The [2+2]-Photocycloaddition of Aromatic Aldehydes and Ketones to 3,4-Dihydro-2-pyridones: Regioselectivity, Diastereoselectivity, and Reductive Ring Opening of the Product Oxetanes

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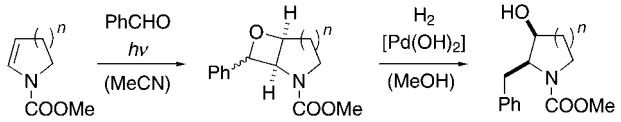
Abstract: 3,4-Dihydro-2-pyridones [3,4-Dihydropyridin-2(1*H*)-ones] **6** were evaluated with respect to their use as alkene components in stereoselective Paternò–Büchi reactions. The parent compound **6a** was shown to be a versatile synthetic building block that reacted with various photoexcited aromatic carbonyl compounds (benzaldehyde, benzophenone, acetophenone, methyl phenylglyoxylate, 3-pivaloyloxybenzaldehyde) with high regio- and diastereoselectivity (51–63% yield). The products can be subjected to hydrogenolysis, opening a new and efficient route for the synthesis of 2-arylmethyl-3-piperidinols. As examples, the oxetanes **7a** and **8a** were hydrogenolytically cleaved and yielded the products **12** (88%) and **13** (93%). The ability of compound **6a** to bind to a chiral lactam host through two hydrogen bonds was used favorably to differentiate the enantiotopic faces of its double bond. In the photocycloaddition to the chiral aldehyde **15**, which was conducted at $-10\,^{\circ}C$ in toluene, a high facial diastereoselectivity (>90% *de*, 56% yield) was recorded. The stereoselectivity results from a 1:1 association of dihydropyridone **6a** to the aldehyde. The 4-substituted dihydropyridones **6b**–**6d** (R = methyl, isopropyl, phenyl) were found to be less suited for potential use in photochemistry. The yields and facial diastereoselectivities recorded in their photocycloaddition to benzophenone remained low.

Keywords: asymmetric synthesis · cycloaddition · hydrogen bonds · Paternò–Büchi reactions · photochemistry

Introduction

The [2+2]-photocycloaddition of carbonyl compounds to alkenes, the Paternò–Büchi reaction, allows the regio- and stereoselective functionalization of olefinic double bonds.[1, 2] The simultaneous formation of a C–C and a C–O bond makes the reaction a versatile tool frequently employed in organic synthesis.[3] Recent interest from our group has centered on the use of the Paternò–Büchi reaction for the carbohydroxylation of nitrogen heterocycles.[4, 5] It was shown that *N*-alkoxycarbonyl-substituted 2,3-dihydropyrroles (e.g. **1a**) react with aromatic aldehydes to form 6-oxa-2-azabicyclo[3.2.0]heptanes (e.g. **2a**), which can be successively cleaved by hydrogenolysis to yield pyrrolidinols (Scheme 1). This method was applied to the synthesis[4b,c] of the naturally occurring pyrrolidinol alkaloid (+)-preussin, which exhibits interesting biological properties.[6] Other biologically active pyrrolidinoles are equally well accessible by this route.[4c] In an attempt to extend the carbohydroxylation procedure to six-membered nitrogen heterocycles, we had to realize that the corresponding *N*-alkoxycarbonyl tetrahydropyridines react sluggishly in the Paternò–Büchi reaction.[4c] The comparison of compounds **1** in the photocycloadditon to benzaldehyde as depicted in Scheme 1 illustrates this point. The yield of isolated 7-oxa-2-azabicyclo[4.2.0]octane **2b** obtained from compound **1b** was only 17% as compared to 57% yield obtained in the photocycloaddition of the dihydropyrrole **1a**.



1a	*n* = 1	**2a**	(57%)	**3a**	(96%)
1b	*n* = 2	**2b**	(17%)	**3b**	(88%)

Scheme 1. Paternò–Büchi reaction of the N-acylated cyclic enamines **1a** and **1b** and the hydrogenolysis of the product oxetanes **2a** and **2b**.

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[++] Crystal structure determination.

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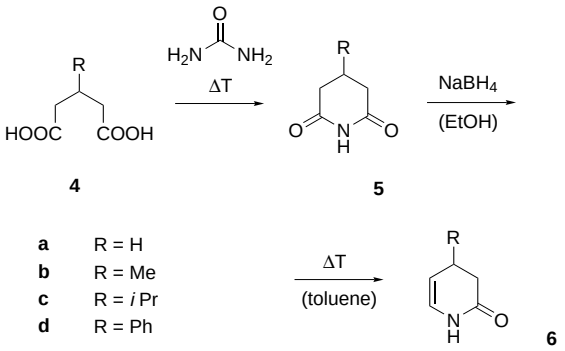
Hydrogenolysis to the desired monocyclic products **3** proceeded smoothly in both cases.

In the search for other cyclic enamides that may be employed in possible syntheses of biologically relevant piperidinols we considered 3,4-dihydro-2-pyridone (**6a**, Scheme 2) to be a useful substrate. The following account



Scheme 2. Preparation of the 3,4-dihydropyridones **6** from the corresponding diacids **4**.

reports on the results of its photocycloaddition to various aromatic aldehydes and ketones. Its capability to bind to other lactams through two hydrogen bonds was used favorably for the association to a chiral aldehyde, and for the differentiation of its enantiotopic faces in the subsequent photocycloaddition.[7]

Abstract in German: *3,4-Dihydro-2-pyridone [3,4-Dihydropyridin-2(1H)-one]* ***6*** *wurden als Alkenkompenenten in der Paternò-Büchi-Reaktion getestet. Die Stammverbindung* ***6a*** *erwies sich als vielseitiger Synthesebaustein, der mit verschiedenen photoangeregten aromatischen Carbonylverbindungen (Benzaldehyd, Benzophenon, Acetophenon, Phenylglyoxylsäuremethylester, 3-Pivaloyloxybenzaldehyd) mit hoher Regioselektivität und Diastereoselektivität reagiert (51–63% Ausbeute). Die Produktoxetane lassen sich einer Hydrogenolyse unterwerfen, was einen neuen und effizienten Syntheseweg zur Herstellung von 2-Arylmethyl-3-piperidinolen eröffnet. Beispielhaft wurden die Oxetane* ***7a*** *und* ***8a*** *hydrogenolytisch gespalten, wobei die Produkte* ***12*** *(88%) und* ***13*** *(93%) erhalten werden konnten. Die Fähigkeit von Verbindung* ***6a****, über zwei Wasserstoffbrücken an einen chiralen Lactamwirt zu binden, wurde genutzt, um die enantiotopen Seiten ihrer Doppelbindung zu differenzieren. In der Photocycloaddition an den chiralen Aldehyd* ***15****, die bei* $-10\,^{\circ}C$ *in Toluol als Lösungsmittel durchgeführt wurde, wurde eine hohe faciale Diastereoselektivität (>90% de, 56% Ausbeute) beobachtet. Die Stereoselektivität resultiert aus einer 1:1-Assoziation des Dihydropyridons* ***6a*** *an den Aldehyd. Die 4-substitutierten Dihydropyridone* ***6b–6d*** *(R = Methyl, iso-Propyl, Phenyl) erwiesen sich für eine Anwendung in der Photochemie als weniger gut geeignet. Die Ausbeuten und facialen Diastereoselektivitäten, die bei ihren [2+2]-Photocycloadditionen an Benzophenon gemessen wurden, waren nicht zufriedenstellend.*

Results and Discussion

Preparation of dihydropyridones: There is ample literature precedence for the synthesis of 3,4-dihydro-2-pyridones.[8] We planned to employ the parent compound for photocycloaddition reactions with various carbonyl compounds and 4-substituted derivatives for studies regarding facial diastereoselectivity. For the preparation of these compounds, the reduction of glutarimides **5**, combined with a subsequent elimination, was considered to be the most versatile sequence (Scheme 2). Dihydropyridone **6a** has been previously prepared by this route.[9] Glutarimides were available from substituted glutaric acids **4** by heating with urea.[10] The 3-substituted glutaric acids **4b–4d** were in turn synthesized by the procedure of Heathcock et al.[11] To this end, the corresponding aldehyde RCHO was initially condensed with ethyl cyanoacetate. A subsequent Michael addition of dimethyl malonate yielded the direct precursor for the glutaric acid, which was obtained after acidic hydrolysis and concurrent decarboxylation. The conversion of the acids **4** to the desired dihydropyridones **6** proceeded cleanly. The results are summarized in Table 1.

Table 1. Preparation of the dihydropyridones **6** by cyclization of glutaric acids **4** and subsequent reduction of glutarimide **5** (cf. Scheme 2).

Entry	Acid	R	Imide	Yield[a] [%]	Product	Yield[a] [%]
1	**4a**	H	**5a**	78	**6a**	46
2	**4b**	Me	**5b**	87	**6b**	61
3	**4c**	*i*Pr	**5c**	65	**6c**	36
4	**4d**	Ph	**5d**	58	**6d**	68

[a] Yield of isolated product.

Chemoselectivity, regioselectivity, and simple diastereoselectivity: In a set of experiments with acyclic *N*-acyl enamines[4a, 12] we had previously employed NH-acidic enamine substrates. Although they did react fairly well in the photocycloaddition to benzaldehyde the yield and diastereoselectivities were inferior to the results obtained with N-alkylated derivatives. *N*-Vinylacetamide proved to be prone to polymerization and reacted sluggishly. We were more pleased to realize that the reaction of benzaldehyde and dihydropyridone (**6a**) in acetonitrile turned out to be a clean reaction that produced the corresponding bicyclic product **7a** in reasonable yield. As a major side reaction, the photopinacolization of benzaldehyde was observed. An increase in the dihydropyridone concentration helped to suppress the side reaction, but we routinely kept the ratio of carbonyl compound:**6a** above 1:2 to facilitate purification of the product. As a consequence, the reaction time and yields vary slightly depending on the precise ratio. Some results that were obtained with various carbonyl substrates are summarized in Scheme 3 and Table 2.

The formation of regioisomeric products was not observed. The tendency of photoexcited carbonyl compounds to attack the more electron-rich position of an enamine substrate has been previously demonstrated.[12] As a consequence, 7-oxa-2-azabicyclo[4.2.0]octan-3-ones were formed as major products from dihydropyridone **6a**. In the case of the benzophenone

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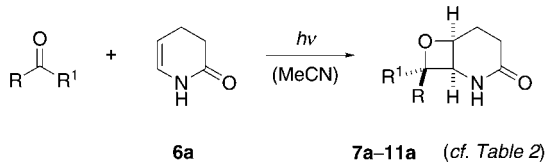


Scheme 3. [2 + 2]-Photocycloaddition of various carbonyl compounds with dihydropyridone **6a**.

Table 2. Paternò–Büchi reaction of 3,4-dihydro-2-pyridone (**6a**) with aromatic carbonyl compounds $RR^1C{=}O$ (cf. Scheme 3).

Entry	R	R^1	Time [h][a]	Product	d. r.[b]	Yield[c] [%]
1	Ph	H	8	**7a**	92/8	63
2	Ph	Ph	16	**8a**	–	56
3	3-PivOPh[d]	H	10	**9a**	88/12	54
4	Ph	Me	48	**10a**	90/10	51
5	Ph	COOMe	40	**11a**	90/10	52

[a] Irradition time (entries 1 and 3: $\lambda = 300$ nm; entries 2, 4, 5: $\lambda = 350$ nm). [b] The ratio of diastereoisomers was determined by integration of appropriate ^{1}H NMR signals. [c] Yield of isolated product. [d] Piv = Pivaloyl, solvent: benzene.

photocycloadduct **8a** we were able to unequivocally establish the structure by single crystal X-ray crystallography.[13] The result of this study is depicted in Figure 1. It shows nicely the planarity of the oxetane ring and the anticipated *cis*-connection between the four- and six-membered rings.

