Photocycloaddition of *N*-Acyl Enamines to Aldehydes and Its Application to the Synthesis of Diastereomerically Pure 1,2-Amino Alcohols

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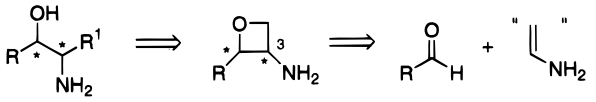
The regio- and stereoselective synthesis of the protected *cis*-3-aminooxetanes *cis*-**5** and *cis*-**7** is reported. The oxetanes were obtained by the photocycloaddition of aliphatic (**6c**−**e**) and aromatic (**4**, **6a**) aldehydes to the corresponding enamides (**1a**−**d**,**h**) or enecarbamates (**1e**−**g**). The enamine derivatives used in the Paternò−Büchi reaction were either commercially available or prepared from the corresponding acetaldehyde imines **2** by acylation. The oxetane formation proceeded with good-to-excellent simple diastereoselectivity for aromatic aldehydes (56−82% yield) and moderate selectivity for aliphatic aldehydes (46−55% yield). The *cis*-3-aminooxetanes are precursors for *syn*- and *anti*-1,2-amino alcohols. The relative configuration established in the photochemical step was retained upon nucleophilic ring opening between the oxygen atom and carbon atom C-4. By this means, *syn*-1,2-amino alcohols such as **8** and **10** were available in good yields. In contrast, the *N*-Boc-protected *cis*-3-aminooxetanes *cis*-**5e** and *cis*-**5f** were transformed into *anti*-1,2-amino alcohols. Upon treatment with trifluoroacetic acid, they underwent an intramolecular nucleophilic substitution at the carbon atom C-2 of the oxetane and the oxazolidinones **11** and **12** were formed. Because the substitution occurs with inversion of configuration, *anti*-1,2-amino alcohols, e.g., ephedrine (**15**), are accessible.

Introduction

3-Heteroatom-substituted oxetanes are versatile synthetic building blocks that can be transformed into 1,2-difunctional or 1,2,3-trifunctional compounds by subsequent ring-opening reactions.[1] The Paternò−Büchi reaction[2] of 3-heteroatom-substituted alkenes and aldehydes represents a short and straightforward route to these heterocycles.[3] As a result of the photochemical "umpolung" of the carbonyl compound, a 1,2-connectivity of the former carbonyl carbon atom and the former α-carbon atom of the alkene, which is more difficult to attain by other methods, is established. In this respect, enamines may serve as precursors for 3-aminooxetanes, which in turn can be further used for the synthesis of 1,2-amino alcohols[4] (Scheme 1).

Scheme 1



Prior to our work, some studies were reported in regard to the search for suitably protected cyclic or acyclic enamines that undergo the Paternò−Büchi reaction with good regio- and stereocontrol. Typical enamines derived from secondary amines had proven unsuited for the photochemical aminooxetane formation.[5] 1,3-Oxazoline and its derivatives reacted well with aldehydes in a [2 + 2] photocycloaddition, but the regioselectivity was not satisfactory.[6] *N*-Substituted pyrroles gave almost exclusively 1,3-difunctional 2-aminooxetanes.[7] The consecutive

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(3) Review on synthetic applications: Bach, T. *Synthesis* **1998**, 683.

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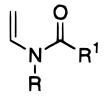
reactions of these adducts with an additional equivalent of aldehyde delivered 3-aminooxetanes, but the reaction was not exploited any further.[7c] Good regio- and stereoselectivities were observed in the Paternò–Büchi reaction of α-aminoacrylonitriles with benzil and its derivatives.[8] The 3-amino-3-cyanooxetanes so obtained are less suited for applications in stereoselective synthesis, however.

Our approach to 3-aminooxetanes was based on the use of acceptor-substituted enamines, which we hoped would be electron-rich enough to account for the addition of the photoexcited carbonyl compound and which should be electron-deficient enough to avoid side reactions based on a single electron transfer (SET). Indeed, it turned out that *N*-acyl- and *N*-alkoxycarbonyl-protected enamines (enamides and enecarbamates) are excellent substrates for the Paternò–Büchi reaction. They react cleanly with a variety of aldehydes to the corresponding oxetanes, and their addition products can be further manipulated in several ways. The following report gives a full account on the preparation of these enamines, their photocycloaddition to aldehydes,[9] and the ring-opening reactions of 3-aminooxetanes to 1,2-amino alcohols.[10]

Results and Discussion

Preparation of Enamides and Enecarbamates. The structures of the alkene components used in this study are shown. *N*-Vinylformamide (**1a**) and *N*-vinylpyrrolidinone (**1h**) are industrially used monomer building blocks and are consequently commercially available. *N*-Vinylacetamide (**1b**) was obtained from vinyl isocyanate via a published procedure.[11] All other alkenes were prepared by the *N*-acylation of acetaldehyde imines. For the acetylation, we followed the procedure by Breederveld in which acetic anhydride was used as the acylating agent.[12] In an analogous fashion, the *tert*-butyloxycarbonylation (*tert*-butyloxycarbonyl = Boc) could be conducted with Boc_2O and NEt_3 in benzene or toluene. By this means, the enecarbamates **1e** and **1f** were obtained from the imines **2a** and **2b** in 80% and 69% yield (Scheme 2). Attempts to use alkoxycarbonyl chlorides as *N*-acylation agents did not give satisfactory results.

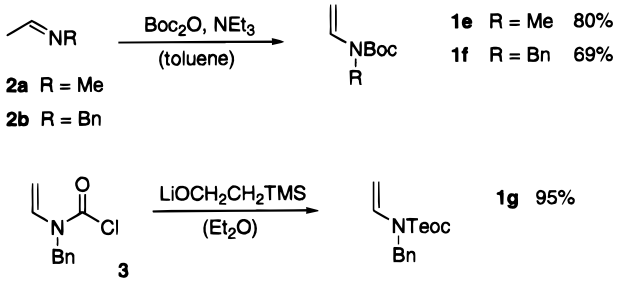


1

a R = H R^1 = H **e** R = Me R^1 = O*t* Bu
b R = H R^1 = Me **f** R = Bn R^1 = O*t* Bu
c R = Bn R^1 = Me **g** R = Bn R^1 = OCH_2CH_2TMS
d R = Pr R^1 = Me **h** R, R^1 = $CH_2CH_2CH_2$

The 2-trimethylsilylethyloxycarbonyl (Teoc)-protected enamine **1g** was available from carbamoyl chloride **3**, which in turn was synthesized by the reaction of aldimine **2b** with diphosgene ($Cl_3COCOCl$) according to a published procedure (Scheme 2).[13]

Scheme 2



Scheme 3

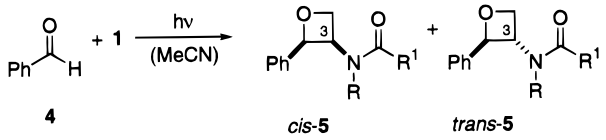


Table 1. Photocycloaddition of Alkenes 1 to Benzaldehyde (4) in Acetonitrile Solution

entry	alkene[a]	time[b] [h]	product	d.r.[c]	yield[d] [%]
1	**1a**	18	**5a**	71/29	74
2	**1b**	120	**5b**	79/21	58[e]
3	**1c**	14	**5c**	89/11	81
4	**1d**	14	**5d**	>90/10	71
5	**1e**	14	**5e**	90/10	56
6	**1f**	14	**5f**	87/13	77
7	**1g**	14	**5g**	>90/10	74
8	**1h**	18	**5h**	88/12	82

[a] In most cases an excess (2 equiv) of alkene was used (see the Experimental Section). [b] Irradiation time. [c] Diastereomeric ratio *cis*-**5**/*trans*-**5** as determined from GLC and ^{1}H NMR analysis of the crude product mixture. [d] Yield of isolated oxetane product. In most cases, the *cis*-isomer *cis*-**5** strongly prevails (d.r. = ≥90/10), although a complete separation could not always be achieved (for the precise diastereomeric composition of the isolated product see the Experimental Section). [e] The yield relative to the converted amount of benzaldehyde is 79%.

