Preparation and Use in Amino Acid Synthesis of a New Chiral Glycine Derivative – (*R*)- and (*S*)-*tert*-Butyl 2-*tert*-Butyl-4-methoxy-2,5-dihydroimidazole-1-carboxylate (BDI)☆

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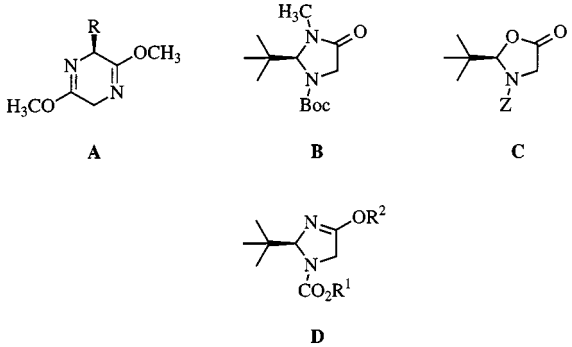
The title compound BDI is prepared on multigram scale, either by resolution of the precursor 2-*tert*-butylimidazolidin-4-one (from glycine amide and pivalaldehyde) through diastereomeric salts (Scheme 2) or by preparative chromatographic enantiomer separation on a chiral column. Lithiated BDI derivatives are highly nucleophilic species, combining the structural elements of a Li enaminate, of an enolether and of an *N*-Boc-enaminate (**E, G**). They react with complete diastereoselectivity (NMR analysis) from the face *trans* to the *tert*-butyl group. The electrophiles employed are primary and secondary alkyl, allyl, benzyl, and propargyl halides (Schemes 3 and 5), enoates (in Michael additions, Scheme 7), as well as aliphatic and aromatic aldehydes (in aldol additions, Scheme 8). When a third, exocyclic, stereocenter is formed in these reactions, there is a high degree of enantiomer differentiation (with *rac. sec.* halides, products **10–12**) and of enantiotopic face differentiation (with enoates and aldehydes, products **40–50**). The reactions are so clean that highly efficient in-situ double alkylations are feasible, in which the sequence of addition of the two different electrophiles determines the configuration at the newly formed stereogenic center (Scheme 5). In contrast to derivatives of previously reported chiral glycine reagents, the products from BDI are converted to methyl esters of amino acids under mild conditions *and* without concomitant formation (... and the need for recovery or removal) of a chiral auxiliary; the method is compatible with acid-sensitive side chains in the α-amino acids and α-branched α-amino acids to be synthesized (Schemes 4 and 6). The addition of Li-BDI to aldehydes furnishes, after hydrolysis, α-amino-β-hydroxy acids of *erythro* configuration (*allo*-threonine analogs, Scheme 8); a model for the stereochemical course of this reaction (rel. topicity *unlike*) is proposed, and compared with the corresponding conversions of analogous oxazolidinone and imidazolidinone Li enolates which occur with rel. topicity *like*.

Introduction

The non-catalytic methods of enantioselective amino acid synthesis can be divided into two subgroups: those employing a chiral auxiliary and those using an enantiomer separation, the most versatile strategy involving C,C-bond formation with chiral glycine derivatives to which one or two side chains are added stereoselectively[1]. The prototype of the first group is the bis-lactim ether **A**: an amino acid (usually valine, preferably *tert*-leucine) serves as the chiral auxiliary, and two amino acid esters have to be separated in the process of isolation of the desired product[2].



A **B** **C**

D

The most commonly used reagent of the second group is the cyclic acetal **B** (Boc-BMI) prepared in enantiopure form by resolution[3] of the non-Boc-protected precursor heterocycle with mandelic acid[4][5]. The harsh conditions for hydrolysis of Boc-BMI derivatives to the free amino acids can be circumvented by using the oxo-oxazolidine **C** (BOX) which can be resolved[3][6] by chromatography on chiral stationary phases (CSP). We have developed a new and superior chiral glycine derivative **D** (R^1 = *t*Bu, R^2 = CH_3; *tert*-butyl 2-*tert*-butyl-4-methoxy-2,5-dihydroimidazole-1-carboxylate, BDI)[7][8], combining the advantages of the Schöllkopf reagent **A** with those of our Boc-BMI **B**: the products of mono- and dialkylation are formed with extremely high stereoselectivity, hydrolysis of the heterocycle takes place under mildly acidic conditions, and the side product pivalaldehyde is volatile under evaporative solvent removal during work-up.

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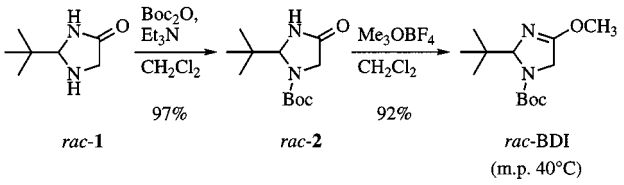
Preparation of Enantiopure BDI

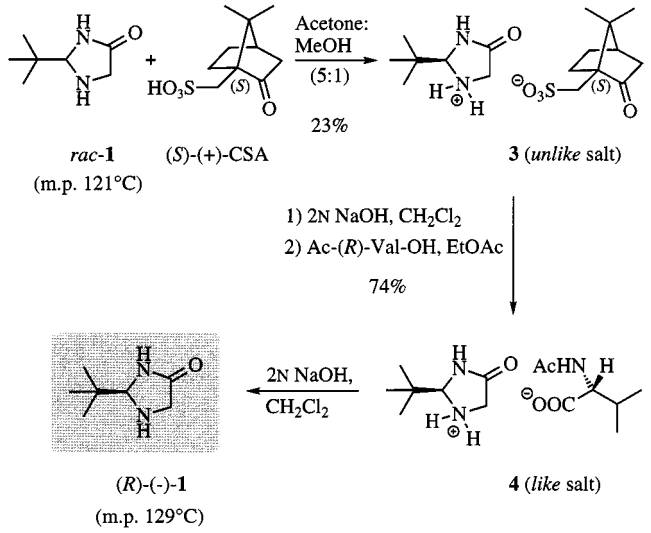
The two methods used by us to prepare larger amounts (10−60 g) of BDI are the enantiomer separation on CSP of BDI itself and the classical resolution of the imidazolidinone **1** through diastereomeric salt formation. The preparation of *rac*-**1** from commercial glycine amide and pivalaldehyde, its conversion to the Boc-derivative *rac*-**2**, and the subsequent *O*-methylation with Meerwein salt to give *rac*-BDI (Scheme 1), as well as the CSP enantiomer separation of BDI and configurational assignment have been described in full detail elsewhere[9][10][11].

Scheme 1



The resolution of *rac*-**1** with camphor sulfonic acid (CSA), as described[7][11] originally, turned out not to be applicable to large scale[12]. We therefore looked for other chiral acids to use instead of or in addition to CSA. After extensive experimentation (27 different carboxylic acids were tested in four different solvents each!)[13], the procedure shown in Scheme 2 was chosen for the resolution[8]: the salt **3** precipitating from acetone/methanol and consisting of the two diastereomeric *u*- and *l*-forms in a ca. 92:8 ratio is isolated, and the heterocycle liberated with aqueous base, and then converted to the *l*-salt **4** with *N*-acetyl-(*R*)-valine; this is so pure that no further crystallization is necessary: the enantiopure imidazolidinone (*R*)-**1** (enantiomer ratio ≥ 99.5:0.5) can be isolated by treatment with base.

Scheme 2



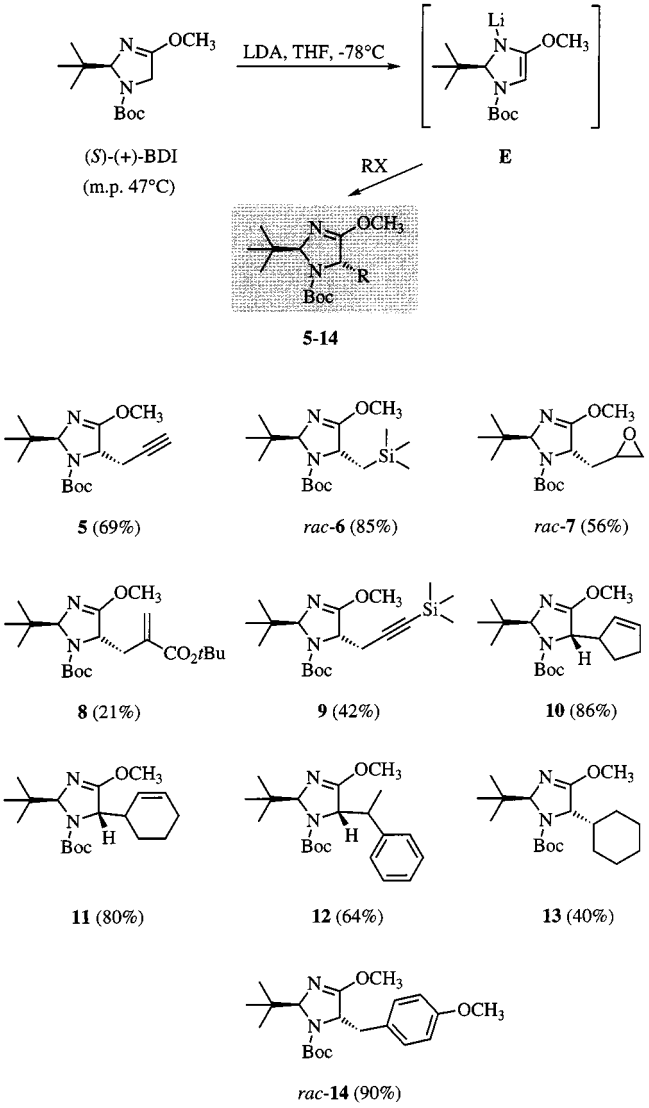
The overall yield of (*R*)-**1**[14] from *rac*-**1** is ca. 34% of theory; (*S*)-**1** can be prepared in the same way, since both chiral acids are commercially available in either enantiomeric form.

Following the procedure outlined in Scheme 1 for *rac*-**1**, the enantiopure (*R*)-**1** is converted to (*S*)-BDI without loss of configurational purity. BDI-analogs with protecting groups other than Boc have, of course, also been prepared from *rac*-[10] or from enantiopure imidazolidinone **1**[15]. In preliminary experiments, the (*Z*)-protected analog of BDI turned out to be an inferior reagent for C,C-bond coupling processes[11][13].

Alkylation of BDI through the Li-Enaminate E and Preparation of Amino Acid Methyl Esters

Racemic or enantiopure BDI was deprotonated with lithium diisopropyl amide (LDA) to form the enaminate **E**, which was alkylated with various electrophiles RX (Scheme 3). The halides used may be primary or secondary, propargylic, allylic, or benzylic.

Scheme 3. (Only one enantiomer of the *rac* products is shown)



The corresponding products of alkylation **5**−**14** were generally isolated in good yields (of purified materials[16]) and, according to ^{1}H-NMR spectroscopy of the crude products, in diastereopure form. Only with the least reactive

halides, such as iodo cyclohexane, warming of the reaction mixture to the stability limit of the enaminate **E** (hours at room temperature) was necessary. By nuclear Overhauser effect (NOE) NMR measurements of the products and by an X-ray crystal structure analysis[17], we confirmed that of the two possible diastereoisomers the one with the new substituent *trans* to the *tert*-butyl group at position 2 of the heterocycle was formed exclusively[11].

