-C_3H_5^+$], 111 (100) [$M-C_5H_8^+$], 95 (18), 82 (32), 67 (18), 53 (16), 41 (27) [$C_3H_5^+$]; HRMS (70 eV): *m*/*z* calcd for $C_{11}H_{17}NO$: 179.1310 [M^+]; found: 179.1309.

3-(3′-Butenyl)-3-(phenylselanyl)piperidin-2-one (12): A solution of *n*-butyllithium (2.5 M, 2.61 mL, 6.52 mmol) in hexane was added dropwise to a solution of 3-(3′-butenyl)piperidin-2-one (**9**;[14] 500 mg, 3.26 mmol) in dry THF (30 mL) in an inert atmosphere at −78 °C. The resulting mixture was stirred for 1 h and allowed to warm to 0 °C. After the reaction mixture was cooled again to −78 °C, phenylselenyl bromide (2.31 g, 9.78 mmol) was added immediately, and the resulting mixture was allowed to warm to 0 °C within 15 min. After the addition of saturated aqueous NH_4Cl (50 mL), the mixture was extracted with EtOAc (3× 50 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography (pentane/EtOAc 1:1) to give **12** as a colorless oil (854 mg, 2.77 mmol, 85 %). R_f = 0.27 (pentane/EtOAc 1:1; CAM, UV); ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ = 7.67–7.64 (m, 2H), 7.40–7.35 (m, 1H), 7.32–7.28 (m, 2H), 5.94 (br s, 1H), 5.78–5.70 (m, 1H), 5.01–4.89 (m, 2H), 3.32–3.28 (m, 2H), 2.21–2.04 (m, 4H), 2.00–1.97 (m, 2H), 1.84–1.70 ppm (m, 2H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ = 173.0 (s), 138.3 (d), 138.0 (d), 129.3 (d), 128.9 (d), 127.6 (s), 115.0 (t), 52.3 (s), 42.6 (t), 38.0 (t), 32.2 (t), 29.8 (t), 20.3 ppm (t); IR (film): $\tilde{\nu}$ = 3185 (m), 3073 (m), 2933 (m), 1649 (vs), 1483 (m), 1436 (m), 1415 (m), 1354 (m), 1327 (m), 1304 (m), 1276 (m), 1208 (m), 1116 (m), 1021 (m), 921 (m), 835 (m), 827 (m), 740 (m), 698 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 309 (18) [M^+], 255 (38) [$M-C_4H_6^+$], 152 (100) [$M-C_6H_5Se^+$], 112 (18), 99 (35), 81 (17), 41 (14) [$C_3H_5^+$]; HRMS (70 eV): *m*/*z* calcd for $C_{15}H_{19}NOSe$: 309.0632 [M^+]; found: 309.0645.

3-(4′-Pentenyl)-3-(phenylselanyl)piperidin-2-one (13): A solution of *n*-butyllithium (2.5 M, 2.39 mL, 5.98 mmol) in hexane was added dropwise to a solution of 3-(4′-pentenyl)piperidin-2-one (**10**;[14] 500 mg, 2.99 mmol) in dry THF (30 mL) in an inert atmosphere at −78 °C. The resulting mixture was stirred for 1 h and allowed to warm to 0 °C. After the reaction mixture was again cooled to −78 °C, phenylselenyl bromide (2.12 g, 8.97 mmol) was added immediately and the resulting mixture was then allowed to warm to 0 °C within 15 min. After addition of saturated aqueous NH_4Cl (50 mL), the mixture was extracted with EtOAc (3×50 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography (pentane/EtOAc 1:1) to give **13** as a colorless solid (800 mg, 2.48 mmol, 83 %). R_f = 0.29 (pentane/EtOAc 1:1; CAM, UV); m.p. 85 °C; ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ = 7.67–7.64 (m, 2H), 7.38–7.35 (m, 1H), 7.31–7.28 (m, 2H), 6.12 (br s, 1H), 5.78–5.69 (m, 1H), 4.98–4.90 (m, 2H), 3.28–3.27 (m, 2H), 2.15–1.88 (m, 6H), 1.78–1.65 (m, 2H), 1.60–1.30 ppm (m, 2H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ = 173.2 (s), 138.5 (d), 138.2 (d), 129.2 (d), 128.9 (d), 127.7 (s), 114.8 (t), 52.5 (s), 42.6 (t), 38.4 (t), 34.0 (t), 32.3 (t), 24.8 (t), 20.3 ppm (t); IR (powder): $\tilde{\nu}$ = 3176 (m), 3054 (m), 2928 (m), 1650 (vs), 1485 (m), 1435 (m), 1414 (m), 1355 (m), 1328 (m), 1304 (m), 1275 (m), 1204 (m), 1120 (m), 1021 (m), 998 (m), 907 (m), 741 (m), 697 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 323 (4) [M^+], 255 (10) [$M-C_5H_8^+$], 166 (100) [$M-C_6H_5Se^+$], 112 (21), 81 (10), 77 (6) [$C_6H_5^+$]; HRMS (70 eV): *m*/*z* calcd for $C_{16}H_{21}NOSe$: 323.0788 [M^+]; found: 323.0782.

3-(5′-Hexenyl)-3-(phenylselanyl)piperidin-2-one (14): A solution of *n*-butyllithium (2.5 M, 2.21 mL, 5.52 mmol) in hexane was added dropwise to a solution of 3-(5′-hexenyl)piperidin-2-one (**11**;[14] 500 mg, 2.76 mmol) in dry THF (30 mL) in an inert atmosphere at −78 °C. The resulting mixture was stirred for 1 h and allowed to warm to 0 °C. After the reaction mixture was again cooled to −78 °C, phenylselenyl bromide (1.95 g, 8.27 mmol) was added immediately, and the resulting mixture was then allowed to warm to 0 °C within 15 min. After the addition of saturated aqueous NH_4Cl (50 mL), the mixture was extracted with EtOAc (3× 50 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography (pentane/EtOAc 1:1) to give **14** as a colorless oil (752 mg, 2.24 mmol, 81 %). R_f = 0.31 (pentane/EtOAc 1:1; CAM, UV); ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ = 7.67–7.63 (m, 2H), 7.37–7.26 (m, 3H), 6.20 (br s, 1H), 5.81–5.70 (m, 1H), 4.99–4.90 (m, 2H), 3.29–3.25 (m, 2H), 2.15–1.90 (m, 6H), 1.78–1.64 (m, 2H), 1.45–1.25 ppm (m, 4H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ = 173.6 (s), 139.1 (d), 138.5 (d), 129.5 (d), 129.1 (d), 128.0 (s), 114.8 (t), 52.9 (s), 42.9 (t), 39.0 (t), 34.0 (t), 32.5 (t), 29.5 (t), 25.1 (t), 20.6 ppm (t); IR (film): $\tilde{\nu}$ = 3168 (m), 3058 (m), 2932 (m), 2859 (m), 1656 (vs), 1484 (m), 1475 (m), 1436 (m), 1351 (m), 1319 (m), 1018 (m), 989 (m), 912 (m), 741 (m), 693 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 337 (8) [M^+], 256 (10) [$M-C_6H_{10}^+$], 180 (100) [$M-C_6H_5Se^+$], 152 (11) [$C_6H_5Se^+$], 112 (23), 100 (11), 81 (22), 67 (10), 55 (13), 41 (14) [$C_3H_5^+$]; HRMS (70 eV): *m*/*z* calcd for $C_{17}H_{23}NOSe$: 337.0945 [M^+]; found: 337.0944.

