# Asymmetric Electrophilic Substitutions at the α-Position of γ- and δ-Lactams

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*Dedicated to Professor Jean François Normant on the occasion of his 65th birthday*

**Keywords:** Alkylations / Asymmetric synthesis / Lactams / Michael additions / Nitroalkenes

Enantioselective electrophilic substitutions with Michael acceptors and alkylating agents at the α-positions of γ- and δ-lactams are presented. The asymmetric Michael addition of lactam **1a** to nitroalkenes **2** was used as the key step for the synthesis, over three steps, of α-(β-aminoalkyl)-γ-lactams **5** in good overall yields (37–61%) and with very good diastereomeric and enantiomeric excesses (*de* ≥ 96%, *ee* = 82 to ≥ 96%). Conjugate addition to alkenylsulfones **6a** and **6b** afforded Michael adducts **7a** and **7b** in good yields, but with only moderate diastereoselectivities (*de* = 38–41%). α-Substituted *N*-dialkylamino lactams **9a–c** were obtained by asymmetric alkylation of *N*-(dialkylamino)lactam **1a** with functionalised electrophiles **8a–c** in good yields (66–84%) and with moderate to excellent diastereomeric excesses (66 to ≥ 96%). The auxiliary was removed by reductive N–N bond cleavage to afford the lactam **10** (*ee* = 83%). A second alkylation of α-alkylated d *N*-(dialkylamino)lactams **11** yielded α-disubstituted γ-butyrolactams (**12a**, **12b**) in good yields and diastereomeric excesses (*de* = 83–88%) and α-disubstituted δ-valerolactams (**12c–e**) in good yields but with low to moderate diastereoselectivities (*de* = 6–52%). The α-silylated γ-lactam **15** was obtained in good yield (53% over two steps) and with an enantiomeric excess of 83% by α-silylation of *N*-(dialkylamino)lactam **1a** and subsequent reductive removal of the auxiliary.

## Introduction

The lactam functionality is a widespread structural feature in many natural and biologically active products. β-Lactams[1] are by far the largest class of lactams and they are of enormous interest as antibiotics. γ-Lactams and δ-lactams are also of importance, as many derivatives have been shown to possess biological activity.[2] The highly functionalised γ-lactam (−)-pramanicin,[2b] for instance, displays antifungal activity towards several fungal pathogens. The α-substituted δ-lactam L-724,217 (Merck) may be used as an antithrombotic agent, thanks to its antiplatelet activity.[2d] As lactams can be converted into the corresponding acyclic amino acids, they are valuable precursors for the synthesis of these compounds. γ-Aminobutyric acids (GABAs), which are acyclic derivatives of γ-lactams, are used in the regulation of neurological disorders such as Parkinson's disease and epilepsy.[3] Recently, Suh et al. have used (*S*)-3-ethylpiperidin-2-one as a precursor in the total synthesis of the macrolactam antibiotic fluvirucinin $A_1$,[4] while α-disubstituted γ- and δ-lactams have been employed as precursors in the synthesis of alkaloids.[5] Some 3,3-dialkyl-2-pyrrolidinones have shown anticonvulsive activity and may be useful in the treatment of human epilepsies.[6]

Thanks to the importance of chiral α-substituted lactams, several methods for their asymmetric synthesis have been reported. Meyers et al., for instance, developed the bicyclic lactam methodology,[7] while Royer, Quirion, and Husson et al. have used γ- and δ-lactams with chiral auxiliaries attached to the lactam nitrogen atoms to carry out diastereoselective alkylations at the α-positions.[8] Fuji's asymmetric nitroolefination, in which the chirality information is transferred from the electrophile, is an efficient method for the generation of a quaternary stereogenic centre adjacent to the lactam carbonyl group.[9] A catalytic method for the enantioselective generation of stereogenic centres in positions α to lactam carbonyl functions was developed by Porter et al.,[10] who utilised a chiral bis(oxazoline)zinc complex in the radical allylation of an α-bromolactam.

We have already reported on asymmetric electrophilic substitutions at the α-positions of γ- and δ-lactams with alkyl halides,[11] enoates,[12a] and nitroalkenes.[12b] We now wish to report in detail on the nitroalkene additions and to present new results using alkenylsulfones as Michael acceptors, an aziridine, alkyl halides carrying an additional functionality, and trimethylsilyl chloride as electrophiles. We also report on the asymmetric synthesis of α-disubstituted lactams with quaternary stereogenic centres.

## Results and Discussion

Because of their utility in C−C bond formation, a great variety of asymmetric Michael additions has been developed in recent years.[13] Nitroalkenes are excellent Michael acceptors, as the nitro group can be converted into a broad range of functionalities,[14] and so various methods for asymmetric Michael additions to nitroalkenes are available.[15] The addition of lactam **1a** to aliphatic nitroalkenes

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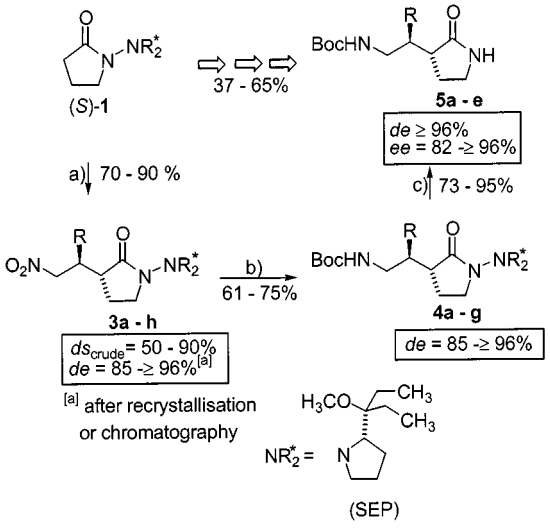
**2a−c** was conducted after lithiation of the *N*-(dialkylamino)-lactam (3−4 h at −78 °C with 1.2 equiv. of LDA in THF) and subsequent addition of the aliphatic nitroalkenes[16] at −100 °C: the same conditions as used for the addition to enoates.[12] The crude adducts **3a−c** were obtained with moderate to good diastereoselectivities after aqueous workup at room temperature. In the case of compound **3a** only two diastereomers were observed (*de* = 81%), while the other aliphatic examples gave three diastereomers in ratios of 7:7:86 for **3b** and 8.5:11.5:80 for **3c**. The major diastereomer of **3a** was obtained in diastereomerically pure form after column chromatography and the major diastereomer of **3b** after recrystallization from diethyl ether/pentane. For adduct **3c** it was only possible to remove one diastereomer by column chromatography, and it was consequently isolated in 85% diastereomeric excess (Table 1, Scheme 1).

Table 1. Results of the diastereoselective Michael addition of (*S*)-**1** to nitroalkenes **2**

| Product | R | Yield [%] | *dr*[a][b] [a] | *de* [%][a] |
|---|---|---|---|---|
| **3a** | Me | 90 | 10:90 | ≥ 96[c] |
| **3b** | Et | 73 | 7:7:86 | ≥ 96[d] |
| **3c** | *n*Pr | 74 | 8.5:11.5:80 | 85[c] |
| **3d** | Ph | 72 | 5:18:77 | ≥ 96[e] |
| **3e** | 2-Furyl | 76 | 17:33:50 | ≥ 96[e] |
| **3f** | 2-Naphthyl | 72 | 4.5:21.5:74 | ≥ 96[e] |
| **3g** | 3,4-$OCH_2OC_6H_3$ | 70 | 10:18:72 | ≥ 96[e] |
| **3h** | 3,4,5-$(MeO)_3C_6H_3$ | 60 | 10:17:63 | ≥ 96[c] |

[a] Determined by $^1$H NMR and $^{13}$C NMR spectroscopy. [b] Crude product. [c] After column chromatography. [d] After recrystallization. [e] After HPLC.




Scheme 1. Synthesis of α-(β-aminoalkyl)lactams by asymmetric Michael addition to nitroalkenes: a) 1. LDA, THF, −78 °C; 2. (*E*)-$RCH{=}CH_2NO_2$ (**2a−g**), −40 °C or −100 °C; b) 1. $NaBH_4$, Pd/C, THF, MeOH; 2. $Boc_2O$, $NEt_3$; c) Li, $NH_3$, −33 °C

At first we conducted additions to aromatic nitroalkenes[12b,16] **2d−g** under the same conditions as used for additions to the aliphatic nitroalkenes **2a−c**. Product **3d** was obtained with a yield of 67% and a diastereoselectivity of 70%. We carried out some experiments to optimize this result and it turned out that the best diastereoselectivities and yields could be achieved by changing the reaction temperature from −100 °C to −40 °C and the reaction time from 14 h to 1−1.5 h (Table 2). The other additions to nitroalkenes **2d−g** were conducted under these optimized conditions and, after aqueous workup at −40 °C, the crude aryl-substituted Michael adducts were obtained as mixtures of three diastereomers with diastereomeric ratios between 17:33:50 (**3e**) and 5:18:77 (**3d**). Separation of these mixtures could be achieved by HPLC (**3d−f**) or column chromatography (**3g**), so the major and first minor diastereomer of each adduct **3d−g** were obtained in diastereomerically pure form. The least abundant diastereomers, formed in the smallest amounts in the crude mixtures, were not isolated (Table 1, Scheme 1).

Table 2. Results of optimization of the preparation of Michael addition to **2d**

| Experiment | Solvent | Reaction time [h] | *T* [°C] (start)[a] | *T* [°C] (end)[b] | Yield [%] | *ds* [c] [%] |
|---|---|---|---|---|---|---|
| 1 | THF | 14 | −100 | −78 | 67 | 70 |
| 2 | $Et_2O$ | 14 | −100 | −78 | 50 | n.d. |
| 3 | THF | 1.5 | −100 | −78 | 77 | 57 |
| 4 | THF | 1.5 | −40 | −40 | 90 | 78 |
| 5 | THF | 1.5 | −20 | −20 | 84 | 75 |
| 6 | THF | 1.5 | 0 | 0 | 56 | 64 |

[a] Temperature of addition of nitroalkene. [b] Temperature at quenching of the reaction. [c] Determined by $^1$H NMR and $^{13}$C NMR spectroscopy on the crude product.

The relative and absolute configurations of the newly formed stereogenic centres in the major diastereomer of **3b** were determined by X-ray crystallography as given in Figure 1. The sense of asymmetric induction α to the carbonyl group for the major diastereomers is in agreement with that observed previously in the α-alkylation of *N*-(dialkylamino)-lactams.[11] The relative configuration (*anti*) is in accordance with our findings for the formation of Michael adducts of enoates and lithiated *N*-(dialkylamino)lactams,[12a] The stereochemistry of the major diastereomers of the other Michael adducts **3** is based on the assumption of a uniform reaction mechanism operating in the addition to nitroalkenes.

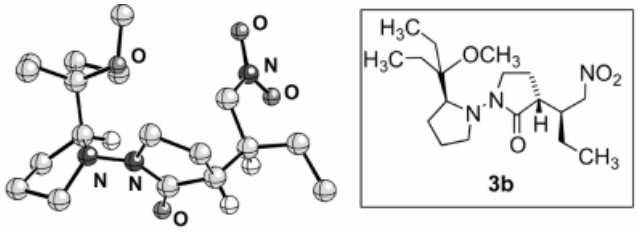
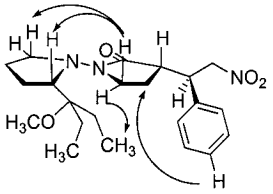



Figure 1. Crystal structure of lactam

The relative and absolute configuration of the first minor diastereomer formed in the addition was determined by NOE experimentation on **3d** (Figure 2). The configuration at the α-position is the opposite of that observed with the major diastereomers of other α-substituted *N*-(dialkylamino)-lactams. The relative configuration of the newly formed centres is *syn*. It was necessary to conduct the NOE experiment in [$D_6$]benzene at 50 °C, because lower temperatures and other solvents such as $CDCl_3$ resulted in broadening of the NMR signals. This phenomenon occurs in every NMR spectrum of *N*-(dialkylamino)lactams and is caused by hindered rotation of the N−N bond.




**3d**

Figure 2. NOE measurements on **3d**

Before removal of the auxiliary by reductive cleavage of the N−N bond, with lithium in liquid ammonia,[17] it was necessary to convert the nitro compounds **3** into the corresponding amines, by using $NaBH_4$ in a mixture of MeOH and THF in the presence of a catalytic amount of Pd on charcoal.[18] Without this reduction of the nitro group to the more stable amine, compounds **3** may have suffered from decomposition by elimination of nitrous acid. The crude amines were immediately protected as *tert*-butylcarbamates (Boc). The *N*-protected amines **4** were obtained in moderate to good yields (61−76%). Epimerisation during the conversion into **4** was not observed; the *de* values of the products were found to be the same as of the starting material. However, several attempts to convert the nitro adduct **3h** into the corresponding protected amine gave poor yields (20−30%) and partial epimerisation (Table 3).

Table 3. Results of the synthesis of protected aminolactams **4** by reduction of **3** and subsequent amine protection

| Product | R | Yield [%] | *de* [%][a] |
|---|---|---|---|
| **4a** | Me | 76 | ≥ 96 |
| **4b** | Et | 74 | ≥ 96 |
| **4c** | *n*Pr | 64 | 85 |
| **4d** | Ph | 75 | ≥ 96 |
| **4e** | 2-Furyl | 68 | ≥ 96 |
| **4f** | 2-Naphthyl | 71 | ≥ 96 |
| **4g** | 3,4-$OCH_2O$-$C_6H_3$ | 61 | ≥ 96 |

[a] Determined by $^1$H NMR and $^{13}$C NMR spectroscopy.

Removal of the auxiliary from compounds **4a**−**e** was achieved by cleavage of the N−N bond using lithium in ammonia. The corresponding α-substituted lactams **5** were obtained in good yields and with excellent diastereomeric excesses (*de* ≥ 96%) and good to excellent enantiomeric excesses (*ee* = 82 to ≥ 96%) (Table 4). However, the reductive cleavage showed limitations in the application of substituted aromatic compounds, owing to Birch reduction (**4f**) or lithium/alkoxy exchange (**4g**), resulting in complex product mixtures in those cases.

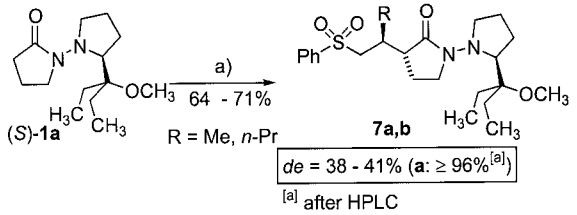
Table 4. Results of the preparation of α-(β-ethylamino)lactams **5** by reductive cleavage of the N−N bond from *N*-(dialkylamino)lactams **4**

| Product | R | Yield [%] | *de* [%][a] | *ee* [%][b] |
|---|---|---|---|---|
| (*R*,*R*)-**5a** | Me | 95 | ≥ 96 | ≥ 96 |
| (*R*,*R*)-**5b** | Et | 73 | ≥ 96 | ≥ 96 |
| (*R*,*R*)-**5c** | *n*Pr | 78 | ≥ 96 | 82 |
| (*S*,*R*)-**5d** | Ph | 95 | ≥ 96 | ≥ 96[c] |
| (*S*,*R*)-**5e** | 2-Furyl | 88 | ≥ 96 | ≥ 96 |

[a] Determined by $^1$H NMR and $^{13}$C NMR spectroscopy. [b] Determined by GC on a chiral stationary phase (Chirasil-L-Val 25 m). [c] Based on the *de* value of the corresponding Mosher amide ($^1$H NMR).

The diastereomeric excesses of the α-substituted lactams **5** were determined by $^1$H and $^{13}$C NMR spectroscopy. The enantiomeric excesses of **5a**, **5b**, **5c**, and **5e** were determined by gas chromatography with a chiral stationary phase. The *ee* value for **5d** was deduced from the *de* value of the corresponding (*R*)-MTPA-amide (**5d′**), which was synthesized from **5d** by removal of the Boc protecting group with TFA and subsequent amide formation with (*S*)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride.[19]

To extend the methodology of asymmetric Michael additions of *N*-(dialkylamino)lactams we used alkenyl sulfones as acceptors.[20] The addition of **1a** to sulfones **6a** and **6b** was conducted under the conditions used in additions to enoates or aliphatic substituted nitroalkenes (Scheme 2). The products were obtained in good yields (64−71%), with two diastereomers being produced. The diastereomeric excesses were moderate (38−41%), and only **7a** could be isolated in diastereomerically pure form by HPLC (Table 5). This configuration for the major diastereomer is based on the assumption of a reaction pathway similar to that of Michael addition of *N*-(dialkylamino)lactams to nitroalkenes.




Scheme 2. Asymmetric Michael addition of *N*-(dialkylamino)lactam (*S*)-**1** to alkenyl sulfones: a) 1. LDA, THF, −78 °C; 2. (*E*)-RCH=$CHSO_2$Ph (**6a, 6b**), −100 °C

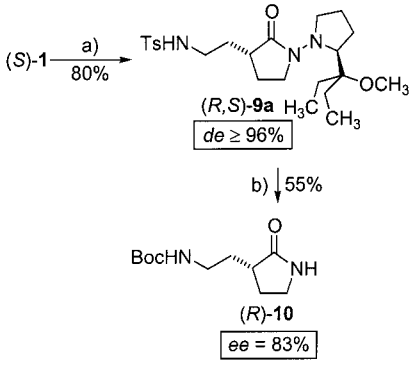
In addition, we investigated the use of electrophiles bearing functional groups for the synthesis of α-substituted lactams. We used *N*-tosylaziridine[21] for the β-aminoethylation of lactam **1a**, affording compound **9a**. *N*-Tosylaziridine (**8a**)

Table 5. Results of Michael additions of *N*-(dialkylamino)lactam (*S*)-**1a** to alkenylsulfones

| Product | R | Yield [%] | *de* [%][a] |
|---|---|---|---|
| **7a** | Me | 71 | 38 (≥ 96[b]) |
| **7b** | *n*Pr | 64 | 43 |

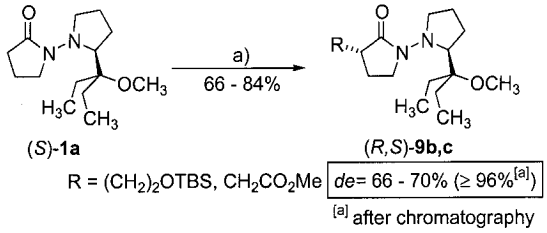
[a] Determined by $^1$H NMR and $^{13}$C NMR spectroscopy. [b] After HPLC.

has already been used successfully in our group for the asymmetric β-aminoethylation of SAMP-hydrazones.[22] The β-aminoethylated lactam **9a** was obtained in a good yield (80%) and diastereomeric excess (*de* ≥ 96%) (Scheme 3). In order to remove the auxiliary we again used the reductive cleavage of the N−N bond with lithium in liquid ammonia. Under these conditions the tosyl group should be removed by cleavage of the N−S bond as well. On treatment with less than 10 equiv. of lithium, only the tosyl group was removed. When 10 equiv. of Li were used, the β-aminoethylated lactam **10** was isolated after protection of the amine with $Boc_2O$ in 30% yield and with an enantiomeric excess of 95%. With 12.5 equiv. of Li the yield was higher (55%) but the basic conditions had resulted in partial racemization, as the enantiomeric excess was 83%. Further investigations and extension of the aziridine addition are in progress.3




Scheme 3. Ring-opening of aziridine **8a** with the lithium enolate of lactam (*S*)-**1a**: a) 1. LDA, THF, −78 °C; 2. $(CH_2)_2NTs$ (**8a**), −100 °C; b) 1. Li, $NH_3$, −33 °C; 2. $Boc_2O$, $NEt_3$, room temp.