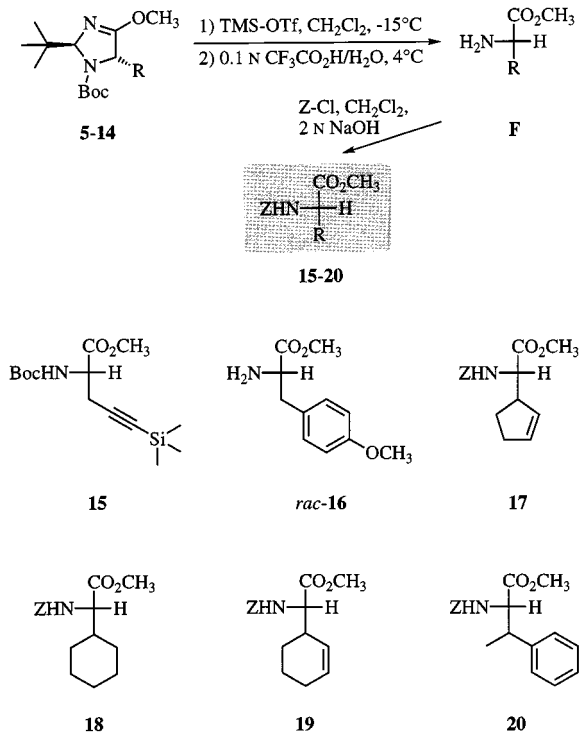
The reactions of enaminate **E** with two equivalents of *rac*-3-bromocyclopentene or *rac*-3-bromocyclohexene are especially noteworthy: the corresponding products **10** and **11** are formed with diastereoisomer ratios of >98:2 and 91:9, respectively, as derived from the ^{1}H-NMR spectra of the crude products. We are sure that these alkylations, again, occur exclusively from the face *trans* to the *tert*-butyl group on the dihydroimidazole ring, and that the second diastereoisomer formed besides **11** is epimeric at the stereocenter in the aliphatic ring. A similar reaction with excess *rac*-1-phenylethylbromide gave the dihydroimidazole derivative **12** with a diastereoisomer ratio of >98:2[18][19]. Thus, the enaminate **E** has an unusually high enantiomer-differentiating ability which leads to an efficient kinetic resolution of racemic mixtures of allylic and benzylic halides. Unfortunately, the configuration of the stereocenters in the aliphatic rings of **10**−**12** could not be determined so far (no crystals suitable for X-ray analysis could be obtained).

Although the yields of analytically pure products **5**−**14**, as given in Scheme 3, are not excellent[16], the conversions in these alkylation reactions are complete (no BDI starting material by thin-layer test of the crude reaction mixture), signalling an excellent nucleophilicity of the Li enaminate **E**. This high reactivity is especially important for applications of the new chiral glycine synthetic building block BDI with in situ double alkylations (vide infra).

Of course we had hoped to be able to hydrolyze BDI derivatives to Boc-protected amino acid esters, and acids, ready for peptide synthesis. Inspite of many attempts, we did not succeed in finding conditions sufficiently acidic to cleave the imino ester functionality but not the Boc group[20]. Furthermore, we observed partial racemization upon treatment of products of type **5**−**14** with acid, aqueous or non-aqueous. Therefore, we chose a two-step procedure, first removing the Boc-group under aprotic conditions, and then cleaving the heterocycle hydrolytically. The Boc deprotection was achieved with trimethylsilyl triflate[21], and the resulting dihydroimidazoles hydrolyzed (without purification) to the free amino acid esters **F** under mildly acidic conditions. The overall yields of the two steps range from 78 to 95%.

The crude-product methyl esters **F** are generally pure enough to be used in subsequent reactions. In order to obtain analytically pure samples, however, the amino acid esters **F** were (*Z*)-protected[22] and the products **15** and **17**−**20** purified by flash-chromatography (FC)[23]. Since all these compounds are oils, it was again not possible to determine the configurations at the stereocenters in the β-positions of the esters **17**, **19**, and **20**. The amino acid derivatives thus obtained were enantiopure[24].

Scheme 4. (Only one enantiomer of the *rac* product is shown)



In Situ Double Alkylation of BDI through the Li-Enaminate G and Preparation of α-Branched Amino Acid Methyl Esters

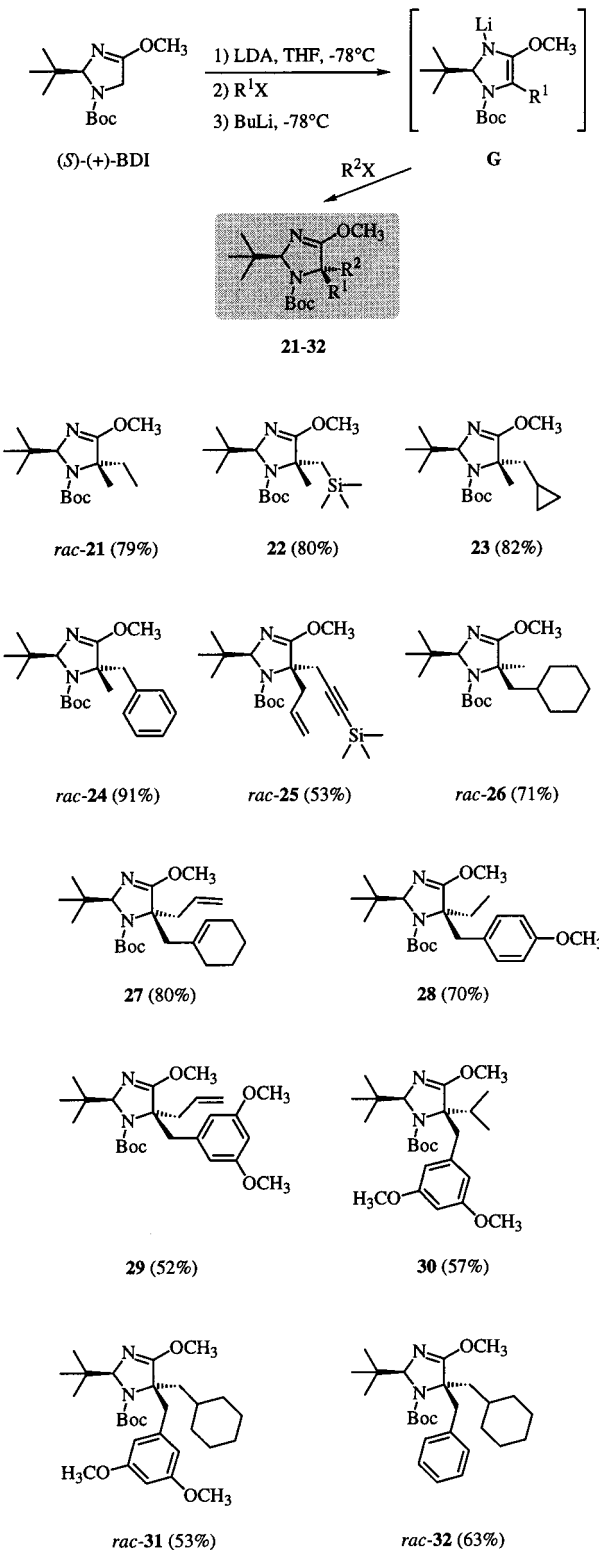
The high nucleophilicity and the complete conversions in the monoalkylations of enaminate **E** gave us the confidence to try in situ double alkylations by adding a second equivalent of base after the first alkylation step to generate the Li-enaminate **G** with tetrasubstituted double bond. The low electrophilicity of the iminoester group in the dihydroimidazole ring enabled us to achieve this second deprotonation with butyllithium (BuLi) (see Scheme 5).

The *gem.* disubstituted products **21**−**32** are formed in yields which depend upon the degree of crowding. In all cases, the bath temperature was allowed to rise to 10−20°C in the second alkylation step. Polar impurities arising from decomposition of enaminate **G** could be readily removed in the chromatographic purification of the products (the yields in Scheme 5 refer to analytically pure samples).

According to ^{1}H-NMR spectroscopy of the crude products single diastereoisomers **21**−**32** were formed. It was, again, confirmed by NOE NMR measurements and by an X-ray crystal structure analysis[25] that of the two possible diastereoisomers the one with the substituent R^2 *trans* to the *tert*-butyl group at position 2 of the dihydroimidazole ring was formed exclusively[11]. Thus, the configuration of the *gem.* disubstituted stereocenter can be determined by the order of addition of the two electrophiles R^1X and R^2X. The unusually high nucleophilicity of the enaminate **G** is demonstrated by the isopropylation of the benzyl derivative leading to an almost 60% yield of product **30**.

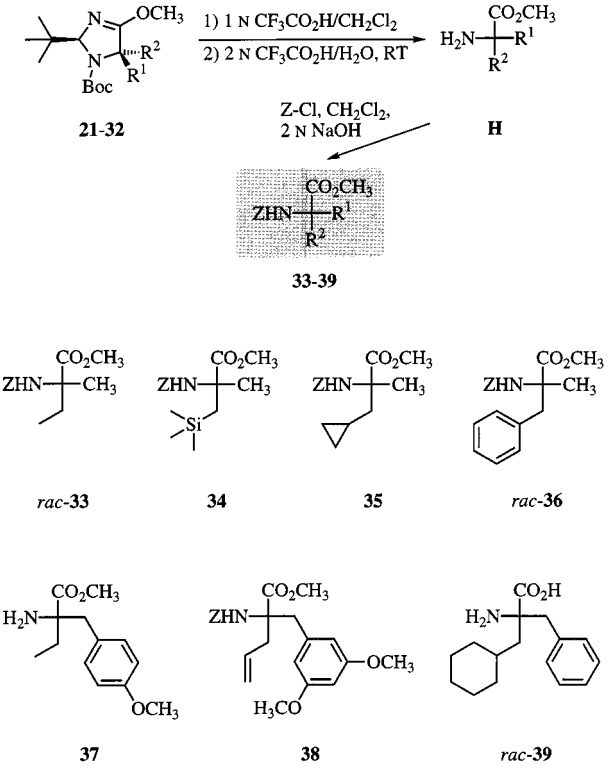
For the hydrolysis of the dialkylated dihydroimidazole derivatives **21**−**32** to the free amino acid esters of type **H** the same concept as for the monoalkylated compounds

Scheme 5. (Only one enantiomer of the *rac* adducts is shown)



5−**14** (Scheme 4) was chosen: the Boc-protecting group was removed first and then the heterocycle hydrolyzed without prior purification. Both steps were performed under mild reaction conditions at room temperature: stirring in 1 N TFA in CH_2Cl_2 (8 h) for the removal of the Boc-group and in 2 N TFA in H_2O (0.5−4 d) for cleavage of the ring (Scheme 6).

Scheme 6. (Only one enantiomer of the *rac* products is shown)



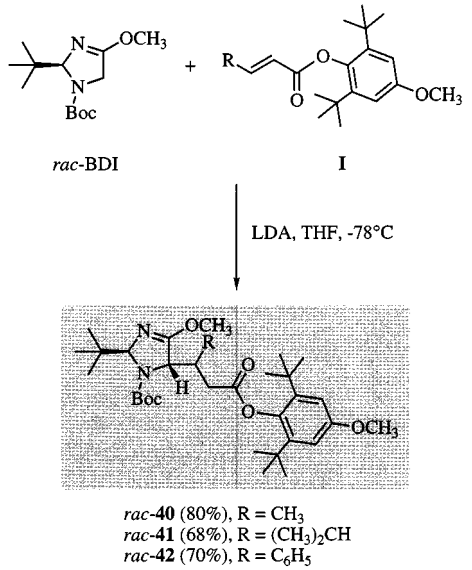
Since the conditions employed in the hydrolysis step are so mild, the preparation of amino acid esters **H** with acid-labile side chains is possible[26]. Like the "monosubstituted" amino acid esters **F**, the *gem.* disubstituted esters **H** thus obtained (yields ranging from 69 to 98%) were (*Z*) protected, and the products **33**−**36** and **38** purified by FC in order to obtain analytically pure samples. The crude ester **37** was purified by FC without prior protection of the free amino group. All esters **33**−**38** are isolated as oils. The dihydroimidazole *rac*-**32** with the most congested substitution could not be hydrolyzed under the mild reaction conditions as outlined in Scheme 6. Since there is no acid-sensitive group in **32**, we used the harsh conditions of reflux in 6 N HCl to set the amino acid *rac*-**39** free (purification by crystallization from $MeOH/H_2O$).

Michael Additions of the Li-Enaminate E to α,β-Unsaturated 2,6-Di-*tert*-butyl-4-methoxyphenylesters I

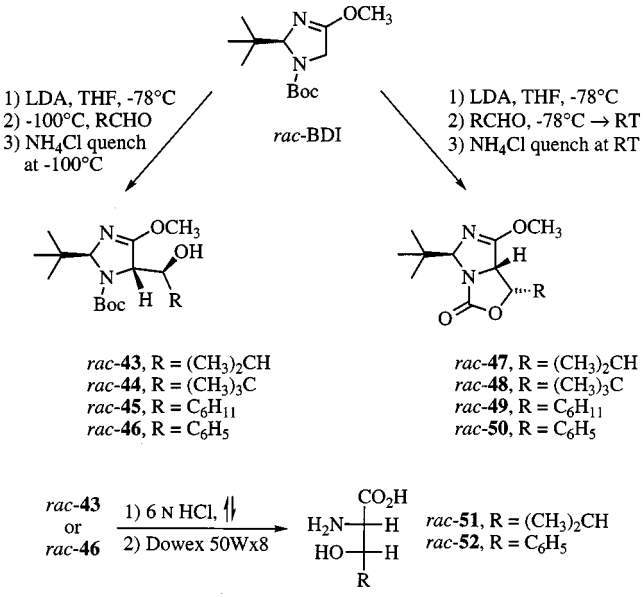
The new chiral glycine derivative BDI was also tested in Michael additions to α,β-unsaturated esters. We chose the hindered 4-methoxyphenylesters **I** as the Michael acceptors (Scheme 7), knowing that such derivatives with "sterically protected but electronically activating" carbonyl groups are ideal substrates to study this reaction. Hydroquinone-derived esters of this type can be cleaved by Ce^{IV} oxidation[19][27][28][29].

