The Synthesis of (+)-Preussin and Related Pyrrolidinols by Diastereoselective Paternò–Büchi Reactions of Chiral 2-Substituted 2,3-Dihydropyrroles

Thorsten Bach,*[a, b] Harm Brummerhop,[a] and Klaus Harms[a, c]

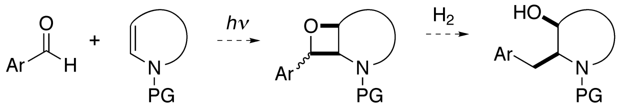
Dedicated to Professor Bernd Giese on the occasion of his 60th birthday

Abstract: The *N*-alkoxycarbonyl substituted 2,3-dihydropyrroles **3** and **8** are converted to 2-benzyl-3-pyrrolidinols by the Paternò–Büchi reaction followed by hydrogenolysis. Since the addition of the photoexcited benzaldehyde at the unsaturated heterocycle proceeds in a *syn* fashion, the benzyl group at C-2 and the hydroxy group at C-3 of the product are *cis* oriented. The simple and facial diastereoselectivities of the Paternò–Büchi reaction were studied more closely and the relative configuration of the products was elucidated. The thermodynamically less stable *endo* product is formed as a result of simple diastereoselection. The face differentiation in 2-substituted 2,3-dihydropyrroles is presumably due to the nonplanarity of these heterocycles, which forces attack of the carbonyl group on the face with the existing substituent. All-*cis*-pyrrolidinols are consequently formed after hydrogenolysis. Following this route, a total synthesis of the pyrrolidinol alkaloid (+)-preussin (**1**) was conducted, which yielded the target compound in a total yield of 11% over nine steps starting from L-pyroglutaminol (**11**).

Keywords: asymmetric synthesis · oxetanes · Paternò–Büchi reactions · photochemistry · pyrrolidines

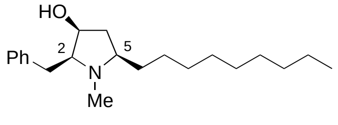
Introduction

The regio- and stereoselective functionalization of double bonds is a key strategy in organic synthesis.[1] In this respect, the [2+2] photocycloaddition of carbonyl compounds and alkenes, commonly called the Paternò–Büchi reaction,[2, 3] allows an efficient carbohydroxylation reaction to occur at the olefinic precursor. In particular, heteroatom-substituted alkenes, which undergo the reaction readily and with high regioselectivity,[4] can be converted effectively to oxetanes by this means. Subsequent O–C bond cleavage generates the carbohydroxylation products.[5, 6] We have used this strategy for the synthesis of various 1,2-diols and 1,2,3-triols from acyclic silyl enol ethers.[7] If cyclic unsaturated olefins are employed as substrates, *cis*-substituted heterocycles with vicinal arylmethyl and hydroxy groups should be obtained. The general route for unsaturated nitrogen heterocycles is outlined in Scheme 1 (PG = protecting group).



Scheme 1. The carbohydroxylation of unsaturated nitrogen heterocycles.

From our previous experience with *N*-acylated enamines in the Paternò–Büchi reaction,[8] we expected the photocycloaddition–hydrogenolysis sequence to proceed with ease and we planned to use this sequence for the construction of biologically active five- and six-membered nitrogen heterocycles. Prominent examples for potentially accessible pyrrolidinols and piperidinols include (+)-preussin (**1**),[9, 10] an



(+)-Preussin (**1**)

antifungal agent isolated from *Aspergillus ochraceus* and from *Preussia* sp., and FR 901483,[11, 12] an immunosuppressant isolated from *Cladobotryum* sp. No. 11231.

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Crystal structure determination

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Our initial efforts, which we would like to report in this account, were directed towards the synthesis of pyrrolidinols. The general propensity of *N*-protected 2,3-dihydropyrroles to the Paternò–Büchi reaction was studied, the regio- and stereoselectivity of the reaction was investigated for chiral 2-substituted substrates and attempts to induce the hydrogenolytic ring opening were undertaken. The work culminated in the synthesis of enantiomerically pure (+)-preussin[13] and related pyrrolidinols.

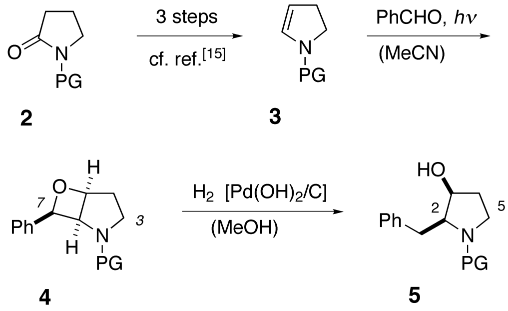
Table 1. Preparation and photocycloaddition/hydrogenolysis of 2,3-dihydropyrroles **3** according to Scheme 2.

	Substrate	PG	**3** [%][a]	**4** [%][b]	**5** [%][c]
1	**2a**	COOMe	42	57	96
2	**2b**	COOEt	43	52	53
3	**2c**	Boc[d]	53	41	56
4	**2d**	Ts[e]	65	–[f]	–[g]

[a] Yield of isolated product over three steps (reduction, acetalization, elimination). [b] Yield of the isolated major oxetane diastereoisomer. [c] Yield of isolated pyrrolidinol **5** according to Scheme 2. [d] Boc = *tert*-butyloxycarbonyl. [e] Ts = *p*-toluenesulfonyl. [f] The desired product was not isolated. [g] The hydrogenolysis experiment was not conducted.

Results and Discussion

Choice of protecting group and simple diastereoselectivity: Various *N*-protected 2,3-dihydropyrroles can be considered as substrates for the Paternò–Büchi reaction. An acceptor substituent appeared to be the best choice, as it decreases the oxidation potential of the enamines and avoids side reactions arising from single electron transfer. Four substrates **3a–d** were prepared which bear an electron-withdrawing group (Scheme 2, Table 1). Starting from the corresponding *N*-substituted pyrrolidinone **2** these dihydropyrroles are readily accessible.[14–16] Reduction with diisobutylaluminum hydride (DIBAL-H) or superhydride ($LiBEt_3H$) yields the corresponding lactamols, which can be converted into the *N*,*O*-acetals by treatment with 2,2-dimethoxypropane. The final elimination step was advantageously carried out with trimethylsilyl trifluoromethanesulfonate (TMSOTf) and *N*,*N*-diisopropylethylamine as the base.[15, 17] The photocycloaddition was conducted in acetonitrile as the solvent and with benzaldehyde as the carbonyl substrate. Rayonet lamps (RPR 3000 Å) were employed as the irradiation source (λ = 300 nm). In general, a 1:2 aldehyde/dihydropyrrole ratio was required to suppress intermolecular side reaction of the aldehyde (photopinacolization). Unreacted dihydropyrrole could be recovered by flash chromatography. The three alkoxycarbonyl-substituted substrates **3a–c** all reacted reasonably well and yielded the desired oxetanes **4** (Table 1, entries 1–3). Substrate **3d**, however, failed to undergo the Paternò–Büchi reaction and decomposed under the irradiation conditions (Table 1, entry 4). No defined decomposition products could be isolated.



Scheme 2. The photochemical synthesis of simple 2-benzyl-3-hydroxypyrrolidines **5** from dihydropyrroles **3** (cf. Table 1).

Abstract in German: *Durch eine Sequenz aus Paternò–Büchi-Reaktion und /Hydrogenolyse lassen sich die N-Alkoxycarbonyl-substituierten 2,3-Dihydropyrrole **3** und **8** in 2-Benzyl-3-pyrrolidonole überführen. Da die Addition des photoangeregten Benzaldehyds an den ungesättigten Heterocyclus als syn Addition verläuft, stehen im Produkt die Benzylgruppe an C-2 und die Hydroxylgruppe an C-3 cis zueinander. Die einfache und faciale Diastereoselektivität der Paternò–Büchi-Reaktion wurden genauer untersucht und die Relativkonfiguration der Produkte einwandfrei aufgeklärt. Als Resultat der einfachen Diastereoselektivität entsteht bevorzugt das thermodynamisch ungünstigere endo-Produkt. Die Seitendifferenzierung in chiralen 2-substituierten 2,3-Dihydropyrrolen basiert vermutlich auf der Nichtplanarität dieser Heterocyclen, die einen Angriff der Carbonylkomponente auf die Seite bedingen, auf der auch der Substituent steht. Nach Hydrogenolyse entstehen deshalb all-cis-Pyrrolidinole. Auf diesem Weg wurde eine Totalsynthese des Pyrrolidinol-Alkaloids (+)-Preussin (**1**) durchgeführt, die ausgehend von* L*-Pyroglutaminol (**11**) in einer Gesamtausbeute von 11 % über neun Stufen die Zielverbindung liefert.*

The relative configuration of the oxetanes **4a–c** was established by NOE and NOESY studies (Figure 1). All hydrogen atoms within the oxetane ring are evidently oriented *cis* to each other. The relative configuration of the oxetanes **4** is in accord with earlier findings we made in our work on acyclic enamides.[8] According to a proposal by Griesbeck et al., the major diastereoisomer arises from a favored intersystem crossing (ISC) transition[18] of the intermediate biradical. This phenomenon is common to heteroatom-substituted alkenes which bear no additional α-substituent, whereas α-substituted alkenes show a preference for the thermodynamically more stable product.[19] Possible reasons for this behavior have been discussed in detail elsewhere[4b, 19] although further data are required if a unified

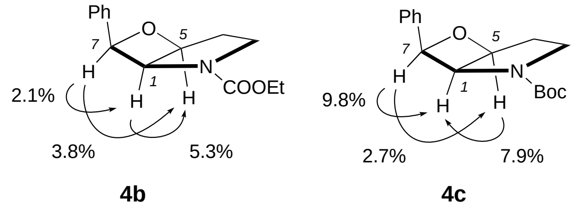


Figure 1. Principal ^1H NOE data recorded for compounds **4b** and **4c**.

picture is to be obtained. Figure 1 shows typical NOE data recorded at 233 K (500 MHz) for the major rotamers of oxetanes **4b** and **4c**. Additional data for these compounds and for oxetane **4a** can be found in the Experimental Section. The subsequent hydrogenolysis of oxetanes **4a–c** turned out to be more dependent on the protecting group than we had anticipated. Under the standard conditions which we had previously employed for the hydrogenolysis of acid-sensitive oxetanes,[6] the *N*-methoxycarbonyl-substituted oxetane **4a** clearly outperfomed the other two hydrogenolysis substrates **4b** and **4c**. We ascribe the lower yields for pyrrolidinols **5b** and **5c** to the higher lability of the protecting group. Even in the case of the most stable oxetane **4a**, we found it better to use a high catalyst/substrate ratio instead of prolonged reaction times to facilitate a complete hydrogenolysis. The expected relative configuration of the pyrrolidinol **5a** was again confirmed by NOE studies. Product **5c** delivered crystals suitable for single-crystal X-ray analysis. The crystal structure is depicted in Figure 2.[20]

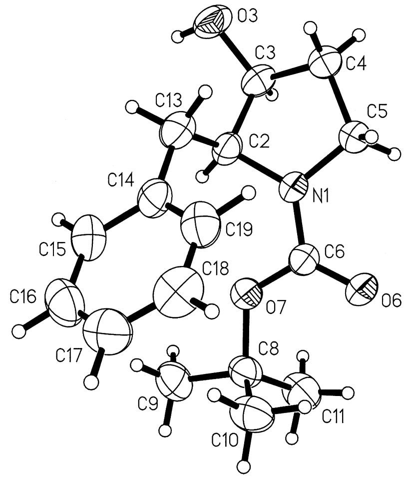
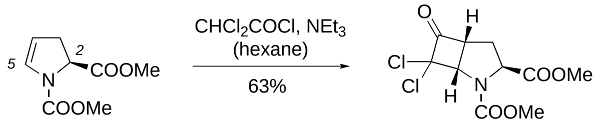


Figure 2. A molecule of compound **5c** in the crystal.

As a major consequence of these preliminary studies, we selected *N*-methoxycarbonyl-substituted dihydropyrroles for our further experiments. The facial diastereoselectivity of their Paternò–Büchi reaction was examined for substrates which bear a stereogenic center at the C-2 carbon atom. Benzaldehyde remained the standard aldehyde although there are ample precedents for the employment of other aromatic aldehydes and ketones in the Paternò–Büchi reaction.[3, 21]

Facial diastereoselectivity: The 2-substituted 2,3-dihydropyrrole **6** was employed as a substrate in thermal addition reactions (Scheme 3). It carries the methoxycarbonyl group at the stereogenic center and is prepared either from L-proline[22] or from L-pyroglutamic acid.[16] Correia et al. showed that ketene additions to this substrate occur with good facial diastereoselectivity.[23] The ketene adds to the dihydropyrrole from the face opposite the methoxycarbonyl group, the cyclobutanone **7** being the major product. Heck reactions of 2-alkoxymethyl-2,3-dihydropyrroles occur at the C-5 carbon atom and exhibit similar diastereoselectivies.[24]



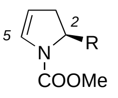
6 **7**

Scheme 3. Stereoselective ketene addition to dihydropyrrole **6**.

In photocycloaddition reactions to *N*-acylated pyrroles the mono adduct, which still contains a 2,3-dihydropyrrole substructure, was reported to react further to a tricyclic product with two oxetane rings attached to the central pyrrolidine.[25] The second photocycloaddition occured from the more accessible face of the concave bicyclic 2-aza-7-oxabicycloheptene.

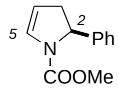
In the present study, we concentrated on 2-alkyl- and 2-aryl-substituted 2,3-dihydropyrroles as olefin components. This selection was based on our interest in the synthesis of pyrrolidinols related to (+)-preussin and possible epimers thereof. The dihydropyrroles **8** were prepared in enantiomerically pure form starting from the corresponding enantiomerically pure *N*-methoxycarbonylpyrrolidinones, which were in turn obtained from L-pyroglutamic acid according to known procedures.[15, 26–30] The procedure will be detailed briefly for the 2-nonylderivative **8d** in a later section. The 2-phenyl-2,3-dihydropyrrole *rac*-**8e** was prepared by Heck reaction of phenyl iodide and dihydropyrrole **3a** employing Pd(OAc)$_2$/P(*o*-Tol$_3$)$_3$ as the catalyst.[31]

The photocycloaddition reactions of the dihydropyrroles **8** were conducted with benzaldehyde as the carbonyl compound. Disappointingly, the initial irradiation experiments failed although they were carried out under conditions fully identical to those successfully employed for the conversion of dihydropyrrole **3a** (room temperature, acetonitrile as the solvent, RPR 3000 Å). Rapid decomposition of the starting materials **8** was observed and the yield of oxetane products remained low. As we suspected that the long-wavelength absorption of the dihydropyrroles (λ_{max} = ca. 240 nm), which partially intersects the emission band of the RPR 3000 Å lamps, was responsible for the decomposition, an irradiation source which emits at longer wavelenghts (RPR 3500 Å, λ = 350 nm) was used. Indeed, we observed only minor dihydropyrrole decomposition under these conditions and the oxetane yields were satisfactory. As expected, the reaction yielded two major products **9** and **10** which could be separated by flash chromatography. Diastereoisomer **9** prevailed in all cases to a significant extent. The results of the study are summarized in Scheme 4 and Table 2.