We also used methyl bromoacetate and (*tert*-butyldimethylsilyloxy)ethyl bromide as electrophiles for the alkylation of lactam **1a** (Scheme 4), employing the same conditions as used in the alkylation of *N*-(dialkylamino)lactams with normal electrophiles.[11] The α-alkylated *N*-(dialkylamino)lactams **7b** and **7c** were obtained in good yields and with moderate diastereoselectivities (*de* = 66−70%), and the major diastereomers were isolated in diastereomerically pure form after chromatography (Table 6). The absolute configurations of the major diastereomers of **9a**−**c** were assigned on the assumption of a uniform pathway for the mechanism of α-alkylation of *N*-(dialkylamino)lactams.




Scheme 4. Alkylation of lactam (*S*)-**1a** with functionalized electrophiles: a) 1. LDA, THF, −78 °C; 2. RBr (**8b, 8c**), −100 °C

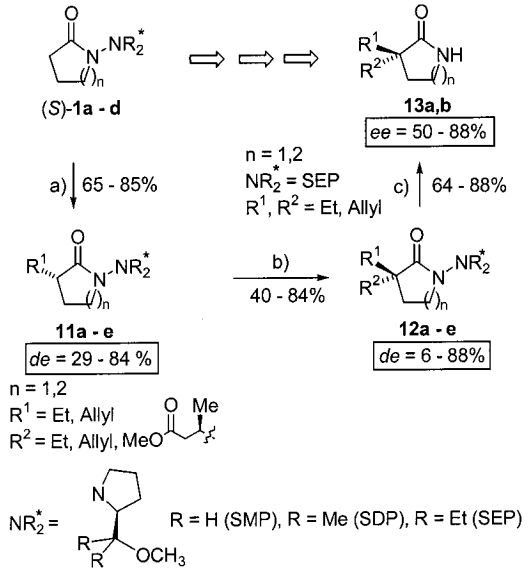
Table 6. Alkylation of *N*-(dialkylamino)lactam **1** with functionalised electrophiles

| Product | R | Yield [%] | *de* [%][a] |
|---|---|---|---|
| (*R*,*S*)-**9a** | $(CH_2)_2NHTs$ | 80 | ≥ 96 |
| (*R*,*S*)-**9b** | $CH_2CO_2Me$ | 84 | 66 (≥ 96[b]) |
| (*R*,*S*)-**9c** | $(CH_2)_2OTBS$ | 66 | 70 (≥ 96[b]) |

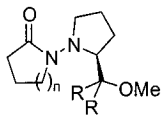
[a] Determined by $^1$H NMR and $^{13}$C NMR spectroscopy. [b] After column chromatography.

We have already emphasized the importance of α-disubstituted lactams in natural product synthesis. Six-membered lactams have particularly been used for the synthesis of alkaloids.

We investigated the synthesis of some 5- and 6-membered α-disubstituted lactams by an *N*-(dialkylamino)lactam double alkylation sequence. As shown in Scheme 5, *N*-(dialkylamino)lactams **1a**−**d**, which were synthesized by literature procedures,[23] were first alkylated by a methodology developed in our group.[11a,11b]




Scheme 5. Synthesis of α-dialkylated lactams **13**: a) 1. LDA, THF, −78 °C; 2. $R^1Br$, −100 °C; b) 1. LDA, THF, −78 °C; 2. $R^2Br$ or (*E*)-$CH_3CH{=}CHCO_2CH_3$, −100 °C; c) Li, $NH_3$, −33 °C



**1a**: n = 1, R = Et
**1b**: n = 2, R = H
**1c**: n = 2, R = Me
**1d**: n = 2, R = Et

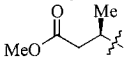
The α-alkylated *N*-(dialkylamino)lactams (Table 7) underwent a second electrophilic substitution under the same conditions as the first step. The γ-lactams **12a** and **12b** were obtained in good yields and diastereomeric excesses (*de* = 83−88%). The second alkylation of α-alkylated δ-lactams **11b**−**e** afforded the α-disubstituted products **12c**−**e** in moderate to good yields, but with rather low to moderate diastereoselectivities (6−52%). We conducted several experiments in which we varied the reaction conditions (temperature, solvent, base) but the results could not be improved (Table 8).

Table 7. Alkylation of *N*-(dialkylamino)lactams **1**

| Product | *n* | $NR_2$* | $R^1$ | Yield [%] | *de* [%][a] |
|---|---|---|---|---|---|
| (*S*,*S*)-**11a** | 1 | SEP | Et | 85 | 84 (≥ 96[b]) |
| (*S*,*S*)-**11b** | 2 | SMP | Et | 66 | 34 |
| (*S*,*S*)-**11c** | 2 | SDP | Et | 65 | 67 (≥ 96[b]) |
| (*S*,*S*)-**11d** | 2 | SEP | Et | 83 | 32 |
| (*R*,*S*)-**11e** | 2 | SEP | Allyl | 82 | 54 |

[a] Determined by $^1$H NMR and $^{13}$C NMR spectroscopy. [b] After column chromatography.

Table 8. Alkylation of α-substituted *N*-(dialkylamino)lactams **11**, preparation of dialkylated *N*-(dialkylamino)lactams **12**

| Product | *n* | $NR_2$* | $R^1$ | $R^2$ | Yield [%] | *de* [%][a] |
|---|---|---|---|---|---|---|
| **12a** | 1 | SEP | Et | Allyl | 84 | 88 |
| **12b** | 1 | SEP | Et |  | 84 | 83 |
| **12c** | 2 | SMP | Et | Allyl | 64 | 25 |
| **12d** | 2 | SDP | Et | Allyl | 71 | 6 |
| **12e** | 2 | SEP | Et | Allyl | 45 | 52 |
| **12e** | 2 | SEP | Allyl | Et | 40 | 31 |

[a] Determined by $^1$H NMR and $^{13}$C NMR spectroscopy.

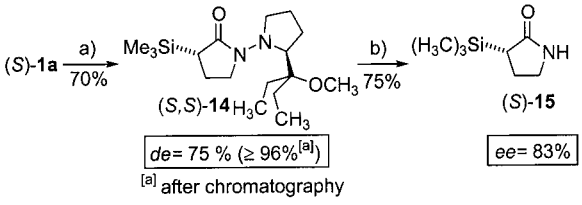
The auxiliaries in lactams **12a**, **12c**, and **12e** were removed by N−N bond cleavage with lithium in ammonia, and the α-disubstituted lactams **13a** and **13b** were obtained in good yields. The enantiomeric excesses were determined by gas chromatography on chiral stationary phases and were in agreement with the diastereomeric excesses of their precursors (Table 9).

Table 9. Synthesis of α-disubstituted lactams **13** by removal of the auxiliary from *N*-(dialkylamino)lactams **12**

| Product | *n* | $R^1$ | $R^2$ | Yield [%] | *ee* [%][a] |
|---|---|---|---|---|---|
| (*S*)-**13a** | 1 | Et | Allyl | 84 | 88 |
| (*R*)-**13b** | 2 | Et | Allyl | 55 | 51 |
| (*S*)-**13b** | 2 | Allyl | Et | 60 | 42 |

[a] Determined by GC on a chiral stationary phase (Chirasil-Dex 25 m).

Finally, we investigated the asymmetric α-silylation of **1a**. After metallation with LDA the lactam enolate of **1a** was trapped with trimethylsilyl chloride to yield **14** in a good yield and with a moderate diastereomeric excess (*de* = 75%). The major diastereomer could be obtained in diastereomerically pure form after chromatography (Scheme 6). The N−N bond cleavage with lithium in liquid ammonia afforded the α-silylated lactam **15** with a relatively low degree of racemization, as the enantiomeric excess was determined by gas chromatography on a chiral stationary phase to be 83%. We are currently investigating the use of other silyl electrophiles, such as isopropoxydimethyl silyl chloride, which should allow the synthesis of α-hydroxylactams after Tamao oxidation[24] of the α-silylated lactam.




Scheme 6. Synthesis of α-silylated lactam **15**: a) 1. LDA, THF, −78 °C; 2. TMSCl, −100 °C; b) Li, $NH_3$, −33 °C

## Conclusion

In conclusion, we have developed an efficient method for asymmetric electrophilic substitution at the α-positions in γ- and δ-lactams, to afford ω-functionalised α-alkylated lactams and α-disubstituted lactams with quaternary stereogenic centres. α-(β-Aminoethyl)-γ-lactams, which represent "double" GABA derivatives, were synthesized in three steps, with an asymmetric Michael addition of a metallated enantiopure *N*-(dialkylamino)lactam to nitroalkenes as the key step. Alkenyl sulfones were also used as Michael acceptors. Diastereoselective α-alkylation with electrophiles, such as *N*-tosylaziridine or trimethylsilyl chloride, yielded the α-substituted lactams with functionalities suitable for further reactions.

## Experimental Section

**General Remarks:** All reactions were carried out under dry argon, using standard Schlenk techniques. All reagents were of commer-

cial quality and used from freshly opened containers. Solvents were dried and purified by conventional methods prior to use. THF and $Et_2O$ were freshly distilled from Na under Ar. *n*BuLi (1.6 N in hexane) was purchased from Merck, Darmstadt. Preparative column chromatography: Merck silica gel 60, particle size 0.040−0.063 mm (230−400 mesh, flash). Analytical TLC: Silica gel 60 $F_{254}$ plates, Merck, Darmstadt. All melting points (Büchi 510) are uncorrected. Optical rotation values were measured using a Perkin−Elmer P 241 polarimeter, solvents used were of Merck UVASOL quality. Analytical GC: Siemens Sichromat 2 or 3 equipped with Shimadzu Chromopac C-R3A, FID, using SE-54 capillary column (25 m × 0.25 mm), carrier gas: nitrogen. Preparative HPLC: GILSON Abimed; Merck. Lichrosorb® column (25 cm × 25 mm, silica 60, particle size 0.007 mm); solvent: $Et_2O$/pentane mixtures, UV detection. Microanalyses were obtained with an Elementar Vario EL element analyzer. MS: Varian MAT 212 (EI 70 eV or CI, isobutane, 100 eV) with DIE ionisation. IR spectra: Perkin−Elmer FT/IR 1750. $^1$H NMR spectra (300, 400, and 500 MHz), $^{13}$C NMR (75, 100 and 125 MHz): Varian VXR 300, Gemini 300, Varian Inova 400 or Varian Unity 500, TMS was used as internal standard. The chiral auxiliaries SAMP [(*S*)-1-amino-2-(methoxymethyl)pyrrolidine], SADP [(*S*)-1-amino-2-(1-methoxy-1-methylethyl)pyrrolidine] and SAEP [(*S*)-1-amino-2-(1-ethyl-1-methoxypropyl)pyrrolidine] were prepared from (*S*)-proline according to literature procedures.[25,26]

**General Procedure 1a (GP 1a) for the Michael Addition of Lithiated *N*-(Dialkylamino)lactams (*S*)-1 to Aliphatic Substituted Nitroalkenes and Alkenyl Sulfones:** A solution of lithium diisopropylamide (1.8 mmol) in THF (15 mL) was slowly added at −78 °C, by double-ended needle, to a solution of *N*-(dialkylamino)lactam **1** (1.5 mmol) in THF (7 mL). The mixture was stirred for 3−4 h at −78 °C. The reaction mixture was cooled to −100 °C and the Michael acceptor **2** (1.8 mmol, neat) was added dropwise. The mixture was stirred overnight at −78 °C and then warmed to −30 °C. The reaction was quenched by addition of a saturated aqueous $NH_4Cl$ solution (15 mL). The aqueous phase was extracted three times with $CH_2Cl_2$ (50 mL). The combined organic phases were washed with $H_2O$ (25 mL) and dried with $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography ($SiO_2$; diethyl ether/pentane, 1:2) to afford the Michael adducts **3**.

**3a:** This compound was prepared according to GP 1a; Michael addition of lactam **1a** (1.5 mmol, 380 mg) to (*E*)-nitroprop-1-ene (**2a**) (1.8 mmol, 160 mg) afforded adduct **3a** as a colourless solid. Yield: 400 mg; 78%; *de* = 81% (≥ 96%, after chromatography); $[\alpha]_D^{24}$ = −24.9 (*c* = 1.12, $CHCl_3$, *de* ≥ 96%); m.p. 71−73 °C. IR ($CHCl_3$): $\tilde{\nu}$ = 2970 cm$^{-1}$ (s), 2880, 2840 (s), 2830 (m) 1680 (s), 1550 (s), 1460 (s), 1435, 1415 (m), 1380 (s), 1280 (s), 1120 (m), 1080 (s), 950 (w), 920 (m). $^1$H NMR (300 MHz, $CDCl_3$): δ = 0.84, 0.88 (2 t, *J* = 7.4 Hz, 6 H, $2CH_2CH_3$), 1.08 (d, *J* = 7.1 Hz, 3 H, $CHCH_3$), 1.50−2.20 (m, 10 H, $2CH_2CH_3$, $NCH_2CH_2$, $CH_2CH_2CH_2N$), 2.51 (dt, *J* = 3.7, 9.1 Hz, 1 H, CHCHCO), 2.63 (m, 1 H, CHCHCO), 3.12 (m, 2 H, $NCH_2$), 3.24 (s, 3 H, $COCH_3$), 3.47 (m, 2 H, $CONCH_2$), 3.72 (br. s, 1 H, NCH), 4.52 (dd, *J* = 8.4, 12.8 Hz, 1 H, $CHHNO_2$), 4.74 (dd, *J* = 5.7, 12.8 Hz, $CHHNO_2$). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 7.98, 8.75, 12.93, 21.10, 24.01, 24.16, 26.16, 33.90, 42.64, 49.94, 52.35, 65.00, 79.16, 79.94, 172.03. MS (EI): *m*/*z* (%) = 341 (0.1) [M$^+$], 241 (13), 240 (100) [M$^+$ − $C[CH_2CH_3]_2OCH_3$], 152 (8), 97 (12), 68 (5), 55 (5). $C_{17}H_{31}N_3O_4$ (341.45): calcd. C 59.80, H 9.15, N 12.31; found C 60.07, H 9.35, N 12.06.

**3b:** This compound was prepared according to GP 1a; Michael addition of lactam **1a** (1.5 mmol, 380 mg) to (*E*)-nitrobut-1-ene (**2b**) (1.8 mmol, 180 mg) afforded adduct **3b** as a colourless solid. Yield: 390 mg (73%); *dr* = 7:7:86 (*de* ≥ 96%, after recrystallisation from $Et_2O$/pentane); $[\alpha]_D^{24}$ = −26.2 (*c* = 0.69, $CHCl_3$, *de* ≥ 96%); m.p. 75−76 °C. IR ($CHCl_3$): $\tilde{\nu}$= 2970 cm$^{-1}$ (s), 2935 (s), 2880 (m), 2830 (w) 1675 (s), 1550 (s), 1460, 1440, 1415, 1385, 1355 (m), 1300 (w), 1275 (m), 1245 (w), 1180, 1165 (w), 1140, 1095, 1170, 1095, 1070, 1045 (m), 925, 910 (m), 740, 720 (w). $^1$H NMR (400 MHz, $CDCl_3$): δ = 0.84, 0.89 (2 t, *J* = 7.7 Hz, 6 H, $2CH_2CH_3$), 0.98 (t, *J* = 7.4 Hz, 3 H, $CH_2CH_3$), 1.45−2.12 (m, 12 H, $3CH_2CH_3$, $NCH_2CH_2$, $CH_2CH_2CH_2N$), 2.50 (m, 1 H, CHCHCO), 2.62 (dt, *J* = 3.7, 9.1 Hz, 1 H, CHCHCO), 3.13 (m, 2 H, $NCH_2$), 3.23 (s, 3 H, $COCH_3$), 3.45 (m, 2 H, $CONCH_2$), 3.70 (br. s, 1 H, NCH), 4.37 (dd, *J* = 7.2, 12.6 Hz, 1 H, $CHHNO_2$), 4.77 (dd, *J* = 6.3, 12.9 Hz, 1 H, $CHHNO_2$). $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 7.97, 8.84, 11.61, 20.42, 21.20, 24.00, 24.28, 26.13, 26.27, 39.84, 41.25, 49.88, 52.38, 65.09, 80.04, 76.85, 172.32. MS (CI, isobutane): *m*/*z* (%) = 357 (21) [M$^+$ + 2], 356 (100) [M$^+$ + 1], 326 (7), 325 (5), 324 (25), 322 (5), 311 (5), 254 (7) [M$^+$ − $C[CH_2CH_3]_2OCH_3$]. $C_{18}H_{33}N_3O_4$ (355.48): calcd. C 60.82, H 9.36, N 11.82; found C 60.74, H 9.34, N 11.66. Crystal data of lactam **3b** and experimental details: The compound was crystallized from $Et_2O$/pentane after column chromatography. The compound crystallizes in the orthorhombic space group $P2_12_12_1$ (no. 19), *a* = 8.3263(3), *b* = 11.029(1), *c* = 21.192(3) Å. At *Z* = 4, *V* = 1946.16 Å$^3$ and $M_r$ = 355.48 the calculated density is $\rho_{calcd.}$ = 1.213 g/cm$^3$. The structure was solved by direct methods as implemented in the program XTAL 3.4.[27] A total of 4697 reflections was collected with an ENRAF-NONIUS CAD4 diffractometer at 150 K. Cu-$K_\alpha$ radiation (λ = 1.54179 Å), μ = 6.59 cm$^{-1}$, no absorption correction; 3681 reflections with $I > 2\sigma(I)$ were used in the final full-matrix, least-squares refinement process of 358 variables, terminating at *R* = 0.049 [$R_w$ = 0.072, $w = 1/\sigma^2(F)$]. Residual electron density ρ = −0.30/+ 0.38 e Å$^{-3}$. Hydrogen positions were located and refined isotropically. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CDDC-140025. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033, E-mail: deposit@ccdc.cam.ac.uk].