The esters **I** derived from crotonic, 4-methylpentenoic and cinnamic acid were added to −78°C cold solutions of

Scheme 7. (Only one enantiomer of BDI and of the *Michael* adducts is shown)



Scheme 8. (Only one enantiomer of BDI and of the main diastereoisomer of the hydroxyalkylation products **43**−**46**, of the bicyclic products **47**−**50**, and of the amino hydroxy acids **51** and **52** is shown)



rac-BDI enaminate, and the reactions were quenched after 3 h reaction time at this temperature (TLC sampling indicating complete conversions). Work-up gave two diastereoisomers in ratios of 94:6 for *rac*-**40**, 83:17 for *rac*-**41**, and >98:2 for *rac*-**42**. The crude products were purified by FC which led to the isolation of colorless solids in yields ranging from 68−80%.

Based on the results of the mono- and dialkylations of BDI, we are confident that the Michael-addition reactions of the Li-enaminate **E** to the methoxyphenylesters **I** proceed with complete diastereoselectivity *trans* to the *tert*-butyl group at position 2 of the dihydroimidazole ring, and that the minor diastereoisomer formed in the reaction leading to *rac*-**40** and *rac*-**41** is epimeric at the exocyclic stereocenter. The configurations of this stereocenter in the major diastereoisomers are, as yet, unknown.

Aldol Additions of the Li-Enaminate E from *rac*-BDI to Aldehydes

Aldol additions to *rac*-BDI were carried out in two different ways (Scheme 8): After reaction of enaminate **E** with isobutyric aldehyde, pivalaldehyde, cyclohexane carbaldehyde or benzaldehyde at −100°C for 5 min, followed by low-temperature quenching, mainly the expected protonated primary adducts *rac*-**43** − *rac*-**46** were formed in yields ranging from 61−88%[30]. When, however, the aldehyde was added at −78°C to the enaminate solution, and the reaction solution allowed to warm up to room temperature, the bicyclic compounds *rac*-**47** − *rac*-**50** were formed as the main products (yields between 26 and 79%). In both ways of conducting the aldol addition, a mixture of the two types of products was formed and easily separated by FC to give the pure compounds which were fully characterized. The hydroxyalkylation products were thus obtained as colorless oils, the bicyclic compounds as amorphous solids.

In order to determine the relative configurations at the exocyclic stereocenters of the main aldol adducts, compounds *rac*-**43** and *rac*-**46** were hydrolyzed to the corresponding amino acids *rac*-**51** and *rac*-**52** as shown in Scheme 8.

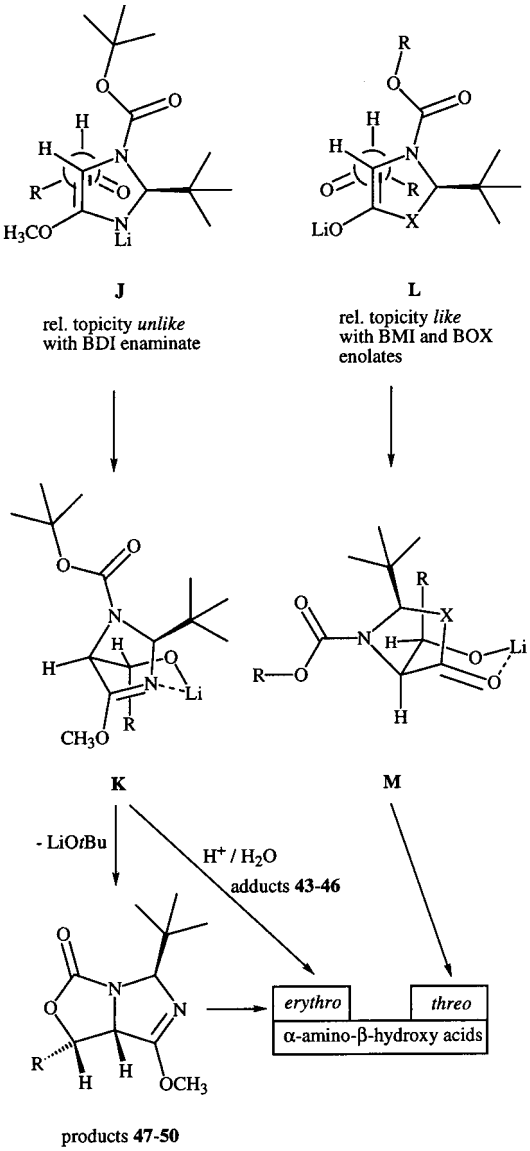
Comparison of the ^{1}H-NMR spectra of the products *rac*-**51** and *rac*-**52** with spectra found in the literature[31] revealed that the amino hydroxy acids of *erythro* configuration had been formed[34]. Hydrolysis of the corresponding bicyclic products *rac*-**47** and *rac*-**50** under the same conditions also led to the formation of products *rac*-**51** and *rac*-**52**. Furthermore, the relative configurations of the stereocenters in the bicyclic products *rac*-**47** − *rac*-**50** were also verified to be as depicted in Scheme 8, using NOE ^{1}H-NMR spectroscopy[13]. The amount of epimer at the 1′-position of **43**−**46** and at the 4-position of the bicyclic carbamates **47**−**50** varies from <2 to 33% and is given in the Experimental Section[35].

Thus, it is clearly established that the reaction of lithiated BDI with aldehydes and subsequent hydrolysis lead to amino hydroxy carboxylic acids of *erythro* configuration, i.e. to analogs of *allo*-threonine (see **51** and **52** in Scheme 8).

Using the Zimmerman-Traxler model[36], the approach of the trigonal centers of enaminate **E** and aldehyde and the primary adduct can be pictured as shown in **J** and **K** of Scheme 9.

The cyclization of Li-alkoxides such as **K** to bicyclic carbamates (**47**−**50**) is a process which we have observed previously with analogous reactions of other *N*-alkoxycarbonyl-protected heterocyclic glycine derivatives[6][37]. For a comparison, we also show in Scheme 9 the approach of oxo-oxazolidine (**L**, **M**, X = O) or oxo-imidazolidine (**L**, **M**, X = NCH_3) Li enolates to aldehydes[38]. In this presentation, the surprising reversal of the relative topicity *like*

Scheme 9. Comparison of the stereochemical course of addition of enaminate **E** and of BMI or BOX enolates to aldehydes using the Zimmerman-Traxler model (only one enantiomer of the products and precursors is shown)



with the enolates to *unlike* with the enaminate is directly correlated to the *exo*-cyclic position of Li on oxygen in the first case and its *endo*-cyclic position on nitrogen in the second case[39].

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Experimental Section

General Methods: THF used for alkylations was freshly distilled from potassium/benzophenone ketyl under an inert gas atmosphere of Ar. Flasks, stirring bars and hypodermic needles used for the generation and reactions of organolithium reagents were dried for ca. 12 h at 150°C and allowed to cool in a desiccator over anhydrous $CaCl_2$. The side arms of the reaction flasks were connected to an Ar line by three-way taps. A positive pressure of Ar was established by following the operation "flask evacuation/Ar introduction" several times. − The electrophiles used for the reactions were passed through a short column of basic Al_2O_3 prior to injection. − Diisopropylamine and triethylamine were distilled from CaH_2 under Ar and stored over molecular thieves (4 A), solvents for chromatography and work-up were distilled, all other solvents were used as purchased from Fluka. − Thin layer chromatography (TLC) analyses were performed on silica gel plates (Merck 60 F_{254}, 0.25 mm thickness), components were detected by UV light and/or by dipping into a soln. of 5.25 g of *N,N,N′,N′*-tetramethyl-4,4′-methylenebis[aniline] (TDM), 10.20 g of KI, 3.4 mg of ninhydrine, 23.6 ml of CH_3CO_2H and 310 ml of H_2O followed by dipping into hot water. − For flash chromatography (FC) Merck silica gel 60, 230−400 mesh was used. − Melting points were determined in open capillaries in a Büchi 510 apparatus with Anschütz thermometers and are uncorrected. − Optical rotations $[\alpha]_D^{r.t.}$ were measured with a Perkin Elmer 241 polarimeter using a 1.00 dm cell at room temp. (ca. 22°C); concentration *c* (in g/100 ml) and solvent in parenthesis. − Infrared spectra were recorded with a Perkin Elmer FT-IR 1600 spectrometer. − ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Varian XL 300 or a Gemini 300 (300 MHz/75 MHz) and a Gemini 200 (200 MHz/50 MHz). $CDCl_3$ was used as solvent and as internal reference (δ = 7.26/77.0) unless otherwise stated. Coupling constants *J* are given in Hertz (Hz); multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Carbon multiplicities were assigned by DEPT techniques. − Mass spectra were obtained on a Hitachi-Perkin-Elmer RMU-6M spectrometer. − Elemental analyses were performed by the "Mikroelementaranalytisches Laboratorium der ETH Zürich".

General Procedures (GP's)

Monoalkylations of tert-Butyl 2-tert-Butyl-4-methoxy-2,5-dihydroimidazole-1-carboxylate (BDI) *(GP1):* A soln. of 1 eq. of BDI (usually ca. 5 mmol) in THF (15 ml) was cooled to −78°C. A freshly prepared and precooled (−78°C) soln. of LDA (1.5 eq.) in THF (15 ml) was slowly added. The reaction soln. was stirred at −78°C for 40 min. The corresponding electrophile was then injected using a syringe. After letting the reaction mixture warm up to room temp. in 12 h, saturated NH_4Cl soln. (75 ml) was added. The aqueous phase was extracted three times with Et_2O (100 ml), and the combined organic phases washed with saturated NaCl soln. (150 ml) and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product purified by FC.

Dialkylations of tert-Butyl 2-tert-Butyl-4-methoxy-2,5-dihydroimidazole-1-carboxylate (BDI) *(GP2):* A soln. of 1 eq. of BDI (usually ca. 5 mmol) in THF (15 ml) was cooled to −78°C. A freshly prepared and precooled (−78°C) soln. of LDA (1.5 eq.) in THF (15 ml) was slowly added. The reaction soln. was stirred at −78°C for 40 min. The first electrophile was then injected using a syringe. After letting the reaction warm up to room temp. in 12 h, it was again cooled to −78°C. The same amount of BuLi as was used for the preparation of the LDA soln. was added and the reaction mixture stirred at −78°C for 40 min. The second electrophile was then injected using a syringe. After letting the reaction warm up to room temp. in 12 h, saturated NH_4Cl soln. (75 ml) was added. The aqueous phase was extracted three times with Et_2O (100 ml), and the combined organic phases washed with saturated NaCl soln. (150 ml) and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product purified by FC.

Hydrolysis of 4-Monosubstituted Methoxydihydroimidazoles and Protection to the Corresponding (Z)-Protected Amino Acid Methyl Esters (GP3): A soln. of the methoxydihydroimidazole in CH_2Cl_2 was cooled to −15°C. TMSO-Tf (6 eq.) was added using a syringe and the reaction soln. stirred for 12 h at −15°C. The reaction soln. was diluted with an equal volume of saturated $NaHCO_3$ soln., extracted three times with Et_2O and the combined organic phases dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product dissolved in THF. 0.1 N CF_3CO_2H/H_2O (2 eq.) was added and the reaction soln. stirred at 4°C for 4 d. The mixture was washed with half a volume of Et_2O (which was discarded), set to pH > 10 with a 10%-NH_3 soln. and the aqueous phase extracted three times with Et_2O. The combined organic phases were dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude amino acid methylester dissolved in CH_2Cl_2. Benzylchloroformate (1.5 eq.) and 2 N NaOH (1.5 eq.) were added and the reaction stirred at room temp. for 1 d. An equal volume of CH_2Cl_2 was added. The combined organic phases were washed with half a volume of saturated $NaHCO_3$ soln. and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product purified by FC.