3-Chloro-3-(phenylselanyl)piperidin-2-one (16): Phenylselenyl chloride (153 mg, 800 μmol) was added to a solution of 3-diazo-piperidin-2-one (**15**;[17] 100 mg, 799 μmol) in dry CH_2Cl_2 (5 mL) at room temperature. The reaction mixture was stirred for 15 min at room temperature and the evolution of nitrogen was observed. The solvent was removed under reduced pressure, and the crude product was purified by flash chromatography (pentane/EtOAc 1:1) to give **16** as a colorless oil (180 mg, 623 μmol, 78 %). R_f = 0.58 (EtOAc, 100 %); UV); ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ = 7.68–7.66 (m, 2H), 7.48–7.30 (m, 3H), 7.25 (br s, 1H), 3.48–3.22 (m, 2H), 2.45–2.22 (m, 1H), 2.18–2.04 (m, 1H), 2.00–1.71 ppm (m, 2H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ = 168.6 (s), 137.8 (d), 130.0 (d), 129.2 (d), 126.8 (s), 76.3 (s), 42.4 (t), 40.1 (t), 19.8 ppm (t); MS (EI, 70 eV): *m*/*z* (%): 288 (1) [M^+], 255 (19) [$M-Cl^+$], 253 (100), 172 (32), 115 (66), 105 (53), 77 (20), 51 (13); HRMS (70 eV): *m*/*z* calcd for $C_{11}H_{12}ClNOSe$: 288.9773 [M^+]; found: 288.9759.

3-(Allyloxy)-3-(phenylselanyl)piperidin-2-one (17): Sodium hydrogencarbonate (293 mg, 3.49 mmol) was added to a solution of **16** (200 mg, 693 μmol) in dry allylic alcohol (2 mL) in an argon atmosphere, and the reaction mixture was stirred for 15 h at room temperature. After the allylic alcohol was removed under reduced pressure and brine (20 mL) added, the mixture was extracted with EtOAc (3×20 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography (pentane/EtOAc 1:1) to give **17** as a colorless solid (148 mg, 478 μmol, 69 %). R_f = 0.75 (EtOAc, 100 %; CAM, UV); m.p. 88–90 °C; ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ = 7.57–7.55 (m, 2H), 7.34–7.28 (m, 3H), 6.20 (br s, 1H), 5.99 (ddt, ^3J = 17.1, ^3J = 10.5, ^3J = 5.4 Hz, 1H), 5.33 (ddt, ^2J = 3.2, ^3J = 17.1, ^4J = 1.4 Hz, 1H), 5.19 (ddt, ^2J = 3.2, ^3J = 10.5, ^4J = 1.4 Hz, 1H), 4.78 (ddt, ^2J = 13.0, ^3J = 5.4, ^4J = 1.4 Hz, 1H), 4.25 (ddt, ^2J = 13.0, ^3J = 5.4, ^4J = 1.4 Hz, 1H), 3.39–3.25 (m, 2H), 2.10 (ddd, ^2J = 14.9, ^3J = 11.4, ^3J = 3.5 Hz, 1H), 1.98–1.85 (m, 2H), 1.77–1.65 ppm (m, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ = 168.7 (s), 137.2 (d), 134.5 (d), 128.9 (d), 128.5 (d), 128.0 (s), 116.7 (t), 89.4 (s), 68.1 (t), 42.6 (t), 36.6 (t), 19.7 ppm (t); IR (powder): $\tilde{\nu}$ = 3185 (m), 3054 (m), 2934 (m), 1670 (vs), 1644 (vs), 1489 (m), 1476 (m), 1437 (m), 1421 (m), 1352 (m), 1327 (m), 1275 (m), 1208 (m), 1201 (m), 1157 (m), 1118 (m), 1041 (m), 984 (m), 943 (m), 918 (m), 827 (m), 741 (m), 730 (m), 689 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 311 (1) [M^+], 154 (100) [$M-C_6H_5Se^+$], 157 (16) [$C_6H_5Se^+$], 126 (13), 114 (40) [$M-C_6H_5Se-C_3H_5^+$], 86 (15), 77 (11) [$C_6H_5^+$], 41 (40) [$C_3H_5^+$]; HRMS (70 eV): *m*/*z* calcd for $C_{14}H_{17}NO_2Se$: 311.0424 [M^+]; found: 311.0412.

3-(3′-Butenyloxy)-3-(phenylselanyl)piperidin-2-one (18): Sodium hydrogencarbonate (293 mg, 3.49 mmol) was added to a solution of **16** (200 mg, 693 μmol) in dry but-3-en-1-ol (2 mL) in an argon atmosphere, and the reaction mixture was stirred for 15 h at room temperature. After the allylic alcohol had been removed under reduced pressure and brine (20 mL) added, the mixture was extracted with EtOAc (3×20 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography (pentane/EtOAc 1:1) to give **18** as a colorless solid (144 mg, 444 μmol, 64 %). R_f = 0.77 (EtOAc, 100 %; CAM, UV); m.p. 105 °C; ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ = 7.64–7.58 (m, 2H), 7.39–7.28 (m, 3H), 6.20 (br s, 1H), 5.85 (ddt, ^3J = 17.0, ^3J = 10.2, ^3J = 6.7 Hz, 1H), 5.15–5.03 (m, 2H), 4.18 (dt, ^2J = 9.5, ^3J = 6.7 Hz, 1H), 3.72 (dt, ^2J = 9.5, ^3J = 6.7 Hz, 1H), 3.39–3.21 (m, 2H), 2.41–2.38 (m, 2H), 2.08 (ddd, ^2J = 3.6, ^3J = 14.3, ^3J = 11.6 Hz, 1H), 1.98–1.88 (m, 2H), 1.75–1.63 ppm (m, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ = 168.8 (s), 137.1 (d), 135.5 (d), 128.8 (d), 128.4 (d), 128.2 (s), 116.6 (t), 89.6 (s), 66.2 (t), 42.6 (t), 36.6 (t), 34.2 (t), 19.6 ppm (t); IR (powder): $\tilde{\nu}$ = 3187 (m), 3049 (m), 2938 (m), 1671 (vs), 1644 (vs), 1487 (m), 1477 (m), 1436 (m), 1325 (m), 1271 (m), 1202 (m), 1150 (m), 1123 (m), 1071 (m), 1001 (m), 954 (m), 911 (m), 827 (m), 741 (m), 692 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 325 (1) [M^+], 168 (49) [$M-C_6H_5Se)^+$], 157 (13) [$C_6H_5Se^+$], 114 (100) [$M-C_6H_5Se-C_4H_7^+$], 86 (10), 77 (9) [$C_6H_5^+$], 55 (22) [$C_4H_7^+$]; HRMS (70 eV): *m*/*z* calcd for $C_{15}H_{19}NO_2Se$: 325.0581 [M^+]; found: 325.0581.