**3c:** This compound was prepared according to GP 1a; Michael addition of lactam **1a** (1.5 mmol, 380 mg) to (*E*)-nitropent-1-ene (**2c**) (1.8 mmol, 210 mg) afforded adduct **3c** as a colourless solid. Yield: 410 mg (74%); *dr* = 8.5:11.5:80 (*de* = 85%, after chromatography); $[\alpha]_D^{24}$ = −19.0 (*c* = 1.00, $CHCl_3$, *de* = 85%); m.p. 47−48 °C. IR (KBr): $\tilde{\nu}$ = 2965 cm$^{-1}$ (s), 2935, 2875 (s), 2830 (m), 1675 (s), 1550 (s), 1465, 1415, 1385, 1373, 1355 (m), 1305 (m), 1230 (w), 1180, 1165 (w), 1135, 1105, 1090, 1070, 1050 (m), 930, 915 (m), 735 (w). $^1$H NMR (400 MHz, $CDCl_3$): δ = 0.84, 0.90, 0.93 (3 t, *J* = 7.4 Hz, 9 H, $3CH_2CH_3$), 1.50−2.20 (m, 14 H, $2CH_2CH_3$, $CH_2CH_2CH_3$, $NCH_2CH_2$, $CH_2CH_2CH_2N$), 2.60 (m, 2 H, CHCHCO), 3.13 (m, 2 H, $NCH_2$), 3.24 (s, 3 H, $COCH_3$), 3.46 (m, 2 H, $CONCH_2$), 3.72 (br. s, 1 H, NCH), 4.37 (dd, *J* = 9.9, 12.6 Hz, $CHHNO_2$), 4.78(dd, *J* = 6.6, 12.6 Hz, $CHHNO_2$). $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 7.91, 8.85, 14.04, 20.29, 20.51, 24.05, 24.35, 26.14, 26.31, 30.35, 38.14, 41.43, 49.86, 52.41, 65.17, 77.18, 80.04, 172.31. MS (CI, isobutane): *m*/*z* (%) = 371 (18) [M$^+$ + 2], 370 (100) [M$^+$ + 1], 338 (19), 325 (11), 268 (13) [M$^+$ − $C[CH_2CH_3]_2OCH_3$]. $C_{19}H_{35}N_3O_4$ (369.51): calcd. C 61.76, H 9.55, N 11.37; found C 61.75, H 9.47, N 11.30.

**7a:** This compound was prepared according to GP 1a; Michael addition of lactam **1a** (1.5 mmol, 380 mg) to phenyl (*E*)-prop-1-en-1-yl sulfone (**6a**) (1.8 mmol, 330 mg) afforded adduct **7a** as a

colourless oil. Yield: 465 mg (71%); *de* = 38% (*de* ≥ 96%, after HPLC); $[\alpha]_D^{24} = -50.1$ (*c* = 0.21, $CHCl_3$, *de* ≥ 96%). IR ($CHCl_3$): $\tilde{\nu}$ = 2970 $cm^{-1}$ (s), 2880, 2840 (s), 2830 (m) 1680 (s), 1460 (s), 1435, 1415 (m), 1380 (s), 1280 (s), 1120 (m), 1080 (s), 950 (w), 920 (m). $^1$H NMR (400 MHz, $CDCl_3$), major diastereomer: δ = 0.83, 0.85 (2 t, *J* = 7.4 Hz, 6 H, $CH_2CH_3$), 1.14 (d, *J* = 7.2 Hz, 3 H, $CHCH_3$), 1.46−2.15 (m, 10 H, $CH_2CH_3$, $NCH_2CH_2$, $CH_2CH_2CH_2N$), 2.50 (m, 1 H, CHCHCO), (dt, *J* = 3.0, 8.8 Hz, 1 H, CHCHCO), 3.09 (br. m, 2 H, $NCH_2$), 3.23 (dd, *J* = 7.7, 14.3 Hz, $CHHSO_2Ph$), 3.22 (s, 3 H, $COCH_3$), 3.42 (m, 2 H, $CONCH_2$), 3.62 (dd, *J* = 5.0, 14.0 Hz, $CHHSO_2Ph$), 3.67 (br. s, 1 H, NCH), 7.56 (m, 2 H, Ar-H), 7.64 (m, 1 H, Ar-H), 7.91 (m, 2 H, Ar-H). $^{13}$C NMR (100 MHz, $CDCl_3$), major diastereomer: δ = 8.01, 8.67, 15.29, 21.08, 23.98, 26.10, 26.19, 29.60, 44.58, 50.01, 52.29, 60.17, 64.97, 79.89, 127.81, 129.23, 133.57, 140.15, 172.47. MS (CI, isobutane): *m*/*z* (%) = 438 (26) [$M^+$ + 2], 437 (100) [$M^+$ + 1], 405 (24), 335 (14) [$M^+ - C[CH_2CH_3]_2OCH_3$], 297 (36), 268 (46), 172 (12), 170 (15), 143 (16), 140 (12), 128 (12), 87 (14), 70 (16). $C_{23}H_{36}N_3O_4S$ (436.61): calcd. C 63.27, H 8.31, N 6.42; found C 63.10, H 8.45, N 6.64.

**7b:** This compound was prepared according to GP 1a; Michael addition of lactam **1a** (1.5 mmol, 380 mg) to (*E*)-pent-1-en-1-yl phenyl sulfone (**6b**) (1.8 mmol, 360 mg) afforded adduct **7b** as a colourless oil. Yield: 446 mg (64%); *de* = 43%; $[\alpha]_D^{24} = -33.5$ (*c* = 0.49, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3065 $cm^{-1}$ (w), 2965, 2875 (s), 2830 (s), 1680 (s), 1585 (w), 1450, 1410 (s), 1380 (m), 1305 (s), 1150 (s), 1085 (s), 1030, 1000 (w), 915 (m), 880, 850, 830 (w), 790 (w), 755, 725, 690 (s), 600, 570, 645 (s). $^1$H NMR (300 MHz, $CDCl_3$), major diastereomer: δ = 0.76−0.88 (m, 9 H, $3CH_3$), 1.45−2.15 (m, 14 H, $CH_2CH_2CH_3$, $2CH_2CH_3$, $NCH_2CH_2$, $CH_2CH_2CH_2N$), 2.90 (dt, *J* = 3.0, 9.4 Hz, 1 H, CHCHCO), 3.01 (dd, *J* = 4.7, 14.1 Hz, 1 H, $CHHSO_2Ph$), 3.11 (br. m, 2 H, $NCH_2$), 3.21 (s, 3 H, $COCH_3$), 3.30−3.50 (m, 2 H, $CONCH_2$), 3.70 (br. s, 1 H, NCH), 3.78 (dd, *J* = 7.1, 14.1 Hz, $CHHSO_2Ph$), 7.50−7.68, 7.91 (m, 5 H, Ar-H). $^{13}$C NMR (75 MHz, $CDCl_3$), major diastereomer: δ = 7.98, 8.74, 13.89, 20.24, 20.92, 24.05, 24.19, 26.19, 31.45, 34.32, 42.32, 49.94, 52.30, 57.29, 65.18, 79.94, 127.90, 129.20, 133.54, 140.01, 172.84. MS (CI, isobutane): *m*/*z* (%) = 464 (18) [$M^+$], 211 (100) [$M^+ - CH_3CH_2CH_2CH{=}CHSO_2Ph$]. $C_{25}H_{40}N_3O_4S$ (464.66): calcd. C 64.62, H 8.68, N 6.03; found C 64.52, H 8.93, N 6.43.

**General Procedure 1b (GP 1b) for the Michael Addition of the Lithiated *N*-(Dialkylamino)lactam (*S*)-1 to Aromatic Substituted Nitroalkenes 2d−h:** A solution of lithium diisopropylamide (1.8 mmol) in THF (15 mL) was slowly added at −78 °C, by double-ended needle, to a solution of *N*-(dialkylamino)lactam **1** (1.5 mmol) in THF (7 mL). The mixture was stirred for 3−4 h at −78 °C. The solution was allowed to warm to −40 °C and the Michael acceptors **2d−h** (1.8 mmol), dissolved in THF (1−2 mL), were added. The reaction mixture was stirred for 1−1.5 h at this temperature. The reaction was quenched by addition of a saturated aqueous $NH_4Cl$ solution (15 mL). The aqueous phase was extracted three times with $CH_2Cl_2$ (50 mL). The combined organic phases were washed with $H_2O$ (25 mL) and dried with $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography ($SiO_2$; diethyl ether/pentane, 1:2) to afford the Michael adducts **3**.

**3d:** This compound was prepared according to GP 1b; Michael addition of lactam **1a** (1.5 mmol, 380 mg) to (*E*)-1-nitro-2-phenylethene (**2d**) (1.8 mmol, 270 mg) afforded adduct **3d** as a colourless oil. Yield: 538 mg (72%); *dr* = 5:18:77 (*de* ≥ 96%, after HPLC); $[\alpha]_D^{24}$= +56.6 (*c* = 0.49, $CHCl_3$, *de* ≥ 96%). IR ($CHCl_3$): $\tilde{\nu}$ = 2970 $cm^{-1}$ (s), 2940, 2880, 2830 (s), 1685 (s), 1590, 1550 (s), 1510 (m), 1460 (s), 1425 (m), 1380 (m), 1330, 1280 (m), 1240 (m), 1130, (s), 1005 (w), 910 (w). $^1$H NMR (500 MHz, $C_6D_6$, 50 °C), major diastereomer: δ = 0.76, 0.84 (2 t, *J* = 7.6 Hz, 6 H, $2CH_2CH_3$), 1.23−1.60 (m, 7 H, $2CH_2CH_3$, $NCH_2CHHCH_2$, $CONCH_2CH_2$), 1.64 (m, 1 H, $NCH_2CH_2CHH$), 1.78 (m, 1 H, $NCH_2CHHCH_2$), 1.91 (m, 1 H, $NCH_2CH_2CHH$), 2.27 (ddd, *J* = 4.0, 9.2, 9.4 Hz, 1 H, CHCHCO), 2.76 (dd, *J* = 6.7, 8.6 Hz, 2 H, $CONCH_2$), 2.91 (m, 1 H, NCHH), 2.93 (s, 3 H, $OCH_3$), 3.01 (m, 1 H, NCHH), 3.45 (ddd, *J* = 4.0, 6.7, 8.6 Hz, 1 H, CHCHCO), 3.66 (br. s, 1 H, NCH), 4.94 (dd, *J* = 8.6, 13.4 Hz, 1 H, $CHHNO_2$), 5.08 (dd, *J* = 6.7, 13.4 Hz, 1 H, $CHHNO_2$), 6.97−7.05 (m, 3 H, Ar-H), 7.13 (m, 2 H, Ar-H); minor diastereomer: δ = 0.83, 0.92 (2 t, *J* = 7.6 Hz, 6 H, $2CH_2CH_3$), 1.14−1.23 (m, 2 H, $CONCH_2CH_2$), 1.38−1.48 (m, 4 H, $2CH_2CH_3$), 1.50−1.62 (m, 2 H, $NCH_2CHHCH_2$, $NCH_2CH_2CHH$), 1.84 (m, 1 H, $NCH_2CHHCH_2$), 1.93 (m, 1 H, $NCH_2CH_2CHH$), 2.08 (q, *J* = 8.9 Hz, 1 H, CHCHCO), 2.81 (dt, *J* = 7.5, 9.2 Hz, 1 H, $CONCHHCH_2$), 3.00 (m, 1 H, NCHH), 3.05 (s, 3 H, $OCH_3$), 3.10 (br. m, 1 H, $CONCHHCH_2$), 3.24 (br. q, *J* = 7.6 Hz, 1 H, NCHH), 3.67 (dt, *J* = 5.2, 9.4 Hz, 1 H, CHCHCO), 3.94 (br. q, *J* = 4.6 Hz, NCH), 4.41 (dd, *J* = 10.1, 12.8 Hz, 1 H, $CHHNO_2$), 5.39 (dd, *J* = 5.2, 13.1 Hz, 1 H, $CHHNO_2$), 6.94 (m, 2 H, Ar-H), 6.98−7.06 (m, 3 H, Ar-H). $^{13}$C NMR (125 MHz, $C_6D_6$, 50 °C), major diastereomer: δ = 8.22, 8.56, 21.26, 24.51, 24.69, 26.23, 26.57, 43.21, 44.58, 45.26, 49.55, 52.12, 65.84, 77.51, 79.82, 128.05, 128.78, 129.57, 137.06, 171.38; minor diastereomer: δ = 8.23, 8.97, 22.60, 25.25, 24.41, 26.39, 26.87, 43.13, 45.25, 45.58, 49.53, 52.47, 64.95, 78.45, 80.05, 126.78, 128.55, 128.90, 138.34, 171.50. MS (CI, isobutane): *m*/*z* (%) = 405 (22) [$M^+$ + 2], 404 (100) [$M^+$ + 1], 373 (6), 372 (25), 359 (11), 302 (19). $C_{22}H_{33}N_3O_4$ (403.52): calcd. C 65.48, H 8.24, N 10.41; found C 65.49, H 8.39, N 10.73.

**3e:** This compound was prepared according to GP 1b; Michael addition of lactam **1a** (1.8 mmol, 380 mg) to (*E*)-2-(furan-2-yl)-1-nitroethene (**2e**) (1.8 mmol, 250 mg) afforded adduct **3e** as a colourless oil. Yield: 450 mg (76%); *dr* = 17:33:50 (*de* ≥ 96%, after HPLC); $[\alpha]_D^{24} = +29.5$ (*c* = 0.55, $CHCl_3$, *de* ≥ 96%). IR ($CHCl_3$): $\tilde{\nu}$ = 2945 $cm^{-1}$ (s), 2830 (s), 1680 (s), 1550 (s), 1455, 1430, 1380 (m), 1285 (w), 1150, 1110 (s), 1070, 1030 (s), 920 (w), 885, 740 (w). $^1$H NMR (400 MHz, $CDCl_3$), major diastereomer: δ = 0.81, 0.85 (2 t, *J* = 7.4 Hz, 6 H, $2CH_2CH_3$), 1.45−2.19 (m, 10 H, $2CH_2CH_3$, $NCH_2CH_2CH_2$, $CONCH_2CH_2$), 2.79 (dt, *J* = 3.9, 8.5 Hz, 1 H, CHCHCO), 2.96 (br. m, 1 H, NCHH), 3.06−3.15 (m, 2 H, NCHH, CONCHH), 3.19 (s, 3 H, $OCH_3$), 3.34 (br. q, *J* = 8.1 Hz, 1 H, CONCHH), 3.51 (br. s, 1 H, NCH), 3.95 (m, 1 H, CHCHCO), 5.01 (dd, *J* = 6.3, 13.5 Hz, 1 H, $CHHNO_2$), 5.07 (dd, *J* = 8.5, 13.8 Hz, 1 H, $CHHNO_2$), 6.27, 6.30 (m, 2 H, CH=CHCO), 7.34 (m, 1 H, CH=CHO). $^{13}$C NMR (100 MHz, $CDCl_3$), major diastereomer: δ = 7.97, 8.65, 21.31, 23.92, 26.11, 26.17, 38.89, 42.36, 50.00, 51.92, 65.02, 75.69, 79.90, 108.46, 110.63, 142.39, 150.65, 171.45. MS (CI, isobutane): *m*/*z* (%) = 395 (18) [$M^+$ + 2], 394 (100) [$M^+$ + 1], 362 (13), 292 (28) [$M^+ - CH_3OC[CH_3CH_2]_2$]. $C_{20}H_{31}N_3O_5$ (393.48): calcd. C 61.05, N 7.94, H 10.68; found C 60.86, N 8.16, H 10.79.

**3f:** This compound was prepared according to GP 1b; Michael addition of lactam **1a** (1.8 mmol, 380 mg) to (*E*)-1-(2-naphthalenyl)-2-nitroethene (**2f**) (1.8 mmol, 360 mg) afforded adduct **3f** as a colourless solid. Yield: 490 mg (72%); *dr* = 4.5:21.5:74 (*de* ≥ 96%, after HPLC); $[\alpha]_D^{24} = +58.0$ (*c* = 0.92, $CHCl_3$, *de* ≥ 96%); m.p. 52−54 °C. IR ($CHCl_3$): $\tilde{\nu}$ = 2970 $cm^{-1}$ (s), 2940, 2880, 2830 (s), 1685 (s), 1590, 1550 (s), 1510 (m), 1460 (s), 1425 (m), 1380 (m), 1330, 1280 (m), 1240 (m), 1130, (s), 1005 (w), 910 (w). $^1$H NMR (300 MHz, $C_6D_6$), major diastereomer: δ = 0.67, 0.73 (2 t, *J* =

7.6 Hz, 6 H, $2CH_2CH_3$), 1.20−1.70 (m, 7 H, $2CH_2CH_3$, $NCH_2CH_2CH_2$, $CONCH_2CH_2$, $NCH_2CH_2CHH$), 1.91 (m, 1 H, $NCH_2CH_2CHH$), 2.27 (dt, $J$ = 4.0, 9.4 Hz, 1 H, CHCHCO), 2.69 (br. s, 1 H, CONCHH), 2.62 (br. m, 1 H, CONCHH), 2.80 (s, 3 H, $OCH_3$), 2.89 (dt, $J$ = 4.0, 8.5 Hz, 1 H, NCHH), 2.95 (br. m, 1 H, NCHH), 3.59 (ddd, $J$ = 4.0, 7.1, 8.1 Hz, 1 H, CHCHCO + br. m, 1 H, NCH), 5.09 (dd, $J$ = 8.4, 13.4 Hz, 1 H, $CHHNO_2$), 5.17 (dd, $J$ = 7.1, 13.4 Hz, 1 H, $CHHNO_2$), 7.15−7.32 (m, 4 H, Ar-H), 7.47−7.62 (m, 4 H, Ar-H); minor diastereomer: δ = 0.81, 0.87 (2 t, $J$ = 7.4 Hz, 6 H, $2CH_2CH_3$), 1.05−1.62 (m, 8 H, $CONCH_2CH_2$, $2CH_2CH_3$, $NCH_2CHHCHH$), 1.84−2.00 (m, 2 H, $NCH_2CHHCHH$), 2.09 (q, $J$ = 8.7 Hz, 1 H, CHCHCO), 2.77 (q, $J$ = 7.7 Hz, 1 H, $CONCHHCH_2$), 2.99 (m, 1 H, NCHH), 3.02 (s, 3 H, $OCH_3$), 3.05 (br. m, 1 H, $CONCHHCH_2$), 3.25 (br. m, 1 H, NCHH), 3.87 (dt, $J$ = 5.0, 9.7 Hz, 1 H, CHCHCO), 3.94 (br. s, 1 H, NCH), 4.52 (dd, $J$ = 10.1, 13.1 Hz, 1 H, $CHHNO_2$), 5.53 (dd, $J$ = 5.0, 13.1 Hz, 1 H, $CHHNO_2$), 7.05, 7.24, 7.40−7.60 (m, 6 H, Ar-H). $^{13}$C NMR (75 MHz, $C_6D_6$), major diastereomer: δ = 8.30, 8.55, 21.26, 24.56, 24.63, 26.38, 26.55, 43.31, 44.40, 45.55, 49.47, 51.99, 65.65, 77.40, 79.63, 126.32, 126.43, 127.31, 127.80, 127.24, 128.24, 128.59, 128.74, 133.32, 133.74, 134.60, 171.44; minor diastereomer: δ = 8.23, 8.94, 22.55, 24.41, 25.13, 26.32, 26.77, 42.95, 45.35, 45.72, 49.47, 52.56, 64.81, 78.31, 79.92, 125.76, 126.37, 127.57, 127.95, 128.10, 128.93, 133.33, 133.79, 134.61, 171.50. MS (EI): $m/z$ (%) = 453 (0.2) [$M^+$], 353 (23), 352 (100) [$M^+ - CH_3OC(CH_3CH_2)_2$], 167 (5), 154 (4), 153 (4), 152 (9), 101 (6), 97 (13), 68 (3). $C_{26}H_{35}N_3O_4$ (453.58): calcd. C 68.85, H 7.78, N 9.26; found C 68.59, H 7.85, N 8.97.