Hydrolysis of 4,4-Disubstituted Methoxydihydroimidazoles and Protection to the Corresponding (Z)-Protected Amino Acid Methyl Esters (GP4): A soln. of the methoxydihydroimidazole in 1 N CF_3CO_2H/CH_2Cl_2 was stirred at room temp. for 8 h. The reaction solution was diluted with an equal volume of saturated $NaHCO_3$ soln., extracted three times with Et_2O and the combined organic phases dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product dissolved in THF. 2 N CF_3CO_2H/H_2O (8 eq.) was added and the reaction soln. stirred at room temp. for 4 d. The mixture was washed with half a volume of Et_2O (which was discarded), set to pH > 10 with a 10%-NH_3 soln. and the aqueous phase extracted three times with Et_2O. The combined organic phases were dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude amino acid methylester dissolved in CH_2Cl_2. Benzylchloroformate (1.5 eq.) and 2 N NaOH (1.5 eq.) were added and the reaction stirred at room temp. for 1 d. An equal volume of CH_2Cl_2 was added. The combined organic phases were washed with half a volume of saturated $NaHCO_3$ soln. and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product purified by FC.

Michael Additions with rac-tert-Butyl 2-tert-Butyl-4-methoxy-2,5-dihydroimidazole-1-carboxylate (*rac*-BDI) *(GP5):* A soln. of 1 eq. of *rac*-BDI (usually ca. 5 mmol) in THF (15 ml) was cooled to −78°C. A freshly prepared and precooled (−78°C) soln. of LDA (1.5 eq.) in THF (15 ml) was slowly added. The reaction soln. was stirred at −78°C for 40 min. The corresponding Michael acceptor (1.5 eq.) dissolved in THF was then injected using a syringe. After stirring the reaction solution at −78°C for 3 h, saturated NH_4Cl soln. (75 ml) was added. The aqueous phase was extracted three times with Et_2O (100 ml), and the combined organic phases washed with saturated NaCl soln. (150 ml) and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product purified by FC.

Hydroxyalkylation of rac-BDI at −100°C (GP6): A soln. of 1 eq. of *rac*-BDI (usually ca. 5 mmol) in THF (15 ml) was cooled to −78°C. A freshly prepared and precooled (−78°C) soln. of LDA (1.5 eq.) in THF (15 ml) was slowly added. The reaction soln. was stirred at −78°C for 40 min and then cooled to −100°C. The corresponding aldehyde (2.5 eq.) was injected using a syringe. After stirring the reaction for 5 min at −100°C, saturated NH_4Cl soln. (75 ml) was added. The aqueous phase was extracted three times with Et_2O (100 ml), and the combined organic phases washed with saturated NaCl soln. (150 ml) and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product purified by FC.

Formation of Bicyclic Carbamates from rac-BDI and Aldehydes at −78 to +20°C (GP7): A soln. of 1 eq. of *rac*-BDI (usually ca. 5 mmol) in THF (15 ml) was cooled to −78°C. A freshly prepared and precooled (−78°C) soln. of LDA (1.5 eq.) in THF (15 ml) was slowly added. The reaction soln. was stirred at −78°C for 40 min. The corresponding aldehyde (2.5 eq.) was then injected using a syringe. After letting the reaction warm up to room temp., saturated NH_4Cl soln. (75 ml) was added. The aqueous phase was extracted three times with Et_2O (100 ml), and the combined organic phases washed with saturated NaCl soln. (150 ml) and dried with anhydrous $MgSO_4$. The solvent was removed by rotary evaporation and the crude product purified by FC.

Hydrolysis of Aldol-Addition Products to the Corresponding erythro α-Amino-β-hydroxy Carboxylic Acids (GP8): A sample of aldol addition product was heated in 6 N HCl at reflux for 12 h. The reaction solution was extracted with Et_2O and the phases separated. The aqueous phase was evaporated on a rotary evaporator and the crude product purified by ion exchange chromatography on a Dowex 50W×8 column with a 1%-NH_3 soln. as eluent.

Enantiomer Resolution of rac-2-tert-Butylimidazolidin-4-one (*rac*-**1**) *through Diastereoisomeric Salt Formation*

(R)-2-tert-Butylimidazolidin-4-onium-N-acetyl-D-valinate (**4**): Imidazolidinone *rac*-**1** (30.0 g, 211 mmol) and (*S*)-(+)-CSA (49.0 g, 211 mmol) were dissolved in acetone/MeOH (83:17, 1.7 l) at reflux temp. After cooling to room temp. over night, colorless crystals of *unlike* salt **3**[11] (18.0 g, 23%) with a diastereoisomer ratio of 92.5:7.5 (determined by GC analysis of a sample of enriched **1** obtained after basic hydrolysis of **3**) were formed. The *unlike* salt **3** was dissolved in 2 N NaOH (150 ml) and the solution three times extracted with CH_2Cl_2 (250 ml). The organic phases were combined, dried with anhydrous $MgSO_4$ and the solvent removed using a rotary evaporator. The free imidazolidinone **1** was isolated and dissolved in AcOEt (300 ml) at reflux together with *N*-acetyl-D-valine (7.65 g, 48 mmol). After cooling to room temp. over night, colorless crystals of *like* salt **4** (10.72 g, 74%) with a diastereoisomer ratio of >99.5:0.5 were isolated, m.p. 125.4−126.6°C. − IR (KBr): 3293*m*, 3077*m*, 2962*m*, 1719*s*, 1639*s*, 1541*m*, 1404*m*, 1376*m*, 1349*m*, 1321*m*, 1299*m*, 1152*w*, 1088*w*, 1056*w*, 975*w*, 843*w*, 757*m*. − ^{1}H NMR (300 MHz, CD_3OD): δ = 4.32 [s, 1 H, *H*C-C(Me)$_3$], 4.30 (d, *J* = 6 Hz, 1 H, HC-COO), 3.44 [d, *J* = 16 Hz, 1 H, H-C(5)], 3.36 [d, *J* = 16 Hz, 1 H, H-C(5)], 2.22−2.10 (m, 1 H, HCMe$_2$), 2.00 (s, 3 H, H_3C-CO), 0.97 (d, *J* = 3 Hz, 3 H, H_3C-CH), 0.95 (d, *J* = 3 Hz, 3 H, H_3C-CH), 0.91 (s, 9 H, *Me*$_3$-C). − ^{13}C NMR (75 MHz, CD_3OD): δ = 178.7, 175.2, 173.4, 81.0, 59.3, 36.4, 31.7, 24.7, 22.4, 19.6, 18.4. − $C_{14}H_{27}N_3O_4$ (301.39): calcd. C 55.79, H 9.03, N 13.94; found C 56.05, H 8.85, N 13.85.

The free imidazolidinone (*R*)-(−)-**1** was obtained after basic hydrolysis of *like* salt **4** as described above. All analytical data were identical to the ones published in[11].

Monoalkylations of BDI

(2S,5S)-tert-Butyl 2-tert-Butyl-4-methoxy-5-prop-2-inyl-2,5-dihydroimidazole-1-carboxylate (**5**): The alkylation of (*S*)-(+)-BDI (1.35 g, 5.3 mmol) with propargylbromide (0.94 g, 7.9 mmol) was performed according to *GP1*. Purification of the crude product by

FC (hexane/AcOEt, 15:1) gave **5** (1.08 g, 69%) as a colorless solid, m.p. 71.8−72.2°C. − $[\alpha]_D^{r.t.}$ = +157.53 (*c* = 0.97, $CHCl_3$). − IR (KBr): 3274*m*, 2982*m*, 1685*s*, 1477*w*, 1453*w*, 1398*m*, 1368*m*, 1295*w*, 1266*m*, 1177*m*, 1121*m*, 1076*w*, 1006*m*, 962*w*, 904*w*, 864*w*, 781*m*, 668*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 94.5°C): δ = 5.19 [s, 1 H, H-C(2)], 4.28−4.25 [m, 1 H, H-C(5)], 3.82 (s, 3 H, H_3C-O), 3.33 (d, *J* = 17 Hz, 1 H, H-CC≡C), 2.58 (s, 1 H, H-C≡C), 2.46 (d, *J* = 17 Hz, 1 H, H-CC≡C), 1.43 (s, 9 H, *Me*$_3$C-O), 0.87 [s, 9 H, *Me*$_3$C-C(2)]. − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 165.9, 152.6, 88.4, 79.2, 78.5, 73.6, 59.6, 55.5, 27.8, 25.9, 20.4, 18.3. − MS (70 eV); *m*/*z* (%): 237 (15), 221 (5), 181 (100), 137 (64), 122 (6), 110 (3), 98 (5), 57 (95), 41 (18), 29 (6). − $C_{16}H_{26}N_2O_3$ (294.39): calcd. C 65.28, H 8.90, N 9.52; found C 65.35, H 8.83, N 9.52.

rac-tert-Butyl 2-tert-Butyl-4-methoxy-5-trimethylsilanylmethyl-2,5-dihydroimidazole-1-carboxylate (*rac*-**6**): The alkylation of *rac*-BDI (2.10 g, 8.2 mmol) with trimethylsilylmethyliodide (2.64 g, 12.3 mmol) was performed according to *GP1*. Purification of the crude product by FC (pentane/Et_2O, 16:1) gave *rac*-**6** (2.39 g, 85%) as a colorless oil. − IR ($CHCl_3$): 2976*m*, 2904*w*, 1669*s*, 1480*w*, 1448*w*, 1393*s*, 1367*s*, 1119*m*, 1074*w*, 997*m*, 913*w*, 879*w*, 840*m*. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.25−5.21 [br, 1 H, H-C(2)], 4.43−4.41 [br, 1 H, H-C(5)], 3.84 (s, 3 H, H_3C-O), 1.48 (s, 10 H), 1.33 [dd, *J* = 13 und 3 Hz, 1 H, *H*-C-Si(Me)$_3$], 0.91 [s, 9 H, *Me*$_3$C-C(2)], 0.00 (s, 9 H, *Me*$_3$Si). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.4, 153.4, 88.4, 79.9, 59.2, 55.0, 39.5, 28.5, 26.4, 19.2, 16.9, 0.0. − MS (70 eV); *m*/*z* (%): 343 (1) [M^+], 285 (23), 271 (18), 229 (100), 185 (27), 153 (4), 125 (12), 89 (8), 81 (14), 73 (17), 57 (43), 41 (9), 29 (5). − $C_{17}H_{34}N_2O_3Si$ (342.55): calcd. C 59.61, H 10.00, N 8.18; found C 59.58, H 10.07, N 8.27.

rac-tert-Butyl 2-tert-Butyl-4-methoxy-5-oxiranylmethyl-2,5-dihydroimidazole-1-carboxylate (*rac*-**7**): The alkylation of *rac*-BDI (1.13 g, 4.4 mmol) with epibromohydrin (0.91 g, 6.6 mmol) was performed according to *GP1*. Purification of the crude product by FC (pentane/Et_2O, 2:1) gave *rac*-**7** (0.78 g, 56%) as a colorless solid, m.p. 62.2−63.0°C. − IR (KBr): 2974*m*, 1687*s*, 1672*s*, 1482*w*, 1451*w*, 1395*m*, 1364*s*, 1267*m*, 1185*m*, 1139*m*, 1103*m*, 1082*w*, 1000*m*, 949*w*, 913*w*, 887*w*, 815*w*, 805*w*, 764*w*. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.29 [br, 1 H, H-C(2)], 4.36 [br, 1 H, H-C(5)], 3.90 (s, 3 H, H_3C-O), 2.84−2.68 (m, 3 H), 2.53-2.46 (m, 1 H), 2.01−1.95 (m, 1 H), 1.48 (s, 9 H, *Me*$_3$C-O), 0.92 [s, 9 H, *Me*$_3$C-C(2)]. − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.8, 153.5, 88.8, 80.3, 59.4, 55.5, 47.9, 46.6, 39.3, 30.4, 28.4, 26.2. − MS (70 eV); *m*/*z* (%): 255 (12), 239 (4), 225 (11), 199 (100), 155 (29), 137 (3), 125 (6), 111 (35), 99 (10), 57 (8), 41 (4). − $C_{16}H_{28}N_2O_4$ (312.41): calcd. C 61.51, H 9.03, N 8.97; found C 61.74, H 9.21, N 8.71.