Oxetane Formation. The Paternò–Büchi reaction of *N*-acyl enamines **1** was first studied with benzaldehyde (**4**) as the carbonyl substrate. A clean photocycloaddition was observed, which yielded the corresponding 3-aminooxetanes **5** (Scheme 3, Table 1). The oxetanes were formed with good-to-excellent simple diastereoselectivity in favor of the *cis*-products. The relative configuraton was assigned on the basis of NOE and NOESY studies on oxetanes **5b**, **5c**, **5f**, and **5h**, the results of which are given in the Experimental Section. The correlations accomplished by ring-opening reactions (vide infra) further support the stereochemical assignments. Acetonitrile proved to be a superior solvent for the photocycloaddition as compared to aromatic (benzene, toluene) or aliphatic (cyclohexane, *n*-hexane) hydrocarbons. The influence of the solvent on the diastereoselectivity was minor, and the diastereomeric ratio recorded for the irradiation of benzaldehyde and enamide **1h** in benzene, for example, did not differ significantly from the results obtained in acetonitrile solution. In most examples, except for oxetanes **5c** and **5d**, the diastereomeric oxetane products *cis*-**5** and *trans*-**5** could not be fully separated by chromatography. An enrichment of the major stereoisomer

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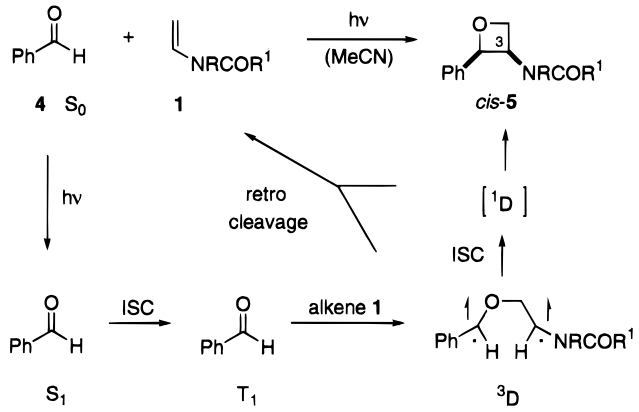
Scheme 4



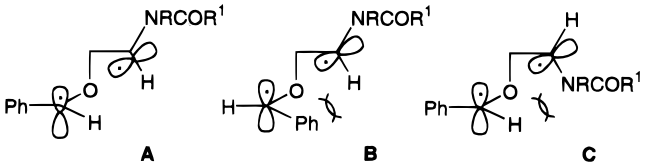
was possible, however (see Table 1 and Experimental Section). Regioisomeric products were not detected in significant quantities. Although the propensity of heteroatom-substituted alkenes to be attacked at the more electron-rich β-position in Paternò−Büchi reactions is well-known,[14] the almost exclusive preference in favor of this addition mode is remarkable. Indeed, α-unsubstituted enol derivatives such as enol acetates[15] and enol ethers[16] react only with modest regioselectivity (65/35 to 75/25) in the Paternò−Büchi reaction. The regioselectivity increases if an α-alkyl substituent is present.[1] Good regioselectivities have been previously reported for the photocycloaddition of vinyl sulfides to benzophenone.[14,17]

Preparatively, the [2 + 2] photocycloaddition of benzaldehyde and *N*-acyl enamines is easy to conduct, and no precautions were taken to avoid exposure of the reaction mixture to oxygen or water. In general, major side reactions were not noticed except for the inevitable pinacol formation, which is due to hydrogen abstraction by the photoexcited benzaldehyde and its subsequent addition to another benzaldehyde molecule.[18] In the case of the secondary enamides **1a** and **1b**, the formation of polymeric byproducts was detected (entries 1 and 2). The resulting precipitate retarded the velocity of the photocyloaddition as it partially covered the glass wall of the reaction vessel. Nonetheless, the yields of oxetanes **5a** and **5b** are satisfactory. Apparently, the Paternò−Büchi reaction can efficiently compete with a radical-type polymerization of the alkene substrates.

For a mechanistic explanation of the high simple diastereoselectivities recorded in the enamide photocycloaddition, we rely on the picture of a stepwise formation of the oxetane ring (Scheme 4).[19] Initial O−C bond formation by attack of the photoexcited aldehyde in its triplet nπ* state at the alkene is succeeded by the C−C bond-forming step, which occurs after intersystem crossing (ISC). Indeed, it is known that the irradiation of aromatic carbonyl compounds results in an efficient conversion to the corresponding nπ* triplet states (T_1) via a fast ISC step ($k = >10^{10}$ s^{-1}),[2d] and the O−C bond formation has been shown to be the first step in the Paternò−Büchi reaction of electron-rich alkenes leading to a biradical intermediate (^{3}D).[2] Indications for a single-electron transfer have not been found in our case. An exciplex formation prior to the bond forming steps cannot be excluded, however.

According to mechanistic arguments given above, the C−C bond formation can be singled out as the stereoselectivity-determining step. For systems in which a singlet biradical ^{1}D (Scheme 4) either is extremely short-lived or does not even represent a minimum on the energy hypersurface, the ISC step of triplet biradical ^{3}D is responsible for the simple diastereoselectivity. On the basis of earlier arguments put forward by Salem and Rowland,[20] Griesbeck and co-workers identified certain ISC geometries that are suited to the facilitation of this step by the maximization of the obligatory spin−orbit coupling.[21] According to their analysis, the orbitals which bear the unpaired electrons are required to be orthogonal to each other to allow a fast ISC to occur. Depending on steric interactions in these conformations, the ISC rates can differ significantly. This difference finally leads to the preferential formation of a single oxetane diastereoisomer.

The biradical conformation **A** encounters the least steric strain because only the hydrogen atoms at the radical centers get into close proximity to each other. Any



other conformation (**B** or **C**) requires that a larger substituent resides in the congested situation, disfavoring this arrangement and thus retarding the ISC step to the *trans*-oxetane. The *cis*-product that is accessed from conformation **A** is consequently obtained as the major product. It should be noted, however, that these arguments are valid only if the singlet biradical ^{1}D (Scheme 4) cannot account for a separate selection step as a result of the aforementioned reasons. On the basis of literature precedent, indeed this appears to be the case for terminal alkenes.[15,16]

As a variety of aromatic aldehydes were successfully employed as carbonyl compounds in previous photocycloaddition reactions of 3-heteroatom-substituted alkenes,[1,22] only one additional example (aldehyde **6a**) was tested in this study. Instead, we made an effort to look into other potentially useful aldehydes as reaction partners. Mostly, enecarbamate **1f** served as the alkene substrate. It was a pleasant surprise for us to note that aliphatic aldehydes, which are known to be notoriously sluggish carbonyl substrates for the Paternò−Büchi

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Scheme 5

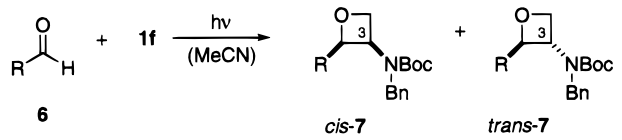


Table 2. Photocycloaddition of Enecarbamate 1f to Various Aldehydes 6 in Acetonitrile Solution

entry[a]	R	aldehyde	time[b] [h]	product	d.r.[c]	yield[d] [%]
1	2-PivOC$_6$H$_4$	**6a**	15	**7a**	>90/10	62
2	*n*-BuOOC	**6b**	15	**7b**	90/10	33
3	*n*-Pr	**6c**	15	**7c**	75/25	55
4	Me	**6d**	15	**7d**	65/35	46[e]
5	TBDMSO(CH$_2$)$_2$	**6e**	40	**7e**	69/31	54

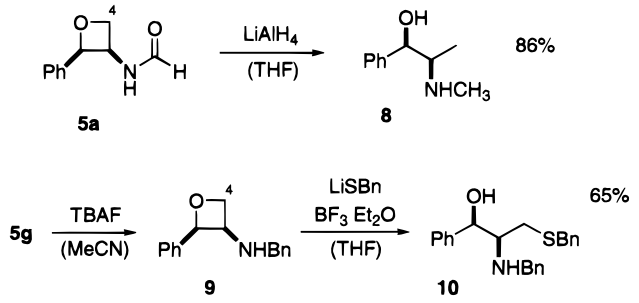
[a] Except for entry 4, an excess of alkene was used (see the Experimental Section). [b] Irradiation time. [c] Diastereomeric ratio *cis*-**7**/*trans*-**7** as determined from GLC and/or ^{1}H NMR analysis of the crude product mixture. [d] Yield of isolated oxetane product. The diastereomeric composition of the isolated product is similar to the crude d.r. (see the Experimental Section). [e] The alkene was used as the limiting agent.

reaction because of competitive Norrish-type cleavage reactions,[2d] underwent a fairly clean photocycloaddition to the corresponding oxetane (Scheme 5). Some examples are listed in Table 2.