**3g:** This compound was prepared according to GP 1b; Michael addition of lactam **1a** (1.5 mmol, 380 mg) to (*E*)-(3,4-methylenedioxyphenyl)-1-nitroethene (**2g**) (1.5 mmol, 350 mg) afforded adduct **3g** as a colourless oil. Yield: 470 mg (70%); $dr$ = 10:18:72 ($de$ ≥ 96%, after HPLC); $[\alpha]_D^{24}$ = +44.2 ($c$ = 0.81, $CHCl_3$, $de$ ≥ 96%). IR ($CHCl_3$): $\tilde{\nu}$ = 2970 $cm^{-1}$ (s), 2940, 2880 (s), 1680 (s), 1610 (w), 1550 (s), 1505, 1490 (s), 1445 (s), 1380 (m), 1280 (m), 1250 (s), 1220 (m), 1110, 1080 (m), 1040 (s), 940, 910 (m), 880 (w), 815 (w), 665, 655 (w). $^1$H NMR (400 MHz, $CDCl_3$), major diastereomer: δ = 0.79, 0.82 (2 t, $J$ = 7.7 Hz, 6 H, $2CH_2CH_3$), 1.40−2.05 (m, 10 H, $2CH_2CH_3$, $NCH_2CH_2CH_2$, $CONCH_2CH_2$), 2.77 (dt, $J$ = 4.1, 8.0 Hz, 1 H, CHCHCO), 2.90−3.06 (br. m, 3 H, $CONCH_2$, NCHH), 3.16 (s, 3 H, $OCH_3$), 3.29 (br. q, $J$ = 8.3 Hz, 1 H, NCHH), 3.47 (br. s, 1 H, NCH), 3.63 (ddd, $J$ = 4.1, 5.2, 10.0 Hz, 1 H, CHCHCO), 5.09 (dd, $J$ = 6.0, 13.5 Hz, 1 H, $CHHNO_2$), 5.18 (dd, $J$ = 9.0, 13.5 Hz, 1 H, $CHHNO_2$), 5.91 (d, $J$ = 1.4 Hz, $OCHHO$), 5.93 (d, $J$ = 1.4 Hz, $OCHHO$), 6.75 (m, 2 H, Ar-H), 6.83 (m, 1 H, Ar-H); minor diastereomer: δ = 0.85, 0.88 (2 t, $J$ = 7.4 Hz, 6 H, $2CH_2CH_3$), 1.50−2.05 (m, 10 H, $CONCH_2CH_2$, $2CH_2CH_3$, $NCH_2CH_2CH_2$), 2.54 (q, $J$ = 8.8 Hz, 1 H, CHCHCO), 3.13 (br. m, 2 H, $NCH_2$), 3.23 (s, 3 H, $OCH_3$), 3.33 (m, 1 H, CONCHH), 3.40 (br. m, 1 H, CONCHH), 3.59 (dt, $J$ = 5.0, 10.2 Hz, 1 H, CHCHCO), 3.75 (br. s, 1 H, NCH), 4.66 (dd, $J$ = 10.7, 13.0 Hz, 1 H, $CHHNO_2$), 5.53 (dd, $J$ = 5.0, 12.9 Hz, 1 H, $CHHNO_2$), 5.94 (s, 2 H, $OCH_2O$), 6.63−6.75 (m, 3 H, Ar-H). $^{13}$C NMR (100 MHz, $CDCl_3$), major diastereomer: δ = 8.06, 8.45, 21.19, 23.77, 25.84, 26.12, 43.34, 45.16, 50.05, 51.84, 64.94, 77.71, 79.78, 101.22, 108.42, 109.02, 122.65, 129.82, 147.38, 147.99, 172.04; minor diastereomer: δ = 7.97, 8.75, 22.59, 23.77, 24.25, 26.09, 26.17, 43.14, 45.19, 49.92, 52.27, 64.38, 78.60, 79.99, 101.25, 108.02, 108.54, 121.69, 131.14, 147.26, 148.12, 172.03. MS (CI, isobutane): $m/z$ (%) = 449 (26) [$M^+$ + 2], 448 (100) [$M^+$ + 1], 418 (19), 417 (10), 416 (31), 414 (13), 404 (14), 403 (57), 401 (9), 371 (10), 172 (10), 170 (29), 140 (14), 87 (13). $C_{23}H_{33}N_3O_6$ (453.58): calcd. C 61.73, H 7.43, N 9.39; found C 62.00, H 7.00, N 9.79.

**3h:** This compound was prepared according to GP 1b; Michael addition of lactam **1a** (1.5 mmol, 380 mg) to (*E*)-1-nitro-2-(3,4,5-trimethoxyphenyl)ethene (**2h**) (1.8 mmol, 430 mg) afforded adduct **3h** as a colourless solid. Yield: 444 mg (60%); $dr$ = 10:17:63 ($de$ ≥ 96%, after chromatography); $[\alpha]_D^{24}$ = +43.3 ($c$ = 1.13, $CHCl_3$, $de$ ≥ 96%); m.p. 87−89 °C. IR ($CHCl_3$): $\tilde{\nu}$ = 2970 $cm^{-1}$ (s), 2940, 2880, 2830 (s), 1685 (s), 1590, 1550 (s), 1510 (m), 1460 (s), 1425 (m), 1380 (m), 1330, 1280 (m), 1240 (m), 1130, (s), 1005 (w), 910 (w). $^1$H NMR (300 MHz, $CDCl_3$), major diastereomer: δ = 0.75, 0.80 (2 t, $J$ = 7.4 Hz, 6 H, $2CH_2CH_3$), 1.40−2.14 (m, 12 H, $2CH_2CH_3$, $NCH_2CH_2CH_2$, $CONCH_2CH_2$), 2.78 (dt, $J$ = 3.7, 9.1 Hz, 1 H, CHCHCO), 2.90−3.02 (br. m, 2 H, $NCH_2$), 3.11 (br. s, 4 H, $OCH_3$, CONCHH), 3.32 (q, $J$ = 7.8 Hz, 1 H, CONCHH), 3.45 (br. s, 1 H, NCH), 3.66 (ddd, $J$ = 3.7, 5.7, 9.4 Hz, 1 H, $CH_2CHCH$), 3.80 (s, 3 H, $OCH_3$), 3.84 (s, 6 H, $OCH_3$), 5.14 (dd, $J$ = 9.1, 13.4 Hz, 1 H, $CHHNO_2$), 5.26 (dd, $J$ = 6.4, 13.4 Hz, 1 H, $CHHNO_2$), 6.55 (s, 2 H, Ar-H). $^{13}$C NMR (75 MHz, $CDCl_3$), major diastereomer: δ = 8.01, 8.39, 21.43, 23.82, 24.03, 26.05, 26.17, 43.58, 45.29, 49.89, 51.94, 56.24, 60.74, 65.25, 76.85, 79.85, 106.19, 131.96, 137.72, 153.31, 171.95. MS (EI): $m/z$ (%) = 493 (0.4) [$M^+$], 394 (5), 393 (27), 392 (100) [$M^+ - C[CH_2CH_3]_2OCH_3$], 194 (3), 152 (6), 101 (6), 97 (12). $C_{25}H_{39}N_3O_7$ (493.60): calcd. C 60.83, H 7.96, N 8.51; found C 60.53, H 7.85, N 8.35.

**General Procedure (GP 2) for the Conversion of Nitro Compounds 3 into *N*-Protected Amines 4:** The Michael adduct **3a**−**f** (1.0 mmol) was dissolved in a 1:1 mixture of MeOH and THF (20 mL/mmol) and cooled to 0 °C. Pd on charcoal (50 mg/mmol) and $NaBH_4$ (4 mmol) were then added. The flask was immediately closed tightly and the mixture was stirred at room temperature overnight. In order to remove the Pd on charcoal, the reaction mixture was filtered through Celite®, washing three times with MeOH (5 mL). $Boc_2O$ (1.0 mmol) and $NEt_3$ (1.2 mmol) were then added and after the mixture had been stirred for 2 h, the solvent was removed in vacuo. The crude product was dissolved in $CH_2Cl_2$ (20 mL/mmol) and washed twice with $H_2O$ (20 mL) and then with brine (20 mL). After drying with $MgSO_4$, the solvent was removed and the residue was purified by flash chromatography [$SiO_2$; diethyl ether/pentane (1:2), containing 1% of $Et_3N$].

**4a:** This compound was prepared according to GP 2; nitrolactam **3a** (0.56 mmol, 190 mg) was treated with $NaBH_4$ (2.24 mmol, 84 mg) and $Boc_2O$ (1.12 mmol, 122 mg), in the presence of $NEt_3$ (0.67 mmol, 67 mg), to afford compound **4a** as a colourless oil. Yield: 175 mg (76%); $de$ ≥ 96%; $[\alpha]_D^{24}$ = −17.4 ($c$ = 0.68, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3345 $cm^{-1}$ (m), 2970, 2940, 2880, (s), 1690 (s), 1515 (s), 1460 (s), 1390, 1365 (m), 1275, 1250 (s), 1175, (s), 1080 (m), 990, 945, 915 (w), 735 (m). $^1$H NMR (300 MHz, $CDCl_3$): δ = 0.86, 0.87 (2 t, $J$ = 7.4 Hz, 6 H, $2CH_2CH_3$), 0.97 (d, $J$ = 7.1 Hz, 6 H, $CH_3$) 1.43 [s, 9 H, $C(CH_3)_3$], 1.50−2.14 (m, 11 H, $2CH_2CH_3$, $NCH_2CH_2CH_2$, $CONCH_2CH_2$, $CHCH_3$), 2.41 (dt, $J$ = 3.9, 9.0 Hz, 1 H, CHCHCO), 3.15 (m, 4 H, $NCH_2$, $CH_2NHCOO$-*t*Bu), 3.26 (s, 3 H, $OCH_3$), 3.42 (m, 2 H, $CONCH_2$), 3.60 (br. s, 1 H, NCH), 5.23 (br. s, 1 H, N*H*-COO-*t*Bu). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 8.10, 8.58, 14.36, 20.59, 23.95, 26.06, 26.26, 28.45, 34.30, 43.62, 44.19, 50.20, 52.27, 64.94, 78.91, 79.86, 156.35, 174.293. MS (CI, isobutane): $m/z$ (%) = 413 (19) [$M^+$ + 2], 412 (100) [$M^+$ + 1], 380 (6), 310 (7) [$M^+ - C(CH_2CH_3)_2OCH_3$], 75 (37). $C_{22}H_{41}N_3O_4$ (411.58): calcd. C 64.20, H 10.04, N 10.21; found C 64.02, H 9.75, N 10.75.

**4b:** This compound was prepared according to GP 2; nitrolactam **3b** (0.38 mmol, 140 mg) was treated with $NaBH_4$ (1.58 mmol, 61 mg) and $Boc_2O$ (0.38 mmol, 85 mg), in the presence of $NEt_3$ (0.46 mmol, 46 mg), to afford compound **4b** as a colourless oil.

Yield: 120 mg (85%); *de* ≥ 96%; $[\alpha]_D^{24} = -15.4$ (*c* = 0.83, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3350 $cm^{-1}$ (m), 2970, 2935, 2880 (s), 1695 (s), 1510 (s), 1455 (s), 1390, 1365 (s), 1275, 1250 (s), 1170 (s), 1120 (s), 920, 875 (w), 665 (w). $^1H$ NMR (300 MHz, $CDCl_3$): δ = 0.86, 0.87, 0.94 (3 t, *J* = 7.4 Hz, 9 H, $3CH_2CH_3$), 1.42 [s, 9 H, $C(CH_3)_3$], 1.30−2.00 (m, 12 H, $3CH_2CH_3$, $NCH_2CH_2CH_2$, $CONCH_2CH_2$), 2.52 (dt, *J* = 3.3, 9.3, Hz, 1 H, CHCHCO), 3.00−3.20 (m, 5 H, $NCH_2CH_2CH_2$, $CH_2NHCOO$-*t*Bu, CHCHCO), 3.28 (s, 3 H, $OCH_3$), 3.42 (m, 2 H, $CONCH_2$), 3.58 (br. s, 1 H, NCH), 5.20 (br. s, 1 H, NHCOO-*t*Bu). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 8.08, 8.64, 11.94, 19.52, 22.44, 23.80, 26.02, 26.25, 28.46, 39.97, 42.58, 41.77, 50.22, 52.27, 64.91, 78.89, 79.89, 156.33, 174.29. MS (CI, isobutane): *m*/*z* (%) = 427 (26) $[M^+ + 2]$, 426 (100) $[M^+ + 1]$, 394 (8), 324 (11) $[M^+ - C(CH_2CH_3)_2OCH_3]$, 257 (18), 201 (28), 201 (16), 140 (5), 101 (5), 87 (5), 70 (7). $C_{23}H_{43}N_3O_4$ (425.61): calcd. C 64.91, H 10.18, N 9.87; found C 64.70, H 10.01, N 10.40.

**4c:** This compound was prepared according to GP 2; nitrolactam **3c** (0.70 mmol, 260 mg) was treated with $NaBH_4$ (2.8 mmol, 105 mg) and $Boc_2O$ (0.7 mmol, 153 mg), in the presence of $NEt_3$ (0.84 mmol, 85 mg), to afford compound **4c** as a colourless oil. Yield: 195 mg (64%); *de* = 85%; $[\alpha]_D^{24} = -10.4$ (*c* = 0.64, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3345 $cm^{-1}$ (m), 2970, 2935, 2875 (s), 1695 (s), 1510 (s), 1460 (s), 1390, 1365 (m), 1275, 1250 (m), 1175 (s), 1120 (s), 920, 875 (w), 665 (w). $^1H$ NMR (400 MHz, $CDCl_3$): δ = 0.86, 0.87 (2 t, *J* = 7.4 Hz, 6 H, $2CH_2CH_3$), 0.90 (t, *J* = 7.4 Hz, 6 H, $CH_2CH_2CH_3$), 1.42 (s, 9 H, $C(CH_3)_3$], 1.25−2.00 (m, 14 H, $CH_2CH_2CH_3$, $2CH_2CH_3$, $NCH_2CH_2CH_2$, $CONCH_2CH_2$), 2.49 (dt, *J* = 3.0, 9.2 Hz, 1 H, CHCHCO), 3.00−3.20 (m, 5 H, $NCH_2CH_2CH_2$, $CH_2NHCOO$-*t*Bu, CHCHCO), 3.27 (s, 3 H, $OCH_3$), 3.41 (m, 2 H, $CONCH_2$), 3.60 (br. s, 1 H, NCH), 5.25 (br. s, 1 H, NHCOO-*t*Bu). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 8.08, 8.65, 14.29, 19.77, 20.55, 23.86, 26.07, 26.26, 28.46, 31.68, 39.97, 42.98, 42.58, 50.19, 52.29, 64.98, 78.84, 79.89, 156.35, 174.21. MS (CI, isobutane): *m*/*z* (%) = 441 (23) $[M^+ + 2]$, 440 (100) $[M^+ + 1]$, 409 (9), 338 (11) $[M^+ - C(CH_2CH_3)_2OCH_3]$. $C_{24}H_{45}N_3O_4$ (439.63): calcd. C 65.57, H 10.32, N 9.56; found C 65.59, H 10.68, N 10.02.

**4d:** This compound was prepared according to GP 2; nitrolactam **3d** (0.35 mmol, 140 mg) was treated with $NaBH_4$ (1.40 mmol, 53 mg) and $Boc_2O$ (0.35 mmol, 76 mg), in the presence of $NEt_3$ (0.42 mmol, 42 mg), to afford compound **4d** as a colourless oil. Yield: 125 mg (75%); *de* ≥ 96%; $[\alpha]_D^{24} = +30.3$ (*c* = 0.57, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3345 $cm^{-1}$ (s), 2970, 2940, 2880, (s), 1690 (s), 1600 (w), 1500 (s), 1455 (s), 1390, 1365 (m), 1275, 1250 (s), 1170, (s), 1080 (m), 920, 840 (w), 760 (s), 700 (m), 665 (w). $^1H$ NMR (300 MHz, $CDCl_3$): δ = 0.81 (2 t, *J* = 7.4 Hz, 6 H, $2CH_2CH_3$), 1.40 (s, 9 H, $C(CH_3)_3$], 1.43−2.18 (m, 10 H, $2CH_2CH_3$, $NCH_2CH_2CH_2$, $CONCH_2CH_2$), 2.74 (m, 1 H, CHCHCO), 2.80−3.30 (m, 5 H, CHCHCO, $NCH_2CH_2CH_2$, $CONCH_2$), 3.22 (br. s, 3 H, $OCH_3$), 3.45 (br. s, 1 H, NCH), 3.69 (br. t, *J* = 6.5 Hz, $CH_2NHCOO$-*t*Bu), 4.91 (br. s, 1 H, NHCOO-*t*Bu), 7.28 (m, 5 H, Ar-H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 8.12, 8.43, 20.91, 23.46, 23.77, 25.68, 26.22, 28.38, 42.63, 43.25, 46.36, 50.26, 51.81, 64.76, 79.07, 79.74, 126.11, 128.56, 128.88, 139.88, 156.05, 173.23. MS (CI, isobutane): *m*/*z* (%) = 474 (100) $[M^+ + 1]$, 170 (21). $C_{27}H_{43}N_3O_4$ (473.65): calcd. C 68.47, H 9.15, N 8.87; found C 68.26, H 9.33, N 8.75.