(2S,5S)-tert-Butyl 5-(2-tert-Butoxycarbonylallyl)-2-tert-butyl-4-methoxy-2,5-dihydroimidazole-1-carboxylate (**8**): The alkylation of (*S*)-(+)-BDI (1.16 g, 4.5 mmol) with *tert*-butyl 2-bromomethylacrylate (1.50 g, 6.8 mmol) was performed according to *GP1*. Purification of the crude product by FC (pentane/Et_2O, 4:1) gave **8** (0.38 g, 21%) as a colorless oil. − $[\alpha]_D^{r.t.}$ = +81.38 (*c* = 1.09, $CHCl_3$). − IR ($CHCl_3$): 2974*m*, 1697*s*, 1672*s*, 1631*w*, 1477*w*, 1456*w*, 1395*m*, 1369*s*, 1318*w*, 1169*m*, 1144*m*, 1077*w*, 1000*m*, 964*w*, 949*w*, 856*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 95.0°C): δ = 5.97 [s, 1 H, H-C(2)], 5.33 (s, 1 H, H-C=C), 5.12−5.11 (m, 1 H, H-C=C), 4.41−4.37 [m, 1 H, H-C(5)], 3.74 (s, 3 H, H_3C-O), 2.78 (d, *J* = 16 Hz, 1 H, H-C-C=C), 1.44 (s, 9 H, *Me*$_3$C-O), 1.40 (s, 9 H, *Me*$_3$C-O), 0.86 [s, 9 H, *Me*$_3$C-C(2)]. − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 167.1, 165.4, 152.6, 137.1, 124.3, 87.9, 80.1, 79.3, 59.7, 55.3, 27.8, 27.6, 26.0. − MS (70 eV); *m*/*z* (%): 397 (47) [M^+], 339 (35), 297 (10), 283 (21), 267 (6), 239 (31), 227 (22), 183 (100), 165 (32), 111 (11), 84 (6), 57 (21). − $C_{21}H_{36}N_2O_5$ (396.53): calcd. C 63.61, H 9.15, N 7.06; found C 63.56, H 8.93, N 6.82.

(2S,5S)-tert-Butyl 2-tert-Butyl-4-methoxy-5-(3-trimethylsilanyl-prop-2-ynyl)-2,5-dihydroimidazole-1-carboxylate (**9**): The alkylation of (*S*)-(+)-BDI (1.44 g, 5.6 mmol) with (3-chloroprop-1-inyl)trimethylsilane[40] (1.23 g, 8.4 mmol) was performed according to *GP1*. Purification of the crude product by FC (hexane/AcOEt, 8:1) gave **9** (0.87 g, 42%) as a colorless solid, m.p. 81.0−81.4°C. − $[\alpha]_D^{r.t.}$ = +172.22 (*c* = 0.93, $CHCl_3$). − IR (KBr): 2969*m*, 2179*w*, 1694*s*, 1674*s*, 1456*w*, 1392*m*, 1354*s*, 1300*w*, 1250*m*, 1168*m*, 1115*m*, 1079*w*, 1010*m*, 980*m*, 903*w*, 864*m*, 841*m*, 782*w*, 758*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 95.0°C): δ = 5.17 [s, 1 H, H-C(2)], 4.28 [s, 1 H, H-C(5)], 3.81 (s, 3 H, H_3C-O), 3.38 (d, *J* = 17 Hz, 1 H, H-CC≡C), 2.46 (d, *J* = 17 Hz, 1 H, H-CC≡C), 1.44 (s, 9 H, *Me*$_3$C-O), 0.86 [s, 9 H, *Me*$_3$C-C(2)], 0.08 (s, 9 H, *Me*$_3$Si). − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 165.9, 152.8, 101.8, 88.8, 79.2, 60.0, 55.5, 27.8, 25.9, 21.8, 19.6. − MS (70 eV); *m*/*z* (%): 367 (1) [M^+], 309 (28), 295 (7), 253 (100), 209 (91), 193 (5), 170 (4), 105 (7), 73 (3), 57 (6). − $C_{19}H_{34}N_2O_3Si$ (366.58): calcd. C 62.25, H 9.35, N 7.64; found C 62.49, H 9.43, N 7.59.

(2S,5S)-tert-Butyl 2-tert-Butyl-5-cyclopent-2-enyl-4-methoxy-2,5-dihydroimidazole-1-carboxylate (**10**): The alkylation of (*S*)-(+)-BDI (1.66 g, 6.5 mmol) with 3-bromocyclopentene[41] (2.38 g, 16.2 mmol) was performed according to *GP1*. Purification of the crude product by FC (pentane/Et_2O, 7:1) gave **10** (1.80 g, 86%) as a colorless solid, m.p. 87.0−88.0°C. − IR (KBr): 2978*m*, 1688*s*, 1665*s*, 1475*m*, 1456*m*, 1396*m*, 1366*s*, 1356*s*, 1296*m*, 1271*m*, 1169*m*, 1120*m*, 1079*m*, 999*m*, 928*w*, 858*w*, 783*w*, 726*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 92.2°C): δ = 5.63 [s, 1 H, H-C(2)], 5.14−5.10 (dd, 1 H), 4.36 (td, 1 H), 4.00−3.89 (br, 1 H), 3.69 (s, 3 H, H_3C-O), 2.34−2.18 (m, 2 H), 1.95−1.85 (m, 1 H), 1.72−1.63 (m, 1 H), 1.42 (s, 9 H, *Me*$_3$C-O), 1.22−1.14 (m, 1 H), 0.85 [s, 9 H, *Me*$_3$C-C(2)]. − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 166.6, 133.3, 131.3, 129.1, 128.5, 87.4, 79.1, 64.5, 63.1, 54.9, 31.2, 25.9, 23.4. − MS (70 eV); *m*/*z* (%): 265 (21), 249 (4), 209 (55), 165 (7), 155 (12), 143 (65), 99 (83), 84 (3), 67 (24), 57 (100), 41 (28), 29 (13). − $C_{18}H_{30}N_2O_3$ (322.45): calcd. C 67.05, H 9.38, N 8.69; found C 66.84, H 9.45, N 8.58.

(2S,5S)-tert-Butyl 2-tert-Butyl-5-cyclohex-2-enyl-4-methoxy-2,5-dihydroimidazole-1-carboxylate (**11**): The alkylation of (*S*)-(+)-BDI (1.55 g, 6.1 mmol) with 3-bromocyclohexene[42] (2.44 g, 15.1 mmol) was performed according to *GP1*. Purification of the crude product by FC (pentane/Et_2O, 7:1) gave **11** (1.62 g, 80%) as a colorless solid, m.p. 81.8−82.6°C. − IR (KBr): 2971*m*, 1694*s*, 1669*s*, 1477*m*, 1449*m*, 1386*m*, 1364*s*, 1351*s*, 1295*m*, 1266*m*, 1184*m*, 1166*m*, 1107*m*, 1079*m*, 1046*w*, 997*m*, 964*w*, 947*w*, 910*w*, 869*w*, 782*w*, 713*w*, 667*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 92.8°C): δ = 5.69−5.50 (m, 2 H), 5.24−5.13 (m, 1 H), 4.23 (d, 1 H), 3.72 (s, 3 H, H_3C-O), 3.45−3.36 (br, 1 H), 1.92 (br, 2 H), 1.77−1.61 (m, 2 H), 1.41 (s, 9 H, *Me*$_3$C-O), 1.02−0.92 (m, 1 H), 0.86 [s, 9 H, *Me*$_3$C-C(2)]. − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 128.6, 128.0, 125.8, 87.4, 79.2, 64.7, 54.9, 27.8, 25.9, 24.6, 24.4, 22.3, 21.2. − MS (70 eV); *m*/*z* (%): 279 (22), 263 (3), 223 (76), 179 (11), 155 (6), 143 (49), 99 (61), 81 (19), 57 (100), 41 (21), 29 (11). − $C_{19}H_{32}N_2O_3$ (336.47): calcd. C 67.82, H 9.59, N 8.33; found C 67.84, H 9.38, N 8.28.

(2S,5S)-tert-Butyl 2-tert-Butyl-4-methoxy-5-(1-phenylethyl)-2,5-dihydroimidazole-1-carboxylate (**12**): The alkylation of (*S*)-(+)-BDI (0.71 g, 2.8 mmol) with *rac*-(1-bromoethyl)benzene (1.29 g, 6.9 mmol) was performed according to *GP1*. Purification of the crude product by FC (pentane/Et_2O, 5:1) gave **12** (0.64 g, 64%) as a colorless oil. − IR ($CHCl_3$): 2977*m*, 1695*s*, 1667*s*, 1478*w*, 1448*w*, 1394*m*, 1368*s*, 1275*w*, 1164*m*, 1128*m*, 1079*w*, 992*w*, 955*w*, 882*w*, 854*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 95.0°C): δ = 7.31−7.15 (m, 5 H, arom. H), 5.17 [s, 1 H, H-C(2)], 4.47−4.45 (m, 1 H), 4.12−4.03 (br,

1 H), 3.64 (s, 3 H, H_3C-O), 1.47 (s, 9 H, Me_3C-O), 1.04 (d, J = 7 Hz, 3 H, H_3C-CPh), 0.86 [s, 9 H, Me_3C-C(2)]. − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 166.0, 153.1, 141.6, 128.3, 127.7, 126.9, 126.0, 87.4, 79.5, 67.0, 54.5, 36.9, 33.7, 27.9, 26.0. − MS (70 eV); *m/z* (%): 361 (7) [M^+], 303 (44), 287 (7), 247 (100), 203 (19), 155 (16), 143 (44), 105 (41), 84 (16), 57 (18). − $C_{21}H_{32}N_2O_3$ (360.50): calcd. C 69.97, H 8.95, N 7.77; found C 69.84, H 8.94, N 7.70.

(2S,5S)-tert-Butyl 2-tert-Butyl-5-cyclohexyl-4-methoxy-2,5-dihydroimidazole-1-carboxylate (**13**): The alkylation of (*S*)-(+)-BDI (1.68 g, 6.6 mmol) with iodocyclohexane (2.07 g, 9.8 mmol) was performed according to *GP1*. Purification of the crude product by FC (pentane/Et_2O, 9:1) gave **13** (0.89 g, 40%) as a colorless solid, m.p. 82.2−82.6°C. − $[\alpha]_D^{r.t.}$ = +122.91 (*c* = 0.90, $CHCl_3$). − IR (KBr): 2971*m*, 2928*m*, 2853*m*, 1693*s*, 1669*s*, 1476*w*, 1399*m*, 1354*s*, 1290*m*, 1256*m*, 1171*m*, 1109*m*, 1076*w*, 1004*m*, 970*w*, 941*w*, 853*w*, 783*w*, 710*w*. − ^1H NMR (300 MHz, [D$_6$]DMSO, 95.0°C): δ = 5.13 [s, 1 H, H-C(2)], 4.07−4.05 [m, 1 H, H-C(5)], 3.79 (s, 3 H, H_3C-O), 1.72−1.64 (m, 3 H), 1.51−1.50 (m, 2 H), 1.42 (s, 9 H, Me_3C-O), 1.09−1.06 (m, 3 H), 0.85 [s, 9 H, Me_3C-C(2)]. − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 166.7, 153.3, 87.5, 79.0, 65.8, 55.0, 37.7, 34.1, 27.8, 25.9. − MS (70 eV); *m/z* (%): 339 (9) [M^+], 281 (28), 265 (6), 225 (100), 181 (44), 143 (14), 99 (13), 84 (4), 57 (7). − $C_{19}H_{34}N_2O_3$ (338.49): calcd. C 67.42, H 10.12, N 8.28; found C 67.53, H 10.39, N 8.26.

rac-tert-Butyl 2-tert-Butyl-4-methoxy-5-(4-methoxybenzyl)-2,5-dihydroimidazole-1-carboxylate (*rac*-**14**): The alkylation of *rac*-BDI (1.28 g, 5.0 mmol) with *p*-methoxybenzyliodide (1.86 g, 7.5 mmol) was performed according to *GP1*. Purification of the crude product by FC (pentane/Et_2O, 7:1) gave *rac*-**14** (1.69 g, 90%) as a colorless oil. − IR ($CHCl_3$): 2978*m*, 1672*s*, 1613*w*, 1514*s*, 1479*w*, 1444*w*, 1394*s*, 1368*s*, 1302*w*, 1127*m*, 1110*m*, 1074*w*, 1035*w*, 993*m*, 834*w*. − ^1H NMR (300 MHz, [D$_6$]DMSO, 100.0°C): δ = 6.95 (d, J = 3 Hz, 2 H, arom. H), 6.78 (d, J = 3 Hz, 2 H, arom. H), 4.77 [s, 1 H, H-C(2)], 4.46−4.43 [m, 1 H, H-C(5)], 3.76 (s, 3 H, H_3C-O), 3.71 (s, 3 H, H_3C-O), 3.57 (dd, J = 15 und 5 Hz, 1 H), 2.82 (dd, J = 15 und 5 Hz, 1 H), 1.45 (s, 9 H, Me_3C-O), 0.83 [s, 9 H, Me_3C-C(2)]. − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 166.5, 157.8, 130.5, 127.3, 113.3, 87.6, 79.3, 62.0, 54.8, 31.0, 27.9, 26.1. − MS (70 eV); *m/z* (%): 319 (25), 303 (4), 263 (59), 219 (17), 155 (5), 121 (100), 99 (15), 78 (4), 57 (74), 41 (16), 29 (9). − $C_{21}H_{32}N_2O_4$ (376.50): calcd. C 66.99, H 8.57, N 7.44; found C 67.11, H 8.30, N 7.27.