Contrary to the 2-aryloxetanes **5** and **7a,** the oxetanes **7c**−**e** obtained from aldehydes **6c**−**e** were formed with only moderate diastereomeric excess. A likely reason for this lack of stereoselectivity is the lower ISC rate of photochemically excited aliphatic aldehydes ($S_1 \rightarrow T_1$).[2d] Subsequent photocycloaddition reactions are known to occur at least partially in the singlet manifold.[2] If this is the case, factors other than the ones discussed above govern the C−C bond-formation step and the simple diastereoselectivity may decrease.[21d] Still, even with aliphatic aldehydes there is an appreciable preference for the *cis*-oxetane, as proven by NOESY studies on **7b** and **7e**, and altogether the Paternò−Büchi reaction of *N*-acyl enamines is certainly the most direct approach for the synthesis of *cis*-3-aminooxetanes. An application of this method to the synthesis of the naturally occurring antibiotic (±)-oxetin via oxetane **7b** has been recently reported.[23]

Synthesis of *syn*-1,2-Amino Alcohols. Nucleophilic displacement reactions were expected to occur at the least-substituted C-4 position of the oxetanes **5** and **7**. The relative configuration established during the photocycloaddition at C-2 and C-3 would be retained by this ring-opening mode, and *syn*-1,2-amino alcohols should be formed. Most of the previously used reagents[24,25] unfortunately failed to facilitate the desired nucleophilic substitution at C-4, and the question arose how this

Scheme 6



failure could be interpreted and this problem might be overcome. The test substrates **5c** and **5f** we frequently employed to screen possible ring-opening reactions bear a fully protected amino group at the C-3 carbon atom. In combination with our work on 3-oxetanols, we had previously noted that the silyl-protected 3-oxetanols are not suited for nucleophilic ring opening at C-4.[26] The parent 3-oxetanols, however, do undergo these reactions with ease.[27] It was postulated that the free hydroxy group in these oxetanes is able to coordinate the metal that carries the potential nucleophile, thus rendering the reaction intramolecular.[25,28] If similar arguments were applicable to 3-aminooxetanes, the secondary 3-oxetanylamides **5a** and **5b** should be amenable to nucleophilic substitution at C-4. Indeed, the formamide **5a** readily reacted with $LiAlH_4$ to yield a ring-opened product that was identified as pseudoephedrine (**8**) by comparison with authentic material (Scheme 6). In a single step, the reduction of the formyl group and the reductive ring opening occurred. It was not possible by TLC to trace back any intermediates, and it remains open what type of reduction occurs more readily in this particular example. In any case, the free NH group is apparently a handle to achieve a successful ring opening of 3-aminooxetanes.

Despite the fact that 3-oxetanylamides such as **5a** are available directly from secondary amides, a drawback to their use is the fact that any nucleophile will have at least two positions to attack, i.e., either the electrophilic C-4 carbon atom of the oxetane ring or the carbonyl group of the amide. In the previous example, the double attack was desirable, but in many other instances, this ambiguity should be avoided. We therefore intended to remove one of the acyl or alkoxycarbonyl protective groups from the doubly protected 3-aminooxetanes **5c**, **5f**, or **5g**, a maneuver that should give access to the corresponding *N*-benzyl-protected aminooxetane **9**. Saponification of **5c** proved difficult under a variety of conditions, and the acidic cleavage of the Boc group in oxetane **5f** yielded an unexpected result (vide infra). The removal of the Teoc group emerged finally as the most reliable way to generate oxetane **9** (Scheme 6). As expected, this oxetane underwent ring-opening reactions and 1,2,3 functionality can be established by this means. As an example, the nucleophilic displacement by benzyl mercaptide,[25e] which yielded compound **10**, is depicted in Scheme 6. The relative configuration established in the photochemical key step is fully retained in these ring-opening reactions,

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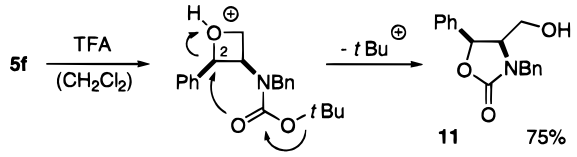
(28) (a) Bach, T.; Lange, C. *Tetrahedron Lett.* **1996**, *37*, 4363. (b) Bach, T.; Eilers, F.; Kather, K. *Liebigs Ann./Recueil* **1997**, 1529−1536.

Scheme 7



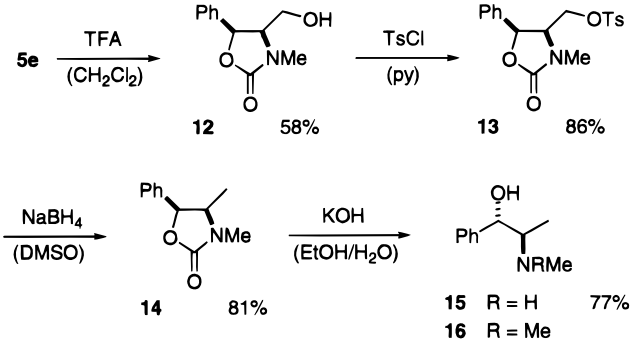
and the synthesis of *syn*-1,2-amino alcohols from *cis*-aminooxetanes can indeed be achieved as suggested in Scheme 1. In analogy to the 2-aryl-3-aminooxetanes, their 2-alkyl-substituted counterparts are equally amenable to nucleophilic attack at the carbon atom C-4. Applications of this route to *syn*-1,2-amino alcohols are currently being studied.

Synthesis of *anti*-1,2-Amino Alcohols. By accident, we found that *anti*-1,2-amino alcohols can be generated from *cis*-aminooxetanes, which is a useful complement to the above-mentioned ring-opening reactions. In attempts to remove the Boc group from oxetane **5f** by trifluoroacetic acid (TFA) catalysis, we noticed the formation of an unexpected major product, which proved to be the oxazolidinone **11**. Because we had used a diastereomeric mixture of *cis*-**5f** and trans-**5f** (90/10) as the starting material, the diastereoisomer of oxazolidinone **11** was also isolated in 5% yield. The relative configuration of the products was established by NMR spectroscopy (NOE experiments). We could demonstrate that the reaction occurs stereospecifically,[10,29] and the mechanism depicted in Scheme 7 can be invoked to explain the results.

The protonation of the carbonyl oxygen of the Boc group, which is a prerequisite for its succesive cleavage, cannot compete against the electrophilic attack of the proton that occurs at the more accessible and more basic[30] oxetane oxygen atom. Activated by this means, the oxetane undergoes displacement at C-2 by the intramolecular oxygen nucleophile, and the *tert*-butyl cation acts as an electrophilic leaving group. The formation of a free carbenium ion can be ruled out on the basis of the stereospecifity of the reaction. On the contrary, in some related cases in which the ring opening of 3-oxetanol derivatives was studied, the intermediacy of carbenium ions appears to be likely.[31] The regioselective attack at C-2 is attributed to the conformational preference of 3-*N*-Boc-amino-2-phenyloxetanes, with the carbonyl oxygen of the Boc group oriented toward the electrophilic center. For 2-alkyloxetanes such as **7c**, the regioselectivity was less pronounced and a mixture of regioisomeric ring-opening products was obtained.

As a short example for the application of the ring opening to *anti*-1,2-amino alcohols, we have prepared ephedrine (**15**) and *N*-methylephedrine (**16**). The aminooxetane **5e** was used as the starting material and upon treatment with TFA underwent smooth ring expansion to oxazolidinone **12**. After conversion of the primary hydroxy group in **12** to a leaving group and subsequent reductive dehydrotosylation[32] of compound **13**, the hydrolysis of oxazolidinone **14** gave the target compound (Scheme 8).

Scheme 8



The conversion of tosylate **13** to *N*-methylephedrine (**16**) was even more facile with $LiAlH_4$ as the reducing agent (97% yield).

Conclusion

The photochemical "umpolung" of a carbonyl compound can be successfully employed for the construction of 1,2-difunctionality in the photocycloaddition of aldehydes and acceptor-substituted enamines. The reactions proceeded with excellent regioselectivity and yielded exclusively the corresponding 3-aminooxetanes. In addition, the simple diastereoselectivity in preference of the *cis*-product is high if aromatic aldehydes are used. An explanation for the preferential formation of the apparently less stable *cis*-products is based on a kinetic scheme in which the ISC rates of a putative triplet 1,4-biradical are responsible for the stereoselection. The rates differ for various conformations of the biradical, and the geometry favored on steric arguments accounts for the fastest ISC. In the singlet manifold, this selection does not apply and aliphatic aldehydes that react partially via their singlet excited states consequently show a lower simple diastereoselectivity in the photocycloaddition.

Preparatively, the *cis*-3-aminooxetanes obtained by the Paternò−Büchi reaction not only are interesting by themselves but also serve as building blocks for the stereoselective construction of 1,2-amino alcohols. The obvious pathway to achieve an oxetane ring opening is a nucleophilic substitution at the less-substituted C-4 carbon atom of the ring, which yields *syn*-1,2-amino alcohols. Indeed, this route is feasible if one ensures the presence of an acidic NH group in the aminooxetanes. If secondary enamides are used as alkene substrates in the photocycloaddition, the NH group is already introduced in the oxetane during this step. Tertiary enecarbamates lead to carbamoyl-protected secondary aminooxetanes, the carbamate protective group of which can be readily removed. For the latter purpose, the trimethylsilylethoxycarbonyl (Teoc) group proved to be best suited.

anti-1,2-Amino alcohols are accessible from *N*-Boc-protected *cis*-2-aryl-3-aminooxetanes via oxazolidinone intermediates. Upon acid treatment, these oxetanes undergo a cyclization with concomitant oxetane ring cleavage, which occurs by an intramolcular nucleophilic substitution at carbon atom C-2 of the oxetane. The oxygen atom of the Boc group attacks the oxetane nucleus in a S_N2-type reaction while the *tert*-butyl cation is simultaneously cleaved. As the substitution proceeds with inversion at the former C-2 carbon atom, the

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(30) pK_a [$HO(CH_2C(CH_3)_2CH_2)^+$] = −2.6, cf. ref 22b; pK_a [$HOC(NMe_2)OR^+$] = −3.1, cf. Homer, R. B.; Johnson, C. D. In *The Chemistry of Functional Groups*; Patai, S., Ed.; *The Chemistry of Amides*; Zabicky, J., Ed.; Interscience: London, 1970; p 211.
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(32) Hutchins, R. O.; Kandasamy, D.; Dux, F., III; Maryanoff, C. A.; Rotstein, D.; Goldsmith, B.; Burgoyne, W.; Cistone, F.; Dalessandro, J.; Puglis, J. *J. Org. Chem.* **1978**, *43*, 2259.

resulting *N*-alkyloxazolidinones have *anti*-configuration and they can be saponified to *anti*-1,2-amino alcohols.