3-(Allyloxy)-5,6-dihydro-1*H*-pyridin-2-one (5): Aqueous hydrogen peroxide (519 μL, 5.08 mmol, 30% v/v) was added to a solution of 3-(allyloxy)-3-(phenylselanyl)piperidin-2-one (**17**) (150 mg, 483 μmol) and pyridine (97.1 μL, 95.5 mg, 1.21 mmol) in CH_2Cl_2 (5 mL) at room temperature and the mixture was stirred for 2 h. Saturated aqueous NH_4Cl (10 mL) was added to the reaction mixture, which was extracted with CH_2Cl_2 (3× 10 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography (EtOAc) to give **5** (58.4 mg, 382 μmol, 79%) as a colorless oil. R_f=0.25 (EtOAc, 100%; CAM, UV); ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ=6.51 (brs, 1H), 6.06–5.95 (m, 1H), 5.45 (t, ^3J=4.6 Hz, 1H), 5.33 (dtd, ^2J=1.4, ^3J=17.3, ^4J=2.9 Hz, 1H), 5.24 (dtd, ^2J=1.4, ^3J=10.5, ^4J=2.9 Hz, 1H), 4.35–4.33 (m, 2H), 3.38–3.33 (AA′XX′, m, 2H), 2.41–2.36 ppm (AA′XX′, m, 2H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ=163.8 (s), 146.6 (s), 132.9 (d), 118.2 (t), 107.2 (d), 69.0 (t), 39.9 (t), 22.9 ppm (t); IR (film): $\tilde{\nu}$=3235 (m), 2885 (m), 2857 (m), 1677 (vs), 1622 (vs), 1480 (m), 1455 (m), 1428 (m), 1338 (m), 1229 (vs), 1188 (m), 1111 (m), 1031 (m), 996 (m), 926 (m), 814 (m), 782 (m), 762 (m), 757 (m), 750 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 153 (9) [M^+], 124 (31), 108 (37), 97 (27), 68 (41), 55 (37), 41 (100) [$C_3H_5^+$]; HRMS (70 eV): *m*/*z* calcd for $C_8H_{11}NO_2$: 153.0790 [M^+]; found: 153.0789.

3-(3′-Butenyloxy)-5,6-dihydro-1*H*-pyridin-2-one (6): Aqueous hydrogen peroxide (397 μL, 3.89 mmol, 30% v/v) was added to a solution of **18** (120 mg, 370 μmol) and pyridine (74.7 μL, 73.2 mg, 925 μmol) in CH_2Cl_2 (5 mL) at room temperature, and the mixture was stirred for 2 h. Saturated aqueous NH_4Cl (10 mL) was added to the reaction mixture, which was extracted with CH_2Cl_2 (3×10 mL). The organic extract was dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by flash chromatography (EtOAc) to give **6** as a colorless solid (46.4 mg, 278 μmol, 75%). R_f=0.27 (EtOAc, 100%; CAM, UV); m.p. 32 °C; ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ=6.18 (brs, 1H), 5.96–5.78 (m, 1H), 5.45 (t, ^3J=4.7 Hz, 1H), 5.17–5.05 (m, 2H), 3.79–3.75 (AA′XX′, m, 2H), 3.39–3.34 (AA′XX′, m, 2H), 2.58–2.52 (AA′XX′, m, 2H), 2.42–2.36 ppm (AA′XX′, m, 2H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ= 163.6 (s), 147.0 (s), 134.2 (d), 117.2 (t), 106.6 (d), 67.3 (t), 40.0 (t), 33.2 (t), 23.0 ppm (t); IR (powder): $\tilde{\nu}$=3343 (m), 2909 (m), 2866 (m), 1687 (vs), 1624 (vs), 1481 (m), 1450 (m), 1428 (m), 1341 (m), 1226 (vs), 1189 (m), 1110 (m), 1065 (m), 1031 (m), 987 (m), 918 (m), 821 (m), 781 (m), 752 (m), 673 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 167 (3) [M^+], 126 (85), 113 (100) [$M-C_4H_7^+$], 98 (12), 84 (50), 69 (18), 55 (82) [$C_4H_7^+$], 39 (24); HRMS (70 eV): *m*/*z* calcd for $C_9H_{13}NO_2$: 167.0946 [M^+]; found: 167.0948.

Irradiation experiments

General procedure for the racemic [2+2] photocycloaddition reactions: In a quartz vessel, a solution of the respective 5,6-dihydro-1*H*-pyridin-2-one derivative in anhydrous, degassed (argon purge under ultrasound for 20 min) CH_2Cl_2 was irradiated at room temperature and λ=254 nm until GC and TLC analysis indicated complete conversion (light source: Rayonet RPR-2537 Å). The solvent was evaporated under reduced pressure, and the remaining residue was purified by column chromatography to give the desired compound.

General procedure for the enantioselective [2+2] photocycloaddition reactions: In a quartz vessel, a solution of the respective 5,6-dihydro-1*H*-pyridin-2-one derivative (c=5 mM) in anhydrous, degassed (argon purge under ultrasound for 20 min) toluene with the addition of the chiral complexing agent was irradiated at −75 °C and λ=254 nm until GC analysis indicated complete conversion (light source: Rayonet RPR-2537 Å). The solvent was evaporated under reduced pressure, and the remaining residue was purified by column chromatography to give the desired compound.

9-Oxa-3-azatricyclo[5.2.1.01,6]decan-2-one (20): *Racemic [2+2] photocycloaddition*: 3-(Allyloxy)-5,6-dihydro-1*H*-pyridin-2-one (**5**; 27.0 mg, 176 μmol) in CH_2Cl_2 (35 mL) was irradiated for 30 min. Column chromatography (EtOAc) yielded the desired product as a colorless solid (17.0 mg, 111 μmol, 63%). M.p. 133 °C.

Enantioselective [2+2] photocycloaddition: Chiral complexing agent (−)-**1** (83.8 mg, 238 μmol, 2.5 equiv) was added to **5** (14.0 mg, 91.4 μmol) in toluene (18.3 mL), and the reaction mixture was irradiated for 5.5 h. Column chromatography (EtOAc) yielded the desired product as a colorless solid (8.54 mg, 55.8 μmol, 61%, 40% *ee*), and the complexing agent was recovered after the reaction (88%). R_f=0.41 (EtOAc, 100%, CAM); $[\alpha]_D^{20}$ = −15.5 (c=0.19 in $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ=5.96 (brs, 1H), 4.00 (d, ^2J=6.0 Hz, 1H), 3.87 (d, ^2J=6.0 Hz, 1H), 3.39–3.35 (m, 2H), 2.90 (brd, ^3J=3.0 Hz, 1H), 2.58 (dd, ^2J=8.2, ^3J=3.0 Hz, 1H), 2.31–2.19 (m, 1H), 2.15–2.06 (m, 2H), 2.00 ppm (dd, ^2J=8.2, ^4J=7.4 Hz, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ=169.0 (s), 82.1 (s), 71.3 (t), 48.8 (d), 43.0 (t), 42.9 (t), 41.1 (d), 24.1 ppm (t); IR (powder): $\tilde{\nu}$=2904 (m), 1667 (vs), 1494 (m), 1464 (m), 1426 (m), 1342 (m), 1246 (m), 1227 (m), 1187 (m), 1123 (m), 1064 (m), 1034 (m), 993 (m), 930 (m), 891 (m), 882 (m), 853 (m), 831 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 153 (6) [M^+], 136 (8), 125 (30), 108 (51), 99 (38), 82 (33), 69 (20), 55 (28), 41 (74); HRMS (70 eV): *m*/*z* calcd for $C_8H_{11}NO_2$: 153.0790 [M^+]; found: 153.0790.

Decahydro-8-oxacyclopenta[1,4]cyclobuta[1,2-*c*]pyridin-1-one (22): *Racemic [2+2] photocycloaddition*: 3-(3′-Butenyloxy)-5,6-dihydro-1*H*-pyridin-2-one (**6**; 28.0 mg, 167 μmol) in CH_2Cl_2 (33 mL) was irradiated for 30 min. Column chromatography (EtOAc) yielded the desired product as a colorless oil (15.4 mg, 91.9 μmol, 55%).