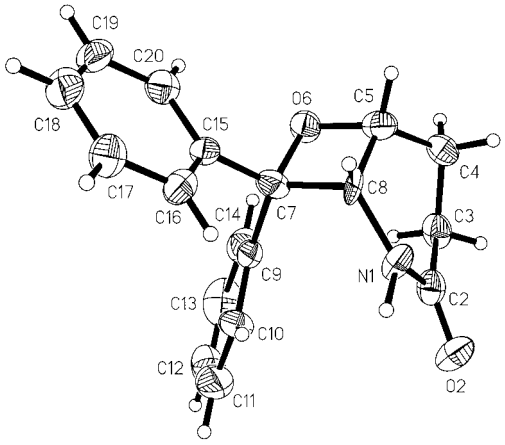


Figure 1. A molecule of compound **8a** from the crystal unit cell.

If nonsymmetrical carbonyl compounds are employed, an additional stereogenic center is created in the course of the photocycloaddition. The simple diastereoselectivity with regard to this C–C bond formation is not exceedingly high but was considered to be sufficient (d.r. ≅ 9/1). The relative configuration of the major diastereoisomer was elucidated by ^{1}H NOESY experiments (Figure 2). The phenyl group adopts the sterically more congested *endo* position relative to the six-membered ring. The substituents that are located *cis* in the oxetane ring show strong (——) or medium (- - - -) NOESY contacts. This stereochemical result has been frequently encountered in the Paternò–Büchi reaction of aldehydes or nonsymmetrical ketones with α-monosubstituted alkenes.[4a, 12e, 14] Reasonable explanations to account for the formation of the *endo* product have been put forward.[15]

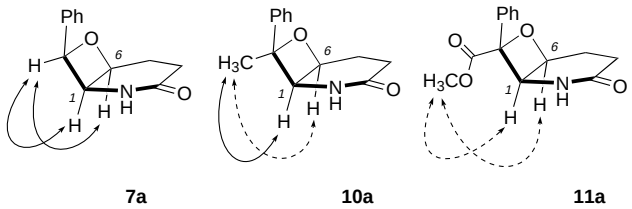
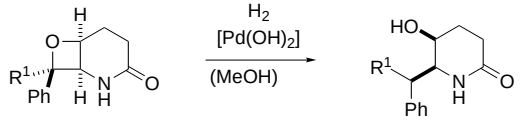


Figure 2. Major ^{1}H NOE data recorded for compounds **7a**, **10a**, and **11a**.

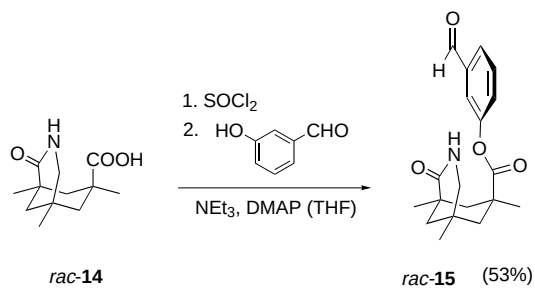
The subsequent hydrogenolysis of the products **7a** and **8a** proceeded smoothly and led to the *cis*-substituted 6-arylalkyl-5-hydroxy-2-piperidones **12** and **13** (Scheme 4). The hydrogenolysis of the other products **9a**–**11a** should be equally possible, but we did not pursue it. Previous work had shown that the process is not stereospecific.[16]



Scheme 4. Hydrogenolysis of the oxetanes **7a** and **8a**.

Hydrogen binding by a chiral aldehyde: A major advantage of a photochemical reaction is the fact that it does not require an additional activation by acids or bases. Accordingly, weak attractions between molecules are not lost in the course of the reaction and can be employed to control relevant selectivity parameters. The lactam **6a** can act as a hydrogen donor via its amide NH group and as hydrogen acceptor through its carbonyl group. If bound to a chiral aldehyde through hydrogen bonds, the two enantiotopic faces of the lactam become diastereotopic and can be diffentiated. It was our goal to prove this selection principle for the Paternò–Büchi reaction as a representative photochemical process. Consequently, we constructed a chiral aldehyde that is capable of hydrogen binding to lactam **6a** and of discriminating its two enantiotopic faces. Starting from the known lactam *rac*-**14**,[17] the aldehyde *rac*-**15** was prepared by O-acylation of 3-hydroxybenzaldehyde (Scheme 5).

The lactam unit of compound *rac*-**15** should be capable of binding to compound **6a** and, provided it did so, the photoexcited aldehyde part would approach the dihydropyridone



Scheme 5. Preparation of the chiral aldehyde host *rac*-**15**.

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6a only from a single face. In addition, any reaction within the stoichiometric complex *rac*-**15**/**6a** should be faster than the comparable intermolecular reaction of *rac*-**15** and **6a**. The face selection should consequently be enhanced by a rate acceleration. Figure 3[18] gives an impression of the face discrimination provided by the aromatic aldehyde backbone in compound *rac*-**15**. In the crystal, the ester and amide carbonyl groups of *rac*-**15** are eclipsed.[18] In solution, the rotation around the C–C bond C7–C13 is certainly free and the approach of the photoexcited aldehyde to the coordinated dihydropyridone should not be hampered by any conformational restriction.

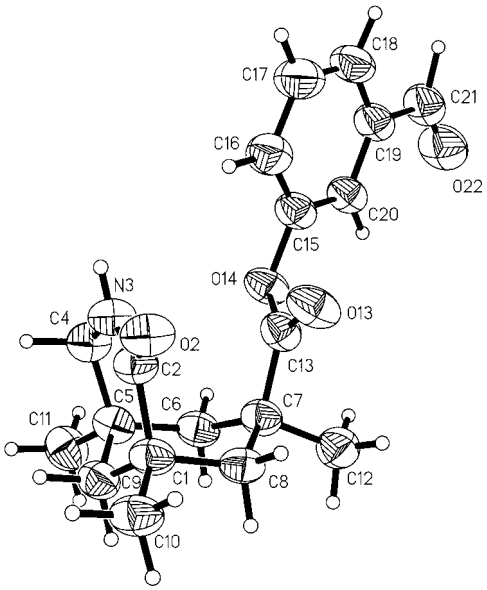
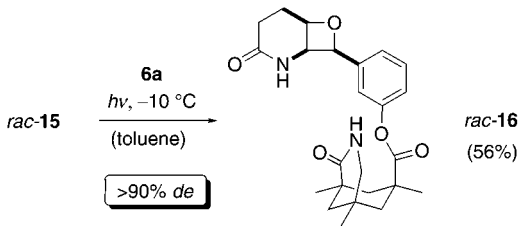


Figure 3. A molecule of compound **15** from the crystal unit cell.

Irradiation experiments of the aldehyde *rac*-**15** in the presence of alkene **6a** were conducted in different solvents and at different temperatures.[7] Not surprisingly, there was no diastereoselection in the polar solvent acetonitrile. The selectivity was significant in benzene and could be optimized by running the reaction at $-10\,^{\circ}C$ in toluene as the solvent (Scheme 6). Under these conditions we could not detect the



Scheme 6. The diastereoselective hydrogen bond mediated Paternò–Büchi reaction of aldehyde *rac*-**15** and dihydropyridone **6a**.

other diastereoisomer in the crude product mixture by ^1H NMR spectroscopy. The detection limit was estimated conservatively at a comparably large value (5%) since the resolution of the relevant signals was not perfect.

The relative configuration of oxetane *rac*-**16** was unambiguously proved by single crystal X-ray crystallography.[7] The preparative investigations were accompanied by NMR titration experiments conducted at $-10\,^{\circ}C$ in [D_8]toluene.[19] The self-association of compound *rac*-**15** was low ($K_a = 24 \pm 1\ M^{-1}$),[20] whereas the dihydropyridone **6a** showed a higher tendency for self association ($K_a = 85 \pm 7\ M^{-1}$). By implementing these values, it was possible to determine the equilibrium constant for the association of **6a** and *rac*-**15** at $K_a = 227 \pm 34\ M^{-1}$. The result of the corresponding titration experiment is depicted in Figure 4. Previous Job plot analysis had revealed a 1/1 stoichiometry for the association complex *rac*-**15**/**6a**.[7]

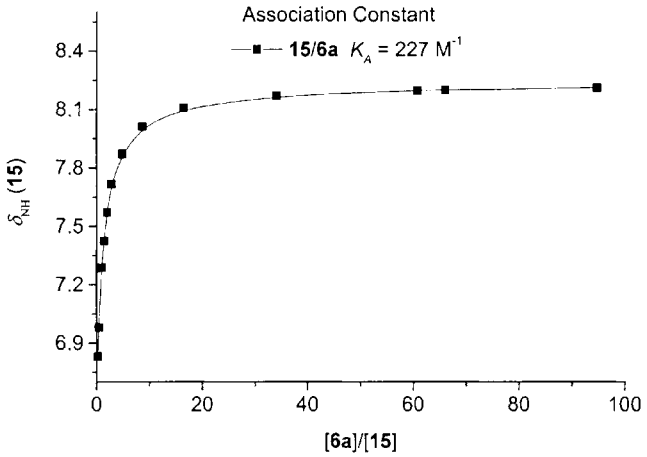
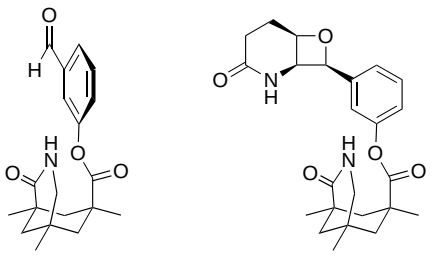


Figure 4. NMR titration of compound **15** and dihydropyridone **6a** at $-10\,^{\circ}C$ in toluene.

Reactions of compound *rac*-**15** with enamides that are not capable of hydrogen binding,[12e] and the reaction of compound **6a** with the N-methylated derivative of *rac*-**15** were conducted in toluene at $-10\,^{\circ}C$ and were not selective. These results provide additional proof for the importance of hydrogen bonds for a successful face discrimination.

Compound **15** was available in enantiomerically pure form by conventional resolution. To this end, the racemate *rac*-**15** was N-acylated with (–)-menthyl chloroformate. Separation of the resulting diastereoisomers by flash chromatography and acidic cleavage of the carbamate yielded (+)- and (–)-**15** in enantiomerically pure forms. The tabulated specific rotations of known 1,5,7-trimethyl-2-oxo-3-azabicyclo[3.3.1]nonanoic acid derivatives that possess only the lactam unit as chiral chromophore[21, 22] were employed to assign an absolute configuration to compound (+)-**15**. All known derivatives with (*1R,5S,7S*) configuration are dextrorotatory whereas their enantiomers are levorotatory. Consequently, compound (+)-**15** {$[\alpha]_D^{20} = +51.8$ ($c = 1.13$, CH_2Cl_2)} should have the (*1R,5S,7S*) configuration as depicted below (Figure 5). Its photocycloaddition to dihydropyridone **6a** gave the enantiomerically pure oxetane (–)-**16** the purity of which was checked by HPLC analysis on a chiral column (Chiracel OD, eluent:hexane/isopropanol = 92/8). The bicyclic oxetano[2,3-*b*]piperidone fragment could be readily cleaved from the host by transesterification.

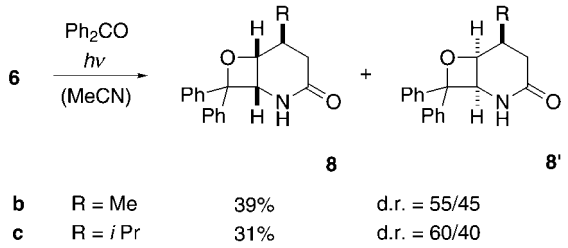


(+)-**15** (–)-**16** (>95% *ee*)

Figure 5. Tentatively assigned absolute configuration of the enantiomerically pure compounds (+)-**15** and (–)-**16**.