Experimental Section

General. All reactions involving water-sensitive chemicals were carried out in flame-dried glassware with magnetic stirring under Ar. Irradiation experiments were performed in acetonitrile (Merck p.a.) or benzene (Merck p.a.) under Ar. Chlorotrimethylsilane, *N,N*-di-*i*-propylamine, triethylamine, DMSO, and pyridine were distilled from calcium hydride. Common solvents (*tert*-butyl methyl ether, pentane, cyclohexane, and ethyl acetate), acetic anhydride, and BF_3-etherate were distilled prior to use. THF and Et_2O were distilled from K/Na immediately prior to use. All other reagents and solvents were used as received. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ as solvent at 303 K unless stated otherwise. Chemical shifts are reported relative to tetramethylsilane as an internal reference. Apparent multiplets which occur as a result of the accidental equality of coupling constants to those of magnetically nonequivalent protons are marked as virtual (virt.). The multiplicities of the ^{13}C NMR signals were determined by attached proton test (APT) experiments. NOESY contacts are reported as weak (′), medium (″), or strong (‴) TLC was performed on Aluminum sheets (0.2 mm silica gel 60 F_{254}), and a pentane (PE)/*tert*-butyl methyl ether (MTBE) mixture or a cyclohexane (CH)/ethyl acetate (EA) mixture was used as eluent. Detection was by UV or by coloration with ceric ammonium molybdate (CAM). Flash chromatography[33] was performed on silica gel 60 (230−400 mesh) (ca 50 g for 1 g of material to be separated), with the eluent given in brackets.

(1,1-Dimethylethyl)-*N*-methyl-*N*-vinylcarbamate (1e). To a solution of 10 mmol of *N*-methylethylidenamine[34] (0.57 g) and 10 mmol of triethylamine (1.01 g, 1.39 mL) in dry toluene (5 mL) was added 10 mmol of di-*tert*-butyl dicarbonate (2.18 g). After the addition, the mixture was stirred for 1 h at room temperature. The solvent was distilled under atmospheric pressure, and nonconverted starting compounds were evaporated by bulb-to-bulb distillation (80 °C/1 mbar). The residue was purified by flash chromatography (PE/MTBE = 90/10). Compound **1e** was obtained as a colorless oil. Yield: 1.3 g (80%). R_f = 0.44 (PE/MTBE = 90/10). IR (film): 1710 cm^{-1} (vs, C=O), 1625 (vs, C=C). ^{1}H NMR (DMSO-d_6, 373 K): δ 1.46 (s, 9 H), 2.94 (s, 3 H), 4.19 (d, J = 9.4 Hz, 1 H), 4.30 (d, J = 15.8 Hz, 1 H), 7.05 (dd, J = 15.8 Hz, J = 9.4 Hz, 1 H). ^{13}C NMR: δ 27.4 (q), 28.0 (q), 81.0 (s), 90.6 (t), 134.3 (d), 146.8 (s). HRMS: Calcd 157.1102; found 157.1095. Anal. Calcd for $C_8H_{15}NO_2$ (157.1): C, 61.12; H, 9.62; N, 8.91. Found: C, 61.22; H, 9.65; N, 8.85.

***N*-Phenylmethyl-(2-trimethylsilyl)-*N*-vinylcarbamate (1g).** To a solution of 36 mmol of 2-(trimethylsilyl)ethanol (4.3 g) in Et_2O (50 mL) was slowly added 30 mmol of *n*-BuLi (19.2 mL, 1.56 M in hexanes) at −5 °C. After 1 h of stirring, 25 mmol of *N*-benzyl-*N*-vinylcarbamoylchlorid (**3**)[13] (4.9 g) was added dropwise to the mixture at this temperature. Stirring was continued for 1 h. The reaction was quenched with a saturated aqueous solution of NH_4Cl (20 mL), and the mixture was extracted with Et_2O (3 × 30 mL). The organic extracts were combined, washed with brine (30 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography (PE/MTBE = 95/5). Compound **1g** was obtained as a colorless oil. Yield: 6.6 g (95%). R_f = 0.90 (PE/MTBE = 90/10). IR (film): 1710 cm^{-1} (vs, C=O), 1630 (vs, C=C). ^{1}H NMR (DMSO-d_6, 373 K): δ 0.02 (s, 9 H), 1.03 (t, J = 8.2 Hz, 2 H), 4.24−4.32 (m, 3 H), 4.38 (d, J = 15.9 Hz, 1 H), 4.76 (s, 2 H), 7.09 (dd, J = 15.9 Hz, J = 9.3 Hz, 1 H), 7.21−7.25 (m, 3 H), 7.30−7.34 (m, 2 H). ^{13}C NMR (DMSO-d_6, 373 K): δ −0.7 (q), 18.2 (t), 47.4 (t), 65.1 (t), 94.0 (t), 127.3 (d), 127.7 (d), 129.2 (d), 133.6 (s), 138.2 (d), 154.8 (s). Anal. Calcd for $C_{15}H_{23}NO_2Si$ (277.4): C, 64.95; H, 8.36; N, 5.05. Found: C, 64.80; H, 8.13; N, 5.20.

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General Irradiation Procedure. In a quartz tube, the aldehyde (1.5 mmol) and the *N*-acyl enamine (3.0 mmol) were dissolved in 10 mL of acetonitrile. This mixture was irradiated for the time period indicated in Tables 1 or 2 (λ = 300 nm; light source: Rayonet RPR 3000). The course of the reaction was monitored by TLC and GLC. Upon complete conversion of the aldehyde, the solvent was evaporated in vacuo. The simple diastereoselectivity (d.r.) was determined by ^{1}H NMR and GLC analysis of the crude product mixture, and the results are listed in Tables 1 and 2. The excess enamide was separated from the desired oxetane by distillation, or it was separated in the course of the subsequent flash chromatography. The diastereomeric ratio of the isolated product as determined by GLC is given in the Experimental Section. The oxetanes were obtained as colorless oils. Relative configurations were determined by ^{1}H NMR spectroscopy (NOE or NOESY experiments). Some selected data are provided.

(2*RS*,3*RS*)-*N*-(2-Phenyloxetan-3-yl)formamide (*cis*-5a). According to the general irradiation procedure, 1.5 mmol of benzaldehyde (159 mg, 152 μL) and 2.5 mmol of *N*-acyl enamine **1a** (178 mg) were irradiated for 15 h. The mixture was filtered, and 1 equiv of *N*-acyl enamine **1a** (1.0 mmol, 71 mg) was added. After further irradiation for 3 h, the mixture was worked up as described in the general procedure. Flash chromatography (CH/EA = 30/70) yielded oxetane **5a** as a mixture of diastereoisomers (196 mg, 74%, d.r. = 90/10). The diastereoisomers were not fully separable. Analytical data are provided for the major diastereoisomer *cis*-**5a**. R_f = 0.15 (CH/EA = 30/70). IR (film): 1670 cm^{-1} (vs, CONH), 995 (s, COC). ^{1}H NMR: δ 4.36 (virt. t, $J \cong$ 6.6 Hz, 1 H), 4.92 (virt. t, $J \cong$ 7.3 Hz, 1 H), 5.21−5.31 (m, 1 H), 5.87 (d, J = 7.6 Hz, 1 H), 5.95−6.15 (s, b, 1 H), 7.21−7.66 (m, 5 H), 7.66 (s, 1 H). ^{13}C NMR: δ 45.7 (d), 76.1 (t), 85.8 (d), 125.4 (d), 128.4 (d), 128.7 (d), 136.8 (s), 160.3 (d). Anal. Calcd for $C_{10}H_{11}NO_2$ (177.2): C, 67.78; H, 7.90; N, 6.26. Found C, 67.84; H, 7.99; N, 6.17.