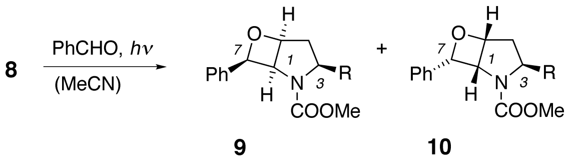
8

a R = CH_3
b R = C_2H_5
c R = CH_2Ph
d R = C_9H_{19}



rac-**8e**

The structure elucidation of compounds **9** and **10** was, to a great extent, performed by NMR studies. Products derived from single diastereoisomeric products **9** confirmed the



Scheme 4. Photochemical oxetane formation from 2-substituted 2,3-dihydropyrroles **8** (cf. Table 2).

Table 2. Yields and facial diastereoselectivities obtained in the Paternò–Büchi reaction of 2,3-dihydropyrroles **8** as shown in Scheme 4.

	Substrate	R	Time [h][a]	dr (**9**/**10**)[b]	Yield [%][c]
1	**8a**	CH_3	6	76/24	57
2	**8b**	C_2H_5	5	71/29	–[d]
3	**8c**	CH_2Ph	6	$\geq 95/5$	57
4	**8d**	C_9H_{19}	6	75/25	65
5	*rac*-**8e**	Ph	7	68/32	63[e]

[a] Irradiation time (RPR 3500 Å) after which the aldehyde had completely disappeared according to GLC. [b] Diastereomeric ratio determined by GLC. [c] Yield of isolated oxetane products. [d] The compound was unstable and could not be isolated. [e] Products *rac*-**9e** and *rac*-**10e** were racemic.

assignment (vide infra). Owing to the bent structure of compounds **9** and **10**, direct NOESY contacts between H-1 and H-3 cannot be expected. However, it is possible to observe NOESY contacts between H-5 and H-4α or H-4β. The protons at C-4 can in turn be related to the proton H-3. If H-5 and H-4α are located *cis* to each other—as is the case for diastereoisomer **10**—a strong contact is expected. For diastereoisomer **9** the contact between H-5 and H-4β is strong. This behavior is exemplified in Figure 3, which depicts the strong (——) and medium (- - - -) NOESY contacts observed for the diastereoisomers **9a** and **10a** (• = COOMe).

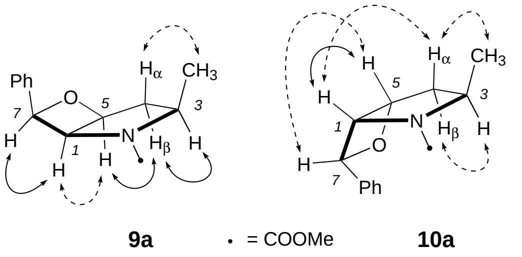
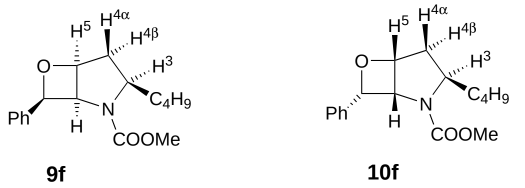


Figure 3. ^{1}H NOESY contacts recorded for compounds **9a** and **10a**.

In addition, the coupling patterns for **9** and **10** are completely different. Force-field calculations[32] and the inspection of simple molecular models reveal that the dihedral angles between H-3 and H-4α and between H-5 and H-4α in compounds **9** are roughly 90°, resulting in two small ^3J coupling constants. By contrast, only one small ^3J coupling is recorded for compounds **10**, that is, for the coupling between H-4β and 5. The dihedral angle between H-4α and H-3 is much larger and the dihedral angle between H-4β and H-3 is much smaller than 90°; this results in larger coupling constants (^3J = ca. 7 Hz). Calculated coupling constants for two model compounds **9f** and **10f** (R = C_4H_9) are shown in Figure 4. They compare well with the real coupling constants for compounds **9** and **10**, which are given in the experimental section.



$J_{4\beta,3}$ = 8.3 Hz $J_{4\beta,5}$ = 5.2 Hz $J_{4\beta,3}$ = 7.3 Hz $J_{4\beta,5}$ = 2.6 Hz

$J_{4\alpha,3}$ = 2.1 Hz $J_{4\alpha,5}$ = < 1 Hz $J_{4\alpha,3}$ = 7.5 Hz $J_{4\alpha,5}$ = 6.8 Hz

Figure 4. Calculated[32] ^{1}H NMR coupling constants in the bicyclic compounds **9f** and **10f**.

The data prove clearly that the attack of the photoexcited carbonyl compound that finally leads to oxetane formation occurs on the 2,3-dihydropyrroles **8** predominantly from the diastereotopic face to which the side chain R points. This facial diastereoselectivity is opposite to the selectivity observed in the thermal [2+2]-cycloaddition (Scheme 3) and in the Heck reaction (vide supra).

Discussion of the facial diastereoselectivity: Our initial hypothesis concerning the facial diastereoselectivity was quickly disproved. We speculated that the hydrophobic side chain R assists the entering photoexcited aromatic aldehyde during its attack on the carbon atom C-4 in the dihydropyrroles **8**. The polar solvent acetonitrile should favor this interaction. Since the diastereoselectivity of the photocycloaddition remained unchanged (e.g. **9d**/**10d** = 75/25) when the reaction was carried out in benzene as the solvent, this idea had to be discarded. The effect of the temperature on the facial diastereoselectivity was marginal and gave no hint of the face-discriminating reaction step.[33] Although the kinetics of the reaction were never followed quantitatively, there was no apparent difference between the reaction velocity in the reaction of the unsubstituted dihydropyrrole **3a** and the substituted dihydropyrroles **8**. In addition, the simple diastereoselectivity remained constant, favoring the thermodynamically less stable *endo* products in which the five-membered ring and the phenyl group are attached to the oxetane in a *cis* fashion. Under the reasonable assumption that the oxetane formation occurs stepwise, that is, by initial formation of the O–C bond and subsequent formation of the C–C bond after ISC, there is no evidence that the latter step influences the facial diastereoselectivity. If it did, it could only occur by a competition between C–C bond formation and ring cleavage. As a consequence, the reaction would slow down and, even more importantly, the simple diastereoselectivity should also change, favoring the more stable *exo* product. On the basis of these considerations, it seems that the C–C bond-forming step is unlikely to be selectivity-determining. The O–C bond-forming step appears to determine the stereoselectivity and the question arises: Why does the photoexcited benzaldehyde attack the carbon atom C-4 of the dihydropyrroles **8** preferentially from the *Si* face? The explanation we currently favor aims at the different environment at the neighboring carbon atom C-3. We assume the dihydropyrroles **8** to be not fully planar during the approach of the photoexcited carbonyl compound. Owing to 1,3-allylic strain[34, 35] the substituent at C-2 prefers a pseudoaxial position; this leads to a discrimination between the protons at C-3 as schematically drawn in Figure 5. If this is correct, the O–C bond formation should occur preferentially antiperiplanar to the bond between C-3 and H_β, avoiding torsional strain and yielding directly a staggered product.

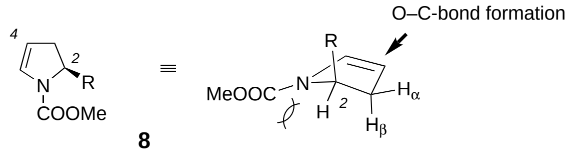
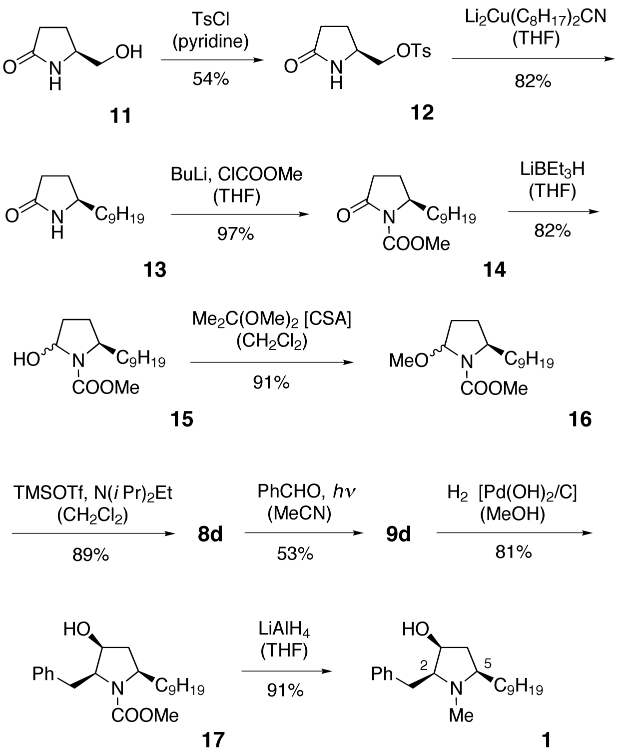


Figure 5. Possible explanation for the facial diastereoselection in the Paternò–Büchi reaction of dihydropyrroles **8**.

In this respect the explanation resembles a recent suggestion put forward by Woerpel et al. to account for the facial diastereoselectivity in nucleophilic displacement reactions via five-membered oxocarbenium ions.[36] It is also in line with the stereochemical results observed in nucleophilic addition reactions to *N*-acyliminium ions.[37] The discrepancy between the selectivities achieved in the photochemical addition to chiral 2,3-dihydropyrroles and the selectivities recorded in thermal reactions which occur at C-5 or simultanously at C-5 and C-4 is also readily explained. The reaction at C-5 requires an attack from the face opposite the substituent R to avoid steric interactions in the transition state.

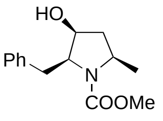
It must be noted, however, that we have no evidence for the nonplanarity of the dihydropyrroles **8** in the ground state. Crystal structure data of these compounds are not available but a related structure was shown by X-ray analysis to contain a nonplanar dihydropyrrole moiety.[38] Our attempts to obtain information about their conformation by NMR have been unsuccessful so far. The spectra were not well resolved because of the restricted rotation around the carbamate bond. Therefore, the question of the possible reasons for the observed facial diastereoselectivity cannot be conclusively answered yet.

Synthesis of (+)-preussin and related pyrrolidinols: We were pleased to note that the hydrogenolyses of the photochemically prepared oxetanes **9** and **10** proceeded smoothly. This reaction paved the way to a short synthesis of (+)-preussin (**1**), the individual steps of which are detailed in Scheme 5. The scheme exemplifies the previously mentioned approach to 2,3-dihydropyrroles. The reaction sequence commenced with the tosylation of L-pyroglutaminol (**11**). Nucleophilic substitution of tosylate **12** with a higher-order cuprate yielded pyrrolidinone **13**, which was *N*-acylated with methyl chloroformate. *N*-Methoxycarbonylpyrrolidinone **14** was reduced with superhydride to the lactamol **15**, which was converted to the *N*,*O*-acetal **16** by treatment with 2,2-dimethoxypropane in the presence of camphorsulfonic acid (CSA). A final elimination gave the desired dihydropyrrole **8d**, the photocycloaddition of which has already been desribed. The major diastereoisomer **9d** of the Paternò–Büchi reaction was isolated in 53 % yield. Its hydrogenolysis was conducted in the presence of Pearlman's catalyst and yielded the known (+)-preussin precursor **17**. The reduction of this compound to (+)-preussin (**1**) has already been described[10a] and was successfully conducted in 91 % yield. The optical rotation ($[\alpha]_D^{25} = +22.1$ in $CHCl_3$, $c = 1$) of synthetic preussin and its analytical data were in accord with the literature data.[9] Moreover, we carried out NOESY experiments which confirmed the all-*cis* configuration, for example by showing a contact between H-2 and H-5, and which supported our assignment of the major oxetane diastereoisomer **9d**.



Scheme 5. The total synthesis of (+)-preussin (**1**).

The total yield of (+)-preussin starting from commercially available L-pyroglutaminol was 11 % over nine steps. Because of the biological potential of (+)-preussin[9] the synthesis of analogs is certainly a topic of current interest. The hydrogenolysis of further oxetane substrates could be readily conducted and we obtained, for example, the pyrrolidinols **18** (89 % yield from **9a**) and **19** (88 % yield from **10d**) by this means.



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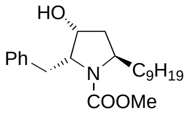

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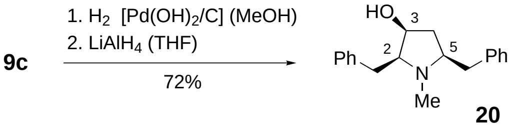
The hydrogenolysis of compounds *rac*-**9e** and *rac*-**10e** could not be performed selectively. Both benzylic C–heteroatom bonds were cleaved and an open-chain amino alcohol was isolated in low yield. This was the only case, however, for which difficulties in the hydrogenolysis step were encountered.

In some instances it proved advantageous to use the hydrogenolysis product further in the $LiAlH_4$ reduction step without prior purification. As an example a reaction which led to the pyrrolidinol **20** is depicted in Scheme 6.



Scheme 6. Preparation of the preussin analogue **20**.

The solid pyrrolidinol **20** gave crystals suitable for single-crystal X-ray analysis.[39] The crystal structure so obtained (Figure 6) showed nicely the all-*cis* arrangement of the three substituents at C-2, C-3, and C-5. As the configuration at these stereogenic centers does not change in the hydrogenolysis step, this provides conclusive evidence for the relative configuration of oxetane **9c**.

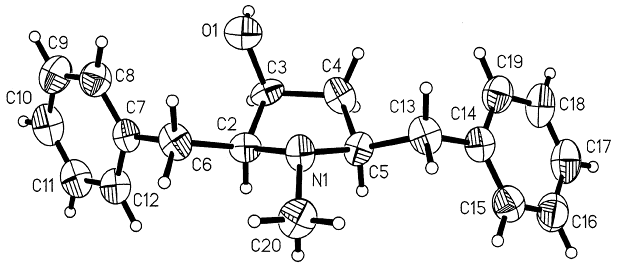
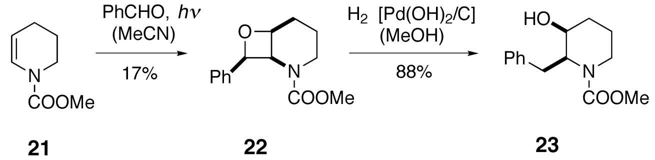


Figure 6. A molecule of compound **20** in the crystal.