Despite these encouraging results, we currently have not pursued the utilization of aldehyde **15** as a chiral auxiliary-based aldehyde. The study described in this section was conducted to prove in principle that a control of stereoselectivity in intermolecular photochemical reactions is possible by hydrogen bonds. To the best of our knowledge, we have provided the first unequivocal evidence for this type of control. In subsequent experiments, hydrogen bonds have been employed in enantioselective photochemical reactions. Chiral host compounds related to compound (+)-**15** serve as templates on which enantioselective intramolecular and intermolecular photochemical reactions proceed.[23]

Chiral dihydropyridones: Finally, we studied the photocycloaddition reaction of the chiral dihydropyridones **6b**–**6d** with benzophenone. The ratio of carbonyl compound to alkene was 1:1.5 in all experiments. Disappointingly, the facial diastereoselectivity was found to be low. The two products **8** and **8′** were formed in almost equal amounts (Scheme 7). In



Scheme 7. [2+2]-Photocycloaddition of benzophenone with the chiral dihydropyridones **6b** and **6c**.

addition, the yields were significantly reduced as compared to the parent compound **6a**. We assume that the ease of hydrogen abstraction at the C-4 carbon atom is enhanced by the substitutent R. The alkyl group R presumably resides in a pseudoequatorial position that facilitates the attack of the photoexcited carbonyl compound at the axial hydrogen atom. The C–H bond to be cleaved is almost perfectly aligned with the π bond of the dihydropyridone. This argument is in line with the fact that no oxetane product formation was observed with dihydropyridone **6d** (R = Ph). The aromatic substituent additionally stabilizes a radical in 4-position and hydrogen abstraction becomes the exclusive reaction pathway. Defined products derived from compound **6d** could not be isolated.

Although the facial diastereoselectivity in the above mentioned photocycloaddition was marginal, we made an attempt to elucidate the relative configuration of the products. The diastereomeric products **8b** (22%) and **8b′** (17%) were separable by flash chromatography, as were the *iso*-propyl substituted products **8c** (18%) and **8c′** (13%). The major diastereoisomer **8b** gave crystals suitable for X-ray analysis. The result of the structure elucidation is shown in Figure 6.[24]

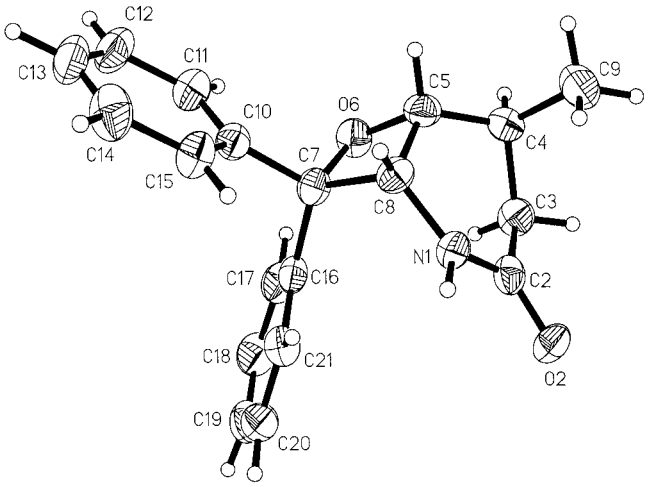


Figure 6. A molecule of compound **8b** from the crystal unit cell.

Apparently, the major diastereoisomer is formed by photochemically initiatied O–C formation from the face opposite to the methyl group. This effect is not pronounced, however, and does not increase significantly with increasing bulk of the R group.

Conclusion

In summary, the parent unsubstituted 3,4-dihydropyridone **6a** was identified as a useful and versatile substrate for the Paternò–Büchi reaction. Its reaction with aldehydes and ketones serves as a useful entry into multiply substituted piperidinones and piperidines. The capacity of compound **6a** to form hydrogen bonds to other lactams was favorably employed for the differentiation of its enantiotopic faces by a chiral aldehyde host. The perfect facial diastereoselectivity (>90% *de*) in the conversion of the host **15** and the pyridone **6a** to the oxetane **16** was shown to be effected by hydrogen bonds. This photocycloaddition represents the first example for an efficient stereocontrol in intermolecular photochemical reactions based on hydrogen bonds and paves the way to further applications of non-covalently chiral hosts in stereoselective photochemical reactions. The chiral dihydropyridones **6b**–**6d** exhibit a lower chemoselectivity in their reaction with photochemically excited carbonyl compounds. Product yields in the conversion of **6b** and **6c** with benzophenone were low and the facial diastereoselectivity disappointing. Compound **6d** did not undergo a [2+2]-photocycloaddition. Hydrogen abstraction in 4-position by the photoexcited carbonyl compound appears to be an efficient side reaction that cannot be suppressed.

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Experimental Section

General: For general remarks, see ref.[12e]. Abbreviations: P = *n*-pentane, TBME = *tert*-butyl methyl ether. Relevant starting materials **4c**, **5b**, **5d**, **6a**, *rac*-**14** that were not commercially available were prepared by known procedures.[9–11, 17]

3-isopropyl glutarimide (5c): 3-Isopropyl glutaric acid (**4c**)[11, 25] (44.7 mmol, 7.79 g) and urea (49.1 mmol, 2.95 g) were mixed without the addition of a solvent. The mixture was heated for 2 h at 145 °C and for an additional 20 min at 180 °C. Upon cooling, the crude product mixture was recrystallized from ethanol. The product **5c** was obtained as a white solid. Yield 4.53 g (29.2 mmol, 65 %); $R_f = 0.15$ (TBME); m.p. 118 °C; ^{1}H NMR (200 MHz): $\delta = 8.72$ (br s, 1H; NH), 2.65 (dd, $^2J = 17.0$ Hz, $^3J = 4.0$ Hz, 2H; CH*H*CHCH*H*), 2.07 (ddd, $^2J = 17.0$ Hz, $^3J = 12.5$ Hz, $^3J = 1.0$ Hz, 2H; C*H*HCHC*H*H), 1.96–1.79 (m, 1H; CH_2CHCH_2), 1.65–1.48 (m, 1H; $(CH_3)_2CH$), 0.90 (d, $^3J = 6.8$ Hz, 6H; CH_3CHCH_3); ^{13}C NMR (50 MHz): $\delta = 173.2$ (2C; CONHCO), 36.5 (CH_2CHCH_2), 35.5 (2C; CH_2CHCH_2), 31.3 ($(CH_3)_2CH$), 19.2 (2C, $(CH_3)_2CH$); IR (film): $\tilde{\nu} = 3200$ (m, NH), 3085 (m), 2930 (s), 2870 (m, C-H), 1720 (s, C=O), 1675 (vs), 1395 (m), 1375 (m), 1250 (m), 1150 cm^{-1} (s, C-H); MS (70 eV, EI): *m*/*z* (%): 155 (37) [M^+], 127 (16) [$M^+ - CO$], 113 (51) [$M^+ - C_3H_7$], 85 (36) [$C_5H_{11}N^+$], 43 (100) [$C_3H_7^+$]; elemental analysis calcd (%) for $C_8H_{13}NO_2$ (155.19): C 61.91, H 8.44, N 9.03; found: C 61.67, H 8.59, N 9.17.

The known compounds **5b**[10] and **5d**[10, 26] were obtained in an analogous fashion. Yields for the individual steps are provided in Table 1.

(*RS*)-3,4-Dihydro-4-methyl-2-pyridone (6b): At 0 °C, sodium borohydride (107 mmol, 2.77 g) was added in portions to a stirred solution of 3-methyl glutarimide (**5b**)[10] (23.6 mmol, 3.00 g) in 100 mL of ethanol. The mixture was stirred for another 2 h at 0 °C. The pH was subsequently adjusted to 3 by addition of an ethanolic HCl solution (2 M). After 45 min at 0 °C the mixture was neutralized with ethanolic KOH solution and warmed to room temperature. The solvent was removed in vacuo and the resulting colorless solid extracted with dichloromethane (200 mL). After filtration the solvent was removed and the resulting 6-ethoxy pyridone dissolved in toluene (150 mL). The solution was refluxed for 7 h to induce the elimination. The toluene was removed in vacuo and the crude product subsequently purified by flash chromatography (TBME). The desired product **6b** was obtained as a colorless oil, which solidified upon standing. Yield 1.60 g (14.4 mmol, 61 %); $R_f = 0.38$ (EtOAc); m.p. 62 °C; ^{1}H NMR (200 MHz): $\delta = 8.31$ (br s, 1H; NH), 5.99 (ddd, $^3J = 7.6$ Hz, $^3J = 4.5$ Hz, $^4J = 1.5$ Hz, 1H; NC*H*CH), 4.95 (dd, $^3J = 7.6$ Hz, $^3J = 3.0$ Hz, 1H; NCHC*H*), 2.65–2.45 (m, 2H; C*H*CH*H*CO), 2.24–2.10 (m, 1H; C*H*HCO), 1.04 (d, $^3J = 6.7$ Hz, 3H; CH_3); ^{13}C NMR (50 MHz): $\delta = 171.9$ (NCO), 123.7 (NCH), 111.5 (NCH*C*H), 38.6 (*C*HCH$_3$), 26.7 (CH_2), 20.1 (CH_3); IR (film): $\tilde{\nu} = 3256$ (m, NH), 2960 (s), 2830 (m, CH), 1730 (vs, C=O), 1690 (vs), 1260 (m), 1230 (m), 1090 (w), 1065 cm^{-1} (m, CH); MS (70 eV, EI): *m*/*z* (%): 111 (20) [M^+], 55 (73) [$C_3H_3O^+$], 42 (100) [$C_2H_2O^+$], 28 (25) [CO^+]; elemental analysis calcd (%) for C_6H_9NO (111.14): C 64.84, H 8.16, N 12.60; found: C 64.74, H 8.24, N 12.71.

(*RS*)-3,4-Dihydro-4-isopropyl-2-pyridone (6c): 3-Isopropyl glutarimide (**5c**) (3.50 g, 22.6 mmol) was converted into the desired product **6c** as previously described for compound **6b**. Yield 1.17 g (8.17 mmol, 36 %); $R_f = 0.43$ (EtOAc); ^{1}H NMR (200 MHz): $\delta = 8.09$ (br s, 1H; NH), 6.02 (dd, $^3J = 7.8$ Hz, $^3J = 4.5$ Hz, 1H; NC*H*CH), 4.93 (dd, $^3J = 7.8$ Hz, $^3J = 3.2$ Hz, 1H; NCHC*H*), 2.50–2.37 (m, 1H; C*H*CH$_2$CO), 2.32–2.27 (m, 2H; CH_2CO), 1.66–1.55 (m, 1H; $(CH_3)_2CH$), 0.83 (d, $^3J = 6.8$ Hz, 6H; CH_3CHCH_3); ^{13}C NMR (50 MHz): $\delta = 172.4$ (NCO), 124.4 (NCH), 108.0 (NCH*C*H), 37.9 (*C*H$_2$CO), 33.8 (*C*HCH$_2$CO), 31.6 ($(CH_3)_2CH$), 19.1 (CH_3), 18.9 (CH_3). IR (film): $\tilde{\nu} = 3240$ (s, NH), 3130 (w), 2960 (s, CH), 2935 (m, CH), 2875 (m, CH), 1685 (vs, C=O), 1655 (vs), 1465 (m), 1355 cm^{-1} (m, CH); MS (70 eV, EI): *m*/*z* (%): 139 (16) [M^+], 96 (100) [$C_5H_6NO^+$], 41 (18) [$C_2H_3N^+$]; HRMS calcd (u) for $C_8H_{13}NO$: 139.0997; found 139.0996.