Enantioselective [2+2] photocycloaddition: Chiral complexing agent (−)-**1** (82.2 mg, 233 μmol, 2.5 equiv) was added to **6** (15.0 mg, 89.7 μmol) in toluene (17.9 mL), and the reaction mixture was irradiated for 4.0 h. Column chromatography (EtOAc) yielded the desired product as a colorless oil (7.95 mg, 47.5 μmol, 53%, 60% *ee*), and the complexing agent was recovered after the reaction (91%). R_f=0.43 (EtOAc, 100%; CAM); $[\alpha]_D^{20}$ = −19.5 (c=0.19, in $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ=6.38 (brs, 1H), 4.47–4.40 (m, 1H), 4.23–4.11 (m, 1H), 3.59–3.51 (m, 1H), 3.44–3.32 (m, 1H), 3.05–2.95 (m, 1H), 2.73–2.60 (m, 1H), 2.07–2.00 (m, 1H), 1.98–1.86 (m, 2H), 1.83–1.66 (m, 2H), 1.65–1.58 ppm (m, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ=172.6 (s), 82.4 (s), 69.2 (t), 42.6 (d), 38.6 (t), 37.2 (d), 32.4 (t), 26.9 (t), 24.6 ppm (t); MS (EI, 70 eV): *m*/*z* (%): 167 (8) [M^+], 151 (59), 136 (54), 126 (67), 97 (100), 55 (43), 41 (32); HRMS (70 eV): *m*/*z* calcd for $C_9H_{13}NO_2$: 167.0946 [M^+]; found: 167.0946.

3-Azatricyclo-[5.2.1.01,6]-decan-2-one (19): *Racemic [2+2] photocycloaddition*: 3-(3′-Butenyl)-5,6-dihydro-1*H*-pyridin-2-one (**2**; 32.0 mg, 212 μmol) in CH_2Cl_2 (42 mL) was irradiated for 1 h. Column chromatography (EtOAc) yielded the desired product as a colorless solid (26.6 mg, 176 μmol, 83%). M.p. 103 °C.

Enantioselective [2+2] photocycloaddition: Chiral complexing agent (−)-**1** (84.9 mg, 241 μmol, 2.5 equiv) was added to **2** (14.0 mg, 92.5 μmol) in toluene (18.5 mL), and the reaction mixture was irradiated for 7.0 h. Column chromatography (EtOAc) yielded the desired product as a colorless solid (11.6 mg, 76.8 μmol, 83%, 69% *ee*), and the complexing agent was recovered after the reaction (76%). R_f=0.49 (EtOAc, 100%; CAM); $[\alpha]_D^{20}$ = −23.6 (c=0.12 in $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$, 300 K): δ=6.00 (brs, 1H), 3.45–3.30 (m, 1H), 3.24 (virt. td, $^2J\cong{}^3J$=12.2, ^3J=3.6 Hz, 1H), 2.45–2.40 (m, 1H), 2.35–2.25 (m, 1H), 2.15–2.01 (m, 2H), 1.97–1.80 (m, 2H), 1.78–1.65 (m, 3H), 1.51 ppm (dd, ^2J=7.3, ^4J= 6.6 Hz, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): δ=174.5 (s), 49.0 (s), 48.3 (d), 43.1 (t), 42.8 (t), 39.9 (d), 28.4 (t), 27.4 (t), 22.6 ppm (t); IR (powder): $\tilde{\nu}$=2930 (m), 1644 (vs), 1485 (m), 1452 (m), 1438 (m), 1413 (m), 1362 (m), 1340 (m), 1310 (m), 1300 (m), 1267 (m), 1250 (m), 1226 (m), 1188 (m), 1151 (m), 1121 (m), 1065 (m), 1045 (m), 1020 (m), 848 (m), 831 (m), 820 (w), 806 (m), 668 cm^{-1} (w); MS (EI, 70 eV): *m*/*z* (%): 151 (100), [M^+], 136 (68), 122 (29), 107 (19), 93 (25), 85 (31), 79 (32), 67 (13), 53 (14), 39 (14); HRMS (70 eV): *m*/*z* calcd for $C_9H_{13}NO$: 151.0997 [M^+]; found: 151.0997.

Decahydro-cyclopenta[1,4]cyclobuta[1,2-*c*]pyridine-1-one (21): *Racemic [2+2] photocycloaddition*: 3-(4′-Pentenyl)-5,6-dihydro-1*H*-pyridin-2-one (**3**; 32.0 mg, 194 μmol) in CH_2Cl_2 (39 mL) was irradiated for 30 min. Column chromatography (EtOAc) yielded the desired product as a colorless solid (26.0 mg, 157 μmol, 81%). M.p. 115 °C.

Enantioselective [2+2] photocycloaddition: Chiral complexing agent (−)-**1** (83.2 mg, 236 μmol, 2.5 equiv) was added to **3** (15.0 mg, 90.7 μmol) in toluene (18.1 mL), and the reaction mixture was irradiated for 4.0 h. Column chromatography (EtOAc) yielded the desired product as a color-

less solid (12.0 mg, 72.6 μmol, 80%, 84% *ee*), and the complexing agent were recovered after the reaction (90%). $R_f = 0.51$ (EtOAc, 100%; CAM); $[\alpha]_D^{20} = -23.6$ ($c = 0.14$ in MeOH); ^{1}H NMR (250 MHz, $CDCl_3$, 300 K): $\delta = 6.42$ (brs, 1H), 3.60–3.48 (m, 1H), 3.33–3.22 (m, 1H), 2.79–2.70 (m, 1H), 2.29–2.15 (m, 2H), 2.04–1.98 (m, 2H), 1.97–1.82 (m, 2H), 1.73–1.52 ppm (m, 5H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): $\delta = 177.4$ (s), 50.8 (s), 43.0 (d), 39.3 (t), 35.6 (t), 34.8 (d), 33.4 (t), 28.7 (t), 27.2 (t), 25.5 ppm (t); IR (powder): $\tilde{\nu} = 2930$ (m), 1644 (vs), 1485 (m), 1452 (m), 1438 (m), 1413 (m), 1362 (m), 1340 (m), 1310 (m), 1300 (m), 1267 (m), 1250 (m), 1226 (m), 1188 (m), 1151 (m), 1121 (m), 1065 (m), 1045 (m), 1020 (m), 848 (m), 831 (m), 820 (w), 806 (m), 668 cm^{-1} (w); MS (EI, 70 eV): *m*/*z* (%): 165 (54) [M^+], 150 (18), 137 (100), 124 (81), 111 (49), 95 (60), 82 (28), 67 (25), 53 (10), 41 (17); HRMS (70 eV): *m*/*z* calcd for $C_{10}H_{15}NO$: 165.1154 [M^+]; found: 165.1152.