**4e:** This compound was prepared according to GP 2; nitrolactam **3e** (0.41 mmol, 160 mg) was treated with $NaBH_4$ (1.64 mmol, 109 mg) and $Boc_2O$ (0.41 mmol, 89 mg), in the presence of $NEt_3$ (0.49 mmol, 50 mg), to afford compound **4e** as a colourless oil. Yield: 130 mg (68%); *de* ≥ 96%; $[\alpha]_D^{24} = +13.0$ (*c* = 0.72, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3350 $cm^{-1}$ (m), 2975, 2940, 2880, (s), 2830 (w), 1695 (s), 1505 (s), 1455 (m), 1390, 1365 (m), 1275, 1250 (s), 1170, (s), 1075 (m), 1010 (w), 915, 865 (w), 625 (w). $^1H$ NMR (300 MHz, $CDCl_3$): δ = 0.84 (2 t, *J* = 7.4 Hz, 6 H, $2CH_2CH_3$), 1.42 (s, 9 H, $C(CH_3)_3$], 1.44−2.10 (m, 10 H, $2CH_2CH_3$, $NCH_2CH_2CH_2$, $CONCH_2CH_2$), 2.76 (ddd, *J* = 4.1, 7.7, 9.3 Hz, 1 H, CHCHCO), 2.80−3.16 (m, 3 H, $NCH_2CH_2CH_2$, CONCH), 3.26 (br. s, 3 H, $OCH_3$), 3.36−3.46 (m, 2 H, NCH, CONCH), 3.60 (m, 2 H, $CH_2NHCOO$-*t*Bu), 5.08 (br. m, 1 H, NHCOO-*t*Bu), 6.17 (d, *J* = 3.0 Hz, 1 H, CCH=CH), 6.31 (m, 1 H, CCH=CH), 7.33 (m, 1 H, CHO). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 8.13, 8.45, 21.20, 23.46, 23.84, 25.85, 26.28, 28.40, 41.41, 40.13, 41.92, 50.33, 51.77, 64.76, 79.16, 79.77, 107.27, 110.34, 141.66, 153.91, 156.04), 172.80. MS (CI, isobutane): *m*/*z* (%) = 465 (22) $[M^+ + 2]$, 464 (100) $[M^+ + 1]$, 463 (5) $[M^+]$, 432 (12), 362 $[M^+ - C(CH_2CH_3)_2OCH_3]$, 170 (11), 87 (22). $C_{25}H_{41}N_3O_5$ (463.61): calcd. C 64.77, H 8.91, N 9.06; found C 64.55, H 8.84, N 9.40.

**4f:** This compound was prepared according to GP 2; nitrolactam **3f** (0.54 mmol, 244 mg) was treated with $NaBH_4$ (2.16 mmol, 82 mg) and $Boc_2O$ (0.54 mmol, 118 mg), in the presence of $NEt_3$ (0.64 mmol, 65 mg), to afford compound **4f** as a colourless solid. Yield: 200 mg (71%); *de* ≥ 96%; $[\alpha]_D^{24} = +43.6$ (*c* = 0.80, $CHCl_3$); m.p. 62−64 °C. IR (KBr): $\tilde{\nu}$ = 3355 $cm^{-1}$ (m), 3055 (m), 2970, 2940, 2880, (s), 1710 (s), 1600 (w), 1455 (s), 1390, 1365 (m), 1275, 1250 (s), 1170, (s), 1080 (m), 920, 860, 820 (w), 750 (m). $^1H$ NMR (400 MHz, $CDCl_3$): δ = 0.76, 0.78 (2 t, *J* = 7.4 Hz, 6 H, $2CH_2CH_3$), 1.39 [s, 9 H, $C(CH_3)_3$], 1.41−2.10 (m, 10 H, $2CH_2CH_3$, $NCH_2CH_2CH_2$, $CONCH_2CH_2$), 2.80 (br. m, 2 H, $NCH_2$), 2.83 (dt, *J* = 4.1, 8.8 Hz, 1 H, CHCHCO), 3.07 (dt, *J* = 5.5, 9.0 Hz, 1 H, CHCHCO), 3.18 (br. s, 3 H, $OCH_3$), 3.22 (br. q, *J* = 8.0 Hz, 1 H, CONCH), 3.42 (br. m, 2 H, NCH, CONCH), 3.80 (br. t, *J* = 6.9 Hz, $CH_2NHCOO$-*t*Bu), 4.91 (br.s, 1 H, NHCOO-*t*Bu), 7.44, 7.70−7.82 (m, 6 H, Ar-H). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 8.11, 8.38, 20.95, 23.53, 23.73, 25.78, 26.22, 28.38, 42.66, 43.42, 46.52, 50.23, 51.84, 64.74, 79.07, 79.74, 125.74, 126.11, 126.96, 1127.56, 127.73, 128.23, 132.23, 133.40, 137.49, 156.07, 173.19. MS (CI, isobutane): *m*/*z* (%) = 525 (34) $[M^+ + 2]$, 524 (100) $[M^+ + 1]$, 492 (10), 424 (13), 422 (12), 355 (11), 170 (19), 87 (17), 70 (14). $C_{31}H_{45}N_3O_4$ (523.71): calcd. C 71.10, H 8.66, N 8.02; found C 70.69, H 9.07, N 8.20.

**4g:** This compound was prepared according to GP 2; nitro lactam **3g** (0.51 mmol, 228 mg) was treated with $NaBH_4$ (2.08 mmol, 78 mg) and $Boc_2O$ (0.51 mmol, 111 mg), in the presence of $NEt_3$ (0.61 mmol, 62 mg), to afford compound **4g** as a colourless oil. Yield: 160 mg (61%); *de* ≥ 96%; $[\alpha]_D^{24} = +30.2$ (*c* = 0.85, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3350 $cm^{-1}$ (m), 2970, 2880 (s), 2830 (m), 1710 (s), 1600 (w), 1505, 1490 (s), 1440 (s), 1390, 1365 (m), 1345 (m), 1250 (s), 1170, (s), 1080 (m), 1040 (s), 935, 865 (s), 810 (m). $^1H$ NMR (300 MHz, $CDCl_3$): δ = 0.83 (t, *J* = 7.4 Hz, 6 H, $2CH_2CH_3$), 1.41 (s, 9 H, $C(CH_3)_3$], 1.41−2.08 (m, 10 H, $CH_2CH_3$, $NCH_2CH_2CH_2$, $CONCH_2CH_2$), 2.71 (dt, *J* = 4.1, 8.8 Hz, 1 H, CHCHCO), 2.80 (br. s, 2 H, $NCH_2$), 3.00−3.15 (m, 2 H, $CONCH_2$), 3.24 (br. s, 3 H, $OCH_3$), 3.26 (m, 1 H, CHCHCO), 3.46 (br. m, 1 H, NCH), 3.80 (br. t, *J* = 6.9 Hz, 2 H, $CH_2NHCOO$-*t*Bu), 4.90 (br. s, 1 H, NHCOO-*t*Bu), 5.93 (m, 2 H, $OCH_2O$), 6.72 (s, 2 H, Ar-H), 6.79 (s, 1 H, Ar-H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 8.17, 8.39, 21.05, 23.54, 23.80, 25.78, 26.21, 28.40, 42.99, 43.18, 46.29, 50.28, 51.80, 64.80, 79.10, 79.77, 101.00, 108.25, 108.98, 122.31, 133.57, 146.61, 147.61, 156.05, 173.23. MS (CI, isobutane): *m*/*z* (%) = 519 (34) $[M^+ + 2]$, 518 (100) $[M^+ + 1]$, 486 (11), 416 (10) $[M^+ - C(CH_2CH_3)_2OCH_3]$. $C_{28}H_{43}N_3O_6$ (517.66): calcd. C 64.97, H 8.37, N 8.12; found C 64.49, H 8.12, N 8.13.

**Removal of the Auxiliary by Reductive N−N Cleavage. − General Procedure 3 (GP 3) for N−N Bond Cleavage in α-(β-Aminoethyl)-*N*-(dialkylamino)lactams:** Pieces of lithium wire (5 equiv.) were added to liquid $NH_3$ in a three-necked flask fitted with a dry ice condenser. The α-substituted *N*-(dialkylamino)lactams **4** (1 mmol), dissolved in dry THF (10 mL/mmol), were then added at −78 °C to the dark blue solution. The cooling bath was removed and the solution was kept under reflux (−33 °C) until the blue colour disappeared (after 5−15 min). The reaction was quenched with solid $NH_4Cl$ (12 equiv.) and the $NH_3$ was evaporated at room temperature. The solid residue was dissolved in a mixture of $CH_2Cl_2$ and pH 7 buffer (20 mL/mmol) and the aqueous phase was extracted twice with $CH_2Cl_2$ (10 mL). The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo, and the crude products were purified by chromatography ($SiO_2$; diethyl ether or diethyl ether/MeOH, 10:1).

**5a:** *N*-(Dialkylamino)lactam **4a** (0.49 mmol, 200 mg) was treated with Li (2.5 mmol, 17 mg) to afford α-(β-aminoalkyl)-substituted lactam **5a** as a colourless solid. Yield: 115 mg (95%); *de* ≥ 96%; *ee* ≥ 96% (GC, chiral stationary phase, Chirasil-Dex 25m); $[\alpha]_D^{24}$ = −0.90 (*c* = 0.67, $CHCl_3$); m.p. 123−124 °C. IR (KBr): $\tilde{\nu}$ = 3390 $cm^{-1}$ (m), 3220 (m), 3090 (w), 2980, 2935 (m), 2900 (w), 1695, 1675 (s), 1520 (s), 1460 (m), 1390, 1365 (m), 1320 (w), 1270 (m), 1180 (s), 1005, 985 (w), 780 (w). $^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.00 (d, *J* = 6.9 Hz, 3 H, C*H*$_3$), 1.44 [s, 9 H, C(C*H*$_3$)$_3$], 1.96 (m, 1 H, CONCH$_2$C*H*H), 2.16 (m, 2 H, CONCH$_2$CH*H*, C*H*CH$_3$), 2.47 (dt, *J* = 3.9, 7.9 Hz, 1 H, CHC*H*CON), 3.14 (m, 1 H, C*H*HNHCOO-*t*Bu), 3.21 (m, 1 H, CH*H*NHCOO-*t*Bu), 3.33 (m, 2 H, CONC*H*$_2$), 5.31 (br. m, 1 H, N*H*COO-*t*Bu), 6.97 (br. s, 1 H, CON*H*). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 14.74, 23.90, 28.43, 33.83, 40.66, 43.99, 43.95 78.84, 156.27, 179.86. MS (EI): *m*/*z* (%) = 242 (1) [$M^+$], 186 (22), 185 (13), 169 (21) [$M^+$ − O-*t*Bu], 141 (22) [$M^+$ − COO-*t*Bu], 1226 (10), 124 (17), 124 (17), 98 (55), 85 ($C_4H_7NO^+$, 100), 84 (18), 57 (58), 55 (14). $C_{12}H_{22}N_2O_3$ (242.32): calcd. C 59.48, H 9.15, N 11.56; found C 59.36, H 9.29, N 11.34.

**5b:** *N*-(Dialkylamino)lactam **4b** (0.28 mmol, 120 mg) was treated with Li (1.4 mmol, 10 mg) to afford α-(β-aminoalkyl)-substituted lactam **5b** as a colourless oil. Yield: 70 mg (98%); *de* ≥ 96%; *ee* ≥ 96% (GC, chiral stationary phase, Chirasil-L-Val, 25m); $[\alpha]_D^{24}$ = +5.3 (*c* = 0.48, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3315 $cm^{-1}$ (s), 2965, 2930, 2875 (s), 1695 (s), 1520 (s), 1460 (m), 1390, 1365 (m), 1275, 1255 (m), 1175 (s), 1070, 1040, 1010 (m). $^1H$ NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.4 Hz, 3 H, CH$_2$C*H*$_3$), 1.43 (s, 9 H, C(C*H*$_3$)$_3$], 1.32−1.45 (m, 2 H, C*H*$_2$CH$_3$), 1.96 (m, 2 H, CONCH$_2$C*H*H, C*H*CHCO), 2.13 (m, 1 H, CONCH$_2$CH*H*), 2.58 (dt, *J* = 3.9, 7.9 Hz, 1 H, CHC*H*CON), 3.13 (m, 1 H, C*H*HNHCOO-*t*Bu), 3.32 (m, 1 H, CH*H*NHCOO-*t*Bu), 3.33 (m, 2 H, CONC*H*$_2$), 5.34 (br. m, 1 H, N*H*COO-*t*Bu), 6.91 (br. s, 1 H, CON*H*). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 11.92, 22.64, 22.77, 28.43, 39.87, 42.66, 41.62, 40.62, 78.85, 156.26, 180.49. MS (EI): *m*/*z* (%) = 257 (99) [$M^+$ + 1], 202 (9), 201 (100) [$M^+$ − CH=C(CH$_3$)$_2$], 157 (16). $C_{13}H_{24}N_2O_3$ (256.34): calcd. C 60.91, H 9.44, N 10.93; found C 60.54, H 9.70, N 11.36.

**5c:** *N*-(Dialkylamino)lactam **4c** (0.52 mmol, 230 mg) was treated with Li (2.6 mmol, 18 mg) to afford α-(β-aminoalkyl)-substituted lactam **5c** as a colourless oil. Yield: 110 mg (78%); *de* ≥ 96%; *ee* = 82% (GC, chiral stationary phase, Chirasil-L-Val, 25m); $[\alpha]_D^{24}$ = +5.5 (*c* = 0.48, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3290 $cm^{-1}$ (s), 2960, 2930 (s), 1695 (s), 1520 (s), 1460 (m), 1390, 1365 (*t*Bu, m), 1275, 1250 (s), 1175 (s), 1040, 1015 (m), 990, 960 (w), 870 (w). $^1H$ NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 6.9 Hz, 3 H, CH$_2$C*H*$_3$), 1.20−1.45 (m, 4 H, C*H*$_2$C*H*$_2$CH$_3$), 1.44 [s, 9 H, C(C*H*$_3$)$_3$], 1.90−2.20 (m, 3 H, C*H*$_2$CH$_2$NCO, C*H*CHCO), 2.58 (dt, *J* = 3.0, 9.6 Hz, 1 H, CHC*H*CON), 3.12 (m, 1 H, C*H*HNHCOO-*t*Bu), 3.23 (br. q, *J* = 7.2 Hz, 1 H, CH*H*NHCOO-*t*Bu), 3.33 (m, 2 H, CONC*H*$_2$), 5.31 (br. m, 1 H, N*H*COO-*t*Bu), 6.65 (br. s, 1 H, CON*H*). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 14.24, 20.47, 22.90, 28.43, 31.86, 37.82, 42.96, 40.55, 41.92, 78.80, 156.22, 180.28. MS (EI): *m*/*z* (%) = 270 (6) [$M^+$] 214 (23), 123 (9), 197 (16), 170 (9), 169 (27), 154 (7), 152 (15), 141 (12), 140 (16), 112 (26), 98 (44), 86 (12), 85 (100), 69 (8), 57 (26), 55 (11). $C_{14}H_{26}N_2O_3$ (270.37): calcd. C 62.19, H 9.69, N 10.36; found C 61.92, H 9.82, N 10.74.

**5d:** *N*-(Dialkylamino)lactam **4d** (0.22 mmol, 110 mg) was treated with Li (0.86 mmol, 6 mg) to afford α-(β-aminoalkyl)-substituted lactam **5d** as a colourless solid. Yield: 64 mg (95%); *de* ≥ 96%; *ee* ≥ 96% (*de* of corresponding Mosher amide **5d′**); $[\alpha]_D^{24}$ = +47.1 (*c* = 0.77, $CHCl_3$); m.p. 142 °C. IR (KBr): $\tilde{\nu}$ = 3310 $cm^{-1}$ (s), 2975 (m), 2930 (m), 2880 (m), 1695 (s), 1495 (s), 1465 (m), 1390, 1365 (m), 1270, 1250 (s), 1170 (s), 1040 (m), 760 (m), 735 (m), 700 (m). $^1H$ NMR (300 MHz, $CDCl_3$): δ = 1.40 [s, 9 H, C(C*H*$_3$)$_3$], 2.00 (m, 1 H, C*H*HCH$_2$), 2.14 (m, 1 H, CH*H*CH$_2$), 2.76 (dt, *J* = 4.1, 9.1 Hz, 1 H, CHC*H*CO), 2.92 (dt, *J* = 4.1, 9.1 Hz, 1 H, CONC*H*H), 3.17 (br. q, *J* = 7.7 Hz, 1 H, CONCH*H*), 3.33 (m, 1 H, C*H*CHCO), 3.64 (m, 2 H, C*H*$_2$NHCOO-*t*Bu), 4.91 (br. t, *J* = 6.9 Hz, 1 H, N*H*COO-*t*Bu), 6.43 (br. s, 1 H, CON*H*), 7.20−7.36 (m, 5 H, Ar-H). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 24.05, 28.37, 40.35, 42.26, 43.83, 45.67, 127.12, 128.51, 128.64, 140.27, 155.97, 179.09. MS (CI, isobutane): *m*/*z* (%) = 306 (19), 305 (100) [$M^+$ + 1], 249 (90), 205 (10). $C_{17}H_{24}N_2O_3$ (304.39): calcd. C 67.08, H 7.95, N 9.20; found C 66.61, H 8.07, N 8.96.

**5e:** *N*-(Dialkylamino)lactam **4e** (0.26 mmol, 120 mg) was treated with Li (1.3 mmol, 9 mg) to afford α-(β-aminoalkyl)-substituted lactam **5e** as a colourless solid. Yield: 65 mg (88%); *de* ≥ 96%; *ee* ≥ 96% (GC, chiral stationary phase, Chirasil-L-Val, 25m); $[\alpha]_D^{24}$ = +46.0 (*c* = 0.40, $CHCl_3$); m.p. 121−123 °C. IR ($CHCl_3$): $\tilde{\nu}$ = 3295 $cm^{-1}$ (m, br), 3005 (m), 2980 (m), 2935 (m), 2895 (m), 1695 (s), 1505 (m), 1460 (m), 1390, 1365 (m), 1275, 1250 (m), 1170 (s), 1010 (w), 600 (w). $^1H$ NMR (400 MHz, $CDCl_3$): δ = 1.42 [s, 9 H, C(C*H*$_3$)$_3$], 2.04 (m, 1 H, C*H*HCH$_2$), 2.21 (m, 1 H, CH*H*CH$_2$), 2.80 (dt, *J* = 3.8, 8.8 Hz, 1 H, CHC*H*CO), 3.07 (dt, *J* = 3.8, 8.8 Hz, 1 H, CONC*H*H), 3.24 (br. q, *J* = 8.0 Hz, 1 H, CONCH*H*), 3.46 (m, 1 H, C*H*CHCO), 3.57 (m, 2 H, C*H*$_2$NHCOO-*t*Bu), 5.06 (br. m, 1 H, N*H*COO-*t*Bu), 6.16 (d, *J* = 3.0 Hz, 1 H, CH=C*H*O), 6.31 (dd, *J* = 1.9, 3.3 Hz, C*H*=CHO), 6.40 (br. s, 1 H, CON*H*), 7.34 (m, 1 H, C*H*=CO). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 24.31, 28.40, 39.46, 42.36, 40.34, 41.10, 79.16, 106.82, 110.30, 141.75, 154.21, 155.96, 178.61. MS (CI, isobutane): *m*/*z* (%) = 296 (12) [$M^+$ + 2], 295 (68) [$M^+$ + 1], 240 (13), 239 (100) [$M^+$ − CH=C(CH$_3$)$_2$], 195 (25). $C_{15}H_{22}N_2O_4$ (294.35): calcd. C 61.21, H 7.53, N 9.52; found C 60.81, H 7.76, N 9.24.