(*RS*)-3,4-Dihydro-4-phenyl-2-pyridone (6d): 3-Phenyl glutarimide (**5d**) (1.33 g, 7.05 mmol)[10, 26] was converted into the desired product **6d** as previously described for compound **6b**. Yield after purification by flash chromatography (EtOAc) 837 mg (4.83 mmol, 68 %); $R_f = 0.37$ (EtOAc); m.p. 158 °C; ^{1}H NMR (200 MHz): $\delta = 8.28$, (s, 1H; NH), 7.30–7.12 (m, 5H; Ph), 6.15 (ddd, $^3J = 7.5$ Hz, $^3J = 4.5$ Hz, $^4J = 2.0$ Hz, 1H; NC*H*CH), 5.12 (dd, $^3J = 7.5$ Hz, $^3J = 3.8$ Hz, 1H; NCHC*H*), 3.70–3.74 (m, 1H; CHPh), 2.74 (dd, $^2J = 16.3$ Hz, $^3J = 7.3$ Hz, 1H; CH*H*CO), 2.54 (dd, $^2J = 16.3$ Hz, $^3J = 9.5$ Hz, 1H; C*H*HCO); ^{13}C NMR (50 MHz): $\delta = 170.9$ (NCO), 142.9 (C_{Ar}), 128.8 (2C; C_{Ar}), 126.94 (2C; C_{Ar}), 126.89 (NCH), 125.0 (C_{Ar}), 108.9 (NCH*C*H), 39.0 (CHPh), 38.0 (CH_2); IR (film): $\tilde{\nu} = 3195$ (m, NH), 3095 (m, CH), 2930 (m, CH), 1680 (vs, C=O), 1635 (s), 1400 (m), 1360 (m), 1340 (m), 945 (w), 770 (m), 700 cm^{-1} (m, CH); MS (70 eV, EI): *m*/*z* (%): 173 (100) [M^+], 144 (44), 130 (88), 68 (24), 28 (59) [CO^+]; elemental analysis calcd (%) for $C_{11}H_{11}NO$ (173.21): C 76.28, H 6.40, N 8.09; found: C 75.88, H 6.40, N 7.86.

General irradiation procedure: Irradiation experiments were performed in a quartz tube. The carbonyl compound (1.0 equiv) and the 3,4-dihydropyridone **6** (1.5–2.0 equiv) were dissolved in an appropriate solvent (Merck p. a.) under argon. This mixture was irradiated for the indicated period of time ($\lambda = 350$ nm: Rayonet RPR 3500 Å; $\lambda = 300$ nm: Rayonet RPR 3000 Å). The course of the reaction was monitored by TLC and GLC. Upon complete conversion of the carbonyl compound, the solvent was evaporated in vacuo. The diastereoselectivity (d.r.) was determined by GLC analysis of the crude product. The desired oxetanes were separated in the course of the subsequent flash chromatography and were obtained as colorless oils or solids. Relative configurations were determined by ^{1}H NMR spectroscopy (NOE or NOESY experiments) or single-crystal X-ray analysis.

(1*RS*,6*SR*,8*RS*)-2-Aza-7-oxa-8-phenylbicyclo[4.2.0]octan-3-one (7a): According to the general irradiation procedure, benzaldehyde (208 mg, 200 μL, 1.95 mmol) and 3,4-dihydropyridone **6a**[9] (380 mg, 3.90 mmol) were irradiated in acetonitrile (20 mL) at $\lambda = 300$ nm for 8 h. The solvent was removed in vacuo and the residue purified by flash chromatography (EtOAc). Yield 250 mg (1.23 mmol, 63 %); $R_f = 0.11$ (EtOAc); m.p. 150 °C; ^{1}H NMR (500 MHz): $\delta = 7.37–7.20$ (m, 5H; H_{Ar}), 6.07 (br s, 1H; NH), 5.91 (d, $^3J = 6.2$ Hz, 1H; PhC*H*), 5.37–5.40 (m, 1H; OCH), 4.53 (ddd, $^3J = 6.2$ Hz, $^3J = 6.2$ Hz, $^3J = 4.3$ Hz, 1H; C*H*NH), 2.74 (ddd, $^2J = 16.8$ Hz, $^3J = 13.5$ Hz, $^3J = 5.8$ Hz, 1H; CHHCH*H*CO), 2.35–2.31 (m, 1H; CHHC*H*HCO), 2.23–2.18 (m, 1H; CH*H*CHHCO), 1.79–1.71 (m, 1H; C*H*HCHHCO); NOESY experiment (500 MHz): H(4.53)-H(5.37–5.40)‴, H(4.53)-H(5.91)″, H(5.37–5.40)-H(5.91)‴; ^{13}C NMR (50 MHz): $\delta = 173.4$ (s; CO), 136.8 (s; C_{Ar}), 129.0 (2C, d; C_{Ar}H), 128.3 (d; C_{Ar}H), 125.5 (2C, d; C_{Ar}H), 85.4 (d; PhCH), 74.8 (OCH), 54.5 (CHN), 28.1 (*C*H$_2$CO), 25.3 (*C*H$_2$CHO); IR (film): $\tilde{\nu} = 3279$ (br s, NH), 2920 (s, CH), 2879 (m, CH), 1665 (s, C=O), 1635 (s), 1485 (m), 1200 (s), 985 (s, COC), 901 (s), 751 (s, CH), 706 cm^{-1} (s, CH); MS (70 eV, EI): *m*/*z* (%): 203 (0.5) [M^+], 119 (8), 97 (100) [M^+ – PhCHO], 91 (6) [$C_7H_7^+$], 77 (13) [$C_6H_5^+$], 69 (78), 54 (21), 43 (22); elemental analysis calcd (%) for $C_{12}H_{12}NO_2$ (203.24): C 70.92, H 6.45, N 6.89; found: C 70.68, H 6.57, N 6.70.

(1*RS*,6*SR*)-2-Aza-8,8-diphenyl-7-oxaazabicyclo[4.2.0]octan-3-one (8a): According to the general irradiation procedure, benzophenone (380 mg, 2.11 mmol) and 3,4-dihydropyridone **6a**[9] (310 mg, 3.16 mmol) were irradiated in acetonitrile (20 mL) at $\lambda = 350$ nm for 16 h. The solvent was removed in vacuo and the residue purified by flash chromatography (EtOAc). Yield 316 mg (1.13 mmol, 54 %). Crystals suitable for single-crystal X-ray analysis were obtained by recrystallization from chloroform. $R_f = 0.21$ (EtOAc); m.p. 170 °C; ^{1}H NMR (200 MHz): $\delta = 7.69–7.35$ (m, 10H; H_{Ar}), 7.18 (br s, 1H; NH), 5.47 (d, $^3J = 7.0$ Hz, 1H; OCH), 4.88 (dd, $^3J = 7.0$ Hz, $^3J = 4.9$ Hz, 1H; CHN), 2.66 (ddd, $^2J = 16.6$ Hz, $^3J = 13.7$ Hz, $^3J = 5.1$ Hz, 1H; CHHCH*H*CO), 2.45–2.34 (m, 2H; CH*H*CH*H*CO), 1.91 (ddd, $^2J = 14.4$ Hz, $^3J = 5.1$ Hz, $^3J = 3.0$ Hz, 1H; C*H*HCHHCO); ^{13}C NMR (50 MHz): $\delta = 184.0$ (NCO), 128.5, 128.3, 127.4, 127.2, 125.3, 124.8, (12C; C_{Ar}H and C_{Ar}), 91.4 (O*C*Ph$_2$), 72.5 (CHO), 59.4 (*C*HN), 27.8 (*C*H$_2$CO), 25.2 (*C*H$_2$CHO); IR (film): $\tilde{\nu} = 3250$ (m, NH), 2930 (w, CH), 1680 (vs, C=O), 1625 (s), 1490 (m), 1450 (s), 1200 (m, CH), 990 (m, COC), 770 (m), 750 (m), 705 cm^{-1} (s, CH); MS (70 eV, EI): *m*/*z* (%): 279 (0.2) [M^+], 183 (71) [Ph_2COH^+], 105 (48) [$PhCO^+$], 97 (100) [$M^+ - Ph_2CO$], 69 (61) [$C_3H_3NO^+$]; HRMS calcd (u) for $C_{18}H_{17}NO_2$: 279.1259; found 279.1265.

3-Pivaloyloxybenzaldehyde: 3-Hydroxybenzaldehyde (3.66 g, 30.0 mmol) was dissoved in CH_2Cl_2 (50 mL) and the solution was cooled to 0 °C. Triethylamine (4.02 g, 5.54 mL, 40.0 mmol) and a catalytic amount of dimethylaminopyridine (DMAP) were added to the stirred solution. Pivaloyl chloride (3.98 g, 4.06 mL, 33.0 mmol) was added dropwise. The mixture was warmed to room temperature and stirred for another 3 h. The solvent was removed in vacuo and the residue purified by flash chromatography (P/TBME = 6/1). Yield 5.90 g (28.6 mmol, 95 %) of the desired aldehyde as a colorless oil; $R_f = 0.37$ (P/TBME = 3/1); ^{1}H NMR (400 MHz): $\delta = 9.97$ (s, 1H; CHO), 7.74 (virt. dt, $^3J = 7.7$ Hz, $^4J = 1.3$ Hz,

1H; H_{Ar}), 7.60 (virt. t, $^4J = 1.8$ Hz, 1H; H_{Ar}), 7.55 (virt. t, $^3J = 7.9$ Hz, 1H; H_{Ar}), 7.34 (ddd, $^3J = 8.1$ Hz, $^4J = 2.6$ Hz, $^4J = 1.1$ Hz, 1H; H_{Ar}), 1.38 (s, 9H; $C(CH_3)_3$); ^{13}C NMR (125 MHz): $\delta = 191.2$ (s; CHO), 176.7 (s; CO), 151.6 (s; C_{Ar}), 137.6 (s; C_{Ar}), 130.0 (d; CH_{Ar}), 127.7 (d; CH_{Ar}), 127.2 (d; CH_{ar}), 122.0 (d; CH_{Ar}), 39.0 (s; $C(CH_3)_3$), 27.0 (3C, q; $C(CH_3)_3$); IR (film): $\tilde{\nu} =$ 2976 (m, CH), 1755 (s, C=O), 1700 (s, C=O), 1590 (m), 1480 (m), 1238 (s), 1139 (s), 1109 cm^{-1} (s); MS (70 eV, EI): *m/z* (%): 206 (2) [M^+], 122 (58), 121 (23) [$M^+ - CO$*t*Bu], 105 (2) [$M^+ - OCO$*t*Bu], 85 (53) [CO*t*Bu$^+$], 77 (4) [$C_6H_5^+$], 65 [$C_5H_5^+$], 57 (100) [*t*Bu$^+$], 41 (33); elemental analysis calcd (%) for $C_{12}H_{14}O_3$ (206.44): C 69.88, H 6.84; found: C 69.63, H 6.87.

2,2-Dimethylpropanoic acid (2-aza-3-oxo-7-oxabicyclo[4.2.0]oct-8-yl)-phenyl ester: According to the general irradiation procedure, 3-pivaloyloxybenzaldehyde (280 mg, 1.36 mmol) and 3,4-dihydropyridone **6a**[9] (263 mg, 2.72 mmol) were irradiated in benzene (10 mL) at $\lambda = 300$ nm for 10 h. The solvent was removed in vacuo and the residue purified by flash chromatography (EtOAc). Yield: **9a** (192 mg, 0.63 mmol; 47%) as a white solid and its (1*RS*,6*SR*,8*SR*)-diastereoisomer (27 mg, 0.09 mmol; 7%) as an oil (54%; *d.r.* = 88/12).