Decahydrobenzo[1,4]cyclobuta[1,2-*c*]pyridine-1-one (23): *Racemic [2+2] photocycloaddition*: 3-(5′-Hexenyl)-5,6-dihydro-1*H*-pyridin-2-one (**4**; 36.0 mg, 201 μmol) in CH_2Cl_2 (40 mL) was irradiated for 2 h. Column chromatography (EtOAc) yielded the desired product as a colorless oil (23.0 mg, 128 μmol, 64%). $R_f = 0.53$ (EtOAc, 100%; CAM); ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): $\delta = 5.76$ (brs, 1H), 3.45–3.32 (m, 1H), 3.27–3.21 (m, 1H), 2.62–2.55 (m, 1H), 2.35–2.30 (m, 1H), 2.05–1.92 (m, 2H), 1.90–1.82 (m, 1H), 1.78–1.65 (m, 4H), 1.55–1.45 (m, 4H), 1.43–1.35 ppm (m, 1H); ^{13}C NMR (90.6 MHz, $CDCl_3$, 300 K): $\delta = 178.8$ (s), 42.6 (s), 40.3 (t), 36.5 (d), 35.4 (d), 31.4 (t), 27.2 (t), 26.6 (t), 26.4 (t), 21.9 (t), 21.3 ppm (t); IR (film): $\tilde{\nu} \sim = 2930$ (m), 1644 (vs), 1485 (m), 1452 (m), 1438 (m), 1413 (m), 1362 (m), 1340 (m), 1310 (m), 1300 (m), 1267 (m), 1250 (m), 1226 (m), 1188 (m), 1151 (m), 1121 (m), 1065 (m), 1045 (m), 1020 (m), 848 (m), 831 (m), 820 (w), 806 (m), 668 cm^{-1} (w); MS (EI, 70 eV): *m*/*z* (%): 179 (100) [M^+], 164 (27), 150 (34), 138 (44), 124 (51), 111 (43), 67 (21), 41 (31); HRMS (70 eV): *m*/*z* calcd for $C_{11}H_{17}NO$: 179.1310 [M^+]; found: 179.1313.

3-(6-Acetoxy-1,2,3,4-tetrahydronaphthene-7-yl)-1,5,7-trimethyl-2,4-dioxo-3-azabicyclo[3.3.1]nonan-7-carboxylic acid (26): The Kemp triacid (**24**; 2.10 g, 8.12 mmol, 1.00 equiv) was heated to reflux in thionyl chloride (20 mL) for 24 h. The solvent was removed by distillation. The residue was washed with toluene (2×10 mL) and dried under reduced pressure. The crude acid chloride was dissolved in pyridine (20 mL) and 3-amino-5,6,7,8-tetrahydronaphthalene-2-ol (**25**;[24] 1.86 g, 11.4 mmol, 1.40 equiv) in pyridine (40 mL) was added dropwise. The resulting solution was heated to reflux for 18 h and cooled to ambient temperature. The volatile compounds were removed under reduced pressure, and the residue was dissolved in EtOAc (200 mL). The organic layer was washed with HCl (1 M, 40 mL), and the aqueous layer was extracted with EtOAc (2× 20 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, filtered, and evaporated. *N*,*N*-Dimethylaminopyridine (137 mg, 1.12 mmol, 0.14 equiv) was added to the resulting residue dissolved in CH_2Cl_2 (120 mL), and the solution was cooled to 0 °C. NEt_3 (4.70 mL, 3.43 g, 33.9 mmol, 4.17 equiv) and acetic anhydride (3.20 mL, 3.46 g, 33.9 mmol, 4.17 equiv) were added dropwise to the reaction mixture, which was warmed to ambient temperature and stirred for an additional 16 h. The solution was diluted with CH_2Cl_2 (100 mL), washed with HCl (1 M, 40 mL), and the aqueous layer extracted with CH_2Cl_2 (3× 50 mL). The combined organic layers were dried over $MgSO_4$, filtered, and evaporated. Column chromatography (CH_2Cl_2/MeOH/AcOH, 100:1:1→100:4:1) yielded the desired product as a colorless solid (3.14 g, 7.31 mmol, 90%). $R_f = 0.32$ (CH_2Cl_2/MeOH/AcOH 95:5:1; UV, $KMnO_4$); m.p. 308 °C; ^{1}H NMR (360 MHz, [D$_6$]DMSO): $\delta = 12.52$ (brs, 1H), 7.01 (s, 1H), 6.88 (s, 1H), 2.71 (brs, 4H), 2.50 (d, $^2J = 13.8$ Hz, 2H), 2.11 (s, 3H), 1.83 (d, $^2J = 13.1$ Hz, 1H), 1.77–1.73 (m, 4H), 1.62 (d, $^2J = 13.1$ Hz, 1H), 1.32 (d, $^2J = 13.8$ Hz, 2H), 1.17 (s, 3H), 1.16 ppm (s, 6H); ^{13}C NMR (90.6 MHz, [D$_6$]DMSO): $\delta = 177.1$ (s), 175.1 (s), 167.3 (s), 143.1 (s), 137.0 (s), 133.8 (s), 129.6 (d), 125.3 (s), 122.2 (d), 42.8 (t), 42.8 (t), 41.0 (s), 40.0 (s), 30.3 (q), 28.5 (t), 28.2 (t), 25.6 (q), 22.4 (t), 22.2 (t), 20.3 ppm (q); IR (powder): $\tilde{\nu} = 3176$ (m), 2959 (m), 2933 (m), 1772 (s), 1731(s), 1707 (s), 1672 (s), 1503 (w), 1450 (m), 1429 (w), 1362 (m), 1190 (vs), 1153 (vs), 1086 (w), 1080 (m), 956 (w), 903 (w), 858 (w), 757 (w), 738 cm^{-1} (w); MS (EI, 70 eV): *m*/*z* (%): 427 (15) [M^+], 385 (48) [$M-C_2H_3O^+$], 367 (96), 323 (100), 296 (10), 267 (54), 214 (40), 187 (22), 163 (48), 121 (80), 107 (38), 44 (74), 43 (48) [$C_2H_3O^+$]; HRMS (70 eV): *m*/*z* calcd for $C_{24}H_{29}NO_6$: 427.1995 [M^+]; found: 427.1989.

6-(7-(Azidoformyl)-1,5,7-trimethyl-2,4-dioxo-3-azabicyclo[3.3.1]nonan-3-yl)-1,2,3,4-tetrahydronaphthene-7-yl-acetate (27): DMF (20 drops) was added to acid **26** (3.04 g, 7.11 mmol, 1.00 equiv) in CH_2Cl_2 (120 mL), and the resulting solution was cooled to 0 °C. Oxalyl chloride (1.81 mL, 2.71 g, 21.3 mmol, 3.00 equiv) was added to the reaction mixture, which was stirred for additional 2 h at 0 °C. All the volatile compounds were removed under reduced pressure at 0 °C, and the residue was dried under reduced pressure. The crude acid chloride was dissolved in dry acetone (80 mL) and cooled to 0 °C. Sodium azide (2.31 g, 35.5 mmol, 5.00 equiv) was carefully added to the reaction mixture, which was slowly warmed to ambient temperature and stirred for 16 h. The solids were removed by filtration and washed with acetone (3×100 mL). The combined organic layers were concentrated at 0 °C. Column chromatography (pentant/Et_2O 6:4→Et_2O 100%) yielded the desired product as a colorless solid (2.89 g, 6.40 mmol, 90%). $R_f = 0.40$ (Et_2O; UV, $KMnO_4$); m.p. 232 °C; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 6.91$ (s, 1H), 6.88 (s, 1H), 2.79–2.76 (m, 6H), 2.15 (s, 3H), 1.97 (td, $^2J = 13.2$ Hz, $^4J = 1.9$ Hz, 1H), 1.80–1.75 (m, 4H), 1.47 (d, $^2J = 13.2$ Hz, 1H), 1.32 (s, 6H), 1.27 (s, 3H), 1.27 ppm (d, $^2J = 12.7$ Hz, 2H); ^{13}C NMR (90.6 MHz, $CDCl_3$): $\delta = 183.9$ (s), 175.0 (s), 167.7 (s), 143.1 (s), 138.6 (s), 135.2 (s), 129.0 (d), 124.5 (s), 122.9 (d), 44.1 (t), 44.1 (s), 43.7 (t), 40.7 (s), 30.7 (q), 29.3 (t), 28.8 (t), 26.0 (q), 22.8 (t), 22.7 (t), 20.8 ppm (q); IR (powder): $\tilde{\nu} = 2932$ (m), 2134 (m), 1770 (m), 1701 (vs), 1506 (w), 1461 (m), 1429 (w), 1360 (m), 1325 (m), 1173 (vs), 1138 (m), 1080 (m), 1029 (m), 956 (w), 914 (w), 852 (w), 733 cm^{-1} (m); MS (EI, 70 eV): *m*/*z* (%): 424 (14) [$M-N_2^+$], 382 (100), 339 (13), 296 (9), 269 (5), 253 (8), 214 (5), 191 (20), 163 (12), 121 (96), 91 (8), 55 (8) [$C_3H_3O^+$]; HRMS (70 eV): *m*/*z* calcd for $C_{24}H_{28}N_2O_5$: 424.1998 [$M-N_2^+$]; found: 424.1995.