Additional experiments: It may seem at first sight as if the successful photocycloaddition of dihydropyrroles such as **3** and **8** to benzaldehyde is straightforward, given the previous experiments conducted with terminal acyclic *N*-acyl and *N*-alkoxycarbonyl enamines.[8] Despite the apparent similarity which was alluded to in the introduction, this conclusion is not fully correct. It is important to note that the 2,3-dihydropyrroles bear a substituent at the *β*-position of the *N*-alkoxycarbonylenamine moiety. Hydrogen abstraction at this site should be facile in particular since the substituent is embedded in a cyclic array. Cyclopentene, for example, is a rather problematic substrate in the Paternò–Büchi reaction and suffers severe photoreduction.[40] In this respect, the 2,3-dihydropyrroles are apparently more closely related to 2,3-dihydrofurans, which undergo the photocycloaddition smoothly and with high simple diastereoselectivity.[41, 42] If this analogy is true, the six-membered tetrahydropyridines should react more sluggishly than do the six-membered dihydropyrans.[40] Indeed, the substrate **21** gave only poor yields of photocycloadduct **22** (Scheme 7) under a variety of conditions.

Although the hydrogenolysis of product **22** to piperidinols **23** was a clean process, the photocycloaddition/hydrogenolysis approach is clearly not suited for the conversion of *N*-alkoxycarbonyl-substituted tetrahydropyridines to piperidinols. Because of the biological significance of 3-piperidinols (vide infra), different photochemical approaches to these compounds are still being pursued in our laboratories. Further results along these lines will be reported in due course.



Scheme 7. Attempted carbohydroxylation of the tetrahydropyridine **21**.

Experimental Section

General: For general remarks, see ref.[8f]. The 2,3-dihydropyrroles **3a-d, 8a-c**, and *rac*-**8e** were prepared according to reported procedures.[15, 32, 44] NOESY contacts are reported as weak (′), medium (″), or strong (‴).

General irradiation procedure: Irradiation experiments were performed in a quartz tube. The aldehyde (1.0 equiv) and the 2,3-dihydropyrrole (1.5 equiv) were dissolved in acetonitrile (Merck p.a.) under Ar. This mixture was irradiated for the indicated period of time ($\lambda = 350$ nm: Rayonet RPR 3500 Å; $\lambda = 350$ nm: Rayonet RPR 3000 Å). The course of the reaction was monitored by TLC and GLC. Upon complete conversion of the aldehyde, the solvent was evaporated in vacuo. The diastereoselectivity (dr) 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. The compounds decomposed rapidly upon standing at 0 °C. Relative configurations were determined by ^{1}H NMR spectroscopy (NOE or NOESY experiments).

(1*RS*,5*SR*,7*RS*)-*N*-Methoxycarbonyl-7-phenyl-6-oxa-2-azabicyclo[3.2.0]-heptane (4a): According to the general irradiation procedure, benzaldehyde (159 mg, 152 μL, 1.50 mmol) and 2,3-dihydropyrrole **3a**[15, 43] (318 mg, 2.50 mmol) were irradiated in acetonitrile (15 mL) at $\lambda = 300$ nm for 4.5 h. The solvent was removed in vacuo and the residue was purified by flash chromatography (pentane/*tert*-butyl methyl ether (P/TBME) = 80:20). A total of 199 mg (57 %) oxetane **4a** was obtained as a colorless oil: $R_f = 0.16$ (P/MTBE = 40/60); ^{1}H NMR (major rotamer, 500 MHz): $\delta = 1.81$ (dddd, ^2J(H,H) = 14.3 Hz, ^3J(H,H) = 10.7 Hz, ^3J(H,H) = 9.2 Hz, ^3J(H,H) = 4.3 Hz, 1H; C*H*HCH$_2$N), 2.22 (dd, ^2J(H,H) = 14.3 Hz, ^3J(H,H) = 6.8 Hz, 1H; CH*H*CH$_2$N), 3.30 (ddd, ^2J(H,H) $\hat{=}$ ^3J(H,H) = 10.9 Hz, ^3J(H,H) = 6.8 Hz, 1H; C*H*HN), 3.35 (s, 3H; OCH$_3$), 3.84 (dd, ^2J(H,H) $\hat{=}$ ^3J(H,H) = 9.8 Hz, 1H; CH*H*N), 4.86 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.6 Hz, 1H; CHN), 5.52 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.4 Hz, 1H; OCH), 5.84 (d, ^3J(H,H) = 4.7 Hz, 1H; C*H*Ph), 7.19–7.39 (m, 5H; Ph); ^{1}H NMR (minor rotamer, 500 MHz): $\delta = 1.79$ (dddd, ^2J(H,H) = 14.3 Hz, ^3J(H,H) = 10.9 Hz, ^3J(H,H) = 9.0 Hz, ^3J(H,H) = 4.5 Hz, 1H; C*H*HCH$_2$N), 2.17 (dd, ^2J(H,H) = 14.3 Hz, ^3J(H,H) = 6.7 Hz, 1H; CH*H*CH$_2$N), 3.44 (s, 3H; OCH$_3$), 3.53 (ddd, ^2J(H,H) $\hat{=}$ ^3J(H,H) = 10.8 Hz, ^3J(H,H) = 6.9 Hz, 1H; C*H*HN), 3.73 (dd, ^2J(H,H) $\hat{=}$ ^3J(H,H) = 9.7 Hz, 1H; CH*H*N), 5.08 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.9 Hz, 1H; CHN), 5.50 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.7 Hz, 1H; OCH), 5.91 (d, ^3J(H,H) = 5.1 Hz, 1H; C*H*Ph), 7.20–7.38 (m, 5H; Ph); ^{13}C NMR (major rotamer, 75.5 MHz): $\delta = 31.3$ (*C*H$_2$CH$_2$N), 46.9 (CH$_2$N), 51.9 (OCH$_3$), 61.0 (CHN), 83.9 (OCH), 84.2 (*C*HPh), 125.3 (C$_{ar}$), 127.8 (2C, C$_{ar}$), 128.0 (2C, C$_{ar}$), 137.0 (C$_{ar}$), 154.8 (*C*OOCH$_3$); ^{13}C NMR (minor rotamer, 75.5 MHz): $\delta = 32.3$ (*C*H$_2$CH$_2$N), 46.1 (CH$_2$N), 52.3 (OCH$_3$), 60.8 (CHN), 83.0 (OCH), 84.3 (*C*HPh), 125.1 (C$_{ar}$), 127.3 (2C, C$_{ar}$), 128.0 (2C, C$_{ar}$), 137.4 (C$_{ar}$), 154.4 (*C*OOCH$_3$); NOE (600 MHz): H (5.84): H (5.52) [0.6 %], H (4.86) [2.9 %]; H (5.52): H (5.84) [0.7 %], H (4.86) [2.2 %]; H (4.86): H (5.84) [3.2 %], H (5.52) [1.9 %]; IR (film): $\tilde{\nu} = 3040$ cm^{-1} (w), 3010 (w), 2930 (s), 2870 (m, C–H), 1680 (vs, C=O), 1440 (s), 1380 (s), 1320 (m), 1220 (m), 1190 (s), 1100 (s), 1030 (m, C–H), 980 (s, C–O–C), 905 (m), 760 (s), 745 (m), 695 (s, C–H); MS (70 eV, EI), *m*/*z* (%): 216 (4) $[M - \mathrm{Me}]^+$, 127 (100) $[M - \mathrm{PhCHO}]^+$, 112 (54) $[M - \mathrm{PhCHO} - \mathrm{Me}]^+$, 105 (16) $[\mathrm{PhCO}]^+$, 82 (28) $[C_5H_8N]^+$, 41 (24) $[C_2H_3N]^+$; elemental analysis calcd (%) for $C_{13}H_{15}NO_3$ (233.26): C 66.94, H 6.48, N 6.00; found C 66.78, H 6.68, N 5.77.

(1*RS*,5*SR*,7*RS*)-2-Ethoxycarbonyl-7-phenyl-6-oxa-2-azabicyclo[3.2.0]heptane (4b): According to the general irradiation procedure, benzaldehyde (212 mg, 202 μL, 2.00 mmol) and dihydropyrrole **3b**[15, 43] (565 mg, 4.00 mmol) were irradiated in acetonitrile (20 mL) at $\lambda = 300$ nm for 3.5 h. The solvent was removed in vacuo and the residue was purified by flash chromatography (P/TBME = 80:20). A total of 155 mg (52 %) of oxetane **4b** was obtained as a colorless oil: $R_f = 0.37$ (P/TBME = 40:60); ^{1}H NMR (major rotamer, 400 MHz): $\delta = 1.09$ (t, ^3J(H,H) = 7.1 Hz, 3H; CH$_2$C*H$_3$*), 1.82 (dddd, ^2J(H,H) = 15.4 Hz, ^3J(H,H) = 10.9 Hz, ^3J(H,H) = 9.2 Hz, ^3J(H,H) = 4.3 Hz, 1H; C*H*HCH$_2$N), 2.22 (ddd, ^2J(H,H) $\hat{=}$ ^3J(H,H) = 15.4 Hz, ^3J(H,H) = 6.8 Hz, 1H; CH*H*CH$_2$N), 3.56 (ddd, ^2J(H,H) $\hat{=}$ ^3J(H,H) = 10.9 Hz, ^3J(H,H) = 6.8 Hz, 1H; CH*H*N), 3.85–3.97 (m, 1H; C*H*HN), 3.87 (q, ^3J(H,H) = 7.1 Hz, 2H; C*H$_2$*CH$_3$), 4.90 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.6 Hz, 1H; CHN), 5.54 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.5 Hz, 1H; CHO), 5.87 (d, ^3J(H,H) = 4.7 Hz, 1H; C*H*Ph), 7.22–7.36 (m, 5H; Ph); ^{1}H NMR (minor rotamer, 400 MHz): $\delta = 1.03$ (t, ^3J(H,H) = 7.1 Hz, 3H; CH$_2$C*H$_3$*), 1.21–1.43 (m, 2H; C*H$_2$*CH$_2$N), 3.34 (ddd, ^2J(H,H) $\hat{=}$ ^3J(H,H) = 10.9 Hz, ^3J(H,H) = 6.7 Hz, 1H; CH*H*N), 3.68–3.80 (m, 1H; C*H*HN), 3.78 (q, ^3J(H,H) = 7.1 Hz, 2H; C*H$_2$*CH$_3$), 5.09 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.8 Hz, 1H; CHN), 5.52 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.5 Hz, 1H; CHO), 5.93 (d, ^3J(H,H) = 5.0 Hz, 1H; C*H*Ph), 7.22–7.36 (m, 5H; Ph); ^{13}C NMR (major rotamer, 50 MHz): $\delta = 14.3$ (CH$_2$*C*H$_3$), 31.1 (*C*H$_2$CH$_2$N), 46.7 (CH$_2$*C*H$_2$N), 60.7 (*C*H$_2$CH$_3$), 60.8 (CHN), 83.9 (OCH), 84.2 (*C*HC$_{ar}$), 125.3 (C$_{ar}$), 127.2 (2C, C$_{ar}$), 127.9 (2C, C$_{ar}$), 137.0 (*C*$_{ar}$), 153.9 (NCOO); ^{13}C NMR (minor rotamer, 50 MHz): $\delta = 13.9$ (CH$_2$*C*H$_3$), 32.1 (*C*H$_2$CH$_2$N), 46.0 (CH$_2$*C*H$_2$N), 60.5 (*C*H$_2$CH$_3$), 60.9 (CHN), 82.9 (OCH), 84.3 (*C*HC$_{ar}$), 125.3 (C$_{ar}$), 126.1 (2C, C$_{ar}$), 127.7 (2C, C$_{ar}$), 137.3 (*C*$_{ar}$), 154.2 (NCOO); NOE (500 MHz): H (5.87): H (4.90) [2.1 %], H (5.54) [3.8 %]; H (5.54): H (1.82) [3.4 %], H (2.22) [0.5 %]; H (4.90): H (5.54) [5.3 %], H (5.87) [8.4 %]; IR (film): $\tilde{\nu} = 2980$ cm^{-1} (m), 2895 (w, C–H), 1700 (vs, C=O), 1470 (s), 1385 (m), 1330 (m, C–H), 1110 (m, C–H), 990 (w, C–O–C), 970 (m), 770 (w), 750 (w), 700 (m, C – H); MS (70 eV, EI), *m*/*z* (%): 247 (0.3) [*M*]$^+$, 202 (0.9) [*M* – OEt]$^+$, 174 (2) [*M* – COOEt]$^+$, 141 (100) [*M* – PhCHO]$^+$, 105 (16) [PhCO]$^+$, 68 (66) [C$_4$H$_8$N]$^+$, 29 (61) [C$_2$H$_5$]$^+$; HRMS calcd (u) for C$_{14}$H$_{17}$NO$_3$ (247.29): 247.1208; found 247.1211.

(1*RS*,5*SR*,7*RS*)-2-*tert*-Butoxycarbonyl-7-phenyl-6-oxa-2-azabicyclo[3.2.0]-heptane (4c): According to the general irradiation procedure benzaldehyde (159 mg, 152 µL, 1.50 mmol) and dihydropyrrole **3c**[15, 43] (634 mg, 3.75 mmol) were irradiated in acetonitrile (15 mL) for 4 h. The mixture was removed in vacuo and the residue was purified by flash chromatography (P/TBME = 80:20). A total of 168 mg (41 %) of oxetane **4c** was obtained as a colorless oil: $R_f = 0.36$ (P/TBME = 40:60); ^{1}H NMR (major rotamer, 500 MHz): $\delta = 1.14$ (s, 9H; C(CH$_3$)$_3$), 1.43–1.56 (m, 1H; C*H*HCH$_2$N), 2.22 (dd, ^2J(H,H) = 14.2 Hz, ^3J(H,H) = 6.1 Hz, 1H; CH*H*CH$_2$N), 3.59 (ddd, ^2J(H,H) $\hat{=}$ ^3J(H,H) = 10.9 Hz, ^3J(H,H) = 7.0 Hz, 1H; C*H*HN), 3.86–3.93 (m, 1H; CH*H*N), 4.79 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.4 Hz, 1H; CHN), 5.52 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.1 Hz, 1H; CHO), 5.83 (d, ^3J(H,H) = 4.3 Hz, 1H; C*H*Ph), 7.24–7.37 (m, 5H; Ph); ^{1}H NMR (minor rotamer, 500 MHz): $\delta = 1.16$ (s, 9H; C(CH$_3$)$_3$), 1.73–1.86 (m, 1H; C*H*HCH$_2$N), 2.16 (dd, ^2J(H,H) = 14.2 Hz, ^3J(H,H) = 6.1 Hz, 1H; CH*H*CH$_2$N), 3.29–3.37 (m, 1H; C*H*HN), 3.64–3.68 (m, 1H; CH*H*N), 4.95 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.7 Hz, 1H; CHN), 5.49 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.3 Hz, 1H; CHO), 5.90 (d, ^3J(H,H) = 4.9 Hz, 1H; C*H*Ph), 7.24–7.37 (m, 5H; Ph); ^{13}C NMR (major rotamer, 125 MHz): $\delta = 27.8$ (*C*H$_2$CH$_2$N), 28.2 (C(*C*H$_3$)$_3$), 30.8 (CH$_2$*C*H$_2$N), 61.0 (CHN), 79.5 (*C*(CH$_3$)$_3$), 84.0 (OCH), 84.3 (CHPh), 125.7 (C$_{ar}$), 126.9 (2C, C$_{ar}$), 128.0 (2C, C$_{ar}$), 136.8 (*C*$_{ar}$), 153.2 (NCOO); ^{13}C NMR (minor rotamer, 125 MHz): $\delta = 26.9$ (*C*H$_2$CH$_2$N), 28.0 (C(*C*H$_3$)$_3$), 31.9 (CH$_2$*C*H$_2$N), 60.0 (CHN), 79.3 (*C*(CH$_3$)$_3$), 83.1 (OCH), 84.4 (CHPh), 125.10 (C$_{ar}$), 126.8 (2C, C$_{ar}$), 127.8 (2C, C$_{ar}$), 137.0 (*C*$_{ar}$), ^{13}C signal for NCOO was not obtained; NOE (500 MHz): H (5.83): H (7.31) [7.3 %], H (5.52) [2.7 %], H (4.79) [9.8 %]; H (5.52): H (5.83) [3.3 %], H (4.79) [7.9 %]; IR (film): $\tilde{\nu} = 3090$ cm^{-1} (w), 3065 (w), 3030 (m), 2970 (s), 2890 (s, C–H), 1695 (vs, C=O), 1480 (s), 1455 (s), 1390 (m), 1370 (m), 1170 (s), 1115 (s, C–H), 990 (m), 970 (m, C–O–C), 770 (m), 750 (m), 700 (m, C–H); MS (70 eV, EI), *m*/*z* (%): 169 (9) [*M* – PhCHO]$^+$, 113 (85) [C$_5$H$_7$NO$_2$]$^+$, 69 (48) [C$_4$H$_7$N]$^+$, 57 (100) [C(CH$_3$)$_3$]$^+$, 41 (30) [C$_2$H$_3$N]$^+$; HRMS calcd (u) for C$_{16}$H$_{21}$NO$_3$ (275.34): 275.1521; found 275.1526.