**5d′:** Trifluoroacetic acid (120 mg, 1.0 mmol) was added to *N*-Boc-protected amine **5d** (30 mg, 0.10 mmol) in $CH_2Cl_2$ (1 mL). After this had stirred overnight at room temperature, the solvent was removed in vacuo, the residue was dissolved in $CHCl_3$ (5 mL), and the evaporation/concentration and dissolution procedure was repeated three times. Finally, the solvent residue was removed in high vacuum. The trifluoroacetate of the amine was dissolved in $CH_2Cl_2$ (1 mL) and triethylamine (26 mg, 0.25 mmol) was added. The mixture was cooled to −78 °C and (*S*)-Mosher chloride (28 mg, 0.11 mmol) was added. After stirring overnight, the reaction mixture was allowed to warm to room temperature and the mixture was then dissolved in a 1:1 mixture of $CH_2Cl_2$/$Et_2O$ (50 mL). The organic phase was washed with a saturated aqueous $NH_4Cl$ solution (2 × 10 mL), a saturated $NaHCO_3$ solution (2 × 10 mL) and

brine (2 × 10 mL). After having been dried with $MgSO_4$, the solvent was removed in vacuo. Product **5d′** was obtained in analytically pure form as an unstable colourless solid after filtration through silica with $Et_2O$ containing 1% $Et_3N$. Yield: 35 mg (83%); *de* ≥ 96% ($^1$H NMR); $[\alpha]_D^{24}$ = +46.6 (*c* = 0.27, $CHCl_3$); m.p.: decomposition beginning at 50 °C. IR (KBr): $\tilde{\nu}$ = 3325 cm$^{-1}$ (s), 3065, 3030 (w), 2960, 2925, 2855 (s), 1690 (s), 1495, 1455 (s), 1380 (m), 1265 (s), 1160, 1105, 1025 (br., s), 950 (m), 920 (w), 865 (m), 800 (s), 765 (m), 720, 700 (s). $^1$H NMR (300 MHz, $CDCl_3$): δ = 1.96 (m, 1 H, C*H*HCH$_2$), 2.13 (m, 1 H, CH*H*CH$_2$), 2.63 (dt, *J* = 4.1, 9.1 Hz, 1 H, CHC*H*CON), 2.93 (dt, *J* = 3.8, 8.5 Hz, 1 H, CONC*H*H), 3.14 (q, *J* = 7.4 Hz, 1 H, CONCH*H*), 3.24 (d, *J* = 1.4 Hz, 3 H, OC$H_3$), 3.40 (ddd, *J* = 3.8, 8.6, 9.6 Hz, 1 H, C*H*CHCO), 3.75 (ddd, *J* = 5.8, 6.6, 13.5 Hz, 1 H, C*H*HNH), 4.02 (ddd, *J* = 6.6, 9.3, 13.7 Hz, 1 H, CH*H*NH), 5.72 (s, 1 H, CON*H*), 7.05 (br. t, *J* = 5.8 Hz, 1 H, N*H*), 7.26−7.34 (m, 10 H, Ar-H). $^{13}$C NMR (75 MHz, $CDCl_3$): 24.25, 40.21, 40.99, 43.95, 45.24, 54.86, 83.90 (q, $^2J$ 6.3 Hz), 123.74 (q, $^1J$ 98.8 Hz), 127.53, 128.41, 128.60, 128.77, 129.27, 132.53, 139.55, 166.42, 178.35. MS (EI): *m*/*z* (%) = 420 (2) [M$^+$], 336 (7), 232 (14), 231 (100) [M$^+$ − C(C$_6$H$_5$)(CF$_3$)(OCH$_3$)], 189 (19), 188 (27), 187 (12), 176 (7), 175 (53), 131 (17), 117 (9), 115 (9), 105 (14), 91 (40), 85 (28), 84 (11), 77 (11).

**General Procedure 4 (GP 4) for the Alkylation of *N*-(Dialkylamino)-lactams:** A solution of lithium diisopropylamide (1.8 mmol) in THF (15 mL) was slowly added at −78 °C, by double-ended needle, to a solution of *N*-(dialkylamino)lactam (**1**) (1.5 mmol) in THF (7 mL). The mixture was stirred for 3−4 h at −78 °C. It was then cooled to −100 °C and the electrophiles were added dropwise. After this had stirred overnight at −78 °C and then warmed to room temperature, a mixture of $H_2O$ (25 mL) and $CH_2Cl_2$ (25 mL) was added. The aqueous phase was extracted three times with $CH_2Cl_2$ (20 mL). The combined organic phases were washed with $H_2O$ (25 mL) and dried with $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography ($SiO_2$; diethyl ether/pentane, 1:2) to afford alkylated lactams **9** and **11**−**12**.

**9a:** Lactam **1a** (1.5 mmol, 380 mg) was alkylated with *N*-tosylaziridine (**8a**) (1.8 mmol, 355 mg) according to GP 4, to afford α-substituted *N*-(dialkylamino)lactam **9a** as a colourless oil. Yield: 540 mg (80%); *de* ≥ 96%; $[\alpha]_D^{24}$ = −34.0 (*c* = 0.68, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3190 cm$^{-1}$ (s), 2965, 2880, 2830 (s), 1680 (s), 1455, 1420 (s), 1380 (m), 1330, 1305, 1290 (s), 1160 (s), 1095 (s), 920 (m), 880, 850 (m), 815 (m), 735 (m), 710 (s), 570, 550 (s). $^1$H NMR (300 MHz, $CDCl_3$): δ = 0.84, 0.87 (2 t, *J* = 7.4 Hz, 6 H, 2CH$_2$C$H_3$), 1.45−2.10, 2.30 (m, 10 H, 2C$H_2$CH$_3$, NCH$_2$C$H_2$CH$_2$, CONCH$_2$C$H_2$, NHCH$_2$C$H_2$), 2.41 (s, 3 H, ArC$H_3$), 2.95 (m, 1 H, C*H*CO), 3.11 (m, 4 H, NHC$H_2$, NC$H_2$CH$_2$), 3.20 (s, 3 H, OC$H_3$), 3.42 (m, 2 H, CONC$H_2$), 3.69 (br. s, 1 H, NC*H*), 6.45 (br. t, *J* = 5.2 Hz, 1 H, N*H*), 7.28 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.75 (d, *J* = 8.2 Hz, 2 H, Ar-H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 8.06, 8.63, 20.58, 23.75, 24.06, 24.60, 26.07, 31.05, 39.97, 41.76, 50.15, 52.17, 64.28, 79.93, 127.06, 129.56, 137.96, 142.96, 174.45. MS (CI, isobutane): *m*/*z* (%) = 453 (20) [M$^+$ + 2], 452 (100) [M$^+$ + 1], 420 (22), 298 (49), 172 (24), 171 (12), 170 (100) [NHTs$^+$], 140 (29), 139 (12), 138 (23), 129 (15), 127 (15), 87 (40), 70 (36). $C_{23}H_{37}N_2O_4S$ (451.62): calcd. C 61.17, H 8.26, N 9.30; found C 60.98, H 8.64, N 9.47.

**10:** α-(β-Aminoethyl)-substituted lactam **9a** (360 mg, 0.82 mmol) was treated with Li (67 mg, 9.60 mmol, 12.5 equiv.) in liquid ammonia according to GP 3. After refluxing for 1 h, the reaction was quenched with solid $NH_4Cl$ (1.2 g). After evaporation of the ammonia the residue was dissolved in MeOH (50 mL), and $Boc_2O$ (715 mg, 3.28 mmol, 4 equiv.) and $Et_3N$ (331 mg, 3.28 mmol, 4 equiv.) were added. After this had stirred for 2 h at room temperature, the solvent was removed in vacuo and the residue was dissolved in $H_2O$ (25 mL). The aqueous phase was extracted three times with $CH_2Cl_2$ (25 mL) and the combined organic phases were washed with brine and dried with $MgSO_4$. Product **10** was obtained as a colourless solid after chromatography (silica; $Et_2O$/MeOH, 10:1). Yield: 103 mg (55%); *ee* = 83% (GC, chiral stationary phase, Chirasil L-Val 25m); $[\alpha]_D^{24}$ = −0.63 (*c* = 1.21, $CHCl_3$); m.p. 102−103 °C. IR ($CHCl_3$): $\tilde{\nu}$ = 3315 cm$^{-1}$ (m), 2975, 2930 (m), 1695 (s), 1525 (m), 1460, 1440 (m), 1390, 1365 (*t*Bu, m), 1275, 1255 (m), 1170 (s), 1060, 1010 (w). $^1$H NMR (300 MHz, $CDCl_3$): δ = 1.44 [s, 9 H, C(C$H_3$)$_3$], 1.62 (m, 1 H, C*H*HCH$_2$NH), 1.83 (m, 1 H, CONCH$_2$C*H*H), 1.94 (m, 1 H, CH*H*CH$_2$NH), 2.35 (m, 1 H, CONCH$_2$CH*H*), 2.41 (dq, *J* = 5.5, 8.5 Hz, C*H*CO), 3.24 (m, 2 H, C$H_2$NHCOO-*t*Bu), 3.35 (m, 2 H, CONC$H_2$), 5.16 (br. s, 1 H, N*H*COO-*t*Bu), 6.80 (br. s, 1 H, CON*H*). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 27.86, 28.43, 31.20, 38.81, 38.80, 40.39, 79.11, 156.12, 180.19. MS (CI, isobutane): *m*/*z* (%) = 229 (30) [M$^+$ + 1], 174 (9), 173 (100= [M$^+$ − CH=C(CH$_3$)$_2$], 167 (5), 129 (23). $C_{11}H_{20}N_2O_3$ (242.32): calcd. C 57.87, H 8.83, N 12.27; found C 57.75, H 8.75, N 11.89.

**9b:** Lactam **1a** (1.5 mmol, 380 mg) was alkylated with (*tert*-butyldimethylsilyloxy)ethyl bromide (**8b**) (1.8 mmol, 430 mg) according to GP 4, to afford α-substituted *N*-(dialkylamino)lactam **9b** as a colourless oil. Yield: 410 mg (66%); *de* = 70% (≥ 96%, after chromatography); $[\alpha]_D^{24}$ = −19.8 (*c* = 0.89, $CHCl_3$, *de* ≥ 96%). IR (film): $\tilde{\nu}$ = 2955 cm$^{-1}$ (s), 2880, 2860 (s), 2825 (w), 1690 (s), 1460 (s), 1405, 1390 (m), 1360 (w), 1270, 1255 (s), 1195 (w), 1095 (s), 1005 (w), 925 (m), 835 (s), 775 (s), 720, 665 (w). $^1$H NMR (400 MHz, $CDCl_3$), major diastereomer: δ = 0.05 [br. s, 6 H, Si(C$H_3$)$_2$], 0.86, 0.87 (2 t, *J* = 7.4 Hz, 6 H, 2CH$_2$C$H_3$), 0.89 [s, 9 H, C(C$H_3$)$_3$], 1.40−2.22 (m, 12 H, 2C$H_2$CH$_3$, NCH$_2$C$H_2$CH$_2$, CONCH$_2$C$H_2$, OCH$_2$C$H_2$), 2.41 (dq, *J* = 4.7, 8.8 Hz, 1 H, C*H*CO), 3.13 (m, 2 H, NC$H_2$), 3.25 (s, 3 H, OC$H_3$), 3.44 (m, 2 H, CONC$H_2$), 3.73 (m, 3 H, OC$H_2$, NC*H*). $^{13}$C NMR (100 MHz, $CDCl_3$), major diastereomer: δ = −5.35, −5.30, 8.17, 8.50, 24.04, 24.72, 26.16, 26.28, 25.94, 34.51, 38.59, 50.15, 52.27, 61.23, 64.51, 79.91, 174.64. MS (CI, isobutane): *m*/*z* (%) = 414 (25) [M$^+$ + 2], 413 (100) [M$^+$ + 1], 381 (13) [M$^+$ − OCH$_3$], 311 (15) [M$^+$ − CH$_3$OC(CH$_2$CH$_3$)$_2$]. $C_{22}H_{44}N_2O_3Si$ (326.52): calcd. C 64.03, H 10.75, N 6.79; found C 63.70, H 10.85, N 7.26.

**9c:** Lactam **1a** (1.5 mmol, 380 mg) was alkylated with methyl bromoacetate (**8c**) (1.95 mmol, 300 mg) according to GP 4, to afford α-substituted *N*-(dialkylamino)lactam **9c** as a colourless oil. Yield: 262 mg (84%); *de* = 66% (≥ 96%, after chromatography); $[\alpha]_D^{24}$ = −14.7 (*c* = 1.04, $CHCl_3$, *de* ≥ 96%). IR ($CHCl_3$): $\tilde{\nu}$ = 2970 cm$^{-1}$ (s), 2880 (s), 2825 (m), 1740 (s), 1690 (s), 1455, 1440 (s), 1415 (m), 1375 (m), 1325, 1305 (w), 1275 (s), 1195, 1170 (s), 1080 (s), 1010, 970 (w), 920, 880 (w). $^1$H NMR (300 MHz, $CDCl_3$), major diastereomer: δ = 0.86, 0.87 (2 t, *J* = 7.4 Hz, 6 H, 2CH$_2$C$H_3$), 1.50−2.00, 2.30 (m, 10 H, 2C$H_2$CH$_3$, NCH$_2$C$H_2$CH$_2$, CONCH$_2$C$H_2$), 2.34 (dd, *J* = 9.3, 16.5 Hz, 1 H, C*H*HCOOCH$_3$), 2.74 (m, 1 H, CH$_2$C*H*CO), 2.87 (dd, *J* = 4.1, 16.5 Hz, 1 H, CH*H*COOCH$_3$), 3.13 (m, 2 H, NC$H_2$), 3.26 (s, 3 H, OC$H_3$), 3.46 (m, 2 H, CONC$H_2$), 3.69 (s + br. s, 4 H, COOC$H_3$, NC*H*). $^{13}$C NMR (75 MHz, $CDCl_3$), major diastereomer: δ = 8.11, 8.57, 23.96, 24.43, 26.11, 26.25, 35.57, 37.85, 50.15, 51.75, 52.30, 64.59, 79.88, 172.46, 172.84. MS (CI, isobutane): *m*/*z* (%) = 328 (18) [M$^+$ + 2], 327 (100) [M$^+$ + 1], 295 (20), 225 (9) [M$^+$ − CH$_3$OC(CH$_2$CH$_3$)$_2$]. $C_{17}H_{30}N_2O_4$ (326.52): calcd. C 62.55, H 9.26, N 8.58; found C 62.13, H 9.67, N 8.89.

**9c:** Lactam **1c** (1.0 mmol, 240 mg) was alkylated with ethyl bromide (1.3 mmol, 141 mg) according to GP 4, to afford α-alkylated *N*-(dialkylamino)lactam **11c** as a colourless solid. Yield: 183 mg (65%); *de* = 67% (≥ 96%, after chromatography); $[\alpha]_D^{24} = -18.6$ (*c* = 1.21, $CHCl_3$); m.p. 67 °C. IR (KBr): $\tilde{\nu}$ = 2965 $cm^{-1}$, 2940, 2870 (s), 2825 (m) 1735 (s), 1460, 1420, 1380, 1370 (m), 1305 (s), 1265 (m), 1200, 1180, 1140, 1075 (m), 975, 965 (m), 915, 895, 870 (w). $^1H$ NMR (300 MHz, $CDCl_3$), major diastereomer: δ = 0.94 (t, *J* = 7.4 Hz, 3 H, $CH_2CH_3$), 1.07, 1.11 (2 s, 6 H, $2CH_3$), 1.40−1.98 (m, 9 H, $CONCHCH_2CHH$, $NCH_2CH_2CH_2$, $CH_2CH_3$), 2.15 (m, 2 H, $CONCHCH_2CHH$, *CH*CO), 3.13 (s, 3 H, $OCH_3$), 3.15 (m, 1 H, NC*H*H), 3.40 (m, 2 H, CONC*H*H, NCH*H*), 3.69 (m, 1 H, CONCH*H*), 3.92 (dd, *J* = 4.7, 9.4 Hz, 1 H, NC*H*). $^{13}C$ NMR (75 MHz, $CDCl_3$), major diastereomer: δ = 11.68, 21.57, 22.17, 22.27, 23.86, 24.88, 25.34, 27.36, 44.54, 48.98, 51.78, 52.34, 63.76, 77.87, 171.42. MS (CI, isobutane): *m*/*z* (%) = 270 (17) [$M^+$ + 2], 269 (100) [$M^+$ + 1], 237 (11), 195 (13) [$M^+$ − $CH_3OC(CH_3)_2$], 128 (9). $C_{15}H_{28}N_2O_2$ (268.40): calcd. C 67.13, H 10.51, N 10.44; found C 67.11, H 10.25, N 10.22.