Hydrolysis of 4-Monosubstituted Methoxy-Dihydro-Imidazoles and Preparation of the Corresponding Amino Acid Methyl Esters

(2S)-Methyl 2-tert-Butoxycarbonylamino-5-trimethylsilanylpent-4-ynecarboxylate (**15**): The monosubstituted dihydroimidazole **9** (0.27 g, 0.7 mmol) was deprotected with TMSO-Tf (0.98 g, 4.4 mmol) in CH_2Cl_2 (10 ml) according to *GP3*. The subsequent hydrolysis of the ring was performed in 0.1 N TFA/H_2O (15 ml) and the protection of the free amino acid methylester (0.12 g, 78%) thus obtained with di-*tert*-butyldicarbonate (0.24 g, 1.1 mmol) in CH_2Cl_2 (5 ml) and Et_3N (0.11 g, 1.1 mmol). Purification of the crude protected amino acid ester by FC (pentane/Et_2O, 7:1) gave **15** (35 mg, 16%) as a colorless oil. − $[\alpha]_D^{r.t.}$ = +66.43 (*c* = 0.28, $CHCl_3$). − IR ($CHCl_3$): 3437*w*, 2958*m*, 2177*w*, 1745*s*, 1711*s*, 1502*s*, 1438*m*, 1368*m*, 1064*m*, 1012*w*, 845*s*. − ^1H NMR (300 MHz, $CDCl_3$): δ = 5.29 (d, J = 8 Hz, 1 H, H-N), 4.48−4.46 (m, 1 H, H-CN), 3.77 (s, 3 H, H_3C-O), 2.78 (dd, J = 17 und 5 Hz, 1 H, H-CC≡C), 2.69 (dd, J = 17 und 5 Hz, 1 H, H-CC≡C), 1.46 (s, 9 H, Me_3C-O), 0.14 (s, 9 H, Me_3Si). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.3, 155.2, 127.6, 100.8, 80.1, 52.4, 52.1, 28.2, 24.2. − MS (70 eV); *m/z* (%): 287 (1), 265 (1), 243 (3), 210 (4), 198 (1), 184 (6), 167 (2), 152 (6), 140 (4), 124 (2), 105 (4), 88 (27), 86 (63), 84 (100), 73 (16), 57 (26).

rac-Methyl 2-Amino-3-(4-methoxyphenyl)propionate (*rac*-**16**): The monosubstituted dihydroimidazole *rac*-**14** (0.61 g, 1.6 mmol) was deprotected with TMSO-Tf (2.16 g, 9.7 mmol) in CH_2Cl_2 (20 ml) according to *GP3*. The subsequent hydrolysis of the ring was performed in 0.1 N TFA/H_2O (32 ml) and the purification of the free amino acid methylester (0.32 g, 95%) by bulb-to-bulb destillation (0.5 Torr, 165°C) gave *rac*-**16** (0.19 g, 55%) as a colorless oil. − ^1H NMR (200 MHz, $CDCl_3$): δ = 7.09 (d, J = 9 Hz, 2 H, arom. H), 6.83 (d, J = 9 Hz, 2 H, arom. H), 3.78 (s, 3 H, H_3C-O), 3.70 (s, 3 H, H_3C-O), 3.02 (dd, J = 14 und 8 Hz, 1 H, H-CAr), 2.79 (dd, J = 14 und 8 Hz, 1 H, H-CAr), 1.64 (br, 2 H, H_2N).

(2S)-Methyl Benzyloxycarbonylaminocyclopent-2-enylacetate (**17**): The monosubstituted dihydroimidazole **10** (0.40 g, 1.3 mmol) was deprotected with TMSO-Tf (1.67 g, 7.5 mmol) in CH_2Cl_2 (16 ml) according to *GP3*. The subsequent hydrolysis of the ring was performed in 0.1 N TFA/H_2O (25 ml) and the protection of the free amino acid methylester (0.16 g, 85%) thus obtained with benzylchloroformate (0.32 g, 1.9 mmol) in CH_2Cl_2 (10 ml) and 2 N NaOH (1.4 ml). Purification of the crude protected amino acid ester by FC (pentane/Et_2O, 3:1) gave **17** (0.15 g, 41%) as a colorless oil. − IR ($CHCl_3$): 3431*w*, 3035*w*, 2954*w*, 1721*s*, 1509*m*, 1455*w*, 1438*w*, 1344*w*, 1062*m*, 1003*w*. − ^1H NMR (200 MHz, $CDCl_3$): δ = 7.36 (s, 5 H, arom. H), 5.96−5.92 (m, 1 H, H-C=C), 5.50−5.46 (m, 1 H, H-C=C), 5.11 (s, 3 H), 4.49−4.38 (m, 1 H), 3.75 (s, 3 H, H_3C-O), 3.37−3.12 (br, 1 H), 2.37−2.29 (br, 2 H), 2.17−1.85 (m, 1 H), 1.77−1.60 (m, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.4, 136.3, 135.6, 133.7, 130.1, 128.5, 128.2, 67.1, 56.8, 52.2, 48.8, 47.9, 32.4, 32.0, 26.1, 24.8. − MS (70 eV); *m/z* (%): 230 (5), 223 (46), 186 (7), 162 (57), 138 (25), 122 (5), 115 (8), 108 (15), 91 (100), 79 (15), 67 (27). − $C_{16}H_{19}NO_4$ (289.33): calcd. C 66.42, H 6.62, N 4.84; found C 66.39, H 6.72, N 4.61.

(2S)-Methyl Benzyloxycarbonylaminocyclohexylacetate (**18**): The monosubstituted dihydroimidazole **13** (0.53 g, 1.6 mmol) was deprotected with TMSO-Tf (2.09 g, 9.4 mmol) in CH_2Cl_2 (20 ml) according to *GP3*. The subsequent hydrolysis of the ring was performed in 0.1 N TFA/H_2O (31 ml) and the protection of the free amino acid methylester (0.22 g, 81%) thus obtained with benzylchloroformate (0.40 g, 2.4 mmol) in CH_2Cl_2 (15 ml) and 2 N NaOH (1.2 ml). Purification of the crude protected amino acid ester by FC (pentane/Et_2O, 4:1) gave **18** (0.27 g, 56%) as a colorless oil. − $[\alpha]_D^{r.t.}$ = +17.38 (*c* = 1.07, $CHCl_3$). − IR ($CHCl_3$): 3436*w*, 3032*w*, 2933*s*, 2856*m*, 1720*s*, 1514*s*, 1451*m*, 1342*m*, 1065*m*, 1028*w*. − ^1H NMR (200 MHz, $CDCl_3$): δ = 7.36 (s, 5 H, arom. H), 5.27 (d, J = 9 Hz, 1 H, H-N), 5.11 (s, 2 H, HC-Ph), 4.31−4.27 (dd, J = 9 und 5 Hz, 1 H, HC-CO_2), 3.74 (s, 3 H, H_3C-O), 1.77−1.55 (m, 6 H), 1.28−1.01 (m, 5 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.5, 156.2, 136.4, 128.6, 128.2, 67.1, 58.8, 52.1, 41.1, 29.5, 28.1, 26.0. − MS (70 eV); *m/z* (%): 305 (6) [M^+], 271 (1), 246 (54), 223 (1), 202 (82), 170 (5), 162 (9), 154 (3), 138 (49), 115 (100), 91 (59), 79 (19), 65 (4), 55 (6). − $C_{17}H_{23}NO_4$ (305.37): calcd. C 66.86, H 7.59, N 4.59; found C 66.70, H 7.46, N 4.43.

(2S)-Methyl Benzyloxycarbonylaminocyclohex-2-enylacetate (**19**): The monosubstituted dihydroimidazole **11** (0.71 g, 2.1 mmol) was deprotected with TMSO-Tf (2.81 g, 12.6 mmol) in CH_2Cl_2 (25 ml) according to *GP3*. The subsequent hydrolysis of the ring was performed in 0.1 N TFA/H_2O (42 ml) and the protection of the free amino acid methylester (0.32 g, 89%) thus obtained with benzylchloroformate (0.54 g, 3.2 mmol) in CH_2Cl_2 (20 ml) and 2 N NaOH (1.6 ml). Purification of the crude protected amino acid ester by FC (pentane/Et_2O, 3:1) gave **19** (0.34 g, 54%) as a colorless oil. −

IR ($CHCl_3$): 3682*w*, 3436*w*, 3015*w*, 2944*w*, 1723*s*, 1600*w*, 1513*s*, 1456*m*, 1436*m*, 1062*m*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 7.36 (s, 5 H, arom. H), 5.79−5.74 (m, 1 H, H-C=C), 5.58−5.54 (m, 1 H, H-C=C), 5.06 (s, 2 H, HC-Ph), 4.01 (m, 1 H), 3.65 (s, 3 H, H_3C-O), 1.95 (br, 2 H), 1.72−1.63 (m, 2 H), 1.51−1.44 (m, 1 H), 1.36−1.29 (m, 1 H). − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 171.9, 156.1, 136.8, 129.1, 128.3, 127.7, 127.6, 65.5, 58.3, 57.7, 51.6, 36.6, 25.2, 24.3, 20.7. − MS (70 eV); *m/z* (%): 286 (3), 260 (20), 244 (8), 223 (15), 212 (2), 200 (13), 178 (14), 168 (6), 162 (39), 152 (78), 132 (5), 120 (7), 108 (11), 91 (100), 81 (37). − $C_{17}H_{21}NO_4$ (303.36): calcd. C 67.31, H 6.98, N 4.62; found C 67.35, H 7.27, N 4.92.

(2S)-Methyl 2-Benzyloxycarbonylamino-3-phenylbutyrate (**20**): The monosubstituted dihydroimidazole **12** (1.13 g, 3.1 mmol) was deprotected with TMSO-Tf (4.17 g, 18.7 mmol) in CH_2Cl_2 (35 ml) according to *GP3*. The subsequent hydrolysis of the ring was performed in 0.1 N TFA/H_2O (62 ml) and the protection of the free amino acid methylester (0.55 g, 91%) thus obtained with benzylchloroformate (0.80 g, 4.7 mmol) in CH_2Cl_2 (15 ml) and 2 N NaOH (2.3 ml). Purification of the crude protected amino acid ester by FC (hexane/AcOEt, 8:1) gave **20** (0.68 g, 66%) as a colorless oil. − IR ($CHCl_3$): 3432*w*, 3032*w*, 1723*s*, 1510*s*, 1454*m*, 1438*w*, 1342*m*, 1076*w*, 1028*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 7.33−7.20 (m, 10 H, arom. H), 4.93 (s, 2 H, HC-Ph), 4.29 (m, 1 H), 3.63 (s, 3 H, H_3C-O), 1.19 (d, *J* = 7 Hz, 3 H, H_3C-CPh). − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 172.1, 155.7, 142.6, 136.8, 128.2, 128.1, 127.5, 65.3, 62.8, 59.6, 51.6, 18.5. − MS (70 eV); *m/z* (%): 268 (2), 236 (1), 223 (7), 192 (2), 176 (30), 162 (7), 117 (4), 105 (100), 91 (33), 79 (10). − $C_{19}H_{21}NO_4$ (327.38): calcd. C 69.71, H 6.47, N 4.28; found C 69.72, H 6.45, N 4.17.