***N*-Methoxycarbonyl-3-methyl-6-oxa-7-phenyl-2-azabicyclo[3.2.0]heptane**: According to the general irradiation procedure benzaldehyde (318 mg, 304 µL, 3.00 mmol) and 2,3-dihydropyrrole **8a**[15, 29, 30] (635 mg, 4.5 mmol) were irradiated in acetonitrile (30 mL) at $\lambda = 350$ nm for 6 h. GLC analysis of the crude product mixture showed a diastereomeric ratio dr = 76/24. After removal of the solvent in vacuo, flash chromatography (P/TBME = 80:20) yielded two separated diastereoisomers as colorless oils. **(1*R*,3*R*,5*S*,7*R*) isomer (9a)** (major product): Yield: 275 mg (37 %): $R_f =$ 0.11 (P/TBME = 40:60); $[\alpha]_D^{25} = -41.9$ ($c = 1.15$; CHCl$_3$); ^{1}H NMR (400 MHz, [D$_6$]DMSO, 373 K): $\delta = 1.07$ (d, ^3J(H,H) = 6.5 Hz, 3H; CH$_3$), 1.79 (dd, ^2J(H,H) = 14.7 Hz, ^3J(H,H) = 2.3 Hz, 1H; C*H*H), 2.18 (ddd, ^2J(H,H) = 14.7 Hz, ^3J(H,H) = 9.4 Hz, ^3J(H,H) = 5.4 Hz, 1H; CH*H*), 3.47 (s, 3H; OCH$_3$), 4.04–4.14 (m, 1H; C*H*CH$_3$), 4.99 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.6 Hz, 1H; C*H*N), 5.41 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 5.1 Hz, 1H; CHO), 5.84 (d, ^3J(H,H) = 4,7 Hz, 1H; C*H*Ph), 7.22–7.32 (m, 5H; Ph); NOESY (400 MHz, [D$_6$]DMSO, 373 K): H (1.07)–H (1.79)″; H (1.07)–H (4.1)‴; H (1.79)–H (2.18)‴; H (1.79)–H (4.1)′; H (2.18)–H (4.1)‴; H (2.18)–H (5.41)‴; H (4.99)–H (5.41)″; H (4.99)–H (5.84)‴; H (5.41)–H (5.84)″; IR (film): $\tilde{\nu} = 2960$ cm^{-1} (m, C–H), 1715 (s) 1700 (sh, C=O), 1450 (s), 1385 (m); MS (EI, 70 eV, EI), *m*/*z* (%): 248 (0.6) [*M*+H]$^+$, 247 (0.3) [*M*]$^+$, 141 (93) [*M* – PhCHO]$^+$, 126 (100) [C$_6$H$_{10}$NO$_2$]$^+$, 105 (37) [PhCO]$^+$; HRMS calcd (u) C$_{14}$H$_{17}$NO$_3$ (247.29): 247.1208; found 247.1215. **(1*S*,3*R*,5*R*,7*S*) isomer (10a)** (minor product): Yield 148 mg (20 %): $R_f = 0.17$ (P/TBME = 40:60); $[\alpha]_D^{25} = -32.5$ ($c = 1.1$; CHCl$_3$); ^{1}H NMR (400 MHz, [D$_6$]DMSO, 373 K): $\delta = 1.28$ (d, ^3J(H,H) = 6.0 Hz, 3H; CH$_3$), 1.65 (ddd, ^2J(H,H) = 14.6 Hz, ^3J(H,H) = 8.3 Hz, ^3J(H,H) = 5.1 Hz, 1H; C*H*H), 2.48 (dd, ^2J(H,H) = 14.6 Hz, ^3J(H,H) = 7.2 Hz, 1H; CH*H*), 3.09 (s, 3H; OCH$_3$), 4.08–4.14 (m, 1H; C*H*CH$_3$), 4.88 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.7 Hz, 1H; C*H*N), 5.35 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.9 Hz, 1H; CHO), 5.74 (d, ^3J(H,H) = 4,7 Hz, 1H; C*H*Ph), 7.24–7.36 (m, 5H; Ph); NOESY (400 MHz, [D$_6$]DMSO, 373 K): H (1.28)–H (1.65)″; H (1.28)–H (2.48)′; H (1.28)–H (4.1)‴; H (1.65)–H (2.48)‴; H (1.65)–H (4.88)″; H (2.48)–H (4.1)″; H (4.88)–H (5.35)″; H (4.88)–H (5.74)‴; H (5.35)–H (5.74)″; IR (film): $\tilde{\nu} = 3075$ cm^{-1} (w), 3020 (w), 2960 (m, C–H), 1700 (vs, C=O), 1450 (s), 1385 (s), 1320 (m), 1200 (m, C–H), 990 (w, C–O–C), 770 (m), 735 (m), 700 (s, C–H); MS (70 eV, EI), *m*/*z* (%): 246 (4) [*M* – H]$^+$, 140 (100) [*M* – H – PhCHO]$^+$, 126 (16) [C$_6$H$_{10}$NO$_2$]$^+$, 105 (31) [PhCO]$^+$, 28 (76) [CO]$^+$.

(1*R*,3*R*,5*S*,7*R*)-*N*-Methoxycarbonyl-3-benzyl-6-oxa-7-phenyl-2-azabicyclo-[3.2.0]heptane (9c): According to the general irradiation procedure benzaldehyde (159 mg, 152 µL, 1.5 mmol) and 2,3-dihydropyrrole **8c**[15] (543 mg, 2.50 mmol) were irradiated in acetonitrile (15 mL) for 6 h at $\lambda = 350$ nm. GLC analysis of the crude product mixture showed a single diastereomer (dr $\geq$ 95/5). After removal of the solvent in vacuo, flash chromatography (P/TBME = 90:10) yielded 277 mg (57 %) of the oxetane **9c** as a colorless oil: $R_f = 0.16$ (P/TBME = 40:60); $[\alpha]_D^{25} = -3.60$ ($c = 1.7$ in CHCl$_3$); ^{1}H NMR (400 MHz, [D$_6$]DMSO, 373 K): $\delta = 1.93$–1.96 (m, 1H; OCHC*H*H), 2.67–2.75 (m, 3H; CH*H*CHC*H$_2$*Ph), 3.47 (s, 3H; OCH$_3$), 4.20–4.26 (m, 1H; C*H*CH$_2$Ph), 5.07 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.4 Hz, 1H; OCHC*H*N), 5.43–5.46 (m, 1H; CHO), 5.93 (d, ^3J(H,H) = 4,5 Hz, 1H; OC*H*Ph), 7.16–7.38 (m, 10H; 2 Ph); NOESY (400 MHz, [D$_6$]DMSO, 373 K): H (1.9)–H (2.7)‴; H (1.9)–H (4.2)‴; H (1.9)–H (5.4)‴; H (2.7)–H (4.2)″; H (2.7)–H (7.2)‴; H (4.2)–H (7.2)‴; H (5.07)–H (5.4)″; H (5.07)–H (5.93)‴; H (5.4)–H (5.93)‴; H (5.93)–H (7.2)″; IR (film): $\tilde{\nu} = 3060$ cm^{-1} (w), 3030 (m), 2970 (m), 2955 (s, C–H);1700 (vs, C=O), 1450 (vs), 1385 (s), 1335 (s), 1200 (s), 1120 (m), 1080 (m, C–H), 985 (m, C–O–C); MS (70 eV, EI), *m*/*z* (%): 323 (0.9) [*M*]$^+$, 292 (0.8) [*M* – OCH$_3$]$^+$, 217 (26) [*M* – PhCHO]$^+$, 126 (100) [C$_6$H$_{10}$NO$_2$]$^+$, 107 (48) [C$_7$H$_7$O]$^+$, 91 (74) [C$_7$H$_7$]$^+$; HRMS calcd (u) for C$_{20}$H$_{21}$NO$_3$ (323.39): 323.1521; found 323.1511.

***N*-Methoxycarbonyl-3-nonyl-6-oxa-7-phenyl-2-azabicyclo[3.2.0]heptane**: According to the general irradiation procedure benzaldehyde (106 mg, 101 µL, 1.00 mmol) and 2,3-dihydropyrrole **8d** (633 mg, 2.50 mmol) were irradiated in acetonitrile (15 mL) at $\lambda = 350$ nm. After 4 h benzaldehyde (53 mg, 51 µL, 0.5 mmol) was added to the reaction mixture and the mixture was further irradiated for another 2 h. GLC analysis of the crude product mixture showed a diastereomeric ratio dr = 75/25. After removal of the solvent in vacuo, flash chromatography (P/TBME = 90:10) yielded two separate diastereoisomers as colorless oils. **(1*R*,3*R*,5*S*,7*R*) isomer (9d)** (major product): Yield: 286 mg (53 %): $R_f = 0.10$ (P/TBME = 80:20); $[\alpha]_D^{25} = -10.7$ ($c = 2.1$; CHCl$_3$); ^{1}H NMR (400 MHz, [D$_6$]DMSO, 373 K): $\delta = 0.88$ (t, ^3J(H,H) = 7.0 Hz, 3H; CH$_2$C*H$_3$*), 1.08–1.32 (m, 16H; (CH$_2$)$_8$), 1.84 (dd, ^2J(H,H) = 14.7 Hz, ^3J(H,H) = 1.9 Hz, 1H, C*H*H), 2.08 (ddd, ^2J(H,H) = 14.7 Hz, ^3J(H,H) = 9.1 Hz, ^3J(H,H) = 5.2 Hz, 1H; CH*H*), 3.51 (s, 3H; OCH$_3$), 3.93–3.99 (m, 1H; NC*H*CH$_2$), 5.02 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.9 Hz, 1H; CHC*H*N), 5.43 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.9 Hz, 1H; CHO), 5.85 (d, ^3J(H,H) = 4,8 Hz, 1H; C*H*Ph), 7.19–7.29 (m, 5H; Ph); NOESY (400 MHz, [D$_6$]DMSO, 373 K): H (1.84)–H (2.08)‴; H (1.84)–H (3.9)′; H (1.84)–H (5.43)″; H (2.08)–H (3.9)‴; H (2.08)–H (5.43)‴; H (5.02)–H (5.43)″; H (5.02)–H (5.85)‴; H (5.43)–H (5.85)‴; H (5.85)–H (7.2)″; IR (film): $\tilde{\nu} = 2955$ cm^{-1} (m), 2925 (s), 2855 (m, C–H), 1725 (vs, C=O), 1450 (s), 1385 (m), 1275 (s), 1110 (m, C–H), 990 (w, C–O–C); MS (70 eV, EI), *m*/*z* (%): 359 (0.3) [*M*]$^+$, 253 (23) [*M* – PhCHO]$^+$, 126 (100) [$C_6H_{10}NO_2$]$^+$; HRMS calcd (u) for $C_{22}H_{33}NO_3$ (359.50): 359.2460; found 359.2458. **(1*S*,3*R*,5*R*,7*S*) isomer (10d)** (minor product): Yield: 65 mg (12%): $R_f = 0.17$ (P/TBME = 80:20); $[\alpha]_D^{25} = -18.3$ ($c = 2.0$; $CHCl_3$); ^{1}H NMR (400 MHz, [D$_6$]DMSO, 373 K): $\delta = 0.87$ (t, ^3J(H,H) = 6.9 Hz, 3H; CH$_2$C*H*$_3$), 1.16–1.39 (m, 16H; (CH$_2$)$_8$), 1.78 (ddd, ^2J(H,H) = 14.6 Hz, ^3J(H,H) = 6.2 Hz, ^3J(H,H) = 2.2 Hz, 1H; C*H*H), 2.49 (ddd, ^2J(H,H) = 14.6 Hz, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 7.2 Hz, 1H, CH*H*), 3.64 (s, 3H; OCH$_3$), 4.03–4.09 (m, 1H; NC*H*CH$_2$), 4.83 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.5 Hz, 1H; CHC*H*N), 5.34 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 5.0 Hz, 1H; CHO), 5.70 (d, ^3J(H,H) = 4.7 Hz, 1H; C*H*Ph), 7.26–7.35 (m, 5H; Ph); NOESY (400 MHz, [D$_6$]DMSO, 373 K): H (1.78) – H (2.49)‴; H (1.78) – H (5.34)‴; H (2.49) – H (4.0)‴; H (2.49) – H (5.34)′; H (4.0) – H (7.2)″; H (4.83) – H (5.34)″; H (4.83) – H (5.70)‴; H (5.34) – H (5.70)′; H (5.70) – H (7.2)″; IR (film): $\tilde{\nu} = 2955$ cm^{-1} (m), 2925 (s), 2855 (m, C–H), 1710 (vs, C=O), 1445 (s), 1375 (m, C–H), 990 (w, C–O–C); MS (70 eV, EI), *m*/*z* (%): 253 (18) [*M* – PhCHO]$^+$, 126 (100) [$C_6H_{10}NO_2$]$^+$, 67 (9) [C_4H_5N]$^+$.