6-(7-Benzyloxycarbonylamino-1,5,7-trimethyl-2,4-dioxo-3-azabicyclo-[3.3.1]nonan-3-yl)-1,2,3,4-tetrahydronaphthene-7-yl-acetate (28): Azide **27** (2.84 g, 6.27 mmol, 1.00 equiv) and benzylic alcohol (13.0 mL, 13.6 g, 125 mmol, 20.0 equiv) were heated to reflux in toluene (150 mL) for 7 days. All the volatile compounds were removed under reduced pressure and column chromatography (pentane/Et_2O 1:1→Et_2O 100%) yielded the desired product as a colorless solid (3.00 g, 5.64 mmol, 90%). $R_f = 0.45$ (Et_2O; UV, $KMnO_4$); m.p. 206 °C; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 7.26$ (brs, 5H), 6.92 (s, 1H), 6.85 (s, 1H), 5.06 (s, 2H), 4.47 (brs, 1H), 2.71–2.66 (m, 6H), 2.20 (s, 3H), 2.01 (td, $^2J = 13.2$, $^4J = 2.3$ Hz, 1H), 1.70–1.67 (m, 2H), 1.58–1.56 (m, 2H), 1.51 (d, $^2J = 13.2$ Hz, 1H), 1.41 (s, 3H), 1.39 (d, $^2J = 15.9$ Hz, 2H), 1.31 ppm (s, 6H); ^{13}C NMR (90.6 MHz, $CDCl_3$): $\delta = 176.5$ (s), 168.0 (s), 154.5 (s), 143.2 (s), 138.5 (s), 136.2 (s), 135.2 (s), 130.5 (d), 128.4 (d), 127.9 (d), 127.8 (d), 124.4 (s), 122.4 (d), 66.4 (t), 53.0 (s), 46.2 (t), 44.1 (t), 40.2 (s), 29.2 (t), 28.3 (t), 26.2 (q), 26.2 (q), 22.7 (t), 22.6 (t), 20.8 ppm (q); IR (powder): $\tilde{\nu} = 3340$ (s), 2938 (m), 2926 (m), 1764 (m), 1736 (m), 1711 (s), 1682 (vs), 1517 (s), 1455 (m), 1380 (w), 1364 (m), 1267 (m), 1189 (vs), 1070 (m), 1050 (m), 965 (w), 921 (w), 897 (w), 848 (w), 747 (w), 698 cm^{-1} (w); MS (EI, 70 eV): *m*/*z* (%): 532 (4) [M^+], 490 (10) [$M-C_2H_2O^+$], 424 (10), 382 (100) [$M-C_8H_8NO_2^+$], 339 (10), 253 (12), 191 (16), 162 (28), 121 (48) [$C_8H_9O^+$], 91 (38), 43 (12) [$C_2H_3O^+$]; HRMS (70 eV): *m*/*z* calcd for $C_{31}H_{36}N_2O_6$: 532.2573 [M^+]; found: 532.2559.

7-Amino-1,5,7-trimethyl-2,4-dioxo-3-azabicyclo[3.3.1]nonan-3-yl-1,2,3,4-tetrahydronaphthene-7-yl-acetate (29): Carbamate **28** (2.94 g, 5.51 mmol, 1 equiv) and 10% Pd/C (530 mg, 0.50 mmol, 0.09 equiv) were suspended in a mixture of EtOAc (150 mL) and *i*PrOH (15 mL) and stirred for 16 h under an atmosphere of H_2 at ambient temperature. The reaction mixture was filtered through a pad of Celite, and the residue was washed with a mixture of EtOAc (500 mL) and MeOH (10 mL). Evaporation of all solvents yielded the desired compound as a colorless solid (2.19 g, 5.51 mmol, quant.). $R_f = 0.43$ (Et_2O; UV, $KMnO_4$); m.p. 163 °C; ^{1}H NMR (360 MHz, $CDCl_3$): $\delta = 7.04$ (s, 1H), 6.86 (s, 1H), 2.75–2.71 (m, 4H), 2.20 (s, 3H), 1.99 (td, $^2J = 13.0$, $^4J = 2.0$ Hz, 1H), 1.87 (d, $^2J = 14.2$ Hz, 2H), 1.78–1.74 (m, 4H), 1.45 (d, $^2J = 13.0$ Hz, 1H), 1.39 (d, $^2J = 14.2$ Hz, 2H), 1.28 (s, 6H), 1.17 (s, 3H), 0.92 ppm (brs, 2H); ^{13}C NMR (90.6 MHz, $CDCl_3$): $\delta = 177.6$ (s), 168.1 (s), 143.7 (s), 138.1 (s), 134.9 (s), 129.8 (d), 125.5 (s), 122.3 (d), 49.9 (s), 49.1 (t), 44.3 (t), 40.2 (s), 36.5 (q), 29.3 (t),

28.9 (t), 26.4 (q), 22.8 (t), 22.7 (t), 20.7 ppm (q); IR (powder): $\tilde{\nu}$ = 3345 (s), 2921 (s), 1764 (s), 1735 (w), 1682 (vs), 1506 (m), 1459 (w), 1364 (m), 1314 (w), 1186 (vs), 1086 (w), 1050 (m), 921 (w), 902 cm^{-1}; MS (EI, 70 eV): *m/z* (%): 398 (6) [M^+], 356 (38) [$M-C_2H_2O^+$], 163 (100), 149 (10), 121 (8) [$C_8H_9O^+$], 110 (14), 57 (22), 43 (12) [$C_2H_3O^+$]; HRMS (70 eV): *m/z* calcd for $C_{23}H_{30}N_2O_4$: 398.2206 [M^+]; found: 398.2202.