Major (1*RS*,6*SR*,8*RS*)-diastereoisomer (**9a**): $R_f = 0.07$ (EtOAc); m.p. 55–57 °C; ^{1}H NMR (500 MHz): $\delta = 7.24$ (virt. t, $^3J = 7.9$ Hz, 1H; H_{Ar}), 6.85–6.96 (m, 4H; 3H_{Ar}, NH), 5.85 (d, $^3J = 6.0$ Hz, 1H; ArC*H*), 5.27–5.30 (m, 1H; ArCHOC*H*), 4.45 (virt. dt, $^3J = 6.2$ Hz, $^3J = 4.6$ Hz, 1H; CONHC*H*), 2.63–2.55 (m, 1H; NHCOCH*H*), 2.23–2.29 (m, 1H; NHCOC*H*H), 2.11–2.06 (m, 1H; NHCOCH$_2$CH*H*), 1.66–1.59 (m, 1H; NHCOCH$_2$C*H*H), 1.26 (s, 9H; $C(CH_3)_3$); ^{13}C NMR (125 MHz): $\delta = 176.8$ (s; CO), 173.4 (s; CO), 151.2 (s; C_{Ar}), 138.3 (s; C_{Ar}), 129.3 (d; CH_{Ar}), 122.1 (d; CH_{Ar}), 120.5 (d; CH_{Ar}), 118.2 (d; CH_{Ar}), 84.3 (d; Ar*C*HO), 74.5 (d; ArCHO*C*H), 53.4 (d; CONH*C*H), 38.9 (s; $C(CH_3)_3$), 27.5 (t; NHCO*C*H$_2$), 27.0 (q, 3C; $C(CH_3)_3$), 24.7 (t; NHCOCH$_2$*C*H$_2$); IR (film): $\tilde{\nu} = 3391$ cm^{-1} (br s, NH), 2964 (s, CH), 1751 (s, C=O), 1669 (s), 1482 (m), 1262 (s), 1100 (vs, b), 801 (s); MS (70 eV, EI): *m/z* (%): 303 (<1) [M^+], 205 (5), 121 (7), 97 (100) [$M^+ -$ ArCHO], 85 (8) [$C_5H_9O^+$], 77 (3) [$C_6H_5^+$], 69 (43), 57 (67) [$C_4H_9^+$]; elemental analysis calcd (%) for $C_{17}H_{21}NO_4$ (303.35): C 67.31, H 6.98, N 4.62; found: C 67.36, H 6.78, N 4.41.

Minor (1*RS*,6*SR*,8*SR*)-diastereoisomer: $R_f = 0.22$ (EtOAc); ^{1}H NMR (500 MHz): $\delta = 7.24$ (virt. t, $^3J = 7.9$ Hz, 1H; H_{Ar}), 6.90–7.12 (m, 3H; H_{Ar}), 6.59 (br d, $^3J = 5.0$ Hz, 1H; NH), 5.31 (d, $^3J = 4.6$ Hz, 1H; ArC*H*), 5.19–5.23 (m, 1H; ArCHOC*H*), 4.04–4.08 (m, 1H; CONHC*H*), 2.81–2.88 (m, 1H; NHCOCH*H*), 2.47–2.62 (m, 1H; NHCOC*H*H), 2.17–2.22 (m, 1H; NHCOCH$_2$CH*H*), 1.71–1.79 (m, 1H; NHCOCH$_2$C*H*H), 1.27 (s, 9H; $C(CH_3)_3$); ^{13}C NMR (125 MHz): $\delta = 177.0$ (s; CO), 173.8 (s; CO), 151.6 (s; C_{Ar}), 142.1 (s; C_{Ar}), 129.9 (d; CH_{Ar}), 122.0 (d; CH_{Ar}), 121.5 (d; CH_{Ar}), 118.1 (d; CH_{Ar}), 91.1 (d; Ar*C*HO), 76.0 (d; ArCHO*C*H), 56.3 (d; CONH*C*H), 39.1 (s; $C(CH_3)_3$), 28.4 (t; NHCO*C*H$_2$), 27.1 (q, 3C; $C(CH_3)_3$), 26.3 (t; NHCOCH$_2$*C*H$_2$); IR (film): $\tilde{\nu} = 3379$ (br s, NH), 2971 (s, CH), 1752 (s, C=O), 1674 (s, C=O), 1481 (m), 1263 (s), 1114 (s), 806 cm^{-1} (s); MS (70 eV, EI): *m/z* (%): 303 (<1) [M^+], 205 (1), 121 (5), 97 (100) [$M^+ -$ ArCHO], 85 (12) [$C_5H_9O^+$], 77 (4) [$C_6H_5^+$], 69 (52), 57 (73) [$C_4H_9^+$]; HRMS calcd (u) for $C_{17}H_{21}NO_4$: 303.1471; found 303.1462.

(1*RS*,6*SR*,8*RS*)-2-Aza-8-methyl-7-oxa-8-phenylbicyclo[4.2.0]octan-3-one (10a): According to the general irradiation procedure, acetophenone (342 mg, 2.83 mmol) and 3,4-dihydropyridone **6a**[9] (413 mg, 4.26 mmol) were irradiated in acetonitrile (10 mL) at $\lambda = 350$ nm for 48 h. The solvent was removed in vacuo and the residue purified by flash chromatography (EtOAc). Yield: 338 mg (1.44 mmol, 51%). $R_f = 0.11$ (EtOAc); ^{1}H NMR (300 MHz): $\delta = 7.62$ (br s, 1H; NH), 7.36–7.60 (m, 5H; H_{Ar}), 5.45 (d, $^3J =$ 6.1 Hz, 1H; OCH), 4.81 (dd, $^3J = 6.8$ Hz, $^3J = 4.6$ Hz, 1H; C*H*NH), 2.65–2.49 (m, 1H; CH*H*CO), 2.34–2.25 (m, 2H; CH*HCH*HCO), 1.91 (s, 3H; CH_3), 1.86–1.79 (m, 1H; C*H*HCH$_2$CO); ^{13}C NMR (75.5 MHz): $\delta = 173.8$ (NCO), 141.6 (C_{Ar}), 128.1 (2C; $C_{Ar}H$), 126.9 (2C; $C_{Ar}H$), 124.6 ($C_{Ar}H$), 90.3 (CPh), 71.4 (OCH), 57.9 (CHNH), 30.0 (CH_3), 27.6 (*C*H$_2$CO), 24.9 (*C*H$_2$CHO); IR (film): $\tilde{\nu} = 3340$ (s, NH), 2970 (m, CH), 2955 (m, CH), 1675 (s, C=O), 1640 (vs), 1480 (m), 1190 (m), 1030 (m), 915 cm^{-1} (m, COC); MS (70 eV, EI): *m/z* (%): 199 (0.2) [$M^+ - CH_3$], 121 (6) [PhCOHCH$_3^+$], 97 (100) [$M^+ -$ PhCOCH$_3$], 69 (58) [$C_3H_3NO^+$], 43 (22) [$C_3H_7^+$]. The compound was not stable at room temperature. A correct elemental analysis was not obtained.

(1*RS*,6*SR*,8*RS*)-2-Aza-8-methoxycarbonyl-8-phenyl-7-oxabicyclo[4.2.0]-octan-3-one (11a): According to the general irradiation procedure, methyl phenylglyoxylate (760 mg, 4.62 mmol) and 3,4-dihydropyridone **6a**[9] (680 mg, 7.00 mmol) were irradiated in acetonitrile (10 mL) at $\lambda = 350$ nm for 40 h. The solvent was removed in vacuo and the residue purified by flash chromatography (EtOAc). Yield 951 mg (3.64 mmol, 52%); $R_f = 0.32$ (EtOAc); m.p. 158 °C; ^{1}H NMR (300 MHz): $\delta = 7.44-7.04$ (m, 5H; H_{Ar}), 6.56 (d, $^3J = 4.4$ Hz, 1H; NH), 5.34 (d, $^3J = 6.8$ Hz, 1H; OCH), 4.81 (dd, $^3J = 7.3$ Hz, $^3J = 5.4$ Hz, 1H; C*H*NH), 3.73 (s, 3H; CH_3), 2.34 (ddd, $^2J =$ 16.8 Hz, $^3J = 14.2$ Hz, $^3J = 4.7$ Hz, 1H; CH*H*CO), 2.19–2.11 (m, 2H; CH*H*CH*H*CO), 1.67 (dddd, $^2J \cong ^3J = 14.3$ Hz, $^3J = 5.9$ Hz, $^3J = 2.9$ Hz, 1H; C*H*HCH$_2$CO); ^{13}C NMR (50 MHz): $\delta = 173.1$ (NCO), 135.7 (C_{Ar}), 128.5 (2C; C_{Ar}), 125.4 (2C; C_{Ar}), 124.6 (C_{Ar}), 91.3 (CPh), 74.6 (CHO), 56.3 (CHN), 53.1 (CH_3), 27.7 (*C*H$_2$CO), 24.8 (*C*H$_2$CHO); IR (film): $\tilde{\nu} = 3325$ (s, NH), 3060 (w), 2950 (m, CH), 1735 (s, C=O), 1670 (vs), 1440 (m), 1435 (m), 1245 (s), 1195 (m), 1025 (m), 910 cm^{-1} (m, C–O); MS (70 eV, EI): *m/z* (%): 202 (5) [$M^+ -$ COOCH$_3$], 105 (20) [$C_6H_5CO^+$], 97 (100) [$M^+ -$ PhCO-COOCH$_3$], 77 (13) [$C_6H_5^+$], 69 (21) [$C_3H_3NO^+$]; elemental analysis calcd (%) for $C_{14}H_{15}NO_4$ (173.21): C 64.36, H 5.79, N 5.36; found: C 64.52, H 5.63, N 5.79.

(5*RS*,6*RS*)-5-Hydroxy-6-phenylmethyl-2-piperidinone (12): Pd(OH)$_2$/C (20% [w/w], 42 mg, 0.08 mmol) was added to a solution of oxetane **7a** (95 mg, 0.47 mmol) in methanol (4 mL) and the mixture stirred vigorously under atmospheric hydrogen pressure for 3 h. The course of the reaction was monitored by TLC. Upon complete conversion, the catalyst was removed by filtration and the solvent evaporated in vacuo. Flash chromatography (EtOAc) yielded 84 mg (88%) of piperidinone **12** as a white solid. $R_f = 0.50$ (EtOAc/MeOH = 2/1); m.p. 136–138 °C; ^{1}H NMR (500 MHz, [D$_4$]MeOH): $\delta = 7.36-7.20$ (m, 5H; H_{Ar}), 3.81 (virt. dt, $^3J =$ 4.9 Hz, $^3J = 2.6$ Hz, 1H; C*H*OH), 3.61 (virt. dt, $^3J = 7.6$ Hz, $^3J = 2.6$ Hz, 1H; PhCH$_2$C*H*), 3.01 (dd, $^2J = 13.2$ Hz, $^3J = 8.2$ Hz, 1H; PhCH*H*), 2.78 (dd, $^2J = 13.2$ Hz, $^3J = 7.0$ Hz, 1H; PhC*H*H), 2.54 (ddd, $^2J = 18.1$ Hz, $^3J =$ 11.6 Hz, $^3J = 6.9$ Hz, 1H; NHCOCH*H*), 2.26 (ddd, $^2J = 18.1$ Hz, $^3J =$ 6.8 Hz, $^3J = 2.4$ Hz, 1H; NHCOC*H*H), 1.96 (dddd, $^2J = 13.9$ Hz, $^3J =$ 6.9 Hz, $^3J = 4.9$ Hz, $^3J = 2.4$ Hz, 1H; NHCOCH$_2$CH*H*), 1.82 (dddd, $^2J =$ 13.9 Hz, $^3J = 11.6$ Hz, $^3J = 6.8$ Hz, $^3J = 2.2$ Hz, 1H; NHCOCH$_2$C*H*H); ^{13}C NMR (125 MHz, [D$_4$]MeOH): $\delta = 175.1$ (s; CO), 139.1 (s; C_{Ar}), 130.8 (d, 2C; $C_{Ar}H$), 130.0 (d, 2C; $C_{Ar}H$), 128.0 (d; $C_{Ar}H$), 64.2 (d; HOCH), 60.0 (d; PhCH$_2$*C*H), 38.6 (t; PhC*H*$_2$), 28.5 (t; NHCOCH$_2$*C*H$_2$), 27.4 (t; NHCO*C*H$_2$); IR (KBr): $\tilde{\nu} = 3278$ (m, NH), 3219 (m, NH), 2929 (m, CH), 1654 (s, C=O), 1406 (m), 1056 (m), 729 (m, CH), 703 cm^{-1} (m, CH); MS (70 eV, EI): *m/z* (%): 205 (1) [M^+], 133 (2), 120 (10), 114 (100) [$M^+ - C_7H_7$], 91 (20) [$C_7H_7^+$], 86 (15) [114 – CO], 55 (23) [CH$_2$CHCO$^+$]; elemental analysis calcd (%) for $C_{12}H_{15}NO_2$ (205.25): C 70.22, H 7.37, N 6.82; found: C 69.97, H 7.13, N 6.67.