Dialkylations of BDI

rac-tert-Butyl 2-tert-Butyl-5-ethyl-4-methoxy-5-methyl-2,5-dihydroimidazole-1-carboxylate (*rac*-**21**): The double alkylation of *rac*-BDI (2.00 g, 7.8 mmol) with MeI (1.66 g, 11.7 mmol) and EtI (1.82 g, 11.7 mmol) according to *GP2* and purification of the crude product by FC (pentane/Et_2O, 9:1) gave *rac*-**21** (1.84 g, 79%) as a colorless oil. − IR ($CHCl_3$): 2976*m*, 1687*s*, 1480*w*, 1458*w*, 1392*w*, 1366*s*, 1350*s*, 1296*w*, 1171*m*, 1104*w*, 1068*m*, 1021*w*, 996*w*, 915*w*, 865*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 93.6°C): δ = 4.51 [s, 1 H, H-C(2)], 3.75 (s, 3 H, H_3C-O), 3.68−3.57 (br, 1 H), 2.75 (d, *J* = 15 Hz, 1 H), 1.58 [s, 3 H, H_3C-C(5)], 1.50 (s, 9 H, Me_3C-O), 0.83 [s, 9 H, Me_3C-C(2)]. − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 167.9, 154.3, 87.6, 78.9, 67.7, 55.3, 37.4, 29.0, 27.8, 26.4, 23.6, 7.5. − MS (70 eV); *m/z* (%): 241 (12), 225 (5), 185 (100), 141 (25), 125 (1), 114 (4). − $C_{16}H_{30}N_2O_3$ (298.43): calcd. C 64.40, H 10.13, N 9.39; found C 64.23, H 10.36, N 9.46.

(2S,5S)-tert-Butyl 2-tert-Butyl-4-methoxy-5-methyl-5-trimethylsilanylmethyl-2,5-dihydroimidazole-1-carboxylate (**22**): The double alkylation of (*S*)-(+)-BDI (2.08 g, 8.1 mmol) with MeI (1.73 g, 12.2 mmol) and trimethylsilylmethyliodide (2.61 g, 12.2 mmol) according to *GP2* and purification of the crude product by FC (pentane/Et_2O, 11:1) gave **22** (2.33 g, 80%) as a colorless oil. − IR ($CHCl_3$): 2977*m*, 1692*s*, 1480*w*, 1457*w*, 1392*m*, 1365*s*, 1344*s*, 1297*w*, 1123*w*, 1072*w*, 1046*m*, 996*w*, 909*w*, 872*m*, 839*m*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 95.0°C): δ = 5.07 [s, 1 H, H-C(2)], 3.78 (s, 3 H, H_3C-O), 1.81 (d, *J* = 15 Hz, 1 H, H-CSiMe$_3$), 1.48 [s, 3 H, H_3C-C(5)], 1.44 (s, 9 H, Me_3C-O), 1.08 (d, *J* = 15 Hz, 1 H, H-CSiMe$_3$), 0.89 [s, 9 H, Me_3C-C(2)], 0.07 (s, 9 H, Me_3Si). − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 211.9, 170.4, 154.4, 88.2, 80.4, 79.8, 65.8, 55.9, 38.7, 29.0, 27.8, 0.0. − MS (70 eV); *m/z* (%): 357 (2) [M^+], 299 (18), 285 (14), 243 (100), 213 (4), 199 (23), 183 (1), 167 (7), 153 (2), 139 (6), 112 (2), 95 (6), 73 (4), 57 (6). − $C_{18}H_{36}N_2O_3Si$ (356.58): calcd. C 60.63, H 10.18, N 7.86; found C 60.37, H 10.12, N 7.87.

(2S,5S)-tert-Butyl 2-tert-Butyl-5-cyclopropylmethyl-4-methoxy-5-methyl-2,5-dihydroimidazole-1-carboxylate (**23**): The double alkylation of (*S*)-(+)-BDI (2.09 g, 8.2 mmol) with MeI (1.74 g, 12.2 mmol) and cyclopropylmethylbromide (1.65 g, 12.2 mmol) according to *GP2* and purification of the crude product by FC (pentane/Et_2O, 13:1) gave **23** (2.17 g, 82%) as a colorless oil. − $[\alpha]_D^{r.t.}$ = +75.78 (*c* = 1.52, $CHCl_3$). − IR ($CHCl_3$): 2977*m*, 1694*s*, 1480*w*, 1458*w*, 1392*w*, 1366*s*, 1346*s*, 1172*m*, 1123*w*, 1053*m*, 1020*w*, 998*w*, 920*w*, 858*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 93.6°C): δ = 5.13 [s, 1 H, H-C(2)], 3.79 (s, 3 H, H_3C-O), 1.43 (s, 9 H, Me_3C-O), 1.36 [s, 3 H, H_3C-C(5)], 1.22−1.09 (m, 1 H), 0.89 [s, 9 H, Me_3C-C(2)], 0.36−0.21 (m, 3 H), 0.18−0.02 (m, 2 H). − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 168.3, 154.4, 87.6, 78.9, 67.2, 54.9, 37.4, 27.8, 26.5, 23.6, 5.4, 3.8, 2.1. − MS (70 eV); *m/z* (%): 325 (2) [M^+], 267 (21), 251 (5), 225 (1), 211 (100), 167 (38), 157 (4), 152 (1), 113 (7), 57 (5). − $C_{18}H_{32}N_2O_3$ (324.46): calcd. C 66.63, H 9.94, N 8.63; found C 66.44, H 9.93, N 8.56.

rac-tert-Butyl 5-Benzyl-2-tert-butyl-4-methoxy-5-methyl-2,5-dihydroimidazole-1-carboxylate (*rac*-**24**): The double alkylation of *rac*-BDI (1.99 g, 7.8 mmol) with MeI (1.65 g, 11.6 mmol) and benzylbromide (1.99 g, 11.6 mmol) according to *GP2* and purification of the crude product by FC (pentane/Et_2O, 9:1) gave *rac*-**24** (2.28 g, 91%) as a colorless solid, m.p. 112.4−113.2°C. − IR (KBr): 2964*m*, 2892*w*, 1708*s*, 1682*s*, 1477*w*, 1451*m*, 1385*m*, 1364*s*, 1344*s*, 1292*m*, 1256*w*, 1174*m*, 1128*m*, 1092*w*, 1051*s*, 985*m*, 913*w*, 862*w*, 774*w*, 749*w*, 713*w*, 697*m*, 631*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 93.6°C): δ = 7.28−7.18 (m, 3 H, arom. H), 7.02 (d, *J* = 6 Hz, 2 H, arom. H), 4.51 [s, 1 H, H-C(2)], 3.75 (s, 3 H, H_3C-O), 3.72−3.53 (br, 1 H), 2.73 (d, *J* = 15 Hz, 1 H), 1.58 [s, 3 H, H_3C-C(5)], 1.50 (s, 9 H, Me_3C-O), 0.83 [s, 9 H, Me_3C-C(2)]. − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 167.4, 167.2, 153.5, 152.9, 136.1, 129.5, 129.3, 128.0, 127.8, 126.6, 87.4, 79.5, 68.8, 68.3, 54.8, 41.2, 37.6, 37.0, 27.9, 26.8, 23.8. − MS (70 eV); *m/z* (%): 303 (10), 287 (3), 247 (100), 229 (4), 213 (4), 203 (98), 181 (4), 169 (17), 160 (6), 113 (7), 91 (13), 57 (5). − $C_{21}H_{32}N_2O_3$ (360.50): calcd. C 69.97, H 8.95, N 7.77; found C 69.95, H 9.01, N 7.74.

rac-tert-Butyl 5-Allyl-2-tert-butyl-4-methoxy-5-(3-trimethylsilanylprop-2-inyl)-2,5-dihydroimidazole-1-carboxylate (*rac*-**25**): The double alkylation of *rac*-BDI (2.55 g, 9.9 mmol) with allylbromide (1.80 g, 14.9 mmol) and (3-chloroprop-1-inyl)trimethylsilane[40] (2.19 g, 14.9 mmol) according to *GP2* and purification of the crude product by FC (hexane/AcOEt, 15:1) gave *rac*-**25** (2.15 g, 53%) as a colorless oil. − IR ($CHCl_3$): 2977*m*, 2178*w*, 1682*s*, 1480*w*, 1446*w*, 1337*s*, 1172*m*, 1140*w*, 1030*w*, 1009*m*, 921*w*, 845*s*, 644*w*. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.99−5.79 (br, 1 H), 5.23−5.18 (m, 1 H), 5.09−4.95 (m, 2 H), 3.84 (s, 3 H, H_3C-O), 3.33−3.23 (br, 1 H), 2.78−2.38 (m, 3 H), 1.47 (s, 9 H, Me_3C-O), 0.92 [s, 9 H, Me_3C-C(2)], 0.09 (s, 9 H, Me_3Si). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.0, 154.5, 133.7, 117.9, 89.5, 80.1, 55.5, 42.3, 37.4, 28.3, 27.1. − MS (70 eV); *m/z* (%): 407 (8) [M^+], 389 (3), 349 (38), 333 (8), 293 (100), 249 (55), 233 (9), 193 (6), 73 (24), 57 (30).

rac-tert-Butyl 2-tert-Butyl-5-cyclohexylmethyl-4-methoxy-5-methyl-2,5-dihydroimidazole-1-carboxylate (*rac*-**26**): The double alkylation of *rac*-BDI (2.01 g, 7.8 mmol) with iodomethylcyclohexane (2.63 g, 11.7 mmol) and MeI (1.67 g, 11.7 mmol) according to *GP2* and purification of the crude product by FC (pentane/Et_2O, 14:1) gave *rac*-**26** (2.03 g, 71%) as a colorless oil. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 93.6°C): δ = 5.08 [s, 1 H, H-C(2)], 3.74 (s, 3 H, H_3C-O), 2.20 (d, *J* = 15 Hz, 1 H), 1.71−1.48 (m, 10 H), 1.43 (s, 9 H, Me_3C-O), 1.28−1.03 (m, 5 H), 0.92 [s, 9 H, Me_3C-C(2)]. − ^{13}C

NMR (75 MHz, [D$_6$]DMSO): δ = 168.9, 88.1, 79.2, 54.7, 46.0, 37.3, 35.0, 34.6, 34.3, 32.9, 32.5, 32.0, 27.7, 27.1, 26.1, 25.9, 25.7, 25.6. − MS (70 eV); *m*/*z* (%): 335 (100), 291 (27), 251 (4), 239 (15), 207 (10), 195 (40), 155 (8), 111 (22), 97 (5), 84 (10), 57 (9).

(2S,5R)-tert-Butyl 5-Allyl-2-tert-butyl-5-cyclohex-1-enylmethyl-4-methoxy-2,5-dihydroimidazole-1-carboxylate (**27**): The double alkylation of (*S*)-(+)-BDI (1.60 g, 6.2 mmol) with 1-bromomethylcyclohexene (1.64 g, 9.4 mmol) and allylbromide (1.13 g, 9.4 mmol) according to *GP2* and purification of the crude product by FC (pentane/Et$_2$O, 15:1) gave **27** (1.96 g, 80%) as a colorless oil. − $[\alpha]_D^{r.t.}$ = +12.90 (*c* = 0.93, CHCl$_3$). − IR (CHCl$_3$): 2974*m*, 2933*m*, 1692*s*, 1477*w*, 1446*w*, 1390*m*, 1369*s*, 1333*s*, 1169*m*, 1108*w*, 1010*m*, 923*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 92.2°C): δ = 5.47 [br, 1 H, H-C(2)], 5.43−5.28 (m, 1 H), 5.05−4.93 (m, 3 H), 3.77 (s, 3 H, H$_3$C-O), 2.26−2.19 (m, 1 H), 1.99−1.90 (m, 4 H), 1.57−1.47 (m, 4 H), 1.43 (s, 9 H, *Me*$_3$C-O), 0.89 [s, 9 H, *Me*$_3$C-C(2)]. − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 133.1, 131.7, 125.9, 119.5, 87.7, 79.3, 71.1, 54.9, 44.5, 37.1, 29.6, 27.8, 26.9, 24.8, 22.2, 21.2. − MS (70 eV); *m*/*z* (%): 333 (19), 295 (5), 277 (99), 249 (4), 233 (15), 193 (6), 183 (2), 139 (41), 111 (5), 95 (11), 67 (5), 57 (100), 41 (21), 29 (10). − $C_{23}H_{38}N_2O_3$ (390.57): calcd. C 70.73, H 9.81, N 7.17; found C 70.75, H 9.70, N 7.20.