(2*RS*,3*RS*)-*N*-(2-Phenyloxetan-3-yl)acetamide (*cis*-5b). The general irradiation procedure was slightly modified. Six mmol of *N*-acyl enamine **1b**[11] (510 mg) was added in small portions to a solution of 1.5 mmol of benzaldehyde (159 mg, 152 μL) in acetonitrile (10 mL) within 10 h. After irradiation for 140 h, the mixture was worked up as described in the general procedure. Flash chromatography (CH/EA = 40/60 → 20/80) yielded oxetane **5b** as a mixture of diastereoisomers (165 mg, 58%, d.r. = 80/20). Benzaldehyde (40 mg, 25%) was recovered. The diastereoisomers were not fully separable. Analytical data are provided for the major diastereoisomer *cis*-**5b**. R_f = 0.10 (CH/EA = 40/60). IR (film): 3250 cm^{-1} (s, b, NH), 1640 (vs, CONH), 1540 (vs, CONH), 970 (s, COC). ^{1}H NMR: δ 1.70 (s, 3 H), 4.54 (virt. t, $J \cong$ 6.6 Hz, 1 H), 5.05 (virt. t, $J \cong$ 7.2 Hz, 1 H), 5.30−5.38 (m, 1 H), 5.50 (s, b, 1 H), 5.99 (d, J = 7.5 Hz, 1 H), 7.30−7.49 (m, 5 H). NOE experiment (600 MHz) H (5.99): H_N [0.4%]; H_N (5.34): H [0.4%], H_b [0.3%]; H_b (5.05): H_N [0.3%], H_a [1.2%]; H_a (4.54): H_b [1.4%]. ^{13}C NMR: δ 22.7 (q), 47.2 (d), 76.3 (t), 86.2 (d), 125.4 (d), 128.1 (d), 128.6 (d), 137.2 (s), 169.5 (s). $C_{11}H_{13}NO_2$ HRMS: Calcd 191.0946; found 191.0943.

***N*-Phenylmethyl-*N*-(2-phenyloxetan-3-yl)acetamide (5c).** According to the general irradiation procedure, 1.5 mmol of benzaldehyde (159 mg, 152 μL) and 3 mmol of *N*-acyl enamine **1c**[12b] (526 mg) were irradiated for 14 h. Flash chromatography (CH/EA = 75/25 → 70/30) yielded oxetane **5c** as a mixture of separable diastereoisomers (340 mg, 81%, d.r. = 89/11). (2*RS*,3*RS*)-isomer (*cis*-**5c**): R_f = 0.41 (CH/EA = 40/60). IR (film): 1640 cm^{-1} (vs, C=O), 980 (s, COC).^{1}H NMR: δ 1.82 (s, 3 H), 4.06 (d, J = 18.3 Hz, 1 H), 4.32 (d, J = 18.3 Hz, 1 H), 4.52 (virt. t, $J \cong$ 7.2 Hz, 1 H), 4.86 (virt. t, $J \cong$ 8.0 Hz, 1 H), 5.96 (virt. q, $J \cong$ 7.4 Hz, 1 H), 6.07 (d, J = 7.4 Hz, 1 H), 6.87−6.97 (m, 2 H), 7.14−7.46 (m, 8 H). ^{13}C NMR: δ 21.8 (q), 49.0 (t), 52.6 (d), 71.8 (t), 87.3 (d), 124.9 (d), 125.0 (d), 127.3 (d), 127.4 (d), 128.2 (d), 128.9 (d), 137.6 (s), 138.3 (s), 171.8 (s). NOESY experiment (see General): H (6.07)−H (5.96)‴; H (5.96)−H (4.86)‴; H (4.86)−H (4.52)‴. Anal. Calcd for $C_{18}H_{19}NO_2$ (281.4): C, 76.84; H, 6.81; N, 4.98. Found: C, 76.79; H, 6.85; N, 4.83. (2*RS*,3*SR*)-isomer (*trans*-**5c**): R_f = 0.34 (CH/EA = 40/60).^{1}H NMR (DMSO-d_6, 373 K): δ 1.97 (s, 3 H), 4.59

(m, 2 H), 4.85 (s, 2 H), 5.06 (virt. q, $J \cong 7.4$ Hz, 1 H), 5.65 (d, $J = 6.8$ Hz, 1 H), 7.18−7.39 (m, 10 H).^{13}C NMR (75.5 MHz): $\delta = 24.2$ (q), 51.2 (t), 59.7 (d), 74.1 (t), 88.8 (d), 127.7 (d), 128.2 (d), 129.8 (d), 130.6 (d), 130.9 (d), 131.2 (d), 139.1 (s), 142.3 (s), 173.9 (s).

(2*RS*,3*RS*)-*N*-(2-Phenyloxetan-3-yl)-*N*-propylacetamide (*cis*-5d). According to the general irradiation procedure, 1.5 mmol of benzaldehyde (159 mg, 152 μL) and 3.75 mmol of *N*-acyl enamine **1d**[12a] (477 mg) were irradiated for 14 h. Flash chromatography (CH/EA = 80/20 → 40/60) yielded oxetane *cis*-**5d** in diastereomerically pure form (250 mg, 71%, d.r. = >90/10). $R_f = 0.24$ (CH/EA = 40/60). IR (film): 1640 cm^{-1} (vs, C=O), 980 (s, COC). ^{1}H NMR: δ 0.75 (t, $J = 7.4$ Hz, 3 H), 1.12−1.40 (m, 2 H), 1.86 (s, 3 H), 2.74 (ddd, $J = 15.6$ Hz, $J = 10.3$ Hz, $J = 5.7$ Hz, 1 H), 2.95 (ddd, $J = 15.6$ Hz, $J = 10.3$ Hz, $J = 5.5$ Hz, 1 H), 4.80 (virt. t, $J \cong 7.3$ Hz, 1 H), 5.00 (dd, $J = 7.3$ Hz, $J = 8.2$ Hz, 1 H), 5.68 (virt. q, $J \cong 7.8$ Hz, 1 H), 5.97 (d, $J = 7.7$ Hz, 1 H), 7.20−7.42 (m, 5 H).^{13}C NMR: δ 10.7 (q), 21.3 (q), 23.7 (t), 47.2 (t), 52.5 (d), 71.7 (t), 87.6 (d), 125.2 (d), 127.2 (d), 127.9 (d), 138.0 (s), 170.7 (s). Anal. Calcd for $C_{14}H_{19}NO_2$ (233.3): C, 72.07; H, 8.21; N, 6.00. Found: C, 71.74; H, 8.25; N, 6.06.

(2*RS*,3*RS*)-(1,1-Dimethylethyl)-*N*-methyl-*N*-(2-phenyloxetan-3-yl)carbamate (*cis*-5e). According to the general irradiation procedure, 1.5 mmol of benzaldehyde (159 mg, 152 μL) and 2.5 mmol of *N*-acyl enamine **1e** (393 mg) were irradiated for 14 h. Flash chromatography (CH/EA = 90/10) yielded oxetane **5e** as a mixture of diastereoisomers (221 mg, 56%, d.r. = 90/10). The diastereoisomers were not fully separable. Analytical data are provided for the major diastereoisomer *cis*-**5e**. $R_f = 0.47$ (CH/EA = 75/25). IR (film): 1720 cm^{-1} (vs, C=O), 990 (s, COC). ^{1}H NMR (DMSO-d_6, 373K): δ 1.35 (s, 9 H), 2.46 (s, 3 H), 4.85 (virt. t, $J \cong 7.2$ Hz, 1 H), 4.92 (virt. t, $J \cong 7.2$ Hz, 1 H), 5.27 (virt. q, $J \cong 7.2$ Hz, 1 H), 5.85 (d, $J = 7.2$ Hz, 1 H), 7.25−7.43 (m, 5 H). ^{13}C NMR (DMSO-d_6, 373 K): $\delta = 27.5$ (q), 30.2 (q), 53.6 (d), 70.6 (t), 78.6 (s), 86.4 (d), 124.7 (d), 126.6 (d), 127.3 (d), 138.2 (s), 154.0 (s). Anal. Calcd for $C_{15}H_{21}NO_3$ (263.2): C, 68.42; H, 8.04; N, 5.32. Found: C, 68.10; H, 8.21; N, 5.21.

(2*RS*,3*RS*)-(1,1-Dimethylethyl)-*N*-phenylmethyl-*N*-(2-phenyloxetan-3-yl)carbamate (*cis*-5f). According to the general irradiation procedure 1.5 mmol of benzaldehyde (159 mg, 152 μL) and 3.75 mmol of enamine **1f**[23] (875 mg) were irradiated for 14 h. Flash chromatography (CH/EA = 98/2 → 96/4) yielded oxetane **5f** as a mixture of diastereoisomers (395 mg, 77%, d.r. = 87/13). The diastereoisomers were not fully separable. Analytical data are provided for the major diastereoisomer *cis*-**5f**. $R_f = 0.66$ (CH/EA = 60/40). IR (film): 1680 cm^{-1} (vs, C=O), 980 (s, COC). ^{1}H NMR (DMSO-d_6, 373 K): δ 1.30 (s, 9 H), 4.11 (d, $J = 16.8$ Hz, 1 H), 4.25 (d, $J = 16.8$ Hz, 1 H), 4.68−4.76 (m, 2 H), 5.34 (virt. q, $J \cong 7.4$ Hz, 1 H), 5.84 (d, $J = 7.2$ Hz, 1 H), 7.00−7.05 (m, 2 H), 7.15−7.41 (m, 8 H). NOE experiment (360 MHz, DMSO-d_6, 373 K) H (5.84): H_N [15.2%]; H_N (5.34): H [16.9%]. ^{13}C NMR (DMSO-d_6, 373 K): δ 28.6 (q), 48.4 (t), 54.9 (d), 72.1 (t), 80.3 (s), 88.0 (d), 126.6 (d), 126.7 (d), 127.3 (d), 128.1 (d), 128.6 (d), 128.9 (d), 139.2 (s), 139.9 (s), 155.3 (s). Anal. Calcd for $C_{21}H_{25}NO_3$ (339.4): C, 74.31; H, 7.42; N, 4.13. Found: C, 74.34; H, 7.32; N, 4.25.