(5*RS*,6*RS*)-6-Diphenylmethyl-5-hydroxy-2-piperidinone (13): Pd(OH)$_2$/C (20% [w/w], 40 mg, 0.10 mmol) was added to a solution of oxetane **8a** (168 mg, 0.60 mmol) in methanol (10 mL) and the mixture stirred vigorously under atmospheric hydrogen pressure for 3.5 h. The course of the reaction was monitored by TLC. Upon complete conversion, the catalyst was removed by filtration and the solvent evaporated in vacuo. Flash chromatography (TBME) yielded piperidinone **13** (140 mg; 93%) as a white solid. $R_f = 0.42$ (EtOAc); m.p. 168 °C; ^{1}H NMR (200 MHz): $\delta =$ 7.37–7.12 (m, 10H; 2Ph), 5.09 (br s, 1H; NH), 4.70 (dd, $^3J = 7.1$ Hz, $^3J =$ 4.3 Hz, 1H; OCH), 4.19 (dd, $^3J = 5.8$ Hz, $^3J = 1.9$ Hz, 1H; CHN), 2.56 (dd, $^2J = 16.3$ Hz, $^3J = 5.5$ Hz, 1H; CH*H*CO), 2.16 (dd, $^2J = 16.3$ Hz, $^3J = 3.8$ Hz, 1H; C*H*HCO), 2.04–1.94 (m, 1H; C*H*CH$_2$CO), 1.61–1.47 (m, 1H; $(CH_3)_2CH$), 0.91 (d, $^3J = 6.8$ Hz, 6H; C*H*$_3$CHC*H*$_3$); ^{13}C NMR (50 MHz): $\delta = 173.0$ (NCO), 145.3 (2C; C_{Ar}), 130.8 (4C; $C_{Ar}H$), 128.5 (4C; $C_{Ar}H$), 125.3 (2C; $C_{Ar}H$), 91.4 (O*C*Ph$_2$), 74.7 (OCH), 58.7 (CHNH), 42.8 (*C*H$_2$CO), 31.2 (*C*HCH$_2$CO), 28.8 ((CH$_3$)$_2$*C*H), 20.6 (2C; (*C*H$_3$)$_2$CH); IR (film): $\tilde{\nu} = 3230$ (s, NH); 3060 (s), 2960 (s), 2930 (s), 2870 (s, CH), 1730 (s, C=O), 1680 (vs), 1490 (m), 1445 (m), 1275 (m), 1135 (m), 745 (s), 705 cm^{-1} (s, CH); MS (70 eV, EI): *m/z* (%): 167 (38) [CHPh$_2^+$], 114 (100) [$M^+ -$ CHPh$_2$], 28 (22) [CO$^+$].

(*1RS,5SR,7SR*)-3-Aza-2-oxo-1,5,7-trimethylbicyclo[3.3.1]-7-nonanoic acid 3-formylphenyl ester (*rac*-15): Thionyl chloride (2 mL) was added to the solid acid *rac*-**14**[17] (110 mg, 0.49 mmol) under argon. The mixture was refluxed for 2.5 h and excess thionyl chloride was subsequently removed by destillation. The crude acid chloride was dried in vacuo. 3-Hydroxybenzaldehyde (65 mg, 0.53 mmol) was dissolved in a mixture of THF (5 mL) and triethylamine (2 mL). After addition of a catalytic amount of DMAP (5–10 mg), a solution of the crude acid chloride in THF (3 mL) was slowly added to the stirred phenol solution at room temperature. Upon complete

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addition, the solution was stirred for another 18 h. The solvents were removed in vacuo and the crude product was purified by flash chromatography (TBME/P = 3/2). The ester *rac*-**15** was obtained as a white solid. Yield: 85 mg (0.26 mmol, 53 %); $R_f = 0.39$ (EtOAc); m.p. 49–51 °C; ^{1}H NMR (500 MHz): $\delta = 7.60$ (virt. dt, $^3J = 7.5$ Hz, $^4J = 1.3$ Hz, 1H; H_{Ar}), 7.54 (virt. t, $^4J = 1.9$ Hz, 1H; H_{Ar}), 7.42 (virt. t, $^3J = 7.7$ Hz, 1H; H_{Ar}), 7.33 (ddd, $^3J = 7.9$ Hz, $^4J = 2.3$ Hz, $^4J = 1.3$ Hz, 1H; H_{Ar}), 5.63 (br s, 1H; NH), 3.06 (virt. dt, $^2J = 11.7$ Hz, $^4J = 2.3$ Hz, 1H; NCH*H*), 2.93 (d, $^2J = 11.7$ Hz, 1H; NC*H*H), 2.69 (virt. dt, $^2J = 14.2$ Hz, $^4J = 2.2$ Hz, 1H; CH*H*), 9.86 (s, 1H; CHO), 2.45 (virt. dt, $^2J = 14.2$ Hz, $^4J = 2.2$ Hz, 1H; CH*H*), 1.67 (virt. dt, $^2J = 13.0$ Hz, $^4J = 2.2$ Hz, 1H; CH*H*), 1.28 (s, 3H; CH_3), 1.20 (dd, $^2J = 13.0$ Hz, $^4J = 2.1$ Hz, 1H; C*H*H), 1.12 (d, $^2J = 14.2$ Hz, 1H; C*H*H), 1.11 (s, 3H; CH_3), 1.06 (dd, $^2J = 14.2$ Hz, $^4J = 2.1$ Hz, 1H; C*H*H), 0.89 (s, 3H; CH_3); ^{13}C NMR (125 MHz): $\delta = 191.9$ (s; CHO), 176.0 (s; CO), 175.2 (s; CO), 152.0 (s; C_{Ar}), 138.0 (s; C_{Ar}), 130.5 (d; $C_{Ar}H$), 128.5 (d; $C_{Ar}H$), 127.2 (d; $C_{Ar}H$), 123.4 (d; $C_{Ar}H$), 53.6 (t; NCH_2), 46.4 (t; CH_2), 45.5 (t; 2C; CH_2), 43.3 (s; C), 38.9 (s; C), 31.5 (q; CH_3), 31.0 (s; C), 29.2 (q; CH_3), 25.3 (q; CH_3); IR (film): $\tilde{\nu} = 3198$ (m, NH), 3060 (m), 2956 (m, CH), 2924 (m, CH), 1750 (s, C=O), 1699 (s), 1660 (m), 1446 (m), 1458 (m), 1230 (m), 1150 (s), 1074 cm^{-1} (s); MS (70 eV, EI): *m*/*z* (%): 208 (100) [M^+ – OArCHO], 180 (92) [208 – CO], 135 (65), 121 (23), 107 (29), 93 (23), 81 (22), 77 (12) [$C_6H_5^+$], 70 (22), 67 (12); elemental analysis calcd (% for $C_{19}H_{23}NO_4$ (329.39): C 69.28, H 7.04, N 4.25; found: C 69.30, H 7.03, N 4.13.

Resolution of compound 15: *N,N*-Diisopropylamine (160 μL, 1.14 mmol) was dissolved in THF (20 mL) and the solution was cooled −78 °C. *n*-Butyllithium (0.60 mL of a 1.53 M solution in *n*-hexane, 0.92 mmol) was added dropwise to this solution and the mixture subsequently stirred for another 1.5 h at −78 °C. A solution of the bicyclic amide *rac*-**15** (250 mg, 0.76 mmol) in THF (15 mL) was added dropwise to the lithium diisopropylamide (LDA) solution within 45 min. After an additional 1 h at −78 °C (−)-menthyl chloroformate (0.81 mL, 0.835 g, 3.80 mmol) was added slowly over 45 min. The solution was stirred for another 1 h at −78 °C, for 1 h at 0 °C and finally for 15 h at room temperature. It was quenched with a saturated NH_4Cl-solution (12 mL) and the mixture was reduced in vacuo. The residue was partioned between a saturated $NaHCO_3$ solution (10 mL) and CH_2Cl_2 (20 mL). The organic layer was removed and the aqueous layer extracted with CH_2Cl_2 (4 × 20 mL). The combined organic layers were successively washed with a saturated $NaHCO_3$ solution (10 mL) and with brine (10 mL). After drying over $MgSO_4$ and filtration, the solvent was removed in vacuo. The two diastereoisomers were separated by flash chromatography (TBME/P = 1/6 → 1/2).