***N*-Methoxycarbonyl-3,7-diphenyl-6-oxa-2-azabicyclo[3.2.0]heptane**: According to the general irradiation procedure benzaldehyde (159 mg, 152 µL, 1.50 mmol) and dihydropyrrole *rac*-**8e**[31] (508 mg, 2.50 mmol) were irradiated in acetonitrile (15 mL) at $\lambda = 350$ nm for 7 h. GLC analysis of the crude product mixture showed a diastereomeric ratio dr = 68/32. After removal of the solvent in vacuo, flash chromatography (P/TBME = 85:15) yielded two separated diastereoisomers as colorless oils. **(1*SR*,3*SR*,5*RS*,7*SR*) isomer (*rac*-9e)** (major product): Yield: 172 mg (37%): $R_f = 0.14$ (P/TBME = 40:60); ^{1}H NMR (500 MHz, [D$_6$]DMSO, 373 K): $\delta = 2.29$ (d, ^2J(H,H) = 14.9 Hz, 1H; C*H*H), 2.66 (ddd, ^2J(H,H) = 14.9 Hz, ^3J(H,H) = 9.6 Hz, ^3J(H,H) = 5.5 Hz, 1H; CH*H*), 3.11 (s, 3H; OCH$_3$), 5.13 (d, ^3J(H,H) = 4.0 Hz, 1H; CH$_2$C*H*N), 5.16 (ddd, ^3J(H,H) = 5.8 Hz, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.6 Hz, 1H; CHC*H*N), 5.47 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 5.4 Hz, 1H; CHO), 5.88 (d, ^3J(H,H) = 5.2 Hz, 1H; OC*H*Ph), 7.10–7.55 (m, 10H; 2 Ph); NOESY (500 MHz, [D$_6$]DMSO, 373 K): H (2.29) – H (2.66)‴; H (2.29) – H (5.13)′; H (2.29) – H (5.47)′; H (2.66) – H (5.13)‴; H (2.66) – H (5.47)‴; H (5.16) – H (5.47)″; H (5.16) – H (5.88)‴; H (5.47) – H (5.88)′; IR (film): $\tilde{\nu} = 3080$ cm^{-1} (w), 3045 (w), 2980 (m), 2975 (m, C–H), 1715 (vs), 1695 (sh, C=O), 1450 (s), 1380 (m), 765 (w), 700 (m, C–H); MS (EI, 70 eV, EI), *m*/*z* (%): 309 (0.6) [*M*]$^+$, 203 (100) [*M* – PhCHO]$^+$, 144 (48) [*M* – PhCHO – COOCH$_3$)]$^+$, 105 (62) [PhCO]$^+$, 77 (46) [C_6H_5]$^+$, 28 (77) [CO]$^+$; HRMS calcd (u) for $C_{19}H_{19}NO_3$ (309.36): 309.1365; found 309.1361. **(1*SR*,3*RS*,5*RS*,7*SR*) isomer (*rac*-10e)** (minor product): Yield: 121 mg (26%): $R_f = 0.32$; ^{1}H NMR (400 MHz, [D$_6$]DMSO, 373 K): $\delta = 1.92$ (ddd, ^2J(H,H) = 14.9 Hz, ^3J(H,H) = 8.0 Hz, ^3J(H,H) = 5.5 Hz, 1H; C*H*H), 2.78 (dd, ^2J(H,H) = 14.9 Hz, ^3J(H,H) = 7.8 Hz, 1H, CH*H*), 2.93 (s, 3H; OCH$_3$), 5.08–5.15 (m, 2H; C*H*NC*H*), 5.47 (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 4.9 Hz, 1H; CHO), 5.83 (d, ^3J(H,H) = 4,6 Hz, 1H; C*H*Ph), 7.07–7.40 (m, 10H; 2 Ph); NOESY (400 MHz, [D$_6$]DMSO, 373 K): H (1.92) – H (2.78)‴; H (1.92) – H (5.47)″; H (2.78) – H (5.47)″; H (2.78) – H (5.1)″; H (5.83) – H (5.1)‴; IR (film): $\tilde{\nu} = 3065$ cm^{-1} (w), 3030 (m), 2955 (m), 2900 (m, C–H), 1700 (s, C=O), 1450 (s), 1380 (s), 1350 (m), 1325 (m), 1200 (s), 1125 (m, C–H), 985 (m, C–O–C), 765 (s), 755 (s), 700 (s, C–H); MS (70 eV, EI), *m*/*z* (%): 309 (0.7) [*M*]$^+$, 203 (100) [*M* – PhCHO]$^+$, 144 (58) [*M* – PhCHO – COOCH$_3$]$^+$, 128 (61) [$C_6H_{12}NO_2$]$^+$, 107 (77) [C_7H_7O]$^+$, 91 (23) [C_7H_7]$^+$, 79 (55) [C_6H_7]$^+$; HRMS calcd (u) for $C_{19}H_{19}NO_3$ (309.36): 309.1365; found 309.1361.

(1*SR*,6*RS*,8*SR*)-*N*-Methoxycarbonyl-8-phenyl-7-oxa-2-azabicyclo[4.2.0]-octane (22): According to the general irradiation procedure benzaldehyde (250 mg, 0.24 mL, 2.40 mmol) and trihydropyridine **21** (550 mg, 3.90 mmol) were irradiated in acetonitrile (25 mL) at $\lambda = 300$ nm for 3.5 h. GLC analysis of the crude product showed a mixture of simple diastereomers (dr = 75/25). After removal of the solvent in vacuo, flash chromatography (P/TBME = 85:15) yielded 100 mg (17%) of compound **22** as a colorless oil: $R_f = 0.24$ (P/TBME = 40:60); ^{1}H NMR (500 MHz): $\delta = 1.40$–2.25 (m, 4H; NCH$_2$C*H*$_2$C*H*$_2$), 2.80–3.77 (m, 2H; NCH$_2$), 3.35 [3.55] (s, 3H; OCH$_3$), 4.79 [5.11] (dd, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 6.8 Hz, 1H; NCH), 5.28 [5.39] (dd, 1H; ^3J(H,H) $\hat{=}$ ^3J(H,H) = 3.6 Hz, CH$_2$C*H*O), 5.88 [5.99] (d, ^3J(H,H) = 6.4 Hz, 1H; C*H*Ph), 7.23–8.08 (m, 5H; Ph); ^{13}C NMR (125 MHz): $\delta = 18.6$ (NCH$_2$*C*H$_2$), 26.8 (CH*C*H$_2$), 41.7 [41.9] (NCH$_2$), 53.6 (NCH), 66.0 (OCH$_3$), 75.2 (CH$_2$*C*HO), 83.1 [83.2] (Ph*C*H), 125.0 [126.1] (C$_{ar}$), 127.7 [128.3] (2 C, C$_{ar}$), 129.5 [129.7] (2C, C$_{ar}$), 136.8 [137.5] (C$_{ar}$), 156.0 [156.7] (COO); NOESY (500 MHz): H (4.8) – H (5.3)″; H (4.8) – H (5.9)‴; H (5.3) – H (5.9)′; IR (film): $\tilde{\nu} = 3435$ cm^{-1} (m), 3060 (w), 3030 (w), 2955 (m), 2875 (m, C–H), 1705 (s, C=O), 1495 (s, C–H); MS (70 eV, EI), *m*/*z* (%): 247 (0.2) [*M*]$^+$, 141 (100) [*M* – PhCHO]$^+$, 126 (56) [$C_6H_{10}NO_2$]$^+$, 105 (40) [PhCO]$^+$, 77 (28) [C_6H_5]$^+$; HRMS calcd (u) for $C_{14}H_{17}NO_3$ (247.30): 247.1208; found 247.1212.

(2*SR*,3*SR*)-*N*-Methoxycarbonyl-2-benzyl-3-pyrrolidinol (5a): Typical hydrogenolysis procedure: Pd(OH)$_2$/C (20% [w/w], 204 mg, 0.30 mmol) was added to a solution of oxetane **4a** (233 mg, 1.00 mmol) in methanol (30 mL), and the mixture was stirred vigorously under atmospheric hydrogen pressure for 2 h. The course of the reaction was monitored by TLC. Upon complete conversion, the catalyst was removed by filtration and the solvent was evaporated in vacuo. Flash chromatography (P/TBME = 80:20) yielded 220 mg (94%) of the pyrrolidinol **5a** as a colorless oil: $R_f = 0.14$ (P/TBME = 40:60); ^{1}H NMR (400 MHz, [D$_6$]DMSO, 373 K): $\delta = 1.67$ (dddd, ^2J(H,H) = 12.3 Hz, ^3J(H,H) $\hat{=}$ ^3J(H,H) $\hat{=}$ ^3J(H,H) = 7.5 Hz, 1H; C*H*HCHOH), 1.89 (dddd, ^2J(H,H) = 12.3 Hz, ^3J(H,H) = 8.0 Hz, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 6.1 Hz, 1H; CH*H*CHOH), 2.86 (dd, ^2J(H,H) = 13.4 Hz, ^3J(H,H) = 4.8 Hz, 1H; C*H*HPh), 2.99 (dd, ^2J(H,H) = 13.4 Hz, ^3J(H,H) = 7.4 Hz, 1H; CH*H*Ph), 3.27 (ddd, ^2J(H,H) = 10.7 Hz, ^3J(H,H) = 8.1 Hz, ^3J(H,H) = 5.9 Hz, 1H; C*H*HPh), 1H; C*H*HN), 3.35 (ddd, ^2J(H,H) = 10.7 Hz, ^3J(H,H) = 8.0 Hz, ^3J(H,H) = 6.9 Hz, 1H; CH*H*N), 3.48 (s, 3H; OCH$_3$), 3.90 (ddd, ^3J(H,H) $\hat{=}$ ^3J(H,H) $\hat{=}$ ^3J(H,H) = 6.2 Hz, 1H; C*H*CH$_2$Ph), 4.17 (ddd, ^3J(H,H) $\hat{=}$ ^3J(H,H) $\hat{=}$ ^3J(H,H) = 6.4 Hz, 1H; C*H*OH), 7.10–7.28 (m, 5H; Ph); ^{13}C NMR (100 MHz, [D$_6$]DMSO, 373 K): $\delta = 30.8$ (*C*H$_2$CHOH), 33.3 (*C*H$_2$Ph), 42.9 (CH$_2$N), 50.9 (OCH$_3$), 61.4 (*C*HCH$_2$Ph), 69.5 (CHOH), 124.9 (C$_{ar}$), 127.1 (2C, C$_{ar}$), 128.9 (2C, C$_{ar}$), 139.4 (C$_{ar}$), 154.5 (NCOO); NOE (400 MHz, [D$_6$]DMSO, 373 K): H (4.17): H (3.90) [7.3%], H (3.90): H (4.17) [7.1%]; IR (film): $\tilde{\nu} = 3400$ cm^{-1} (vs, b, OH), 3030 (w), 3005 (m), 2940 (s), 2860 (sh, C–H), 1690 (vs, C=O), 1590 (m), 1440 (s), 1380 (s), 1330 (s), 1260 (s), 1190 (s), 1110 (s, C–H); MS (70 eV, EI), *m*/*z* (%): 235 (7) [*M*]$^+$, 234 (41) [*M* – H]$^+$, 144 (54) [*M* – C_7H_7]$^+$, 128 (100) [*M* – C_7H_7O]$^+$, 91 (35) [C_7H_7]$^+$; elemental analysis calcd (%) for $C_{13}H_{17}NO_3$ (235.28): C 66.36, H 7.28, N 5.95; found C 66.21, H 7.55, N 5.93.

(2*SR*,3*SR*)-*N*-Ethoxycarbonyl-2-benzyl-3-pyrrolidinol (5b): According to the typical hydrogenolysis procedure oxetane **4b** (126 mg, 0.51 mmol) was cleaved hydrogenolytically in 3 h. Flash chromatography (P/TBME = 90:10) yielded 67.4 mg (53%) pyrrolidinol **5b** as a colorless oil: $R_f = 0.11$ (P/TBME = 60:40); ^{1}H NMR (200 MHz, CDCl$_3$): $\delta = 1.25$ (t, ^3J(H,H) = 7.0 Hz, 3H; CH$_2$C*H*$_3$), 1.38–1.93 (m, 2H; C*H*$_2$CHOH), 2.85–2.96 (m, 2H; C*H*$_2$Ph), 3.24–3.51 (m, 2H; C*H*$_2$N), 3.98–4.17 (m, 1H; C*H*CH$_2$Ph), 4.01 (q, ^3J(H,H) = 7.0 Hz, 2H; C*H*$_2$CH$_3$), 4.47–4.51 (m, 1H; C*H*OH), 7.08–7.19 (m, 5H; Ph); ^{13}C NMR (50 MHz, CDCl$_3$): $\delta = 14.7$ (CH$_2$*C*H$_3$), 26.9 (*C*H$_2$CHOH), 28.6 (CH$_2$Ph), 47.4 (CH$_2$N), 60.0 (*C*HCH$_2$Ph), 61.9 (*C*H$_2$CH$_3$), 79.1 (CHOH), 126.0 (C$_{ar}$), 128.3 (2C, C$_{ar}$), 129.5 (2C, C$_{ar}$), 139.4 (C$_{ar}$), ^{13}C signal for NCOO was not obtained; IR (film): $\tilde{\nu} = 3425$ cm^{-1} (s, b, OH), 3065 (w), 3030 (w), 2980 (s), 2885 (sh, C–H), 1700, 1675 (s, C=O), 1425 (s), 1380 (s), 1335 (s), 1115 (s, C–H), 775 (m), 750 (m), 705 (m, C–H); MS (70 eV, EI), *m*/*z* (%): 249 (0.2) [*M*]$^+$, 158 (15) [*M* – C_7H_7]$^+$, 142 (100) [*M* – C_7H_7O]$^+$, 98 (19) [$C_6H_{12}N$]$^+$, 70 (53) [C_4H_8N]$^+$, 69 (11) [C_4H_7N]$^+$, 29 (25) [CHO]$^+$; HRMS calcd (u) for $C_{14}H_{19}NO_3$ (249.31): 249.1365; found 249.1367.