(2*RS*,3*RS*)-*N*-Phenylmethyl-(2-trimethylsilyl)-*N*-(2-phenyloxetan-3-yl)carbamate (*cis*-5g). According to the general irradiation procedure, 1.5 mmol of benzaldehyde (159 mg, 152 μL) and 3 mmol of *N*-acyl enamine **1g** (832 mg) were irradiated for 14 h. Flash chromatography (PE/MTBE = 90/10) yielded oxetane *cis*-**5g** in diastereomerically pure form (427 mg, 74%, d.r. = >90/10). $R_f = 0.20$ (PE/MTBE = 90/10). IR (film): 1695 cm^{-1} (vs, C=O), 985 (m, COC). ^{1}H NMR (DMSO-d_6, 373 K): δ −0.01 (s, 9 H), 0.87 (t, $J = 8.1$ Hz, 2 H), 3.93−4.20 (m, 3 H), 4.32 (d, $J = 16.8$ Hz, 1 H) 4.72 (m, 2 H), 5.37 (virt. q, $J \cong 7.3$ Hz, 1 H), 5.86 (d, $J = 7.2$ Hz, 1 H), 6.99−7.43 (m, 10 H). ^{13}C NMR (DMSO-d_6, 373 K): δ −2.9 (q), 16.8 (t), 47.1 (t), 53.7 (d), 62.4 (t), 70.8 (t), 86.6 (d), 125.2 (d), 125.5 (d), 126.2 (d), 127.0 (d), 127.5 (d), 127.8 (d), 137.9 (s), 138.3 (s), 155.1 (s). Anal. Calcd for $C_{22}H_{29}NO_3Si$ (383.5): C, 68.89; H, 7.62; N, 3.65. Found: C, 68.62; H, 7.58; N, 3.82.

***N*-(2-Phenyloxetan-3-yl)-pyrrolidin-2-one (5h).** According to the general irradiation procedure, 1.5 mmol of benzaldehyde (159 mg, 152 μL) and 4.5 mmol of enamine **1h** (500 mg, 480 μL) were irradiated for 14 h. Flash chromatography (CH/EA = 40/60 → 20/80) yielded oxetane **5h** as a mixture of diastereoisomers (270 mg, 82%, d.r. = 88/12). The diastereoisomers were not fully separable. Analytical data are provided for both diastereoisomers. (2*RS*,3*RS*)-isomer (*cis*-**5h**): $R_f = 0.19$ (EA). IR (film): 1680 cm^{-1} (vs, C=O), 980 (s, COC); ^{1}H NMR: δ 1.36 (m, 1 H), 1.71 (m, 1 H), 2.12 (ddd, $J = 16.9$ Hz, $J = 9.4$ Hz, $J = 5.6$ Hz, 1 H), 2.23 (ddd, $J = 16.9$ Hz, $J = 9.3$ Hz, $J = 7.8$ Hz, 1 H), 2.75 (virt. dt, $J \cong 8.8$ Hz, $J = 4.7$ Hz, 1 H), 3.22 (virt. q, $J \cong 8.0$ Hz, 1 H), 4.84 (virt. t, $J \cong 6.8$ Hz, 1 H), 5.06 (virt. t, $J \cong 7.8$ Hz, 1 H), 5.54 (virt. q, $J \cong 7.4$ Hz, 1 H), 6.03 (d, $J = 7.8$ Hz, 1 H), 7.20−7.40 (m, 5 H). NOE experiment (360 MHz) H_{ar} (7.25): H [2.7%], H_a [0.5%], H_5 [0.7%]; H (6.03): H_N [4.4%]; H_N (5.54): H [5.9%], H_b [2.2%]; H_b (5.06): H_N [4.4%], H_a [11.8%]; H_a (4.84): H_b [18.0%], H_5 [2.8%]; H_5 (3.22): H_a [2.5%]. ^{13}C NMR: δ 18.7 (t), 30.8 (t), 44.9 (t), 49.7 (d), 71.1 (t), 86.8 (d), 124.2 (d), 127.2 (d), 128.0 (d), 138.2 (s), 175.2 (s). $C_{13}H_{16}NO_2$ HRMS: Calcd. 218.1181; found 218.1179. (2*RS*,3*SR*)-isomer (trans-**5h**): $R_f = 0.19$ (EA).^{1}H NMR: δ 2.07−2.17 (m, 2 H), 2.42 (virt. t, $J \cong 8.1$ Hz, 2 H), 3.73 (virt. t, $J \cong 8.8$ Hz, 2 H), 4.75 (m, 1 H), 4.82−4.86 (m, 1 H), 5.13 (virt. q, $J \cong 7.6$ Hz, 1 H), 6.03 (d, $J = 6.6$ Hz, 1 H), 7.15−7.35 (m, 5 H). NOE experiment (360 MHz) H_N (5.13): H_a [2.0%]; H_b (4.85): H_a [12.3%]; H_5 (3.73): H [5.9%]. ^{13}C NMR: δ 18.0 (t), 31.0 (t), 44.0 (t), 53.7 (d), 70.2 (t), 85.8 (d), 125.3 (d), 128.2 (d), 128.4 (d), 140.0 (s), 174.8 (s).

(2*RS*,3*RS*)-(1,1-Dimethylethyl)-*N*-[2-[2-(1,1-dimethylethylcarbonyloxy)phenyl]oxetan-3-yl]-*N*-phenylmethylcarbamate (*cis*-7a). According to the general irradiation procedure, 1.5 mmol of aldehyde **6a** (1.5 mmol) and 3 mmol of *N*-acyl enamine **1f**[23] (699 mg) were irradiated for 15 h. Flash chromatography (CH/EA = 90/10) yielded oxetane *cis*-**7a** in diastereomerically pure form (409 mg, 62%, d.r. = >90/10). $R_f = 0.25$ (CH/EA = 90/10). IR (film): 1695 cm^{-1} (vs, C=O), 985 (m, COC). ^{1}H NMR (DMSO-d_6, 373 K): δ 1.14 (s, 9 H), 1.18 (s, 9 H), 4.13 (d, $J = 17.0$ Hz, 1 H), 4.26 (d, $J = 17.0$ Hz, 1 H), 4.72 (virt. t, $J \cong 7.7$ Hz, 1 H), 4.88 (virt. t, $J \cong 7.7$ Hz, 1 H), 5.52 (virt. q, $J \cong 7.7$ Hz, 1 H), 5.96 (d, $J = 7.7$ Hz, 1 H), 6.94−7.72 (m, 9 H). ^{13}C NMR: δ 27.0 (q), 28.2 (q), 39.3 (s), 47.7 (t), 53.5 (d), 73.3 (t), 80.2 (s), 85.1 (d), 122.2 (d), 125.4 (d), 126.5 (d), 127.0 (d), 128.3 (d), 128.6 (d), 130.3 (s), 139.9 (s), 147.9 (s), 155.1 (s). Anal. Calcd for $C_{26}H_{33}NO_5$ (439.6): C, 71.05; H, 7.57; N, 3.19. Found C, 70.82; H, 8.08; N, 3.21.

(2*RS*,3*RS*)-(1,1-Dimethylethyl)-*N*-phenylmethyl-*N*-(2-propyloxetan-3-yl)carbamate (*cis*-7c). According to the general irradiation procedure, 1.5 mmol of aldehyde **6c** (108 mg) and 22.5 mmol of *N*-acyl enamine **1f**[23] (5.25 g) were irradiated for 15 h. Flash chromatography (PE/MTBE = 95/5) yielded oxetane **7c** as a mixture of diastereoisomers (250 mg, 55%, d.r. = 75/25). The diastereoisomers were not fully separable. The collection of selected chromatography fractions yielded diastereoisomer *cis*-**7c** in diastereomerically pure form (168 mg, 37%). $R_f = 0.37$ (PE/MTBE = 90/10). IR (film): 1695 cm^{-1} (vs, C=O), 975 (m, COC). ^{1}H NMR (DMSO-d_6, 373 K): δ 0.89 (t, $J = 7.4$ Hz, 3 H), 1.26 (m, 1 H), 1.35 (m, 1 H), 1.39 (s, 9 H), 1.47 (m, 1 H), 1.70 (m, 1 H), 4.36−4.54 (m, 3 H), 4.68 (m, 1 H), 4.74 (d, $J = 16.5$ Hz, 1 H), 4.91 (virt. q, $J \cong 6.9$ Hz, 1 H), 7.16−7.34 (m, 5 H). ^{13}C NMR (DMSO-d_6, 373 K): δ 14.4 (q), 18.3 (t), 28.8 (q), 33.1 (t), 49.2 (t), 53.8 (d), 71.0 (t), 80.5 (s), 87.3 (d), 127.2 (d), 127.6 (d), 129.2 (d), 140.2 (s), 156.0 (s). Anal. Calcd for $C_{18}H_{27}NO_3$ (305.4): C, 70.79; H, 8.91; N, 4.59. Found C, 70.59; H, 8.68; N, 4.61.