***N*-(3-Hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-1,3,5-trimethyl-7-oxo-6-azabicyclo[3.2.1]octane-3-carboxamide (30)**: K_2CO_3 (2.61 g, 18.9 mmol, 3.5 equiv) was added to amine **29** (2.15 g, 5.40 mmol, 1 equiv) dissolved in MeOH (250 mL), and the reaction mixture was stirred for 6 h at ambient temperature. All the volatile compounds were removed under reduced pressure, the residue was dissolved in water (100 mL), and the aqueous layer was extracted with EtOAc (3×300 mL). The combined organic layers were washed with brine (100 mL), dried over $MgSO_4$, and filtered. Evaporation of the solvent yielded the desired compound as a colorless solid (1.92 g, 5.40 mmol, 100%). R_f = 0.25 (Et_2O; UV, $KMnO_4$); m.p. 156–158 °C; ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.82 (br s, 1H), 7.48 (br s, 1H), 6.88 (s, 1H), 6.66 (s, 1H), 5.60 (br s, 1H), 2.89 (d, ^2J = 13.9 Hz, 1H), 2.68–2.60 (m, 4H), 2.19 (d, ^2J = 15.1 Hz, 1H), 1.80 (d, ^2J = 10.5 Hz, 1H), 1.73–1.70 (m, 4H), 1.58 (d, ^2J = 10.5 Hz, 1H), 1.53 (d, ^2J = 15.1 Hz, 1H), 1.33 (s, 3H), 1.27 (d, ^2J = 13.9 Hz, 1H), 1.25 (s, 3H), 1.16 ppm (s, 3H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 180.2 (s), 175.8 (s), 147.9 (s), 136.4 (s), 129.0 (s), 125.3 (d), 122.4 (s), 118.7 (d), 55.9 (s), 55.2 (t), 44.1 (s), 43.7 (s), 43.6 (t), 43.1 (t), 30.4 (q), 29.1 (t), 28.5 (t), 24.8 (q), 23.3 (t), 23.1 (t), 20.1 ppm (q); IR (powder): $\tilde{\nu}$ = 3357 (m), 3269 (m), 3236 (m), 2926 (s), 2856 (m), 1683 (vs), 1511 (s), 1455 (w), 1426 (w), 1294 (w), 1246 (w), 727 cm^{-1} (w); MS (EI, 70 eV): *m/z* (%): 356 (30) [M^+], 339 (1) [$M-HO^+$], 214 (2), 194 (4), 163 (100), 146 (5), 135 (8), 110 (14), 87 (8), 57 (38), 43 (20); HRMS (70 eV): *m/z* calcd for $C_{21}H_{28}N_2O_3$: 356.2100 [M^+]; found: 356.2100.

1,3,5-Trimethyl-3-(5,6,7,8-tetrahydronaphtho[2,3-*d*]oxazol-2-yl)-6-azabicyclo[3.2.1]octan-7-one (31): Bisamide 30 (1.92 g, 5.40 mmol, 1 equiv) and pyridine (3.05 mL, 2.98 g, 37.7 mmol, 7.00 equiv) were dissolved in benzene (40 mL) and cooled to 0 °C. Thionyl choride (1.95 mL, 3.20 g, 26.9 mmol, 5.00 equiv) was added dropwise to the reaction mixture, which was warmed to ambient temperature, stirred for 15 min, and heated to reflux for 4 h. The solution was cooled to ambient temperature, and all the volatile compounds were removed under reduced pressure. The residue was dissolved in EtOAc (500 mL) and washed with HCl (1 M, 100 mL) and brine (100 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated. Column chromatography ($Et_2O \rightarrow CH_2Cl_2$/MeOH 20;1) yielded the desired product as a colorless solid (1.42 g, 4.20 mmol, 78%). The enantiomers were separated using chiral HPLC (Daicel Chiralpak AD-H; *i*PrOH/hexane 95:5). R_f = 0.21 (Et_2O; UV, $KMnO_4$); m.p. 237 °C; ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.28 (s, 1H), 7.13 (s, 1H), 5.33 (br s, 1H), 2.98 (td, ^2J = 14.2, ^4J = 2.0 Hz, 1H), 2.86–2.83 (m, 5H), 1.81–1.77 (m, 4H), 1.70 (td, ^2J = 10.5, ^4J = 2.2 Hz, 1H), 1.59 (dd, ^2J = 10.5, ^4J = 1.7 Hz, 1H), 1.54 (d, ^2J = 14.2 Hz, 1H), 1.45 (d, ^2J = 13.8 Hz, 1H), 1.35 (s, 3H), 1.28 (s, 3H), 1.13 ppm (s, 3H); ^{13}C NMR (90.6 MHz, $CDCl_3$): δ = 178.7 (s), 171.5 (s), 149.1 (s), 139.4 (s), 133.9 (s), 133.0 (s), 119.0 (d), 110.0 (d), 55.2 (s), 51.8 (t), 44.0 (s), 43.6 (t), 43.3 (t), 37.8 (s), 31.8 (q), 30.1 (t), 29.8 (t), 25.2 (q), 23.2 (t), 23.2 (t), 20.3 ppm (q); IR (powder): $\tilde{\nu}$ ~ = 3079 (m, NH), 2922 (m), 2856 (m), 1707 (vs), 1561 (m), 1465 (w), 1477 (w), 1319 (w), 1247 (w), 1140 (w), 1077 cm^{-1} (w); MS (EI, 70 eV): *m/z* (%): 338 (60) [M^+], 321 (8) [$M-HO^+$], 282 (10), 228 (14), 214 (100), 187 (8); HRMS (70 eV): *m/z* calcd for $C_{21}H_{26}N_2O_2$: 338.1994 [M^+]; found: 338.1991.

(−)-31: $[\alpha]_D^{20}$ = −56 (*c* = 0.95 in $CHCl_3$); HPLC (Daicel Chiralpak AD-H; *i*PrOH/hexane 95:5): t_R = 18.8 min. **(+)-31**: $[\alpha]_D^{20}$ = +56 (*c* = 0.98 in $CHCl_3$); HPLC (Daicel Chiralpak AD-H; *i*PrOH/hexane 95:5): t_R = 19.9 min.

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[1] Reviews: a) T. Bach in *Asymmetric Synthesis—The Essentials* (Eds.: S. Bräse, M. Christmann), Wiley-VCH, Weinheim, **2006**, pp. 166–170; b) S. Breitenlechner, P. Selig, T. Bach in *Ernst Schering Foundation Symposium Proceedings "Organocatalysis"* (Eds.: M. T. Reetz, B. List, S. Jaroch, H. Weinmann), Springer, Berlin, **2008**, pp. 255–280; c) C. Müller, T. Bach, *Aust. J. Chem.* **2008**, *61*, 557–564.

[2] a) T. Bach, H. Bergmann, K. Harms, *Angew. Chem.* **2000**, *112*, 2391–2393; *Angew. Chem. Int. Ed.* **2000**, *39*, 2302–2304; b) T. Bach, H. Bergmann, *J. Am. Chem. Soc.* **2000**, *122*, 11525–11526; c) T. Bach, H. Bergmann, B. Grosch, K. Harms, *J. Am. Chem. Soc.* **2002**, *124*, 7982–7990; d) S. Brandes, P. Selig, T. Bach, *Synlett* **2004**, 2588–2590; e) P. Selig, T. Bach, *J. Org. Chem.* **2006**, *71*, 5662–5673.

[3] a) P. Selig, T. Bach, *Angew. Chem.* **2008**, *120*, 5160–5162; *Angew. Chem. Int. Ed.* **2008**, *47*, 5082–5084; b) P. Selig, E. Herdtweck, T. Bach, *Chem. Eur. J.* **2009**, *15*, 3509–3525.

[4] a) H. Bergmann, B. Grosch, S. Sitterberg, T. Bach, *J. Org. Chem.* **2004**, *69*, 970–973; b) A. Bauer, T. Bach, *Tetrahedron: Asymmetry* **2004**, *15*, 3799–3803.