(2*SR*,3*SR*)-*N*-*tert*-Butoxycarbonyl-2-benzyl-3-pyrrolidinol (5c): According to the typical hydrogenolysis procedure, oxetane **4c** (71.0 mg, 0.26 mmol) was cleaved hydrogenolytically in 4 h. Flash chromatography (P/TBME = 90:10) yielded 40.3 mg (56%) pyrrolidinol **5c** as a colorless oil. A crystalline sample for X-ray crystal structure analysis could be obtained by crystallization of **5c** from pentane at –18 °C: $R_f = 0.29$ (P/TBME = 60:40); ^{1}H NMR (300 MHz, CDCl$_3$): $\delta = 1.35$ (s, 9H; C(CH$_3$)$_3$), 1.61–1.80 (m, 2H; C*H*$_2$CHOH), 2.87–2.90 (m, 2H; C*H*$_2$Ph), 3.27–3.38 (m, 1H; CH*H*N), 3.64–3.69 (m, 1H; C*H*HN), 3.96 (ddd, ^3J(H,H) $\hat{=}$ ^3J(H,H) $\hat{=}$ ^3J(H,H) = 6.3 Hz, 1H; C*H*CH$_2$Ph), 4.20 (ddd, ^3J(H,H) $\hat{=}$ ^3J(H,H) $\hat{=}$ ^3J(H,H) = 5.9 Hz, 1H; C*H*OH), 7.11–7.22 (m, 5H; Ph); ^{13}C NMR (75.5 MHz, CDCl$_3$): $\delta = 28.4$ (C(*C*H$_3$)$_3$), 31.7 (*C*H$_2$CHOH), 34.8 (CH$_2$Ph), 49.4 (CH$_2$N), 59.9 (*C*HCH$_2$Ph), 71.7 (*C*(CH$_3$)$_3$), 79.4 (CHOH), 126.0 (C$_{ar}$), 128.3 (2C, C$_{ar}$), 129.5 (2C, C$_{ar}$), 139.4 (C$_{ar}$), 154.8 (NCOO); IR (film): $\tilde{\nu} = 3420$ cm^{-1} (s, b, OH), 3030 (w), 3060 (w), 3085 (w), 2975 (m), 2895 (w; C–H), 1670 (s, C=O), 1410 (s), 1455 (m), 1170 (s), 1115 (m), 735 (m), 770 (m), 700 (m, C–H); MS (70 eV, EI), *m*/*z* (%): 277 (0.3) [*M*]$^+$, 186 (15) [*M* – C_7H_7]$^+$, 130 (34) [C_9H_8N]$^+$, 113 (9) [$C_6H_{11}NO$]$^+$, 91 (15) [C_7H_7]$^+$, 86 (67)

$[C_4H_7O_2]^+$, 57 (97) $[C_3H_7N]^+$; HRMS calcd (u) for $C_{16}H_{23}NO_3$ (277.36): 277.1678; found 277.1683.

(*R*)-5-Nonyl-2-pyrrolidinone (13): A suspension of CuCN (1.97 g, 22.0 mmol) in THF (45 mL) was cooled to −78 °C. A 0.61 M solution of *n*-octyllithium in *n*-hexane (72.0 mL, 44.0 mmol) was added. Subsequent warming to 0 °C for 5 min led to a dark, clear solution, which was recooled to −78 °C, after which a solution of tosylate **12**[26] (2.37 g, 8.88 mmol) in THF (30 mL) was added dropwise. The mixture was warmed to room temperature, stirred for 20 h, and subsequently quenched with a saturated aqueous NH_4Cl solution (40 mL). After extraction with dichloromethane (3 × 80 mL) the organic layers were collected, washed with brine, and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography (TBME/EtOAc = 50:50). A quantity of 1.53 g (82 %) of compound **13** was obtained as a white solid: $R_f = 0.22$ (EtOAc); $[\alpha]_D^{25} = +9.40$ ($c = 1.3$ in EtOH); m.p. 61–63 °C; ^{1}H NMR (400 MHz): $\delta = 0.78$ (t, $^3J(H,H) = 6.9$ Hz, 3H; CH_3), 1.16–1.20 (m, 14H; $(CH_2)_7$), 1.36–1.63 (m, 3H; CH*H*CHNC*H*$_2$), 2.13–2.25 (m, 3H; COC*H*$_2$C*H*H), 3.50 (ddd, $^3J(H,H) \hat{=} {}^3J(H,H) \hat{=} {}^3J(H,H) = 6.5$ Hz, 1H; CHN), 6.10 (brs, 1H; NH); ^{13}C NMR (100 MHz): $\delta = 14.1$ (CH_3), 22.6 (CH_2), 25.9 (CH_2), 27.3 (CH_2), 29.3 (CH_2), 29.5 (3C, $(CH_2)_3$), 30.1 (CH_2), 31.8 (*C*H$_2$CH$_2$CO), 36.7 (*C*H$_2$CON), 54.5 (CHN), 178.2 (CON); IR (KBr): $\tilde{\nu} = 3180$ cm^{-1} (m, NH), 2920 (vs), 2855 (s, C−H), 1715 (vs), 1655 (s, C=O); MS (70 eV, EI): *m*/*z* (%): 211 (6) $[M]^+$, 85 (5) $[C_5H_{11}N]^+$, 84 (100) $[C_5H_{10}N]^+$; elemental analysis calcd (%) for $C_{13}H_{25}NO$ (211.34): C 73.88, H 11.92, N 6.63; found C 73.97, H 11.70, N 6.47.

(*R*)-*N*-Methoxycarbonyl-5-nonyl-2-pyrrolidinone (14): A solution of *n*-butyllithium in *n*-hexane (5.60 mL, 1.50 M, 8.40 mmol) was added dropwise to a cooled solution of pyrrolidinone **13** (1.70 g, 8.04 mmol) in THF (30 mL) at −78 °C. The mixture was stirred for 1 h at this temperature, then methyl chloroformate (0.80 mL, 10.3 mmol) was added and the reaction mixture was allowed to warm slowly to room temperature. After 3 h it was quenched with saturated aqueous NH_4Cl solution (25 mL). The aqueous phase was extracted with TBME (3 × 30 mL), then the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The raw product was purified by flash chromatography (TBME). A total of 2.10 g (97 %) of pyrrolidinone **14** was obtained as a colorless oil: $R_f = 0.46$ (TBME); $[\alpha]_D^{25} = -85.43$ ($c = 1.4$ in $CHCl_3$); ^{1}H NMR (400 MHz): $\delta = 0.86$ (d, $^3J(H,H) = 7.1$ Hz, 3H; CH_3), 1.17–1.29 (m, 14H; $(CH_2)_7$), 1.41–1.85 (m, 3H; CH*H*CHNC*H*$_2$), 2.04–2.18 (m, 1H; COCH$_2$CH*H*), 2.43 (ddd, $^2J(H,H) = 17.8$, $^3J(H,H) = 9.5$ Hz, $^3J(H,H) = 2.7$ Hz, 1H; COC*H*H), 2.60 (ddd, $^2J(H,H) = 17.8$, $^3J(H,H) = 9.3$ Hz, $^3J(H,H) = 9.0$ Hz, 1H; COCH*H*), 3.84 (s, 3H; OCH_3), 4.16 (dddd, $^3J(H,H) \hat{=} {}^3J(H,H) = 8.8$ Hz, $^3J(H,H) = 3.2$ Hz, $^3J(H,H) = 1.7$ Hz, 1H; CHN); ^{13}C NMR (75.5 MHz): $\delta = 13.7$ (CH_3), 23.3 (CH_2), 25.1 (CH_2), 28.9 (CH_2), 29.0 (CH_2), 29.1 (CH_2), 31.0 (2 C, $(CH_2)_2$), 31.5 (*C*H$_2$CHN), 33.1 (CH_2), 33.3 (*C*H$_2$CON), 52.9 (OCH_3), 57.8 (CHN), 151.8 (*C*OOCH$_3$), 173.4 (CON); IR (film): $\tilde{\nu} = 2955$ cm^{-1} (s), 2925 (vs), 2855 (s, C−H), 1790 (s), 1755 (s), 1720 (vs, C=O), 1300 (m, C−H); MS (70 eV, EI), *m*/*z* (%): 269 (5) $[M]^+$, 142 (100) $[M-(CH_2)_8CH_3]^+$, 98 (53) $[C_5H_8NO]^+$, 41 (30) $[C_2H_3N]^+$; elemental analysis calcd (%) for $C_{15}H_{27}NO_3$ (269.38): C 66.88, H 10.10, N 5.20; found C 66.60, H 10.34, N 5.49.

(*R*)-*N*-Methoxycarbonyl-2-nonyl-2,3-dihydropyrrole (8d): General procedure A: A 1.0 M solution of $LiEt_3BH$ in THF (4.20 mL, 4.20 mmol) was added dropwise to a cooled solution of 2-pyrrolidinone **14** (1.05 g, 3.90 mmol) in CH_2Cl_2 (40 mL) at −78 °C. The reaction mixture was allowed to reach 0 °C and it was subsequently stirred for 4 h at this temperature. A 1M NaOH solution (6.00 mL, 6.00 mmol) and a 35 % H_2O_2 solution (3.0 mL) were added successively. The organic layer was separated and filtered through a Celite pad. The solution thus obtained was cooled to 0 °C. 2,2-Dimethoxypropane (2.55 g, 3.00 mL, 24.6 mmol) and camphorsulfonic acid (CSA) (75.0 mg, 0.30 mmol) were added. After 30 min a saturated aqueous $NaHCO_3$ solution (20 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were filtered through a Celite pad and concentrated in vacuo. The diastereomeric mixture of 2-methoxypyrrolidines was dissolved in CH_2Cl_2 (20 mL) and cooled to 0 °C. Diisopropylethylamine (0.68 g, 0.90 mL, 5.16 mmol) and TMSOTf (1.11 g, 0.90 mL, 4.80 mmol) were added successively. After 30 min the reaction was stopped by adding pentane (40 mL). The reaction mixture was filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography (PE/TBME = 90/10). A total of 602 mg (61 %) of dihydropyrrole **8d** was obtained as a colorless oil: $R_f = 0.55$ (P/TBME = 80:20); $[\alpha]_D^{25} = -245.7$ ($c = 2.0$ in $CHCl_3$); ^{1}H NMR (300 MHz): $\delta = 0.84$ (d, $^3J(H,H) = 6.6$ Hz, 3H; CH_3), 1.24–1.26 (m, 14H; $(CH_2)_7$), 1.47–1.84 (m, 2H; NCHC*H*$_2$(CH$_2$)$_7$), 2.21–2.27 (m, 1H; C*H*HCHCN), 2.74–2.80 (m, 1H; CH*H*CHCN), 3.69 (s, 3H; OCH_3), 3.96–4.06 (m, 1H; CH$_2$C*H*N), 4.86–4.94 (m, 1H; C*H*CHN), 8.36–6.48 (m, 1H; CHC*H*N); ^{13}C NMR (75.5 MHz): $\delta = 14.0$ (CH_3), 22.6 (CH_2), 24.4 (CH_2), 29.3 (CH_2), 29.5 (5 C, $(CH_2)_5$), 31.8 (CH*C*H$_2$CHN), 52.2 (OCH_3), 57.5 (CH$_2$*C*HN), 107.1 (*C*HCHN), 128.8 (CH*C*HN), 182.9 (*C*OOCH$_3$); IR (film): $\tilde{\nu} = 2955$ cm^{-1} (s), 2925 (vs), 2855 (s, C−H), 1750 (w), 1715 (s), 1620 (m, C=O), 1450 (s), 1395 (s), 1345 (sh), 1265 (m), 1135 (s, C−H); MS (70 eV, EI), *m*/*z* (%): 253 (9) $[M]^+$, 126 (100) $[C_9H_{18}]^+$, 67 (11) $[C_4H_5N]^+$, 41 (9) $[C_2H_3N]^+$; HRMS calcd (u) for $C_{15}H_{27}NO_2$ (253.38): 253.2042; found 253.2038.

(2*S*,3*S*,5*R*)-*N*-Methoxycarbonyl-2-benzyl-5-nonyl-3-pyrrolidinol (17): According to the typical hydrogenolysis procedure, oxetane **9d** (420 mg, 1.17 mmol) was cleaved hydrogenolytical in 3 h. Flash chromatography (P/TBME = 60:40) yielded 343 mg (81 %) pyrrolidinol **17** as a colorless oil. The analytical data were in accordance with those reported in the literature:[10a] $R_f = 0.17$ (P/EtOAc = 3:1); $[\alpha]_D^{25} = -69.5$ ($c = 2.5$ in $CHCl_3$); ^{1}H NMR (300 MHz): $\delta = 0.82$ (t, $^3J(H,H) = 6.9$ Hz, 3H; CH$_2$C*H*$_3$), 1.17–1.39 (m, 16H; $[CH_2]_8$), 1.54–1.68 (m, 1H; C*H*HCHOH), 1.97 (bs, 1H; OH), 2.17 (m, 1H; CH*H*CHOH), 2.89–2.94 (m, 2H; CH$_2$Ph), 3.48 (s, 3H; OCH_3), 3.67–3.74 (m, 1H; NC*H*CH$_2$), 4.10 (ddd, $^3J(H,H) \hat{=} {}^3J(H,H) \hat{=} {}^3J(H,H) = 6.8$ Hz, 1H; NC*H*CHOH), 4.23 (ddd, $^3J(H,H) \hat{=} {}^3J(H,H) \hat{=} {}^3J(H,H) = 6.6$ Hz, 1H; C*H*OH), 7.09–7.23 (m, 5H; Ph); ^{13}C NMR (75.5 MHz): $\delta = 14.0$ (CH$_2$*C*H$_3$), 22.6 (CH_2), 26.4 (CH_2), 29.3 (CH_2), 29.5 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 31.9 (CH$_2$Ph), 36.0 (CH_2), 36.4 (CH_2), 37.5 (*C*H$_2$CHOH), 52.0 (OCH_3), 56.8 (CHOH), 62.9 (N*C*HCH$_2$), 71.4 (*C*HCH$_2$Ph), 126.0 (C$_{ar}$), 128.3 (2C, C$_{ar}$), 129.4 (2C, C$_{ar}$), 139.4 (C$_{ar}$), 156.0 (NCOO).

(2*S*,3*S*,5*R*)-*N*-Methyl-2-benzyl-5-nonyl-3-pyrrolidinol [(+)-preussin] (1): A solution of pyrrolidinol **17** (147 mg, 407 mmol) in THF (4 mL) was added dropwise to a stirred solution of lithium aluminum hydride (75.9 mg, 2.00 mmol) in THF (10 mL). The reaction mixture was refluxed for 2 h, cooled to 0 °C, and quenched by addition of saturated aqueous NH_4Cl solution (5 mL). The aqueous phase was extracted with TBME (3 × 10 mL), then the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. The crude product was purified by flash chromatography (CH_2Cl_2/methanol = 9:1) to give 117 mg (91 %) of (+)-preussin (**1**) as a pale yellow oil: $R_f = 0.44$ (EtOAc); $[\alpha]_D^{25} = +22.1$ ($c = 1.0$ in $CHCl_3$); ^{1}H NMR (500 MHz): 0.88 (t, $^3J(H,H) = 6.9$ Hz, 3H; CH$_2$C*H*$_3$), 1.19–1.34 (m, 16H; $(CH_2)_8$), 1.42 (ddd, $^2J(H,H) = 13.9$ Hz, $^3J(H,H) = 6.4$ Hz, $^3J(H,H) = 1.2$ Hz, 1H; C*H*HCHOH), 1.73 (s, 1H; OH), 2.10–2.13 (m, 1H; NC*H*CH$_2$), 2.21 (ddd, $^2J(H,H) = 13.9$ Hz, $^3J(H,H) = 9.1$ Hz, $^3J(H,H) = 6.6$ Hz, 1H; CH*H*CHOH), 2.27 (ddd, $^3J(H,H) = 10.2$ Hz, $^3J(H,H) \hat{=} {}^3J(H,H) = 4.3$ Hz, 1H; C*H*CH$_2$Ph), 2.34 (s, 3H; CH_3), 2.84 (dd, $^2J(H,H) = 13.3$ Hz, $^3J(H,H) = 4.3$ Hz, 1H; C*H*HPh), 2.91 (dd, $^2J(H,H) = 13.3$ Hz, $^3J(H,H) = 10.2$ Hz, 1H; CH*H*Ph), 3.83–3.87 (m, 1H; C*H*OH), 7.16–7.31 (m, 5H; Ph); ^{13}C NMR (125.5 MHz): 14.1 (CH$_2$*C*H$_3$), 22.6 (CH_2), 26.3 (CH_2), 29.3 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.8 (CH_2), 31.9 (CH$_2$Ph), 33.5 (CH_2), 34.8 (CH_2), 38.6 (NCH$_3$), 39.4 (*C*H$_2$CHOH), 65.9 (N*C*HCH$_2$), 70.3 (CHOH), 73.7 (*C*HCH$_2$Ph), 126.0 (C$_{ar}$), 128.3 (2C, C$_{ar}$), 129.3 (2C, C$_{ar}$), 139.4 (C$_{ar}$); IR (film): $\tilde{\nu} = 3430$ cm^{-1} (s, b, OH), 3065 (w), 3030 (w), 2960 (m), 2925 (s), 2855 (s), 2790 (m, C−H), 1495 (w), 1455 (s, C−H); MS (70 eV, EI); m/z (%): 317 (0.1) $[M]^+$, 316 (0.7) $[M-H]^+$, 227 (15) $[M-{}^{13}CC_6H_7]^+$, 226 (100) $[M-C_7H_7]^+$; HRMS calcd (u) for $C_{21}H_{35}NO$ (317.51): 317.2719, found 317.2711.