(2*RS*,3*RS*)-(1,1-Dimethylethyl)-*N*-(2-methyloxetan-3-yl)-*N*-phenylmethylcarbamate (*cis*-7d). The general irradiation procedure was modified. Aldehyde **6d** (22.5 mmol, 990 mg) and 1.5 mmol of *N*-acyl enamine **1f**[23] (350 mg) were irradiated for 15 h. Flash chromatography (PE/MTBE = 40/60) yielded oxetane **7d** as a mixture of diastereoisomers (190 mg, 46%, d.r. = 86/14). Analytical data are provided for the major diastereoisomer *cis*-**7d**. $R_f = 0.66$ (PE/MTBE = 25/75). IR (film): 1695 cm^{-1} (vs, C=O), 975 (s, COC); ^{1}H NMR (DMSO-d_6, 373 K): δ 1.23 (d, $J = 6.0$ Hz, 3 H), 1.40 (s, 9 H), 4.40 (virt.

t, $J \cong 7.3$ Hz, 1 H), 4.48 (d, $J = 16.5$ Hz, 1 H), 4.57 (virt. t, $J \cong 6.8$ Hz, 1 H), 4.72 (d, $J = 16.5$ Hz, 1 H), 4.75−4.88 (m, 2 H), 7.17−7.24 (m, 3 H), 7.30−7.45 (m, 2 H). ^{13}C NMR (DMSO-d_6, 373 K): δ 17.2 (q), 28.9 (q), 48.9 (t), 53.9 (d), 71.0 (t), 80.5 (s), 83.6 (d), 127.4 (d), 127.7 (d), 129.2 (d), 140.0 (s), 156.0 (s). Anal. Calcd for $C_{16}H_{23}NO_3$ (277.4): C, 69.29; H, 8.36; N, 5.05. Found C, 69.62; H, 8.60; N, 5.44.

(2*RS*,3*RS*)-(1,1-Dimethylethyl)-*N*-[2-[(1,1-dimethylethyl)dimethylsilyloxy]ethyloxetan-3-yl]-*N*-phenylmethylcarbamate (*cis*-7e). According to the general irradiation procedure, 1.5 mmol of aldehyde **6e**[35] (282 mg) and 3 mmol of *N*-acyl enamine **1f**[23] (699 mg) were irradiated for 15 h. Flash chromatography (PE/MTBE = 90/10) yielded oxetane **7e** as a mixture of diastereoisomers (337 mg, 54%, d.r. = 85/15). The diastereoisomers were not fully separable. The collection of selected chromatography fractions yielded diastereoisomer *cis*-**7e** in diastereomerically pure form (284 mg, 45%). $R_f = 0.20$ (PE/MTBE = 90/10). IR (film): 1700 cm^{-1} (vs, C=O), 970 (w, COC). ^{1}H NMR (DMSO-d_6, 373 K): δ 0.05 (s, 6 H), 0.90 (s, 9 H), 1.42 (s, 9 H), 1.73 (ddd, $J = 18.5$ Hz, $J = 7.5$ Hz, $J = 3.7$ Hz, 1 H), 1.92 (ddd, $J = 18.5$ Hz, $J = 10.5$ Hz, $J = 5.3$ Hz, 1 H), 3.64 (m, 2 H), 4.43 (virt. t, $J \cong 7.2$ Hz, 1 H), 4.48 (d, $J = 16.4$ Hz, 1 H), 4.57 (virt. t, $J \cong 7.2$ Hz, 1 H), 4.73 (d, $J = 16.4$ Hz, 1 H), 4.81 (m, 1 H), 4.92 (virt. q, $J \cong 7.1$ Hz, 1 H), 7.17−7.35 (m, 5 H). ^{13}C NMR (DMSO-d_6, 373 K): δ −4.5 (q), 18,7 (t), 26.6 (q), 28.8 (q), 34.5 (s), 49.1 (t), 53.5 (d), 59.2 (t), 71.1 (t), 80.6 (s), 84.3 (d), 127.3 (d), 127.7 (d), 129.2 (d), 140.0 (s), 156.0 (s). NOESY experiment: H (4.92)−H (4.81)″; H (4.92)−H (4.43)″; H (4.57)−H (4.43)‴. $C_{19}H_{30}NSiO_3$ (HRMS): Calcd 348.1995; found 348.2000.

(±)-Pseudoephedrine (8). To a mixture of 3 mmol of $LiAlH_4$ (114 mg) in THF (1 mL) was added a solution of 1 mmol of oxetane **5a** (177 mg, d.r.= 90/10) in THF (5 mL) at 0 °C. The mixture was warmed to room temperature, and stirring was continued for 15 h. To this solution were added successively water (0.11 mL), aqueous NaOH (15%, 0.11 mL), and water (0.33 mL). After 1 hr of stirring, the mixture was filtered, and the residue was washed with EA (30 mL). The organic extracts were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Compound **8** was obtained as a white solid. Yield: 142 mg (86%). According to GLC, the product was ≥95% pure. The NMR data were in agreement with the literature values.[36]

(2*RS*,3*RS*)-2-Phenyl-3-(*N*-phenylmethylamino)oxetane (9). TBAF (6.8 mmol, 2.13 g) was added to a solution of 3.4 mmol of oxetane **5g** (1.30 g, d.r. = >95/5) in acetonitrile (60 mL). After 2 h of stirring at 50 °C, the mixture was concentrated in vacuo. The residue was purified by flash chromatography (PE/MTBE = 60/40). Compound **9** was obtained as a colorless oil. Yield: 500 mg (62%). $R_f = 0.31$ (40/60). IR (film): 3340 cm^{-1} (b, NH), 1750 (vs, C=O), 980 (s, COC). ^{1}H NMR: δ 3.38 (s, 2 H), 4.23 (ddd, $J = 7.5$ Hz, $J = 7.0$ Hz, $J = 6.5$ Hz, 1 H), 4.40 (dd, $J = 6.7$ Hz, $J = 6.5$ Hz, 1 H), 4.92 (dd, $J = 7.5$ Hz, $J = 6.7$ Hz, 1 H), 5.95 (d, $J = 7.0$ Hz, 1 H), 6.93 (m, 2 H), 7.19 (m, 3 H), 7.43 (m, 5 H). ^{13}C NMR: δ 51.6 (t), 56.4 (d), 78.5 (t), 89.0 (d), 126.9 (d), 127.5 (d), 128.5 (d), 128.8 (d), 129.0 (d), 129.0 (d), 138.5 (s), 139.9 (s). Anal. Calcd for $C_{16}H_{17}NO$ (239.3): C, 80.30; H, 7.16; N, 5.85. Found C, 80.31; H, 7.07; N, 6.12.

(1*RS*,2*SR*)-1-Phenyl-2-(*N*-phenylmethylamino)-2-phenylmethylsulfanyl-1-propanol (10).[25e,27b] To a solution of 2 mmol of benzylmercaptan (248 mg, 230 μL) in THF (5 mL) was slowly added 2 mmol of *n*-BuLi (1.3 mL, 1.56 M in hexanes) at 0 °C. After 1 h of stirring, 0.5 mmol of oxetane **9** (120 mg) in THF (1 mL) was added at −78 °C. After 20 min, 2 mmol of BF_3-etherate (1.3 mL) was added to the reaction mixture. Stirring was continued for 1 h, and the reaction was subsequently quenched with a saturated aqueous solution of NH_4Cl (5 mL). The mixture was extracted with Et_2O (3 × 10 mL). The organic extracts were combined, washed with brine (5 mL) and dried over $MgSO_4$. The mixture was filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (PE/MTBE = 40/60). Compound **10** was obtained as a white solid. Yield: 152 mg (84%). Mp: 170 °C. $R_f = 0.26$ (PE/MTBE = 40/60). IR (KBr): 3410 cm^{-1} (b, NH), 3320 (s, OH). ^{1}H NMR (MeOH-d_4): δ 2.54 (dd, $J = 14.7$ Hz, $J = 4.7$ Hz, 1 H), 2.65 (dd, $J = 14.7$ Hz, $J = 7.8$ Hz, 1 H), 3.41 (ddd, $J = 8.2$ Hz, $J = 7.8$ Hz, $J = 4.7$ Hz, 1 H), 3.62 (d, $J = 13.7$ Hz, 1 H), 3.92 (d, $J = 13.7$ Hz, 1 H), 4.20 (s, 2 H), 4.86 (d, $J = 8.2$ Hz, 1 H), 6.90−6.94 (m, 2 H), 7.07−7.10 (m, 3 H), 7.26−7.36 (m, 10 H). ^{13}C NMR (MeOH-d_4): δ 30.2 (t), 36.9 (t), 51.2 (t), 63.4 (d), 73.6 (d), 128.3 (d), 128.6 (d), 130.0 (d), 130.3 (d), 130.4 (d), 130.7 (d), 131.1 (d), 131.5 (d), 132.6 (s), 139.1 (s), 141.9 (s). $C_{23}H_{26}NOS$ HRMS; CI, M + H$^+$: Calcd 364.1735; found 364.1729.