More polar diastereoisomer (89 mg, 0.17 mmol, 23 %): $R_f = 0.38$ (P/TBME = 5/1); $[\alpha]_D^{20} = -46.3$ ($c = 0.99$ in CH_2Cl_2); ^{1}H NMR (500 MHz): $\delta = 10.00$ (s, 1H; CHO), 7.73–7.64 (m, 2H; H_{Ar}), 7.52–7.42 (m, 2H; H_{Ar}), 4.49 (virt. dt, $^3J = 10.9$ Hz, $^3J = 4.3$ Hz, 1H; COOCH), 3.79 (dd, $^2J = 12.5$ Hz, $^4J = 2.3$ Hz, 1H; CONCH*H*), 3.21 (dd, $^2J = 12.5$ Hz, $^4J = 1.7$ Hz, 1H; CONHC*H*H), 2.87 (d, $^2J = 14.2$ Hz, 1H; CH*H*), 2.60 (d, $^2J = 14.2$ Hz, 1H; CH*H*), 1.85 (d, $^2J = 13.0$ Hz, 1H; CH*H*), 1.78 (dsep, $^3J = 7.0$ Hz, $^3J = 2.8$ Hz, 1H; $(CH_3)_2CH$), 1.72–1.62 (m, 1H; CH-Menthyl), 1.61–1.53 (m, 2H; CH*H*-Menthyl, CH*H*-Menthyl), 1.52–1.47 (m, 1H; CH*H*-Menthyl), 1.42 (s, 3H; CH_3), 1.35 (dd, $^2J = 13.0$ Hz, $^4J = 2.4$ Hz, 1H; C*H*H), 1.29 (d, $^2J = 14.4$ Hz, 1H; C*H*H), 1.28 (s, 3H; CH_3), 1.28–1.21 (m, 1H; C*H*H-Menthyl), 1.21 (dd, $^2J = 14.2$ Hz, $^4J = 1.7$ Hz, 1H; C*H*H), 1.07 (s, 3H; CH_3), 0.95–0.90 (m, 1H; CH-Menthyl), 0.78 (d, $^3J = 7.0$ Hz, 3H; CH_3-Menthyl), 0.76–0.70 (m, 2H; C*H*H-Menthyl, C*H*H-Menthyl), 0.69 (d, $^3J = 6.6$ Hz, 3H; CH_3-Menthyl), 0.64 (d, $^3J = 6.9$ Hz, 3H; CH_3-Menthyl); ^{13}C NMR (125 MHz): $\delta = 191.6$ (s; CHO), 174.4 (s; CO), 174.3 (s; CO), 152.2 (s; C_{ar}), 151.5 (s; NCOO), 137.4 (s; C_{Ar}), 129.8 (d; $C_{Ar}H$), 128.3 (d; $C_{Ar}H$), 126.1 (d; $C_{Ar}H$), 123.6 (d; $C_{Ar}H$), 77.0 (d; COO*C*H), 57.6 (t; CON*C*H$_2$), 46.5 (d; CH-Menthyl), 46.0 (t; CH_2), 45.8 (t; CH_2), 44.2 (t; CH_2), 42.7 (s; C), 41.3 (s; C), 40.2 (t; CH_2-Menthyl), 34.0 (t; CH_2-Menthyl), 31.5 (d; CH-Menthyl), 31.2 (q; CH_3), 30.5 (s; C), 29.4 (q; CH_3), 26.0 (q; CH_3), 25.9 (d; CH-Menthyl), 23.1 (t; CH_2-Menthyl), 21.8 (q; CH_3-Menthyl), 20.8 (q; CH_3-Menthyl), 16.1 (q; CH_3-Menthyl); IR (film): $\tilde{\nu} = 2924$ (s, CH), 1749 (br s, C=O), 1699 (br s), 1450 (s), 1148 cm^{-1} (m); MS (EI, 70eV): *m*/*z* (%): 390 (4) [M^+ – OArCHO], 330 (3), 208 (100) [M+H$^+$ – $COOC_{10}H_{19}$], 180 (59) [208 CO], 139 (4) [$C_{10}H_{19}^+$], 135 (8), 121 (13) [OArCHO$^+$], 95 (23), 83 (41), 77 (2) [$C_6H_5^+$], 69 (18), 65 (3) [$C_5H_5^+$], 57 (17), 55 (25).

Less polar diastereoisomer (40 mg, 0.08 mmol, 10 %): $R_f = 0.48$ (P/TBME = 5/1); ^{1}H NMR (500 MHz): $\delta = 10.00$ (s, 1H; CHO), 7.71 (d, $^3J = 7.4$ Hz, 1H; H_{Ar}), 7.65 (s, 1H; H_{Ar}), 7.50–7.42 (m, 2H; H_{Ar}), 4.49 (virt. dt, $^3J = 10.9$ Hz, $^3J = 4.3$ Hz, 1H; COOCH), 3.70 (dd, $^2J = 12.6$ Hz, $^4J = 2.1$ Hz, 1H; CONCH*H*), 3.30 (dd, $^2J = 12.6$ Hz, $^4J = 1.5$ Hz, 1H; CONHC*H*H), 2.87 (d, $^2J = 14.3$ Hz, 1H; CH*H*), 2.62 (d, $^2J = 14.3$ Hz, 1H; CH*H*), 1.92–1.80 (m, 2H; $(CH_3)_2CH$, CH*H*), 1.42 (s, 3H; CH_3), 1.28 (s, 3H; CH_3), 1.09 (s, 3H; CH_3), 0.79 (d, $^3J = 7.2$ Hz, 3H; CH_3-Menthyl), 0.76 (d, $^3J = 6.4$ Hz, 3H; CH_3-Menthyl), 1.75–0.50 (m, 11H; 6 × CHH-Menthyl, 4 × CH-Menthyl, 3 × CHH), 0.42 (d, $^3J = 6.9$ Hz, 3H; CH_3-Menthyl); ^{13}C NMR (125 MHz): $\delta = 191.5$ (s; CHO), 174.2 (s; CO), 174.0 (s; CO), 153.0 (s; C_{Ar}), 151.6 (s; NCOO), 137.4 (s; C_{Ar}), 129.8 (d; $C_{Ar}H$), 128.1 (d; $C_{Ar}H$), 126.0 (d; $C_{Ar}H$), 123.3 (d; $C_{Ar}H$), 76.7 (d; COO*C*H), 58.1 (t; CON*C*H$_2$), 46.5 (d; CH-Menthyl), 46.1 (t; CH_2), 45.7 (t; CH_2), 44.4 (t; CH_2), 42.7 (s; C), 41.4 (s; C), 40.2 (t; CH_2-Menthyl), 34.0 (t; CH_2-Menthyl), 31.5 (d; CH-Menthyl), 31.2 (q; CH_3), 30.5 (s; C), 29.4 (q; CH_3), 26.0 (q; CH_3), 25.4 (d; CH-Menthyl), 22.8 (t; CH_2-Menthyl), 21.9 (q; CH_3-Menthyl), 20.9 (q; CH_3-Menthyl), 15.5 (q; CH_3-Menthyl); MS (70 eV, EI): *m*/*z* (%): 390 (2) [M^+ – OArCHO], 330 (1), 208 (100) [M+H$^+$ – $COOC_{10}H_{19}$], 180 (58) [208 – CO], 139 (5) [$C_{10}H_{19}^+$], 135 (8), 121 (12), 95 (34), 83 (69), 77 (2) [$C_6H_5^+$], 69 (33), 65 (2) [$C_5H_5^+$], 57 (53), 55 (38).

The corresponding *N*-menthoxycarbonyl amide was treated with neat trifluoroacetic acid (TFA; 1 mL) under argon (see below for detailed conditions) and stirred for 15 h at room termperature. Upon complete conversion water was added to the solution and the aqueous layer was thoroughly extracted with CH_2Cl_2. The combined organic layers were successively washed with a saturated $NaHCO_3$ solution (10 mL) and with brine (10 mL). After the solution had been dried over $MgSO_4$ and filtered, the solvent was removed in vacuo.

(+)-(*1R,5S,7S*)-15: According to the procedure outlined above, the more polar diastereoisomer (60 mg, 0.12 mmol) was hydrolyzed. The crude product was purified by flash chromatography (TBME/P = 1/1). Yield of (+)-**15** (23 mg, 0.07 mmol; 60 %). $[\alpha]_D^{20} = +51.8$ ($c = 1.13$ in CH_2Cl_2).

(−)-(*1S,5R,7R*)-15: According to the procedure outlined above, the more polar diastereoisomer (40 mg, 0.08 mmol) was hydrolyzed. The crude product was purified by flash chromatography (TBME/P = 1/1). Yield of (−)-**15** (10 mg, 0.03 mmol; 36 %). $[\alpha]_D^{20} = -52.8$ ($c = 0.86$ in CH_2Cl_2).

(*1RS,5SR,7SR,1'SR,6'RS,8'RS*)-3-Aza-2-oxo-1,5,7-trimethylbicyclo-[3.3.1]-7-nonanoic acid 3-(2′-aza-7′-oxa-3′-oxobicyclo[4.2.0]oct-8'-yl)phenyl ester (16): According to the general irradiation procedure, the aldehyde *rac*-**15** (80 mg, 0.24 mmol) and 3,4-dihydropyridone **6a**[9] (48 mg, 0.49 mmol) were irradiated in toluene (20 mL) at $\lambda = 300$ nm and $\Theta = -10$ °C for 4 h. The solvent was removed in vacuo and the residue purified by flash chromatography (EtOAc). Yield: 58 mg (0.14 mmol, 56 %); $R_f = 0.32$ (EtOAc/EtOH = 5/1); m.p. 194–196 °C; ^{1}H NMR (500 MHz): $\delta = 8.61$ (br s, 1H; NH), 8.00 (br s, 1H; NH), 7.37–7.10 (m, 3H; H_{Ar}), 6.90 (s, 1H; H_{Ar}), 5.95 (d, $^3J = 6.6$ Hz, 1H; ArC*H*), 5.49–5.46 (m, 1H; ArCHOC*H*), 4.80 (virt. dt, $^3J = 7.0$ Hz, $^3J = 4.3$ Hz, 1H; ArCHC*H*), 3.16 (d, $^2J = 12.3$ Hz, 1H; NCH*H*), 2.95 (d, $^2J = 12.3$ Hz, 1H; NC*H*H), 2.82 (d, $^2J = 14.1$ Hz, 1H; CH*H*), 2.54 (d, $^2J = 14.0$ Hz, 1H; CH*H*), 2.31–2.26 (m, 1H; NHCOCH*H*CH$_2$), 2.11–2.00 (m, 2H; NHCOC*H*HCH*H*), 1.74 (d, $^2J = 12.8$ Hz, 1H; CH*H*), 1.66–1.63 (m, 1H; NHCOCH$_2$C*H*H), 1.36 (s, 3H; CH_3), 1.26–1.20 (m, 2H; C*H*H), 1.19 (s, 3H; CH_3), 1.07 (dd, $^2J = 14.1$ Hz, $^4J = 1.6$ Hz, 1H; C*H*H), 0.96 (s, 3H; CH_3); ^{13}C NMR (125 MHz): $\delta = 176.8$ (s; CO), 175.4 (s; CO), 173.9 (s; CO), 149.8 (s; C_{Ar}), 138.7 (s; C_{Ar}), 128.6 (d; $C_{Ar}H$), 121.7 (d; $C_{Ar}H$), 121.3 (d; $C_{Ar}H$), 118.6 (d; $C_{Ar}H$), 84.0 (d; ArCHO), 75.7 (d; ArCHO*C*H), 52.5 (t; NHCH$_2$), 52.0 (d; ArCH*C*H), 45.9 (t; CH_2), 45.4 (t; CH_2), 45.1 (t; CH_2), 42.5 (s; C), 38.1 (s; C), 30.7 (q; CH_3), 30.2 (s; C), 29.0 (q; CH_3), 27.5 (t; NHCO*C*H$_2$CH$_2$), 25.1 (t; NHCOCH$_2$*C*H$_2$), 25.0 (q; CH_3); IR (film): $\tilde{\nu} = 3217$ (s, NH), 2962 (s, CH), 2927 (s, CH), 1754 (s, C=O), 1669 (vs, b), 1489 (m), 1261 (s), 1096 (s), 801 cm^{-1} (m); MS (70 eV, EI): *m*/*z* (%): 426 (<1) [M^+], 330 (85) [M^+ – $NHCOC_4H_5$], 288 (3), 208 (95) [M^+ – $OArC_6H_8NO_2$], 180 (100) [M^+ – $COOArC_6H_8NO_2$], 152 (19), 135 (70), 121 (36), 107 (33), 97 (95) [$NHCOC_4H_6^+$], 81 (27), 69 (73), 55 (34); HRMS calcd (u) for $C_{24}H_{30}N_2O_5$: 426.2155; found 426.2163.

(−)-(*1R,5S,7S,1'S,6'R,8'R*)-(16): In an analogous fashion, the enantiomerically pure compound (+)-**15** was converted into the oxetane (−)-**16**, the optical purity of which was proven by HPLC (column: Chiracel OD; eluent: hexane/isopropanol). $[\alpha]_D^{20} = -25.5$ ($c = 0.55$, CH_2Cl_2).

2-aza-8,8-diphenyl-5-methyl-7-oxabicyclo[4.2.0]octan-3-one (8b/8b′): According to the general irradiation procedure, benzophenone (248 mg,

1.36 mmol) and 3,4-dihydropyridone **6b** (228 mg, 2.05 mmol) were irradiated in acetonitrile (10 mL) at $\lambda = 350$ nm for 11 h. The diastereomeric ratio in the crude product mixture was determined as 55:45 in favor of the major diastereoisomer **8b**. The solvent was removed in vacuo and the residue purified by flash chromatography (P/TBME = 1/1). Compounds **8b** (87 mg, 22%) and **8b′** (69 mg, 17%) were obtained as colorless solids.