(2*S*,3*S*,5*R*)-*N*-Methoxycarbonyl-2-benzyl-5-methyl-3-pyrrolidinol (18): The reaction was carried out as described for the typical hydrogenolysis procedure, starting from oxetane **9a** on a 0.16-mmol scale. The crude product was purified by flash chromatography (P/TBME = 80/20). A total of 36 mg (89 %) of pyrrolidinol **18** was obtained as a colorless oil: $R_f = 0.42$ (TBME); $[\alpha]_D^{25} = -48.1$ ($c = 2.1$ in $CHCl_3$); ^{1}H NMR (400 MHz): $\delta = 1.34$ (t, $^3J(H,H) = 6.3$ Hz, 3H; CH_3), 1.60–1.69 (m, 1H; C*H*HCHOH), 2.24–2.30 (m, 1H; CH*H*CHOH), 2.94–3.01 (m, 2H; C*H*$_2$Ph), 3.55 (s, 3H; OCH_3), 3.87 (m, 1H; C*H*CH$_3$), 4.14 (dd, $^3J(H,H) = 13.7$ Hz, $^3J(H,H) = 6.8$ Hz, 1H; C*H*CH$_2$Ph), 4.28 (dd, $^3J(H,H) = 13.7$ Hz, $^3J(H,H) = 6.7$ Hz, 1H; C*H*OH), 7.15–7.31 (m, 5H; Ph); ^{13}C NMR (100 MHz): $\delta = 22.2$ (CH_3), 35.9 (*C*H$_2$Ph), 39.5 (*C*H$_2$CHOH), 52.0 (OCH_3), 52.4 (*C*HCH$_3$), 63.1 (*C*HCH$_2$Ph), 71.3 (CHOH), 126.1 (C$_{ar}$), 128.3 (2C, C$_{ar}$), 129.7 (2C, C$_{ar}$), 139.4 (C$_{ar}$), 156.1 (*C*OOCH$_3$); IR (film): $\tilde{\nu} = 3435$ cm^{-1} (s, OH), 3060 (m), 3030 (m, C$_{ar}$−H), 2930 (s, C−H), 1675 (vs, C=O), 1455 (m), 1130 (m, C−H);

MS (70 eV, EI), m/z (%): 249 (0.4) $[M]^+$, 158 (100) $[M-\mathrm{CH_2Ph}]^+$, 91 (6) $[\mathrm{C_7H_7}]^+$, 42 (17) $[\mathrm{C_2H_4N}]^+$; HRMS calcd (u) for $\mathrm{C_{14}H_{19}NO_3}$ (249.31): 249.1365; found: 249.1371.

(2*R*,3*R*,5*R*)-*N*-Methoxycarbonyl-2-benzyl-5-nonyl-3-pyrrolidinol (19): According to the typical hydrogenolysis procedure, oxetane **10d** (25.1 mg, 0.07 mmol) was cleaved hydrogenolytical in 3 h. Flash chromatography (P/TBME = 60:40) yielded 22.3 mg (88%) pyrrolidinol **19** as a colorless oil: $R_f = 0.33$ (P/EtOAc = 3:1); $[\alpha]_D^{25} = +13.7$ ($c = 1.9$ in $\mathrm{CHCl_3}$); ^{1}H NMR (300 MHz): $\delta = 0.88$ (t, ^3J(H,H) = 6.8 Hz, 3H; $\mathrm{CH_2C}\mathit{H}_3$), 1.18–1.36 (m, 16H; $\mathrm{(CH_2)_8}$), 1.57 (s, 1H; OH), 1.76–1.91 (m, 2H; $\mathrm{CH_2CHOH}$), 2.89–3.04 (m, 2H; $\mathrm{CH_2Ph}$), 3.67–3.78 (m, 1H; $\mathrm{NC}\mathit{H}\mathrm{CH_2}$), 3.68 (s, 3H; $\mathrm{OCH_3}$), 4.15 (ddd, ^3J(H,H) $\hat{=}$ ^3J(H,H) $\hat{=}$ ^3J(H,H) = 6.1 Hz, 1H; $\mathrm{NC}\mathit{H}\mathrm{CHOH}$), 4.46 (ddd, ^3J(H,H) = 10.3 Hz, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 6.9 Hz, 1H; $\mathrm{C}\mathit{H}\mathrm{OH}$), 7.15–7.29 (m, 5H; Ph); ^{13}C NMR (75.5 MHz): $\delta = 14.1$ ($\mathrm{CH_2}\mathit{C}\mathrm{H_3}$), 22.6 ($\mathrm{CH_2}$), 26.3 ($\mathrm{CH_2}$), 29.3 ($\mathrm{CH_2}$), 29.4 ($\mathrm{CH_2}$), 29.5 ($\mathrm{CH_2}$), 29.6 ($\mathrm{CH_2}$), 31.9 ($\mathrm{CH_2Ph}$), 35.7 ($\mathrm{CH_2}$), 36.2 ($\mathrm{CH_2}$), 37.5 ($\mathit{C}\mathrm{H_2CHOH}$), 52.0 ($\mathrm{OCH_3}$), 55.5 (CHOH), 61.7 ($\mathrm{N}\mathit{C}\mathrm{HCH_2}$), 70.8 ($\mathit{C}\mathrm{HCH_2Ph}$), 126.1 ($\mathrm{C_{ar}}$), 128.3 (2C, $\mathrm{C_{ar}}$), 129.7 (2C, $\mathrm{C_{ar}}$), 139.9 ($\mathrm{C_{ar}}$), 155.1 (NCOO); IR (film): $\tilde{\nu} = 3420$ cm^{-1} (s, OH), 3060 (m), 2955 (m, $\mathrm{C_{ar}{-}H}$), 2925 (s, C–H), 1655 (vs, C=O), 1450 (m), 1190 (m), 1120 (w), 1075 (m, C–H); MS (70 eV, EI); m/z (%): 270 (100) $[M-\mathrm{C_7H_7}]^+$, 254 (21) $[\mathrm{C_{22}H_{35}NO_2}]^+$, 128 (73) $[\mathrm{C_6H_{12}NO_2}]^+$, 41 (20) $[\mathrm{C_2H_3N}]^+$, 28 (29) $[\mathrm{CO}]^+$; HRMS calcd (u) for $\mathrm{C_{15}H_{29}NO_3}$ ($[M\text{-}\mathrm{C_7H_7}]^+$): 270.2069, found 270.2064.

(2*S*,3*S*,5*R*)-*N*-Methyl-2,5-dibenzyl-3-pyrrolidinol (20): The reaction was carried out as described in typical hydrogenolysis procedure starting from oxetane **9c** on a 0.53-mmol scale. The crude product was dissolved in THF (25 mL) and lithium aluminum hydride (95.0 mg, 2.50 mmol) was added at 0 °C. The reaction mixture was refluxed for 3 h and quenched at 0 °C by addition of saturated aqueous $\mathrm{NH_4Cl}$ solution (10 mL). TBME (50 mL) was added and the layers were separated. The aqueous phase was extracted with TBME (3 × 20 mL); the combined organic layers were dried with $\mathrm{MgSO_4}$ and concentrated in vacuo. The crude product was purified by flash chromatography (hexane/EtOAc = 3:1). A total of 107 mg (72%) of pyrrolidinol **20** was obtained as a colorless solid: $R_f = 0.32$ (EtOAc); $[\alpha]_D^{25} = +23.6$ ($c = 1.0$ in $\mathrm{CHCl_3}$); m.p. 79 °C; ^{1}H NMR (300 MHz): $\delta = 1.50$ (ddd, ^2J(H,H) = 14.4 Hz, ^3J(H,H) = 6.0 Hz, ^3J(H,H) = 1.2 Hz, 1H; $\mathrm{C}\mathit{H}\mathrm{HCHOH}$), 1.64 (brs, 1H; OH), 2.33 (ddd, ^2J(H,H) = 14.4 Hz, ^3J(H,H) = 9.3 Hz, ^3J(H,H) = 6.4 Hz, 1H; $\mathrm{CH}\mathit{H}\mathrm{CHOH}$), 2.33 (dt, ^3J(H,H) = 3.6 Hz, ^3J(H,H) = 7.5 Hz, 1H; $\mathrm{C}\mathit{H}\mathrm{CHOH}$), 2.44 (s, 3H; $\mathrm{CH_3}$), 2.48–2.56 (m, 1H; $\mathrm{NCHCH_2}$), 2.64 (dd, ^2J(H,H) = 13.2 Hz, ^3J(H,H) = 8.5 Hz, 1H; $\mathrm{C}\mathit{H}\mathrm{HPh}$), 2.84 (d, ^3J(H,H) = 7.5 Hz, 2H; $\mathrm{C}\mathit{H}_2\mathrm{CHCHOH}$), 3.00 (dd, ^2J(H,H) = 13.2 Hz, ^3J(H,H) = 3.7 Hz, 1H; $\mathrm{CH}\mathit{H}\mathrm{Ph}$), 3.69–3.71 (m, 1H; $\mathrm{C}\mathit{H}\mathrm{OH}$), 7.18–7.29 (m, 10H; 2Ph); ^{13}C NMR (75.5 MHz): $\delta = 33.8$ ($\mathit{C}\mathrm{H_2Ph}$), 38.1 ($\mathit{C}\mathrm{H_2Ph}$), 38.6 ($\mathrm{CH_3}$), 40.8 ($\mathit{C}\mathrm{H_2CHOH}$), 66.4 ($\mathrm{CH_2}\mathit{C}\mathrm{HN}$), 70.3 (CHOH), 73.3 ($\mathrm{CHOH}\mathit{C}\mathrm{HN}$), 126.0 ($\mathrm{C_{ar}}$), 126.1 ($\mathrm{C_{ar}}$), 128.2 (2C, $\mathrm{C_{ar}}$), 128.3 (2C, $\mathrm{C_{ar}}$), 129.2 (2C, $\mathrm{C_{ar}}$), 129.6 (2C, $\mathrm{C_{ar}}$), 139.0 ($\mathrm{C_{ar}}$), 139.4 ($\mathrm{C_{ar}}$); IR (KBr): $\tilde{\nu} = 3465$ cm^{-1} (vs, OH), 3025 (m), 3030 (m, $\mathrm{C_{ar}{-}H}$), 2975 (m), 2920 (m), 2780 (m, C–H), 1495 (m), 1450 (m), 1030 (m), 935 (m), 755 (m), 700 (s, C–H); MS (70 eV, EI), m/z (%): 280 (0.6) $[M-\mathrm{H}]^+$, 190 (100) $[M-\mathrm{C_7H_7}]^+$, 174 (27) $[\mathrm{C_{12}H_{15}N}]^+$, 91 (35) $[\mathrm{C_7H_7}]^+$; HRMS calcd (u) for $\mathrm{C_{19}H_{22}NO}$ ($[M^+-\mathrm{H}]$): 280.1701; found: 280.1707.

***N*-Methoxycarbonyl-4,5,6-trihydropyridine (21)**: The reaction was carried out folowing general procedure A starting from *N*-methoxycarbonyl-2-piperidinone[44] on a 20-mmol scale. After work-up, the residue was purified by flash chromatography (P/TBME = 90:10). A total of 1.78 g (63%) of trihydropyridine **21** was obtained as a colorless oil. The analytical data were in accordance with those reported in the literature:[45] $R_f = 0.62$ (TBME); ^{1}H NMR (300 MHz): $\delta = 1.72$–2.05 (m, 4H; $\mathrm{NCH_2}\mathit{CH_2CH_2}$), 3.48–3.61 (m, 2H; $\mathrm{N}\mathit{CH_2}$), 3.71 (s, 3H; $\mathrm{OCH_3}$), 4.77–4.98 (m, 1H; $\mathrm{NCHC}\mathit{H}$), 6.69 [6.83] (d, 1H; ^3J(H,H) = 8.3 Hz; NCH); ^{13}C NMR (75.5 MHz): $\delta = 21.4$ [21.2] ($\mathrm{NCH_2}\mathit{C}\mathrm{H_2}$), 21.6 ($\mathrm{NCHCH}\mathit{C}\mathrm{H_2}$), 42.3 [42.1] ($\mathrm{NCH_2}$), 52.8 ($\mathrm{OCH_3}$), 106.2 [106.4] ($\mathrm{NCH}\mathit{C}\mathrm{H}$), 125.3 [124.9] ($\mathrm{N}\mathit{C}\mathrm{HCH}$), ^{13}C signal for NCOO was not obtained.