(4*SR*,5*RS*)-4-Hydroxymethyl-5-phenyl-3-phenylmethyloxazolidin-2-one (11). To a stirred solution of 2 mmol of trifluoroacetic acid (226 mg, 160 μL) in CH_2Cl_2 (7 mL) was added 1 mmol of oxetane **5f** (339 mg, d.r. = 87/13) in CH_2Cl_2 (2 mL) at −78 °C. The mixture was slowly warmed to room temperature. The solution was concentrated in vacuo, and the trifluoroacetic acid was removed by azeotropic distillation with toluene (2 × 5 mL). The residue was purified by flash chromatography on silica gel (CH/EA = 80/20). Compound **11** was the major product, obtained as a white solid. Yield: (211 mg, 75%). In addition 15 mg (5%) of the (4*RS*,5*RS*)-isomer of compound **11** was isolated. Mp: 131−132 °C. $R_f = 0.41$ (CH/EA = 40/60). IR (KBr): 1690 cm^{-1} (vs, C=O). ^{1}H NMR (DMSO-d_6): δ 3.02 (virt. dt, $J = 11.4$ Hz, $J \cong 4.2$ Hz, 1 H), 3.20 (virt. dt, $J = 11.4$ Hz, $J \cong 4.2$ Hz, 1 H), 3.92 (dt, $J = 8.4$ Hz, $J = 4.2$ Hz, 1 H), 4.29 (d, $J = 15.6$ Hz, 1 H), 4.68−4.72 (m, 2 H), 5.69 (d, $J = 8.4$ Hz, 1 H), 7.28−7.41 (m, 10 H). ^{13}C NMR: δ 46.5 (t), 59.1 (d), 59.2 (t), 76.2 (d), 125.5 (d), 125.5 (d), 127.6 (d), 127.7 (d), 128.4 (d), 128.5 (d), 134.2 (s), 135.9 (s), 157.8 (s). NOE experiment (600 MHz, DMSO-d_6) H (5.69): H_N [3.6%]; H_N (3.92): H [3.5%]. Anal. Calcd for $C_{17}H_{17}NO_3$ (283.3): C, 72.07; H, 6.05; N, 4.94. Found C, 72.25; H, 6.34; N, 5.00.

(4*SR*,5*RS*)-4-Hydroxymethyl-3-methyl-5-phenyloxazolidin-2-one (12). To a stirred solution of 2 mmol of trifluoroacetic acid (226 mg, 160 μL) in CH_2Cl_2 (7 mL) was added 1 mmol of oxetane **5e** (263 mg, d.r. = 90/10) in CH_2Cl_2 (2 mL) at −78 °C. The mixture was slowly warmed to room temperature. The solution was concentrated in vacuo, and the trifluoroacetic acid was removed by azeotropic distillation with toluene (2 × 5 mL). The residue was purified by flash chromatography on silica gel (CH/EA = 70/30). Compound **12** was obtained as a white solid. Yield: 119 mg (58%). Mp: 66 °C. $R_f = 0.55$ (CH/EA = 40/60). IR (KBr): 1730 cm^{-1} (vs, C=O). ^{1}H NMR (300 MHz): δ = 3.00 (s, 3 H), 3.41 (dd, $J = 11.9$ Hz, $J = 4.3$ Hz, 1 H), 3.49 (dd, $J = 11.9$ Hz, $J = 4.3$ Hz, 1 H), 3.95 (virt. dt, $J = 8.6$ Hz, $J = 4.3$ Hz, 1 H), 5.66 (d, $J = 8.6$ Hz, 1 H), 7.31−7.45 (m, 5 H). ^{13}C NMR: δ 30.1 (q), 59.8 (t), 62.3 (d), 77.5 (d), 125.7 (d), 125.9 (d), 128.9 (d), 134.7 (s), 176.1 (s). Anal. Calcd for $C_{11}H_{13}NO_3$ (207.2): C, 63.76; H, 6.32; N, 6.76. Found C, 63.89; H, 6.42; N, 6.92.

(4*SR*,5*RS*)-3-Methyl-4-(4-methylphenylsulfonyloxymethyl)-5-phenyloxazolidin-2-one (13). To a stirred solution of 0.55 mmol of alcohol **12** (144 mg) in pyridine (2 mL) was added 2.7 mmol of *p*-toluenesulfonyl chloride (525 mg) at 5 °C. After 15 h of stirring, the reaction mixture was quenched with 2 M aqueous HCl (10 mL) and extracted with Et_2O (3 × 30 mL). The organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (CH/EA = 80/20 → 70/30). Compound **13** was obtained as a white solid. Yield: 194 mg (98%). $R_f = 0.24$ (CH/EA = 40/60). IR (KBr): 1735 cm^{-1} (vs, C=O). ^{1}H NMR: δ 2.46 (s, 3 H), 2.90 (s, 3 H), 3.66 (dd, $J = 12.2$ Hz, $J = 4.0$ Hz, 1 H), 3.76 (dd, $J = 12.2$ Hz, $J = 3.8$ Hz, 1 H), 3.95 (m, 1 H), 5.61 (d, $J = 8.4$ Hz, 1 H), 7.20−7.38 (m, 7 H), 7.52−7.59 (m, 2 H). ^{13}C NMR: δ 30.5 (q) 30.9 (q), 60.0 (t), 67.0 (d), 77.3 (d), 126.0 (d), 127.8 (d), 128.8 (d), 129.1 (d), 129.9 (d), 132.2 (s), 137.6 (s), 145.7 (s), 175.1 (s). Anal. Calcd for $C_{18}H_{19}NO_5S$ (361.4): C, 59.82; H, 5.30; N, 3.88; found C, 60.00; H, 5.53; N, 3.99.

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(4*SR*,5*RS*)-3,4-Dimethyl-5-phenyloxazolidin-2-one (14).[32] Sodium borohydride (0.38 mmol, 14.3 mg) was added to a solution of 0.19 mmol of tosylate **13** (70 mg) in DMSO (1 mL). The mixture was heated to 150 °C and kept at this temperature for 2 h. After cooling to room temperature, the solution was diluted with water (5 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The organic extracts were combined, washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. Compound **14** was obtained as a white solid. Yield: 26 mg (72%). $R_f = 0.10$ (CH/EA = 40/60). ^{1}H NMR: $\delta = 0.76$ (d, $J = 6.2$ Hz, 3 H), 2.86 (s, 3 H), 4.02 (m, 1 H), 5.56 (d, $J = 7.9$ Hz, 1 H), 7.28−7.38 (m, 5 H). All other analytical data are in agreement with the literature values.[37]

(±)-Ephedrine (15). An aqueous solution of KOH (20% KOH in water/ethanol 1/1, 1 mL) was added to 0.95 mmol of oxazolidinone **14** (18 mg). After 2 h of refluxing, the mixture was cooled to room temperature and neutralized with a saturated aqueous NH_4Cl solution (10 mL). The product was extracted with CH_2Cl_2 (3 × 20 mL). The organic extracts were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Compound **15** was obtained as a white solid. Yield: 12 mg (77%). According to GLC, the product was ≥95% pure. The NMR data were in agreement with the literature values.[38]

(±)-*N*-Methylephedrine (16). To a mixture of 1.3 mmol of $LiAlH_4$ (49 mg) in THF (1 mL) was added a solution of 0.43 mmol of oxazolidinone **14** (155 mg) in THF (5 mL) at 0 °C. The mixture was refluxed for 2 h. To this solution were added successively water (0.11 mL), aqueous NaOH (15%, 0.11 mL), and water (0.33 mL). After 1 h of stirring, the mixture was filtered and the residue was washed with EA (30 mL). The solution was dried over $MgSO_4$, filtered, and concentrated in vacuo. Yield: 75 mg (97%). According to GLC, the product was ≥95% pure. The NMR data were in agreement with the literature values.[39]

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Supporting Information Available: Further analytical data (NMR assignments, IR, MS) for compounds **1e**, **1g**, **5, 7, 9**−**13** and NMR spectra (^{1}H, ^{13}C) of compounds **5b**, **5h**, **7e**, and **10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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