(1*RS*,5*RS*,6*SR*)-Isomer (8b): $R_f = 0.31$ (EtOAc); m.p. 192°C; ^{1}H NMR (200 MHz): $\delta = 7.49-7.14$ (m, 10H; H_{Ar}), 6.61 (d, $^3J = 4.3$ Hz, 1H; NH), 4.89 (ddd, $^3J = 6.8$ Hz, $^3J \cong {}^4J = 2.0$ Hz, 1H; OCH), 4.68 (dd, $^3J = 6.8$ Hz, $^3J = 4.3$ Hz, 1H; C*H*NH), 2.68 (dd, $^2J = 16.4$ Hz, $^3J = 5.6$ Hz, 1H; CH*H*), 2.41–2.31 (m, 1H; C*H*CH$_3$), 2.07 (d, $^2J = 16.4$ Hz, 1H; C*H*H), 0.90 (d, $^3J = 7.3$ Hz, 3H; CH$_3$); ^{13}C NMR (50 MHz): $\delta = 172.9$ (NCO), 145.4 (C_{Ar}), 140.9 (C_{Ar}), 128.4 (2C, C_{Ar}H), 128.1 (2C, C_{Ar}H), 127.2 (2C, C_{Ar}H), 127.0 (2C, C_{Ar}H), 125.2 (C_{Ar}H), 124.7 (C_{Ar}H), 91.8 (O*C*Ph$_2$), 76.3 (OCH), 58.2 (CHN), 34.6 (*C*HCH$_3$), 30.3 (*C*H$_2$CO), 15.3 (CH$_3$); IR (film): $\tilde{\nu} = 3210$ (m, NH), 2960 (m, CH), 1685 (vs, C=O), 1495 (m), 1450 (s), 980 (m), 745 (w), 705 cm^{-1} (m, CH); MS (70 eV, EI): *m*/*z* (%): 293 (1) [M^+], 111 (72) [M^+ – Ph$_2$CO], 105 (50) [PhCO$^+$], 96 (100) [M^+ – Ph$_2$CO-CH$_3$].

(1*RS*,5*SR*,6*SR*)-Isomer (8b′): $R_f = 0.22$ (EtOAc); m.p. >225°C; ^{1}H NMR (200 MHz): $\delta = 7.57$ (d, $^3J = 4.8$ Hz, 1H; NH), 7.46–7.07 (m, 10H; H_{Ar}), 5.00 (d, $^3J = 7.8$ Hz, 1H; OCH), 4.63 (dd, $^3J = 7.8$ Hz, $^3J = 5.0$ Hz, 1H; C*H*NH), 2.25–1.77 (m, 3H; CHCH$_2$), 1.07 (d, $^3J = 6.8$ Hz, 3H; CH$_3$); ^{13}C NMR (50 MHz): $\delta = 174.3$ (NCO), 145.5 (C_{Ar}), 140.7 (C_{Ar}), 128.4 (2C, C_{Ar}H), 128.2 (2C, C_{Ar}H), 127.3 (2C, C_{Ar}H), 127.1 (2C, C_{Ar}H), 125.4 (C_{Ar}H), 124.8 (C_{Ar}H), 91.8 (O*C*Ph$_2$), 75.9 (OCH), 58.9 (CHN), 35.5 (*C*HCH$_3$), 30.5 (*C*H$_2$CO), 14.6 (CH$_3$); IR (film): $\tilde{\nu} = 3345$ (s, NH), 3020 (w), 2960 (m, CH), 1675 (s, C=O), 1635 (vs), 1450 (s), 1315 (m), 990 (m), 945 (m), 750 (m), 705 cm^{-1} (s, CH); MS (70 eV, EI): *m*/*z* (%): 183 (10) [Ph$_2$COH$^+$], 111 (79) [M^+ – Ph$_2$CO], 105 (25) [PhCO$^+$], 96 (100) [M^+ – Ph$_2$CO–CH$_3$], 68 (30) [C$_5$H$_8^+$]. The compounds were not stable at room temperature. Correct elemental analyses were not obtained.

2-Aza-8,8-Diphenyl-5-*iso*-propyl-7-oxabicyclo[4.2.0]octan-3-one (8c/8c′): According to the general irradiation procedure, benzophenone (610 mg, 3.35 mmol) and 3,4-dihydropyridone **6c** (700 mg, 5.03 mmol) were irradiated in acetonitrile (20 mL) at $\lambda = 350$ nm for 11 h. The diastereomeric ratio in the crude product mixture was determined as 60:40 in favor of the major diastereoisomer **8c**. The solvent was removed in vacuo and the residue purified by flash chromatography (P/TBME = 1/1). Compounds **8c** (192 mg, 18%) and **8c′** (138 mg, 13%) were obtained as colorless solids.

(1*RS*,5*RS*,6*SR*)-Isomer (8c): $R_f = 0.35$ (EtOAc); m.p. 185°C; ^{1}H NMR (300 MHz): $\delta = 7.50-7.35$ (m, 10H; H_{Ar}), 5.49 (br s, 1H; NH), 5.20 (dd, $^3J \cong {}^3J = 5.6$ Hz, 1H; OCH), 4.86 (dd, $^3J = 7.3$ Hz, $^3J = 4.9$ Hz, 1H; C*H*NH), 2.79 (dd, $^2J = 17.8$ Hz, $^3J = 3.7$ Hz, 1H; CH*H*CO), 2.73 (ddd, $^2J = 17.8$ Hz, $^3J \cong {}^4J = 1.7$ Hz, 1H; C*H*HCO), 2.14–2.08 (m, 1H; C*H*CH$_2$CO), 1.68–1.45 (m, 1H; (CH$_3$)$_2$C*H*), 1.08 (d, $^3J = 6.8$ Hz, 6H; C*H*$_3$CHC*H*$_3$); ^{13}C NMR (75.5 MHz): $\delta = 172.1$ (NCO), 144.2 (2C; C_{Ar}), 128.6 (4C; C_{Ar}H), 127.6 (4C; C_{Ar}H), 125.3 (2C; C_{Ar}H), 91.4 (O*C*Ph$_2$), 73.8 (OCH), 60.3 (CHNH), 39.9 (*C*H$_2$CO), 32.1 (*C*HCH$_2$CO), 28.8 ((CH$_3$)$_2$*C*H), 20.4 (2C, (*C*H$_3$)$_2$CH); IR (film): $\tilde{\nu} = 3345$ (s, NH), 3250 (m), 2960 (m, CH), 1660 (vs, C=O), 1490 (m), 1445 (m), 1275 (m), 1175 (w), 750 (s), 700 cm^{-1} (s, CH); MS (70 eV, EI): *m*/*z* (%): 183 (28) [Ph$_2$CO$^+$], 139 (46) [C$_8$H$_{13}$O$^+$], 105 (21) [PhCO$^+$], 96 (100) [C$_5$H$_6$NO$^+$], 77 (13) [C$_6$H$_5^+$], 28 (12) [CO$^+$].

(1*RS*,5*SR*,6*SR*)-Isomer (8c′): $R_f = 0.42$ (EtOAc); m.p. 168°C; ^{1}H NMR (200 MHz): $\delta = 7.37-7.12$ (m, 10H; H_{Ar}), 5.09 (br s, 1H; NH), 4.70 (dd, $^3J = 7.1$ Hz, $^3J = 4.3$ Hz, 1H; OCH), 4.19 (dd, $^3J = 5.8$ Hz, $^3J = 1.9$ Hz, 1H; C*H*NH), 2.56 (dd, $^2J = 16.3$ Hz, $^3J = 5.5$ Hz, 1H; CH*H*CO), 2.16 (dd, $^2J = 16.3$ Hz, $^3J = 3.8$ Hz, 1H; C*H*HCO), 2.04–1.94 (m, 1H; C*H*CH$_2$CO), 1.61–1.47 (m, 1H; (CH$_3$)$_2$C*H*), 0.91 (d, $^3J = 6.8$ Hz, 6H; C*H*$_3$CHC*H*$_3$); ^{13}C NMR (50 MHz): $\delta = 173.0$ (NCO), 145.3 (2C, C_{Ar}), 130.8 (4C, C_{Ar}H), 128.5 (4C, C_{Ar}H), 125.3 (2C, C_{Ar}H), 91.4 (O*C*Ph$_2$), 74.7 (OCH), 58.7 (CHNH), 42.8 (*C*H$_2$CO), 31.2 (*C*HCH$_2$CO), 28.8 ((CH$_3$)$_2$*C*H), 20.6 (2C, (*C*H$_3$)$_2$CH); IR (film): $\tilde{\nu} = 3230$ (s, NH), 3060 (s), 2960 (s), 2930 (s), 2870 (s, C-H), 1730 (m), 1680 (vs, C=O), 1490 (m), 1445 (m), 1275 (m), 1135 (m), 745 (s), 705 cm^{-1} (s, C–H); MS (70 eV, EI): *m*/*z* (%): 279 (8) [M^+ – C$_3$H$_6$], 183 (17) [Ph$_2$CO$^+$], 139 (29) [C$_8$H$_{13}$O$^+$], 105 (28) [PhCO$^+$], 96 (100) [C$_5$H$_6$NO$^+$], 77 (7) [C$_6$H$_5^+$], 43 (16) [C$_3$H$_7^+$].

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[13] a) Crystal data of compound **8a** (hydrogen-bridged dimer with two molecules of $CHCl_3$, $C_{38}H_{36}Cl_6N_2O_4$, $M_r = 797.39$): crystal size $0.60 \times 0.20 \times 0.10$ mm; triclinic; space group $P\bar{1}$; $a = 769.90(11)$, $b = 1372.14(19)$, $c = 1883.08(14)$ pm; $\alpha = 89.963(16)$, $\beta = 80.265(16)$, $\gamma = 76.440(17)°$; $V = 1904.4(4)$ Å^3; $\rho_{calcd} = 1.391$ g cm^{-3}; $Z = 2$; $F(000) = 824$, $\mu = 0.493$ mm^{-1}; Stoe IPDS diffractometer; $\lambda = 0.71069$ Å; ω scan; 6733 reflections ($-h$, $+k$, $\pm l$); $\Theta_{max} = 25.0°$; 2873 independent and 1323 observed reflections [$I_o \geq 4\sigma(I_o)$]; 465 refined parameters; $R = 0.0579$, $wR^2 = 0.1660$; residual electron density 0.302 e Å^{-3}; direct methods; hydrogen atoms calculated (N – H refined). Only the non overlapping reflections of the main domain of the twinned crystal have been used. b) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-158028 (**8a**), CCDC-158026 (**15**), CCDC-158027 (**8b**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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[24] Crystal data of compound **8b** ($C_{19}H_{19}NO_2$, $M_r = 293.35$): crystal size $0.15 \times 0.12 \times 0.06$ mm; monoclinic; space group $P2_1/n$; $a = 1385.7(2)$, $b = 798.15(8)$, $c = 15.117(2)$ pm; $\beta = 113.252(15)^\circ$; $V = 1536.1(3)$ Å^3; $\rho_{calcd} = 1.268$ g cm^{-3}; $Z = 4$; $F(000) = 624$; $\mu = 0.082$ mm^{-1}; Stoe IPDS diffractometer; $\lambda = 0.71073$ Å; ω scan; 7863 reflections ($-h$, $+k$, $\pm l$); $\Theta_{max} = 26.0^\circ$; 2824 independent and 1081 observed reflections [$I_o \geq 4\sigma(I_o)$]; 275 refined parameters; $R = 0.0364$, $wR^2 = 0.0579$; residual electron density 0.163 e Å^{-3}; direct methods; hydrogen atoms refined.

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