**9d:** Lactam **1d** (6.0 mmol, 1.60 g) was alkylated with ethyl bromide (7.8 mmol, 0.48 g) according to GP 4, to afford α-alkylated *N*-(dialkylamino)lactam **11d** as a colourless oil. Yield: 1.48 g (83%); *de* = 32%; $[\alpha]_D^{24} = -15.2$ (*c* = 1.05, $CHCl_3$). IR (film): $\tilde{\nu}$ = 2965 $cm^{-1}$ (s), 2940 (s), 2875 (s), 2825 (m), 1645 (s), 1460 (s), 1415 (m), 1380 (m), 1305 (m), 1245 (w), 1195 (m), 1175 (m), 1120 (m), 1080 (m), 955 (w), 915 (m), 880 (w). $^1H$ NMR (400 MHz,$CDCl_3$), major diastereomer: δ = 0.85−0.96 (m, 9 H, $3CH_2CH_3$), 1.39−2.00 (m, 13 H, $NCH_2CH_2CHH$, $CONCH_2CH_2CH_2$, $3CH_2CH_3$), 2.08−2.20 (m, 2 H, *CH*CO, $NCH_2CH_2CHH$), 3.17 (s, 3 H, $OCH_3$), 3.22−3.34 (m, 1 H, NCH*H*), 3.37−3.52 (m, 2 H, CONCH*H*, NC*H*H), 3.69 (m, 1 H, CONC*H*H), 3.90−4.06 (dd, *J* = 4.1, 9.6 Hz, 1 H, NC*H*). $^{13}C$ NMR (100 MHz, $CDCl_3$), major diastereomer: δ = 8.15, 8.64, 11.58, 22.33, 24.31, 24.75, 24.96, 25.41, 26.11, 26.57, 44.61, 49.49, 51.82, 52.16, 63.79, 80.14, 171.17. MS (CI, isobutane): *m*/*z* (%) = 298 (56) [$M^+$ + 2], 297 (100) [$M^+$ + 1], 295 (9), 266 (9), 265 (59), 196 (9), 195 (73) [$M^+$ − $C(CH_2CH_3)_2OCH_3$], 170 (6). $C_{17}H_{32}N_2O_2$, (296.45): calcd. C 68.88, H 10.88, N 9.45; found C 69.16, H 10.88, N 9.45

**11e:** Lactam **1d** (10.0 mmol, 2.68 g) was alkylated with allyl bromide (14 mmol, 1.87 g) according to GP 4, to afford α-alkylated *N*-(dialkylamino)lactam **11e** as a colourless oil. Yield: 2.53 g (82%); *de* = 54%; $[\alpha]_D^{24} = -1.0$ (*c* = 1.09, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3075 $cm^{-1}$ (w), 2965 (s), 2940 (s), 2875 (s), 2825 (m), 1645 (s), 1455 (m), 1415 (m), 1380 (w), 1350 (w), 1335 (w), 1300 (m), 1250 (w), 1225 (w), 1185 (m), 1120 (m), 1080 (m), 995 (m), 910 (m). $^1H$ NMR (300 MHz, $CDCl_3$), major diastereomer: δ = 0.87 (t, *J* = 7.7 Hz, 6 H, $2CH_2CH_3$), 1.40−2.04 (m, 11 H, $NCH_2CH_2CHH$, $CONCH_2CH_2CH_2$, $2CH_2CH_3$), 2.08−2.36 (m, 3 H, $H_2C$=CHC*H*H, C*H*CO, $NCH_2CH_2CHH$), 2.50−2.70 (m, 1 H, $H_2C$=CHCH*H*), 3.10−3.30 (m, 2 H, $NCH_2$), 3.17 (s, 3 H, $OCH_3$), 3.36−3.52 (m, 1 H, CONC*H*H), 3.69 (m, 1 H, CONCH*H*), 3.94 (dd, *J* = 9.4, 3.7 Hz, 1 H, NC*H*), 4.99−5.10 (m, 2 H, $H_2C$=CH), 5.69−5.86 (m, 1 H, $H_2C$=C*H*). $^{13}C$ NMR (75 MHz, $CDCl_3$), major diastereomer: δ = 8.14, 8.71, 22.28, 24.29, 24.86, 25.59, 26.13, 26.61, 36.50, 42.97, 49.54, 51.87, 52.25, 63.81, 80.29, 116.64, 134.48, 170.69. MS (CI, isobutane): *m*/*z* (%) = 311 (9) [$M^+$ + 3], 310 (26) [$M^+$ + 2], 309 (100) [$M^+$ + 1], 307 (14), 279 (9), 278(21), 277 (82), 207 (42) [$M^+$ − $C(CH_2CH_3)_2OCH_3$], 170 (9), 89 (12). $C_{18}H_{32}N_2O_2$ (308.46): calcd. C 70.09, H 10.46, N 9.08; found C 69.70, H 10.70, N 9.47.

**12a:** α-Alkylated *N*-(dialkylamino)lactam **11a** (1.0 mmol, 280 mg) was alkylated with allyl bromide (1.3 mmol, 160 mg) according to GP 4, to afford α-dialkylated *N*-(dialkylamino)lactam **12a** as a colourless oil. Yield: 270 mg (84%); *de* = 88%; $[\alpha]_D^{24} = -14.4$ (*c* = 0.70, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 3075 $cm^{-1}$ (w), 2965, 2940, 2880 (s), 2825 (m), 1690 (s), 1640 (m), 1460 (s), 1405 (m), 1380 (m), 1275 (m), 1115 (m), 1080 (s), 1000 (m), 915 (s), 880 (w). $^1H$ NMR (300 MHz, $CDCl_3$): δ = 0.85, 0.86, 0.90 (3 t, *J* = 7.4 Hz, 9 H, $3CH_2CH_3$), 1.45−2.10 (m, 12 H, $3CH_2CH_3$, $NCH_2CH_2CH_2$, $CONCH_2CH_2$), 2.14 (dd, *J* = 8.2, 13.7 Hz, 1 H, C*H*HCH=$CH_2$), 2.28 (dd, *J* = 6.6, 13.7 Hz, 1 H, CH*H*CH=$CH_2$), 3.12 (m, 2 H, $NCH_2$), 3.30 (s, 3 H, $OCH_3$), 3.33−3.46 (m, 2 H, $CONCH_2$), 3.67 (br. s, 1 H, NC*H*), 5.04 (m, 2 H, $CH_2$=CH), 5.75 (m, 1 H, $CH_2$=C*H*). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 8.21, 8.51, 8.58, 23.90, 24.27, 25.77, 26.19, 26.37, 29.60, 41.42, 46.36, 50.29, 52.46, 64.94, 79.81, 118.06, 134.29, 175.69. MS (CI, isobutane): *m*/*z* (%) = 324 (20) [$M^+$ + 2], 323 (100) [$M^+$ + 1], 291 (13), 221 (9). $C_{19}H_{34}N_2O_2$ (322.49): calcd. C 70.76, H 10.63, N 8.69; found C 70.69, H 10.91, N 9.18.

**12b:** α-Alkylated *N*-(dialkylamino)lactam **11a** (1.0 mmol, 280 mg) underwent Michael addition to methyl crotonate (1.3 mmol, 130 mg) according to GP 1a to afford α-disubstituted *N*-(dialkylamino)lactam **12b** as a colourless oil. Yield: 309 mg (84%); *de* = 83%; $[\alpha]_D^{24} = -24.4$ (*c* = 0.91, $CHCl_3$). IR ($CHCl_3$): $\tilde{\nu}$ = 2965 $cm^{-1}$ (s), 2880 (s), 2830 (m), 1740 (s), 1685 (s), 1460, 1435 (s), 1415, 1385 (m), 1270 (m), 1195, 1165 (m), 1080 (m), 1015 (m), 915 (m), 880 (w), 735 (w). $^1H$ NMR (300 MHz, $CDCl_3$): δ = 0.84, 0.86, 0.91 (4 t, *J* = 7.6 Hz, 9 H, $3CH_2CH_3$, $CHCH_3$), 1.48−2.05 (m, 12 H, 3 $CH_2CH_3$, $NCH_2CH_2CH_2$, $CONCH_2CH_2$), 2.13 (dd, *J* = 11.3, 15.1 Hz, 1 H, C*H*HCOO$CH_3$), 2.31 (m, 1 H, C*H*$CH_3$), 2.49 (dd, *J* = 2.5, 15.1 Hz, 1 H, CH*H*COO$CH_3$), 3.13 (m, 2 H, $NCH_2$), 3.24 (s, 3 H, $OCH_3$), 3.35−3.45 (m, 2 H, $CONCH_2$), 3.65 (s, 3 H, $COOCH_3$), 3.68 (br. s, 1 H, NC*H*). $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 8.06, 8.63, 11.73, 19.72, 23.95, 24.20, 26.23, 26.28, 35.34, 36.98, 42.70, 50.11, 51.49, 52.94, 65.21, 79.89, 173.59, 173.68. MS (EI): *m*/*z* (%) = 368 (0.5) [$M^+$], 337 (2), 268 (18), 267 (100) [$M^+$ − $CH_3OC(CH_2CH_3)_2$], 168 (10), 140 (7), 101 (5), 97 (6), 68 (4), 55 (4). $C_{21}H_{38}N_2O_4$ (382.54): calcd. C 65.94, H 10.01, N 7.32; found C 66.03, H 9.74, N 7.74.

**12c:** α-Alkylated *N*-(dialkylamino)lactam **11b** (1.5 mmol, 360 mg) was alkylated with allyl bromide (2.0 mmol, 240 mg) according to GP 4, to afford α-dialkylated *N*-(dialkylamino)lactam **12c** as a colourless oil. Yield: 270 mg (64%); *de* = 25%; $[\alpha]_D^{24} = -51.4$ (*c* = 0.80, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3075 $cm^{-1}$ (w), 2965 (s), 2940 (s), 2870 (s), 2825 (m), 1640 (s) 1460 (m), 1415 (m), 1380 (w), 1350 (w), 1305 (m), 1200 (m), 1130 (m), 1105 (s), 1000 (w), 965 (w), 915 (m). $^1H$ NMR (300 MHz, $CDCl_3$), major diastereomer: δ = 0.87 (t, *J* = 7.6 Hz, 3 H, $CH_2CH_3$), 1.40−1.90 (m, 9 H, $CONCH_2CH_2CH_2$, $CH_3CH_2$, $NCH_2CH_2CHH$), 2.00−2.20 (m, 2 H, $H_2C$=CHCH*H*, $NCH_2CH_2CHH$), 2.48 (m, 1 H, $H_2C$=CHC*H*H), 3.11 (td, *J* = 7.7, 3.7 Hz, 1 H, NC*H*H), 3.26−3.31 (m, 2 H, $CH_2OCH_3$), 3.33 (s, 3 H, $OCH_3$), 3.36−3.50 (m, 3 H, $CONCH_2$, NCH*H*) 3.90 (br. s, 1 H, NC*H*), 5.07 (m, 2 H, $H_2C$=CH), 5.68−5.86 (m, 1 H, $H_2C$=C*H*). $^{13}C$ NMR (75 MHz, $CDCl_3$), major diastereomer: δ = 8.68, 20.48, 22.74, 27.16, 28.40, 31.46, 43.07, 45.98, 50.01, 53.35, 58.93, 59.33, 76.29, 117.67, 134.86, 173.40. MS (CI, isobutane): *m*/*z* (%) = 281 (100) [$M^+$ + 1]. $C_{16}H_{28}N_2O_2$ (280.41): calcd. C 68.53, H 10.06, N 9.99; found C 68.04, H 10.05, N 10.34.

**12d:** α-Alkylated *N*-(dialkylamino)lactam **11c** (1.5 mmol, 400 mg) was alkylated with allyl bromide (2.0 mmol, 240 mg) according to GP 4, to afford α-dialkylated *N*-(dialkylamino)lactam **12d** as a colourless oil. Yield: 330 mg (71%); *de* = 6%. IR (film): $\tilde{\nu}$ = 3075 $cm^{-1}$ (w) 2970 (br., s), 2940 (s), 2870 (s), 2825 (m), 1640 (s), 1460 (s), 1415 (m), 1380 (m), 1365 (m), 1335 (w), 1300 (m), 1230 (w),

1190 (m), 1180 (m), 1150 (m), 1135 (m), 1090 (m), 1075 (m), 1000 (w), 985 (w), 915 (m), 860 (w). $^1$H NMR (400 MHz, $CDCl_3$), major diastereomer: δ = 0.88 (t, *J* = 7.4 Hz, 3 H, $CH_2CH_3$), 1.08, 1.11 (2s, 6 H, $2CH_3$), 1.40−2.00 (m, 9 H, $NCH_2CH_2CH$H, $CONCH_2CH_2CH_2$, $CH_2CH_3$), 2.09−2.26 (m, 2 H, $H_2C$=CHCH*H*, $NCH_2CH_2CH$*H*), 2.44 (dd, *J* = 7.1, 13.7 Hz, 1 H, $H_2C$=CHC*H*H), 3.12−3.18 (m, 1 H, NCH*H*), 3.16 (s, 3 H, $OCH_3$), 3.28−3.47 (m, 2 H, CONCH*H*, NC*H*H), 3.62−3.70 (m, 1 H, CONC*H*H), 3.88 (m, 1 H, NC*H*), 5.02 (m, 2 H, $H_2C$=CH), 5.70−5.90 (m, 1 H, $H_2C$=C*H*). $^{13}$C NMR (100 MHz, $CDCl_3$), major diastereomer: δ = 8.73, 21.17, 21.94, 20.34, 24.02, 26.98, 28.27, 30.95, 43.26, 45.75, 49.01, 51.77, 52.76, 65.13, 77.77, 117.28, 134.78, 172.90. MS (CI, isobutane): *m*/*z* (%) = 310 (25) [$M^+$ + 2], 309 (100) [$M^+$ + 1], 277 (20) [$M^+$ − $OCH_3$], 235 (25) [$M^+$ − $C(CH_3)_2OCH_3$]. $C_{18}H_{32}N_2O_2$ (308.46): calcd. C 70.09, H 10.46, N 9.08; found C 69.84, H 10.54, N 9.47.

**12e:** α-Alkylated *N*-(dialkylamino)lactam **11d** (1.5 mmol, 440 mg) was alkylated with allyl bromide (2.0 mmol, 240 mg) according to GP 4, to afford α-dialkylated *N*-(dialkylamino)lactam **12e** as a colourless oil. Yield: 230 mg (45%); *de* = 52%; $[\alpha]_D^{24}$ = +37.6 (*c* = 0.84, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3075 $cm^{-1}$ (w), 2965 (s), 2940 (s), 2875 (s), 2825 (m), 1640 (s) 1460 (s), 1415 (m), 1380 (m), 1350 (m), 1340 (w), 1300 (m), 1250 (w), 1220 (w), 1200 (m), 1185 (m), 1155 (m), 1115 (m), 1080 (m), 1000 (w), 910 (m) 880 (w), 855 (w). $^1$H NMR (400 MHz, $CDCl_3$), (*R*,*S*) diastereomer: δ = 0.87 (m, 9 H, $3CH_2CH_3$), 1.40−2.00 (m, 13 H, $NCH_2CH_2CH$H, $CONCH_2CH_2CH_2$, $3CH_2CH_3$), 2.08−2.23 (m, 2 H, $H_2C$=CHCH*H*, $NCH_2CH_2CH$*H*), 2.51 (dd, *J* = 6.6, 13.5 Hz, 1 H, $H_2C$=CHC*H*H), 3.12−3.26 (m, 2 H, $NCH_2$), 3.20 (s, 3 H, $OCH_3$), 3.35−3.52 (m, 1 H, CONCH*H*), 3.66 (m, 1 H, CONC*H*H), 3.92 (m, 1 H, NC*H*), 5.07 (m, 2 H, $H_2C$=CH), 5.70−5.90 (m, 1 H, $H_2C$=C*H*). $^{13}$C NMR (100 MHz, $CDCl_3$), (*R*,*S*) diastereomer: δ = 8.21, 8.63, 8.67, 20.42, 24.55, 24.76, 26.12, 26.26, 28.60, 31.36, 42.65, 45.75, 49.75, 51.88, 52.60, 64.89, 80.20, 117.68, 134.96, 173.25. MS (CI, isobutane): *m*/*z* (%) = 338 (43) [$M^+$ + 2], 337 (100) [$M^+$ + 1], 335 (6), 306 (8), 305 (39), 235 (46) [$M^+$ − $C(CH_2CH_3)_2OCH_3$]. $C_{20}H_{36}N_2O_2$ (336.52): calcd. C 71.38, H 10.78, N 8.32; found C 71.16, H 10.86, N 8.74.

**12e:** α-Alkylated *N*-(dialkylamino)lactam **11e** (1.10 mmol, 330 mg) was alkylated with ethyl bromide (1.4 mmol, 150 mg) according to GP 4, to afford α-dialkylated *N*-(dialkylamino)lactam **12e** as a colourless oil. Yield: 140 mg (40%); *de* = 31%; $[\alpha]_D^{24}$ = −27.4 (*c* = 0.83, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$), (*S*,*S*) diastereomer: δ = 0.87 (m, 9 H, $3CH_2CH_3$), 1.40−2.00 (m, 13 H, $NCH_2CH_2CH$H, $CONCH_2CH_2CH_2$, $3CH_2CH_3$), 2.08−2.23 (m, 2 H, $H_2C$=CHCH*H*, $NCH_2CH_2CH$*H*), 2.51 (dd, *J* = 6.6, 13.5 Hz, 1 H, $H_2C$=CHC*H*H), 3.12−3.26 (m, 2 H, $NCH_2$), 3.20 (s, 3 H, $OCH_3$), 3.35−3.52 (m, 1 H, CONCH*H*), 3.66 (m, 1 H, CONC*H*H), 3.92 (m, 1 H, NC*H*), 5.07 (m, 2 H, $H_2C$=CH), 5.70−5.90 (m, 1 H, $H_2C$=C*H*). $^{13}$C NMR (75 MHz, $CDCl_3$), (*S*,*S*) diastereomer: δ = 8.20, 8.63, 8.73, 20.46, 24.49, 24.92, 26.12, 26.31, 28.45, 30.98, 43.29, 45.89, 49.67, 51.98, 52.59, 64.71, 80.38, 117.51, 134.85, 173.21. The other spectroscopic data are in accordance with those of (*R*,*S*)-**12e**.

**General Procedure 6 (GP 6) for the Reductive N−N Bond Cleavage of α-Alkylated *N*-(Dialkylamino)lactams:** Pieces of lithium wire (5 equiv.) were added to liquid $NH_3$ (50 mL/mmol) in a three-necked flask, fitted with a dry ice condenser. The α-substituted *N*-(dialkylamino)lactams in dry THF (10 mL/mmol) were added to the dark blue solution at −78 °C. The cooling bath was then removed and the solution was kept under reflux (−33 °C) until the blue colour disappeared (after 1 h). The reaction was quenched with solid $NH_4Cl$ (12 equiv.) and the $NH_3$ was evaporated at room temperature. The solid residue was dissolved in a 1:1 mixture of $CH_2Cl_2$ and $H_2O$ (20 mL/mmol) and the aqueous phase was extracted twice with $CH_2Cl_2$ (10 mL). The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo, and the crude products were purified by chromatography [$SiO_2$; $Et_2O$/pentane (10:1) or $Et_2O$].