(2*SR*,3*SR*)-*N*-Methoxycarbonyl-2-benzyl-3-piperidinol (23): According to the typical hydrogenolysis procedure oxetane **21** (65.0 mg, 0.19 mmol) was cleaved hydrogenolytically in 2 h. Flash chromatography (P/TBME = 80:20) yielded 49.0 mg (88%) piperidinol **23** as a colorless oil: $R_f = 0.13$ (P/TBME = 40:60); ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): $\delta = 1.22$–1.91 (m, 4H; $\mathrm{NCH_2}\mathit{CH_2CH_2}$), 2.79 (d, ^2J(H,H) = 11.2 Hz, 1H; $\mathrm{CH}\mathit{H}\mathrm{Ph}$), 2.83 (d, ^2J(H,H) = 11.2 Hz, 1H; $\mathrm{C}\mathit{H}\mathrm{HPh}$), 2.93 (ddd, ^2J(H,H) = 13.9 Hz, ^3J(H,H) $\hat{=}$ ^3J(H,H) = 2.9 Hz, 1H; $\mathrm{NC}\mathit{H}\mathrm{H}$), 3.03 (dd, ^2J(H,H) = 13.9 Hz, ^2J(H,H) = 3.8 Hz, 1H; $\mathrm{NCH}\mathit{H}$), 3.33 (s, 3H; $\mathrm{OCH_3}$), 3.82–3.92 (m, 1H; NCH), 3.92–4.04 (m, 1H; $\mathrm{C}\mathit{H}\mathrm{OH}$), 4.60 (s, 1H; OH), 7.13–7.29 (m, 5H; Ph); ^{13}C NMR (75.5 MHz, $\mathrm{CDCl_3}$): $\delta = 24.2$ ($\mathrm{NCH_2}\mathit{C}\mathrm{H_2}$), 27.8 ($\mathit{C}\mathrm{H_2CHOH}$), 29.5 ($\mathrm{CH_2Ph}$), 37.8 (CHN), 41.5 ($\mathrm{NCH_2}$), 52.2 ($\mathrm{OCH_3}$), 69.2 (CHOH), 126.0 ($\mathrm{C_{ar}}$), 128.2 (2C, $\mathrm{C_{ar}}$), 129.1 (2C, $\mathrm{C_{ar}}$), 138.9 ($\mathrm{C_{ar}}$), 156.2 (NCOO); IR (film): $\tilde{\nu} = 3430$ cm^{-1} (s, b, OH), 3085 (w), 3065 (w), 3030 (w), 2955 (m), 2935 (s), 2870 (s, C–H), 1680 (s, C=O), 1455 (s, C–H); MS (EI), m/z (%): 249 (0.7) $[M]^+$, 158 (100) $[M-\mathrm{C_7H_7}]^+$, 142 (24) $[M-\mathrm{C_7H_7O}]^+$, 126 (88) $[M-\mathrm{PhCHO}-\mathrm{CH_3}]^+$, 91 (19) $[\mathrm{C_7H_7}]^+$; HRMS calcd (u) for $\mathrm{C_{14}H_{19}NO_3}$ (249.31): 249.1365; found 249.1361.

Acknowledgements

This project was supported by the Deutsche Forschungsgemeinschaft (Ba 1372-3/1 and 3/2) and by the Fonds der Chemischen Industrie. We would like to thank Christian Jasper (undergraduate research participant) for skilful technical assistance. The donation of chemicals by Witco GmbH and Degussa-Hüls AG is gratefully acknowledged.

[1] E. Winterfeldt, *Stereoselektive Synthese—Prinzipien und Methoden*, Vieweg, Braunschweig, **1988**, pp. 13–29.

[2] a) E. Paternò, G. Chieffi, *Gazz. Chim. Ital.* **1909**, *39–1*, 341–361; b) G. Büchi, C. G. Inman, E. S. Lipinsky, *J. Am. Chem. Soc.* **1954**, *76*, 4327–4331.

[3] Reviews: a) J. Mattay, R. Conrads, R. Hoffmann, in *Methoden Org. Chem. (Houben-Weyl) 4th ed., Vol. E21c* (Eds.: G. Helmchen, R. W. Hoffmann, J. Mulzer, E. Schaumann), Thieme, Stuttgart, **1995**, pp. 3133–3178; b) J. A. Porco, S. L. Schreiber, in *Comprehensive Organic Synthesis, Vol. 5* (Ed.: B. Trost), Pergamon, Oxford, **1991**, pp. 151–192; c) H. A. J. Carless, in *Synthetic Organic Photochemistry* (Ed.: W. M. Horspool), Plenum, New York, **1984**, pp. 425–487; c) G. Jones II, in *Organic Photochemistry, Vol. 5* (Ed.: A. Padwa), Dekker, New York, **1981**, pp. 1–123.

[4] Reviews: a) T. Bach, *Synthesis* **1998**, 683–703; b) T. Bach, *Liebigs Ann./Recueil* **1997**, 1627–1634.

[5] D. R. Morton, R. A. Morge, *J. Org. Chem.* **1978**, *43*, 2093–2101.

[6] a) T. Bach, *Tetrahedron Lett.* **1994**, *35*, 1855–1858; b) T. Bach, *Liebigs Ann.* **1995**, 1045–1053.

[7] a) T. Bach, K. Jödicke, K. Kather, R. Fröhlich, *J. Am. Chem. Soc.* **1997**, *119*, 2437–2445; b) T. Bach, F. Eilers, K. Kather, *Liebigs Ann./Recueil* **1997**, 1529–1536.

[8] a) T. Bach, *Angew. Chem.* **1996**, *108*, 976–977; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 884–886; b) T. Bach, J. Schröder, *Tetrahedron Lett.* **1997**, *38*, 3707–3710; c) T. Bach, J. Schröder, *Liebigs Ann./Recueil* **1997**, 2265–2267; d) T. Bach, J. Schröder, T. Brandl, J. Hecht, K. Harms, *Tetrahedron* **1998**, *54*, 4507–4520; e) J. Schröder, T. Bach, *J. Inf. Recording* **1998**, *24*, 285–288; f) T. Bach, J. Schröder, *J. Org. Chem.* **1999**, *64*, 1265–1273.

[9] a) R. E. Schwartz, J. Liesch, O. Hensens, L. Zitano, S. Honeycutt, G. Garrity, R. A. Fromtling, J. Onishi, R. Monaghan, *J. Antibiot.* **1988**, *41*, 1774–1779; b) J. H. Johnson, D. W. Phillipson, A. D. Kahle, *J. Antibiot.* **1989**, *42*, 1184–1185.

[10] Previous syntheses: a) C. S. Pak, G. H. Lee, *J. Org. Chem.* **1991**, *56*, 1128–1133; b) M. Shimazaki, F. Okazaki, F. Nakajima, T. Ishikawa, A. Ohta, *Heterocycles* **1993**, *36*, 1823–1836; c) P. L. McGrane, T. Livinghouse, *J. Am. Chem. Soc.* **1993**, *115*, 11485–11489; d) M. Overhand, S. M. Hecht, *J. Org. Chem.* **1994**, *59*, 4721–4722; e) W. Deng, L. E. Overman, *J. Am. Chem. Soc.* **1994**, *116*, 11241–11250; f) H. Yoda, H. Yamazaki, K. Takabe, *Tetrahedron Asymmetry* **1996**, *7*, 373–374; g) C. Beier, E. Schaumann, *Synthesis* **1997**, 1296–1300; h) R. Verma, S. K. Ghosh, *Chem. Commun.* **1997**, 1601–1602; i) P. de Armas, F. Garcia-Tellado, J. J. Marrero-Tellado, J. Robles, *Tetrahedron Lett.* **1998**, *39*, 131–134; j) A. Kanazawa, S. Gillet, P. Delair, A. E. Greene, *J. Org. Chem.* **1998**, *63*, 4660–4663; k) R. Verma, S. K. Ghosh, *J. Chem. Soc. Perkin Trans. 1* **1999**, 265–270.

[11] K. Sakamoto, E. Tsuji, F. Abe, T. Nakanishi, M. Yamashita, N. Shigematsu, S. Izumi, M. Okuhara, *J. Antibiot.* **1996**, *49*, 37–44.

[12] Synthesis: B. B. Snider, H. Lin, *J. Am. Chem. Soc.* **1999**, *121*, 7778–7786.

0947-6539/00/0620-3847 $ 17.50+.50/0

[13] Preliminary communication: T. Bach, H. Brummerhop, *Angew. Chem.* **1998**, *110*, 3577–3579; *Angew. Chem. Int. Ed.* **1998**, *37*, 3400–3402.

[14] R. K. Dieter, R. R. Sharma, *J. Org. Chem.* **1996**, *61*, 4180–4184.

[15] T. Bach, H. Brummerhop, *J. Prakt. Chem.* **1999**, *341*, 312–315.

[16] D. F. Oliveira, P. C. M. L. Miranda, C. R. D. Correia, *J. Org. Chem.* **1999**, *64*, 6646–6652.

[17] T. Bach, H. Brummerhop, *J. Prakt. Chem.* **1999**, *341*, 410–413.

[18] A. G. Griesbeck, H. Mauder, S. Stadtmüller, *Acc. Chem. Res.* **1994**, *27*, 70–75.

[19] T. Bach, K. Jödicke, *Chem. Ber.* **1993**, *126*, 2457–2466.

[20] Crystal data of compound **5c** ($C_{16}H_{23}NO_3$, $M_r = 277.35$): crystal size 0.5 × 0.3 × 0.15 mm, monoclinic, space group $P2(1)/c$, $a = 1331.8(1)$, $b = 683.6(1)$, $c = 1731.8(1)$ pm, $U = 1567.90(12)\,\text{Å}^3$, $\rho_c = 1.175\,\text{g}\,\text{cm}^{-3}$ for $Z = 4$, $F(000) = 600$, $\mu = 0.648\,\text{mm}^{-1}$, Enraf–Nonius CAD4 diffractometer, $\lambda = 1.54178$ Å, ω-scan, 3109 reflections ($-h$, $+k$, $\pm l$), $\Theta_{\max} = 69.85°$, 2976 independent and 2454 observed reflections [$F \geq 4\sigma(F)$], 274 refined parameters, $R = 0.0397$, $wR^2 = 0.1093$, max. residual electron density $0.207\,\text{e}\,\text{Å}^{-3}$, direct methods, hydrogen atoms located. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-142647. 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..

[21] T. Bach, *Liebigs Ann.* **1995**, 855–866.

[22] T. Shono, Y. Matsumura, K. Tsubata, Y. Sugihara, S.-i. Yamane, T. Kanazawa, T. Aoki, *J. Am. Chem. Soc.* **1982**, *104*, 6697–6703.

[23] M. J. S. Carpes, P. C. M. L. Miranda, C. R. D. Correia, *Tetrahedron Lett.* **1997**, *38*, 1869–1872.

[24] D. F. Oliveira, E. A. Severino, C. R. D. Correia, *Tetrahedron Lett.* **1999**, *40*, 2083–2086.

[25] C. Rivas, R. A. Bolivar, *J. Heterocyclic Chem.* **1976**, *13*, 1037–1040.

[26] Tosyloxydehydroxylation: E. Hardegger, H. Ott, *Helv. Chim. Acta* **1955**, *38*, 312–320.

[27] Bromodehydroxylation: R. B. Silverman, M. A. Levy, *J. Org. Chem.* **1980**, *45*, 815–818.

[28] Alkyldetosyloxylation: a) J. Ackermann, M. Matthes, C. Tamm, *Helv. Chim. Acta* **1990**, *73*, 122–132; b) M. Matthes, C. Tamm, *Helv. Chim. Acta* **1991**, *74*, 1585–1590.

[29] Hydrodebromination: M. Otsuka, T. Masuda, A. Haupt, M. Ohno, T. Shiraki, Y. Sugiura, K. Maeda, *J. Am. Chem. Soc.* **1990**, *112*, 838–845.

[30] *N*-Methoxycarbonylation: T. W. Greene, P. G. Wuts, *Protective Groups in Organic Syntheses*, 3rd ed., Wiley, New York, **1999**, p. 504.

[31] C. Sonesson, M. Larhed, C. Nyqvist, A. Hallberg, *J. Org. Chem.* **1996**, *61*, 4756–4763.

[32] The force-field calculations (MM3*) were performed with Macromodel 4.5 software (G. Chang, W. C. Guida, W. C. Still, *J. Am. Chem. Soc.* **1989**, *111*, 4379–4386). We thank Dipl.-Chem. Trixi Brandl and Dr. Thomas Trieselmann (AK Hoffmann) for performing these calculations.

[33] Information as to the selectivity-determining step can be drawn from Eyring plots of the facial diastereoselectivity: H. Buschmann, H.-D. Scharf, N. Hoffmann, M. W. Plath, J. Runsink, *J. Am. Chem. Soc.* **1989**, *111*, 5367–5373.

[34] F. Johnson, *Chem. Rev.* **1968**, *68*, 375–413.

[35] R. W. Hoffmann, *Chem. Rev.* **1989**, *89*, 1841–1860.

[36] C. H. Larsen, B. H. Ridgway, J. T. Shaw, K. A. Woerpel, *J. Am. Chem. Soc.* **1999**, *121*, 12208–12209.

[37] a) P. Renaud, D. Seebach, *Helv. Chim. Acta* **1986**, *69*, 1704–1710; b) M. Thaning, L.-G. Wistrand, *Acta Chem. Scand.* **1989**, *43*, 290–295; c) M. Skrinjar, L.-G. Wistrand, *Tetrahedron Lett.* **1990**, *31*, 1775–1778.

[38] G. Stoll, J. Frank, H. Musso, H. Henke, W. Herrendorf, *Liebigs Ann. Chem.* **1986**, 1968–1989.

[39] Crystal data of compound **20** ($C_{19}H_{23}NO$, $M_r = 281.38$): crystal size 1.32 × 0.18 × 0.06 mm, monoclinic, space group $P2(1)$, $a = 1165.7(2)$, $b = 532.2(1)$, $c = 1348.3(3)$ pm, $U = 796.3(3)\,\text{Å}^3$, $\rho_c = 1.174\,\text{g}\,\text{cm}^{-3}$ for $Z = 2$, $F(000) = 304$, $\mu = 0.072\,\text{mm}^{-1}$, Stoe IPDS diffractometer, $\lambda = 0.71073$ Å, ω-scan, 3530 reflections ($-h$, $+k$, $\pm l$), $\Theta_{\max} = 21.0°$, 1706 independent and 1104 observed reflections [$F \geq 4\sigma(\text{F})$], 195 refined parameters, $R = 0.0644$, $wR^2 = 0.1586$, residual electron density $0.240\,\text{e}\,\text{Å}^{-3}$, direct methods, hydrogen atoms calculated. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-142648.

[40] A. G. Griesbeck, S. Stadtmüller, *J. Am. Chem. Soc.* **1990**, *112*, 1281–1283.

[41] H. A. J. Carless, D. J. Haywood, *J. Chem. Soc. Chem. Commun.* **1980**, 1067–1068.

[42] a) A. G. Griesbeck, S. Stadtmüller, *Chem. Ber.* **1990**, *123*, 357–362; b) A. G. Griesbeck, S. Stadtmüller, *J. Am. Chem. Soc.* **1991**, *113*, 6923–6928; c) A. G. Griesbeck, H. Mauder, K. Peters, E.-M. Peters, H. G. von Schnering, *Chem. Ber.* **1991**, *124*, 407–410.

[43] G. A. Kraus, K. Neuenschwander, *J. Org. Chem.* **1981**, *46*, 4791–4792.

[44] D. de Oliveira Imbroisi, N. S. Simpkins, *J. Chem. Soc. Perkin Trans. 1* **1991**, 1815–1823.

[45] T. Shono, H. Hamaguchi, Y. Matsumura, *J. Am. Chem. Soc.* **1975**, *97*, 4264–4268.

Received: April 10, 2000 [F2414]