[5] D. Albrecht, B. Basler, T. Bach, *J. Org. Chem.* **2008**, *73*, 2345–2356.

[6] J. P. Hehn, C. Müller, T. Bach in *Handbook of Synthetic Photochemistry* (Eds.: A. Albini, M. Fagnoni), Wiley-VCH, Weinheim, **2009**, pp. 171–215.

[7] D. Albrecht, T. Bach, *Synlett* **2007**, 1557–1560.

[8] Y. Torisawa, T. Soe, C. Katoh, Y. Motohashi, A. Nishida, T. Hino, M. Nakagawa, *Heterocycles* **1998**, *47*, 655–660.

[9] For Sonogashira and Stille cross-coupling reactions, see: a) A. Gagnon, S. J. Danishefsky, *Angew. Chem.* **2002**, *114*, 1651–1654; *Angew. Chem. Int. Ed.* **2002**, *41*, 1581–1584; b) J. Dijkink, J.-C. Cintrat, W. N. Speckamp, H. Hiemstra, *Tetrahedron Lett.* **1999**, *40*, 5919–5922; c) C. D. Cox, T. Siu, S. J. Danishefsky, *Angew. Chem.* **2003**, *115*, 5783–5787; *Angew. Chem. Int. Ed.* **2003**, *42*, 5625–5629.

[10] a) X. Li, P. Huang, J. J. Cui, J. Zhang, C. Tang, *Bioorg. Med. Chem. Lett.* **2003**, *13*, 1939–1942; b) T. G. Back, *The Chemistry of Organic Selenium and Tellurium Compounds* (Ed.: S. Patai), Wiley, New York, **1987**, pp. 91–213.

[11] C. R. Johnson, J. P. Adams, M. P. Braun, C. B. W. Senanayake, P. M. Wovkulich, M. R. Uskokovic, *Tetrahedron Lett.* **1992**, *33*, 917–918.

[12] S. Hou, *Org. Lett.* **2003**, *5*, 423–425.

[13] J. E. Milne, S. L. Buchwald, *J. Am. Chem. Soc.* **2004**, *126*, 13028–13032.

[14] K. T. Potts, T. Rochanapruk, *J. Org. Chem.* **1995**, *60*, 3795–3805.

[15] D. J. Buckley, M. A. McKervey, *J. Chem. Soc. Perkin Trans. 1* **1985**, 2193–2200.

[16] A. Bhalla, P. Venugopalan, K. K. Bhasin, S. S. Bari, *Tetrahedron* **2007**, *63*, 3195–3204.

[17] I. S. Hutchinson, S. A. Matlin, A. Mete, *Tetrahedron* **2002**, *58*, 3137–3143.

[18] a) M. Ikeda, M. Takahashi, K. Ohno, Y. Tamura, M. Kido, *Chem. Pharm. Bull.* **1982**, *30*, 2269–2271; b) F. Toda, H. Miyamoto, K. Takeda, R. Matsugawa, N. Maruyama, *J. Org. Chem.* **1993**, *58*, 6208–6211; c) M. J. Begley, M. Mellor, G. Pattenden, *J. Chem. Soc. Perkin Trans. 1* **1983**, 1905–1912; d) S. M. Ng, S. J. Bader, M. L. Snapper, *J. Am. Chem. Soc.* **2006**, *128*, 7315–7319.

[19] a) N.-Y. Fu, S.-H. Chan, H. N. C. Wong in *The Chemistry of Functional Groups: The Chemistry of Cyclobutanes: The Application of Cyclobutane Derivatives in Organic Synthesis* (Eds.: Z. Rappoport, J. F. Liebman), Wiley, New York, **2005**, pp. 357–440; b) J. M. Tanko in *The Chemistry of Functional Groups: The Chemistry of Cyclobutanes: Rearrangements of Cyclobutanes* (Eds.: Z. Rappoport, J. F. Liebman), Wiley, New York, **2005**, pp. 497–519; c) W. M. Horspool in *The Chemistry of Functional Groups: The Chemistry of Cyclobutanes: Photochemistry of Cyclobutanes: Synthesis and Reactivity*

(Eds.: Z. Rappoport, J. F. Liebman), Wiley, New York, **2005**, pp. 715–805; d) J. C. Namyslo, D. E. Kaufmann, *Chem. Rev.* **2003**, *103*, 1485–1537; e) E. Lee-Ruff, G. Mladenova, *Chem. Rev.* **2003**, *103*, 1449–1483.

[20] S. Breitenlechner, T. Bach, *Angew. Chem.* **2008**, *120*, 8075–8077; *Angew. Chem. Int. Ed.* **2008**, *47*, 7957–7959.

[21] We cordially thank Prof. Dr. S. Grimme (Universität Münster) for performing the calculation reactions: a) R. Bauernschmitt, R. Ahlrichs, *Chem. Phys. Lett.* **1996**, *256*, 454–464; b) F. Furche, R. Ahlrichs, A. Sobanski, F. Vögtle, C. Wachsman, E. Weber, S. Grimme, *J. Am. Chem. Soc.* **2000**, *122*, 1717–1724.

[22] a) K. A. Connors, *Binding Constants - The Measurement of Molecular Complex Stability*, Wiley, New York **1987**; b) C. S. Wilcox, in *Frontiers in Supramolecular Organic Chemistry and Photochemistry* (Eds.: H.-J. Schneider, H. Dürr), VCH, Weinheim **1991**, pp. 123–143.

[23] a) J. D. Trevor, J. Rebek, *J. Am. Chem. Soc.* **2006**, *128*, 4500–4501; b) D. S. Kemp, K. S. Petrakis, *J. Org. Chem.* **1981**, *46*, 5140–5143.

[24] M. Kajino, Y. Shibouta, K. Nishikawa, K. Meguro, *Chem. Pharm. Bull.* **1991**, *39*, 2896–2905.

[25] T. Curtius, *J. Prakt. Chem.* **1895**, *52*, 243–271.

[26] I. Huc, J. Rebek, *Tetrahedron Lett.* **1994**, *35*, 1035–1038.

[27] T. Bach, H. Bergmann, B. Grosch, K. Harms, E. Herdtweck, *Synthesis* **2001**, 1395–1405.

[28] Examples of dipole/dipole repulsion as a conformational control element in stereoselective reactions: a) S. Masamune, W. Choy, F. A. J. Kerdersky, B. Imperali, *J. Am. Chem. Soc.* **1981**, *103*, 1566–1568; b) D. A. Evans, J. Bartroli, T. L. Shih, *J. Am. Chem. Soc.* **1981**, *103*, 2127–2129; c) C. M. Lee, W. D. Kumler, *J. Am. Chem. Soc.* **1961**, *83*, 4593–4596; d) D. A. Evans, M. J. Dart, J. L. Duffy, M. G. Yang, *J. Am. Chem. Soc.* **1996**, *118*, 4322–4343; e) L. E. Overman, E. A. Peterson, *Angew. Chem.* **2003**, *115*, 2629–2632; *Angew. Chem. Int. Ed.* **2003**, *42*, 2525–2528; f) A. Steven, L. E. Overman, *Angew. Chem.* **2007**, *119*, 5584–5605; *Angew. Chem. Int. Ed.* **2007**, *46*, 5488–5508; g) G. K. Friestad, A. K. Mathies, *Tetrahedron* **2007**, *63*, 9373–9381.

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