**13a:** α,α-Dialkylated *N*-(dialkylamino)lactam **12a** (0.72 mmol, 230 mg) was treated with Li (3.5 mmol, 24 mg) to afford α,α-dialkylated lactam **13a** as a colourless oil. Yield: 85 mg (78%); *ee* = 88% (GC, chiral stationary phase, Chirasil-Dex 25m); $[\alpha]_D^{24}$ = +57.8 (*c* = 1.05, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3235 $cm^{-1}$ (m), 3075 (m), 2935, 2880 (m), 1690 (s), 1640 (m), 1440, 1385 (m),1325 (m), 1275 (m), 1070 (w), 1000 (w), 915 (s). $^1$H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.4 Hz, 3 H, $CH_2CH_3$), 1.56 (m, 2 H, C*H*HCH$_3$, $CONCH_2CH$H), 1.96−2.01 (m, 2 H, CH*H*CH$_3$, $CONCH_2CH$*H*), 2.20 (dd, *J* = 8.2, 13.8 Hz, 1 H, C*H*HCH=$CH_2$), 2.31 (dd, *J* = 6.6, 13.8 Hz, 1 H, CH*H*CH=$CH_2$), 3.26 (t, *J* = 7.2 Hz, 2 H, $CONCH_2$), 5.07 (m, 2 H, $CH_2$=CH), 5.87 (m, 1 H, $CH_2$=C*H*), 7.44 (br. s, 1 H, NH). $^{13}$C NMR (100 MHz, $CDCl_3$): δ = 8.66, 23.38, 24.40, 39.37, 41.06, 47.19, 118.12, 134.22, 182.05. MS (EI): *m*/*z* (%) = 153 (4) [$M^+$], 138 (18), 126 (8), 125 (100= [$M^+$ − $C_2H_4$], 124 (44), 113 (6), 112 (13), 111 (12), 110 (13), 98 (33), 96 (12), 95 (6), 83 (7), 82 (17), 81 (15), 79 (11), 70 (9), 69 (38), 67 (20), 55 (12), 54 (5), 53 (11). $C_9H_{15}NO$ (153.12): calcd. C 70.55, H 9.87, N 9.15; found C 70.29, H 10.23, N 9.56.

**13b:** α,α-Dialkylated *N*-(dialkylamino)lactam (*R*,*S*)-**12e** (0.46 mmol, 155 mg) was treated with Li (2.3 mmol, 16 mg) to afford α,α-dialkylated lactam (*R*)-**13b** as a colourless oil. Yield: 42 mg (55%); *ee* = 51% (Chirasil-Dex); $[\alpha]_D^{24}$ = −6.4 (*c* = 0.75, $CHCl_3$). IR (film): $\tilde{\nu}$ = 3290 $cm^{-1}$ (s), 3210 (s), 3074 (s), 2940 (s), 2875 (s), 1660 (s), 1490 (s), 1460 (s), 1415 (s), 1385 (m), 1355 (s), 1310 (s), 1255 (w), 1205 (m), 1175 (w), 1110 (m), 1045 (w), 1000 (m), 915 (s), 730 (m), 655 (m), 610 (w), 555 (w), 465 (w). $^1$H NMR (300 MHz, $CDCl_3$): δ = 0.89 (t, *J* = 7.6 Hz, 3 H, $CH_2CH_3$), 1.40−1.60 (m, 2 H, $CH_2CH_3$), 1.66−1.86 (m, 4 H, $CONCH_2CH_2CH_2$), 2.14−2.26 (dd, *J* = 13.8, 7.1 Hz, 1 H, $H_2C$=CHC*H*H), 2.48 (m, 1 H, $H_2C$=CHCH*H*), 3.26 (m, 2 H, $CONCH_2$), 5.10 (m, 2 H, $H_2C$=CH), 5.70−5.88 (m, 1 H, $H_2C$=C*H*), 6.2 (br. s, 1 H, CON*H*). $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 8.67, 19.70, 28.60, 31.05, 42.63, 42.83, 44.79, 117.81, 134.70, 176.98. MS (CI, isobutane): *m*/*z* (%) = 169 (11) [$M^+$ + 2], 168 (100) [$M^+$ + 1]. HRMS: $^{12}C_{10}{}^1H_{17}{}^{14}N^{16}O$ = [$M^+$]: calcd.: (*m*/*z*): 167.1052; found (*m*/*z*): 167.1055. In analogy, N−N bond cleavage of (*S*,*S*)-**12e** (0.62 mmol, 207 mg) with Li (3.1 mmol, 22 mg) yielded 64 mg (62%) of (*S*)-**13b**; *ee* = 42% (Chirasil-Dex); $[\alpha]_D^{24}$ = +4.7 (*c* = 0.75, $CHCl_3$).

**14:** Lactam (*S*)-**1a** (382 mg, 1.5 mmol) in THF (7 mL) was metallated with LDA (1.8 mmol) in THF (15 mL) for 3 h at −78 °C. The reaction mixture was then cooled to −100 °C and trimethylsilyl chloride (1.8 mmol, 174 mg) was added. After this had warmed to room temperature over about 3 h, a saturated aqueous $NaHCO_3$ solution (20 mL) was added. The aqueous phase was extracted three times with $Et_2O$ (20 mL). The combined organic phases were washed with brine (15 mL) and then dried with $MgSO_4$. After concentration in vacuo, the crude product was purified by chromatography ($SiO_2$; $Et_2O$/pentane, 1:2) to afford α-silylated *N*-(dialkylamino)lactam **14** as a colourless oil. Yield: 342 mg (70%); *de* = 75% (≥ 96%, after chromatography); $[\alpha]_D^{24}$ = +20.1 (*c* = 0.63, $CHCl_3$, *de* ≥ 96%). IR (film): $\tilde{\nu}$ = 2955 $cm^{-1}$ (s), 2880, 2860 (s), 2825 (w), 1675 (s), 1460 (s), 1400 (s), 1250 (s), 1210 (m), 1170 (s), 1080 (s), 920 (w), 845 (s), 775, 760 (w), 710, 695 (w). $^1$H

NMR (400 MHz, $CDCl_3$): δ = 0.13 [s, 9 H, $Si(CH_3)_3$], 0.86 (2 t, $J$ = 7.4 Hz, 6 H, $2CH_2CH_3$), 1.45−2.00 (m, 10 H, $2CH_2CH_3$, $NCH_2CH_2CH_2$, $CONCH_2CHH$, $CHSi$), 2.12 (m, 1 H, $CONCH_2CHH$), 3.00 (m, 1 H, $NCHH$), 3.09 (m, 1 H, $NCHH$), 3.34 (s, 3 H, $OCH_3$), 3.34−3.47 (m, 3 H, $CONCH_2$, $NCH$). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = −2.65, 8.24, 8.33, 18.91, 23.48, 24.12, 25.96, 26.46, 31.29, 50.56, 52.09, 64.94, 79.77, 175.33. MS (CI, isobutane): $m/z$ (%) = 328 (24) [$M^+$ + 2], 327 (100) [$M^+$ + 1], 295 (23), 225 (20) [$M^+ - CH_3OC(CH_2CH_3)_2$]. $C_{17}H_{34}N_2O_2Si$ (326.52): calcd. C 62.53, H 10.49, N 8.58; found C 62.40, H 10.91, N 8.95.

**15:** α-Silylated *N*-(dialkylamino)lactam **14** (0.69 mmol, 225 mg) was treated with Li (3.44 mmol, 24 mg) according to GP 4, to afford α-silylated lactam **15** as a colourless solid. Yield: 80 mg (75%); *ee* = 83% (GC, chiral stationary phase, Lipodex E 25m); $[\alpha]_D^{24}$ = +68.4 ($c$ = 0.96, $CHCl_3$); m.p. 85−87 °C. IR (KBr): $\tilde{\nu}$ = 3220 $cm^{-1}$ (s), 3080 (s), 2955, 2880 (s), 1670 (s), 1460, 1485 (m), 1365 (m), 1275, 1245 (s), 1175 (w), 1145 (m), 1080 (w), 1050 (m), 950, 935 (m), 835 (s), 780, 760 695, 660 (s). $^1H$ NMR (400 MHz, $CDCl_3$): δ = 0.14 [s, 9 H, $Si(CH_3)_3$], 1.91 (dd, $J$ = 4.7, 10.4 Hz, 1 H, $CHSi$), 2.03 (ddd, $J$ = 4.4, 8.2, 12.6 Hz, 1 H, $CONCH_2CHH$), 2.35 (m, 1 H, $CONCH_2CHH$), 3.24 (m, 2 H, $CONCH_2$), 6.45 (br. s, 1 H, $NH$). $^{13}C$ NMR (100 MHz, $CDCl_3$): δ = −2.65, 23.43, 31.99, 41.97, 181.48. MS (CI, isobutane): $m/z$ (%) = 158 (25) [$M^+$ + 1], 142 (29), 89 (100) [$OSiMe_3$], 61 (47). $C_7H_{15}NOSi$ (157.29): calcd. C 53.45, H 9.61, N 8.91; found C 53.23, H 9.62, N 8.80.

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[1] N. de Kimpe, in *Comprehensive Heterocyclic Chemistry II*, vol. 1B (Eds.: A. R. Katritzky, C. W. Rees, J. Scriven), Pergamon, Oxford, **1996**, p. 536−575.

[2] [2a] P. S. Dragovich, T. J. Prins, R. Zhou, S. E. Webber, J. T. Marakovits, S. A. Fuhrman, A. K. Patick, D. A Matthews, C. A. Lee, C. E. Ford, B. J. Burke, P. A. Rejto, T. F. Hendrickson, T. Tuntland, E. L. Brown, J. W. Meador, III, R. A. Ferre, J. E. V. Harr, M. B. Kosa, S. T. Worland, *J. Med. Chem.* **1999**, *42*, 1213−1224. [2b] F. G. Salituro, C. T. Baker, J. J. Court, D. D. Deininger, E. E. Kim, B. Li, P. M. Novak, B. G. Rao, S. Pazhanisamy, M. D. Porter, W. C. Schairer, R. D. Tung, *Bioorg. Med. Chem. Lett.* **1998**, *8*, 3637−3642. [2c] A. G. M. Barrett, J. Head, M. L. Smith, N. S. Stock, *Chem. Commun.* **1999**, 133−134. [2d] M. E. Duggan, A. M. Naylor-Olsen, J. J. Perkins, P. S. Anderson, C. T.-C. Chang, J. J. Cook, R. J. Gould, N. C. Ihle, G. D. Hartman, J. J. Lynch, R. J. Lynch, P. D. Manno, L. W. Schaffer, R. L. Smith, *J. Med. Chem.* **1995**, *38*, 3332−3341.

[3] [3a] E. Roberts, T. N. Chase, D. B. Tower, *GABA in Nervous System Functions*, Raven, New York, **1976**. [3b] P. Krogsgaard-Larsen in *Comprehensive Medicinal Chemistry*, vol. 3 (Eds.: P. G. Sammes, J. B. Taylor), Pergamon, Oxford, **1990**, p. 493−566. [3c] Z H. McAlonan, P. J. Stevenson, *Tetrahedron: Asymmetry* **1995**, *6*, 239−244.

[4] Y.-G. Suh, S.-A. Kim, J.-K. Jung, D.-Y. Shin, K.-H. Min, B.-A. Koo, H.-S. Kim, *Angew. Chem.* **1999**, *111*, 3753−3755; *Angew. Chem. Int. Ed.* **1999**, *38*, 3545−3547.

[5] [5a] J. C. F. Alves, A. B. C. Simas, P. R. R. Costa, *Tetrahedron: Asymmetry* **1999**, *10*, 297−306. [5b] F. Roussi, J.-C. Quirion, A. Tomas, H.-P. Husson, *Tetrahedron* **1998**, *54*, 10363−10378. [5c] A. Padwa, S. R. Harring, M. A. Semones, *J. Org. Chem.* **1998**, *63*, 44−54. [5d] D. Desmaële, K. Mekouar, J. d′Angelo, *J. Org. Chem.* **1997**, *62*, 3890−3901.

[6] P. Amruta Reddy, B. C. H. Hsiang, T. N. Latifi, M. W. Hill, K. E. Woodward, S. M. Rothman, J. A. Ferrendelli, D. F. Covey, *J. Med. Chem.* **1996**, *39*, 1898−1906.

[7] Reviews: [7a] A. I. Meyers, D. Romo, *Tetrahedron* **1991**, *47*, 9503−9569. [7b] M. D. Groaning, A. I. Meyers, *Tetrahedron* **2000**, *56*, 9843−9873.

[8] [8a] I. Baussanne, C. Travers, J. Royer, *Tetrahedron: Asymmetry* **1998**, *9*, 797−804. [8b] T. Varea, M. Dufour, L. Micouin, C. Riche, A. Chiaroni, J.-C. Quirion, H.-P. Husson, *Tetrahedron Lett.* **1995**, *36*, 1035−1038. [8c] L. Micouin, T. Varea, C. Riche, A. Chiaroni, J.-C. Quirion, H.-P. Husson, *Tetrahedron Lett.* **1994**, *35*, 2529−2532.

[9] G. Lakshmaiah, T. Kawabata, M. Shang, K. Fuji, *J. Org. Chem.* **1999**, *64*, 1699−1704.

[10] N. A. Porter, H. Feng, I. K. Kavrakova, *Tetrahedron Lett.* **1999**, *40*, 6713−6716.

[11] [11a] D. Enders, R. Gröbner, G. Raabe, J. Runsink, *Synthesis* **1996**, 941−948. [11b] R. Gröbner, Ph D. Dissertation, Technical University of Aachen, **1996**.

[12] [12a] D. Enders, P. Teschner, G. Raabe, *Heterocycles* **2000**, *52*, 733−749. [12b] Short communication: D. Enders, P. Teschner, G. Raabe, *Synlett* **2000**, 637−640.

[13] For general reviews about asymmetric Michael additions see: [13a] P. Perlmutter, *Conjugate Addition Reactions in Organic Synthesis*, Tetrahedron Organic Chemistry Series, vol. 9 (Eds.: J. E. Baldwin, P. D. Magnus), Pergamon, Oxford, **1992**. [13b] Y. Yamamoto, S. G. Pyne, D. Schinzer, B. L. Feringa, J. F. G. A. Jansen, *Methods Org. Chem. (Houben-Weyl)*, **1995**, vol. E21b, chapter 1.5.2. [13c] B. E. Rossiter, N. M. Swingle, *Chem. Rev.* **1992**, *92*, 771−806. [13d] J. Leonard, E. Diez-Barra, S. Merino, *Eur. J. Org. Chem.* **1998**, 2051−2061.

[14] [14a] S. Patai, *The Chemistry of Amino, Nitroso and Nitro Compounds, and their Derivatives*, supplement F, Wiley, New York, **1982**. [14b] G. A. Olah, S. C. Narang, in *Organic Nitro Chemistry Series* (Ed.: H. Feuer), Verlag Chemie, Weinheim, **1990**. [14c] H. Feuer, A. T. Nielsen, *Nitro Compounds*, Verlag Chemie, Weinheim, **1990**.

[15] [15a] D. Seebach, I. M. Lyapkalo, R. Dahinden, M. Brenner, *Helv. Chim. Acta* **1999**, *82*, 1819−1842. [15b] D. Seebach, *Helv. Chim. Acta* **1999**, *82*, 2365−2379. [15c] D. Enders, T. Otten, *Synlett* **1999**, 747−749. [15d] C. Thominiaux, S. Roussé, D. Desmaële, J. d′Angelo, C. Riche, *Tetrahedron: Asymmetry* **1999**, *10*, 2015−2021. [15e] E. Juaristi, A. K. Beck, J. Hansen, T. Matt, T. Mukhopadhyay, M. Simson, D. Seebach, *Synthesis* **1993**, 1271−1290. [15f] K. Busch, U. M. Groth, W. Kühnle, U. Schöllkopf, *Tetrahedron* **1992**, *48*, 5607−5618. [15g] G. Calderari, D. Seebach, *Helv. Chim. Acta* **1985**, *68*, 1592−1604. [15h] S. J. Blarer, D. Seebach, *Chem. Ber.* **1983**, *116*, 3086−3096. [15i] S. J. Blarer, W. B. Schweizer, D. Schweizer, *Helv. Chim. Acta* **1982**, *65*, 1637−1654.

[16] Aromatic nitroalkenes were prepared from the corresponding aldehydes and nitromethane according to a literature procedure: [16a] D. E. Worrall, *J. Am. Chem. Soc.* **1934**, *56*, 1556−1558. [16b] M. Shiga, H. Kono, I. Motoyama, K. Hata, *Bull. Chem. Soc. Chem.* **1968**, *41*, 1897−1901. For the synthesis of the aliphatic examples, see ref.[18a]

[17] [17a] V. Rautenstrauch, F. Delay, *Angew. Chem.* **1980**, *92*, 764−766; *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 726−728. [17b] S. E. Denmark, O. Nicaise, J. J. Edwards, *J. Org. Chem.* **1990**, *55*, 6219−6223. [17c] D. Enders, D. Bartzen, *Liebigs Ann. Chem.* **1991**, 569−574. [17d] S. E. Denmark, O. Nicaise, *Synlett* **1993**, 359. [17e] M. A. Brimble, C. H. Heathcock, *J. Org. Chem.* **1993**, *58*, 5261−5263. [17f] D. Enders, J. Tiebes, N. DeKimpe, M. Keppens, C. Stevens, G. Smagghe, *J. Org. Chem.* **1993**, *58*, 4881−4884. [17g] D. Enders, J. Schankat, M. Klatt, *Synlett*

**1994**, 795−797. [17h] D. Enders, E. Chelain, G. Raabe, *Bull. Soc. Chim. Fr.* **1997**, 299−306.
[18] [18a] D. Enders, A. Haertwig, G. Raabe, J. Runsink, *Eur. J. Org. Chem.* **1998**, 1771−1792. [18b] M. Petrini, R. Ballini, G. Rosini, *Synthesis* **1987**, 713−714.
[19] J. A. Dale, H. S. Mosher, *J. Am. Chem. Soc.* **1973**, *95*, 512−519.
[20] Alkenyl sulfones were prepared by Horner olefination of the corresponding aldehydes according to a literature procedure: M. W. Rathke, M. Nowak, *J. Org. Chem.* **1985**, *50*, 2624−2626.
[21] [21a] R. Bird, A. C. Knipe, C. J. M. Stirling, *J. Chem. Soc., Perkin Trans. 2* **1973**, 1215−1220. [21b] A. Di Martino, C. Galli, P. Gargano, L. Mandolini, *J. Chem. Soc., Perkin Trans. 2* **1985**, 1345−1349.
[22] D. Enders, C. F. Janeck, *Synlett* **2000**, 641−643.
[23] D. Enders, S. Brauer-Scheib, P. Fey, *Synthesis* **1985**, 393−396.
[24] [24a] D. Enders, S. Nakai, *Chem. Ber.* **1991**, *124*, 219−226. [24b] K. Tamao, T. Kakui, T. Iwahara, R. Kanatani, J. Yoshida, M. Kumada, *Tetrahedron* **1983**, *39*, 983−990.
[25] [25a] D. Enders, H. Eichenauer, *Chem. Ber.* **1979**, *112*, 2933−2960. [25b] D. Enders, P. Fey, H. Kipphardt, *Org. Synth.* **1987**, *65*, 173, 183−202.
[26] D. Enders, H. Kipphardt, P. Gerdes, L. Breña-Valle, V. Bhushan, *Bull. Soc. Chim. Belg.* **1988**, *97*, 691−704.
[27] S. R. Hall, G. S. D. King, J. M. Stewart (Eds.), *XTAL 3.4 User's Manual*, Universities of Western Australia, Leuven and Marylamb, Lamb, Perth, **1995**.

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