(2S,5R)-tert-Butyl 2-tert-Butyl-5-ethyl-4-methoxy-5-(4-methoxybenzyl)-2,5-dihydroimidazole-1-carboxylate (**28**): The double alkylation of (*S*)-(+)-BDI (1.28 g, 5.0 mmol) with *p*-methoxybenzyliodide (1.86 g, 7.5 mmol) and EtI (1.17 g, 7.5 mmol) according to *GP2* and purification of the crude product by FC (pentane/Et$_2$O, 7:1) gave **28** (1.42 g, 70%) as a colorless oil. − $[\alpha]_D^{r.t.}$ = +74.41 (*c* = 0.93, CHCl$_3$). − IR (CHCl$_3$): 2974*m*, 1694*s*, 1612*w*, 1513*s*, 1460*w*, 1392*w*, 1368*m*, 1334*s*, 1107*w*, 1092*w*, 1036*w*, 1004*m*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 100.0°C): δ = 7.05 (d, *J* = 8 Hz, 2 H, arom. H), 6.79 (d, *J* = 8 Hz, 2 H, arom. H), 4.99 [s, 1 H, H-C(2)], 3.80 (s, 3 H, H$_3$C-O), 3.70 (s, 3 H, H$_3$C-O), 3.06 (d, *J* = 14 Hz, 1 H, H-CAr), 3.00 (d, *J* = 14 Hz, 1 H, H-CAr), 2.33−2.21 (m, 1 H, H-CMe), 1.60−1.48 (m, 1 H, H-CMe), 1.43 (s, 9 H, *Me*$_3$C-O), 0.62 [s, 9 H, *Me*$_3$C-C(2)], 0.57 (t, *J* = 8 Hz, 3 H, *Me*-CH$_2$). − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 166.4, 158.1, 131.3, 128.9, 113.5, 87.8, 79.2, 72.8, 55.0, 41.3, 36.9, 28.7, 27.7, 26.3. − MS (70 eV); *m*/*z* (%): 347 (16), 331 (3), 291 (59), 247 (9), 227 (11), 183 (14), 171 (7), 121 (100), 111 (3), 78 (4), 57 (70), 41 (16), 29 (8). − $C_{23}H_{36}N_2O_4$ (404.55): calcd. C 68.29, H 8.97, N 6.92; found C 68.45, H 8.68, N 6.83.

(2S,5R)-tert-Butyl 5-Allyl-2-tert-butyl-5-(3,5-dimethoxybenzyl)-4-methoxy-2,5-dihydroimidazole-1-carboxylate (**29**): The double alkylation of (*S*)-(+)-BDI (1.63 g, 6.3 mmol) with 3,5-dimethoxybenzyliodide (2.65 g, 9.5 mmol) and allylbromide (1.15 g, 9.5 mmol) according to *GP2* and purification of the crude product by FC (pentane/Et$_2$O, 5:1) gave **29** (1.47 g, 52%) as a colorless oil. − IR (CHCl$_3$): 2978*m*, 1699*s*, 1597*s*, 1458*m*, 1430*m*, 1368*s*, 1333*s*, 1153*s*, 1063*m*, 1011*m*, 928*w*, 856*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 92.2°C): δ = 6.34−6.31 (m, 3 H, arom. H), 5.42−5.36 (m, 1 H), 5.06−5.00 (m, 2 H), 4.90 [s, 1 H, H-C(2)], 3.82 (s, 3 H, H$_3$C-O), 3.69 (s, 6 H, H$_3$C-O), 3.13−2.96 (m, 3 H), 2.32−2.25 (m, 1 H), 1.46 (s, 9 H, *Me*$_3$C-O), 0.57 [s, 9 H, *Me*$_3$C-C(2)]. − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 165.8, 160.2, 154.5, 138.6, 131.5, 119.7, 108.3, 99.1, 87.6, 79.5, 72.1, 54.9, 41.8, 36.8, 27.8, 26.3. − MS (70 eV); *m*/*z* (%): 389 (20), 333 (16), 305 (4), 289 (100), 249 (9), 195 (7), 151 (42), 139 (8), 57 (63), 41 (15), 29 (7). − $C_{25}H_{38}N_2O_5$ (446.59): calcd. C 67.24, H 8.58, N 6.27; found C 67.44, H 8.62, N 6.48.

(2S,5S)-tert-Butyl 2-tert-Butyl-5-(3,5-dimethoxybenzyl)-5-isopropyl-4-methoxy-2,5-dihydroimidazole-1-carboxylate (**30**): The double alkylation of (*S*)-(+)-BDI (0.97 g, 3.8 mmol) with 3,5-dimethoxybenzyliodide (1.58 g, 5.7 mmol) and isopropyliodide (0.97 g, 5.7 mmol) according to *GP2* and purification of the crude product by FC (pentane/Et$_2$O, 5:1) gave **30** (0.97 g, 57%) as a colorless solid, m.p. 80.6−81.8°C. − IR (KBr): 2970*m*, 1702*s*, 1676*s*, 1606*s*, 1459*m*, 1428*m*, 1388*m*, 1370*m*, 1322*s*, 1286*m*, 1193*s*, 1174*m*, 1154*s*, 1122*m*, 1096*w*, 1063*m*, 1013*m*, 904*w*, 837*m*, 794*w*, 698*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 92.0°C): δ = 6.36 (s, 2 H, arom. H), 6.28 (s, 1 H, arom. H), 4.84 [s, 1 H, H-C(2)], 3.85 (s, 3 H, H$_3$C-O), 3.67 (s, 6 H, H$_3$C-O), 3.18−3.03 (m, 2 H), 2.65−2.59 (m, 1 H, H-CMe$_2$), 1.48 (s, 9 H, *Me*$_3$C-O), 1.07 (d, *J* = 7 Hz, 3 H, *H*$_3$C-CH), 0.73 (d, *J* = 7 Hz, 3 H, *H*$_3$C-CH), 0.40 [s, 9 H, *Me*$_3$C-C(2)]. − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 165.0, 160.2, 155.2, 139.4, 108.2, 99.3, 87.5, 79.3, 75.9, 54.8, 37.0, 35.6, 27.8, 26.2, 18.3, 17.1. − MS (70 eV); *m*/*z* (%): 391 (21), 375 (3), 335 (15), 305 (5), 291 (100), 249 (8), 197 (3), 151 (32), 139 (4), 57 (12). − $C_{25}H_{40}N_2O_5$ (448.60): calcd. C 66.94, H 8.99, N 6.24; found C 67.18, H 8.73, N 6.33.

rac-tert-Butyl 2-tert-Butyl-5-cyclohexylmethyl-5-(3,5-dimethoxybenzyl)-4-methoxy-2,5-dihydroimidazole-1-carboxylate (*rac*-**31**): The double alkylation of *rac*-BDI (0.90 g, 3.5 mmol) with 3,5-dimethoxybenzyliodide (1.46 g, 5.2 mmol) and iodomethylcyclohexane (1.17 g, 5.2 mmol) according to *GP2* and purification of the crude product by FC (pentane/Et$_2$O, 6:1) gave *rac*-**31** (0.93 g, 53%) as a colorless solid, m.p. 97.8−98.6°C. − IR (KBr): 2975*m*, 2924*m*, 2856*m*, 1701*s*, 1679*m*, 1611*m*, 1596*m*, 1462*m*, 1431*w*, 1390*w*, 1368*m*, 1331*s*, 1291*m*, 1204*m*, 1165*m*, 1148*m*, 1121*w*, 1066*w*, 1014*m*, 905*w*, 844*m*, 692*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 92.0°C): δ = 6.31 (s, 3 H, arom. H), 5.01 [s, 1 H, H-C(2)], 3.80 (s, 3 H, H$_3$C-O), 3.68 (s, 6 H, H$_3$C-O), 3.04−2.89 (m, 2 H), 2.18 (d, *J* = 14 Hz, 1 H), 1.63−1.48 (m, 5 H), 1.44 (s, 9 H, *Me*$_3$C-O), 1.17−0.79 (m, 7 H), 0.59 [s, 9 H, *Me*$_3$C-C(2)]. − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 167.3, 160.1, 138.7, 108.4, 98.9, 87.8, 79.2, 70.8, 54.8, 43.1, 37.1, 34.5, 32.8, 27.7, 26.5, 26.0. − MS (70 eV); *m*/*z* (%): 445 (16), 429 (2), 389 (11), 345 (100), 295 (10), 251 (24), 239 (6), 195 (18), 151 (37), 111 (7), 57 (21). − $C_{29}H_{46}N_2O_5$ (502.69): calcd. C 69.29, H 9.22, N 5.57; found C 69.36, H 9.11, N 5.42.

rac-tert-Butyl 5-Benzyl-2-tert-butyl-5-cyclohexylmethyl-4-methoxy-2,5-dihydroimidazole-1-carboxylate (*rac*-**32**): The double alkylation of *rac*-BDI (2.07 g, 8.1 mmol) with benzylbromide (2.08 g, 12.1 mmol) and iodomethylcyclohexane (2.72 g, 12.1 mmol) according to *GP2* and purification of the crude product by FC (pentane/Et$_2$O, 13:1) gave *rac*-**32** (2.26 g, 63%) as a colorless oil. − IR (CHCl$_3$): 2923*s*, 2851*m*, 1687*s*, 1492*w*, 1477*w*, 1451*m*, 1390*m*, 1339*s*, 1169*m*, 1118*m*, 1077*w*, 1010*m*, 908*w*, 856*w*. − ^{1}H NMR (300 MHz, [D$_6$]DMSO, 93.6°C): δ = 7.23−7.14 (m, 5 H, arom. H), 5.02 [s, 1 H, H-C(2)], 3.78 (s, 3 H, H$_3$C-O), 3.11−2.99 (m, 2 H), 2.20 (d, *J* = 15 Hz, 1 H), 1.64−1.46 (m, 6 H), 1.43 (s, 9 H, *Me*$_3$C-O), 1.18−0.73 (m, 6 H), 0.60 [s, 9 H, *Me*$_3$C-C(2)]. − ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 167.5, 136.8, 130.5, 127.9, 126.4, 87.9, 79.3, 70.7, 54.7, 43.2, 42.7, 37.0, 34.4, 32.8, 32.4, 27.7, 26.6, 26.0, 25.8, 25.6. − MS (70 eV); *m*/*z* (%): 385 (8), 369 (2), 351 (1), 329 (100), 295 (7), 285 (49), 251 (19), 239 (7), 195 (22). − $C_{27}H_{42}N_2O_3$ (442.64): calcd. C 73.26, H 9.56, N 6.33; found C 73.14, H 9.68, N 6.21.

Hydrolysis of 4,4-Disubstituted Methoxy-Dihydro-Imidazoles and Preparation of the Corresponding Amino Acid Methylesters

rac-Methyl 2-Benzyloxycarbonylamino-2-methylbutyrate (*rac*-**33**): The disubstituted dihydroimidazole *rac*-**21** (0.89 g, 3.0 mmol) was, according to *GP4*, deprotected in 1 N TFA/CH$_2$Cl$_2$ (46 ml) and hydrolyzed in 2 N TFA/H$_2$O (12 ml) to give the free amino acid methylester (0.33 g, 85%). After protection of the amino group with benzylchloroformate (0.76 g, 4.5 mmol) in CH$_2$Cl$_2$ (14 ml) and 2 N NaOH (2.2 ml), the crude product was purified by FC (pentane/

Et_2O, 4:1). The amino acid ester *rac*-**33** (0.26 g, 33%) was isolated as a colorless oil. − IR ($CHCl_3$): 3417*w*, 3032*w*, 1720*s*, 1506*s*, 1453*m*, 1375*w*, 1337*w*, 1315*m*, 1161*w*, 1089*m*, 1045*m*. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37−7.29 (m, 5 H, arom. H), 5.59−5.57 (br, 1 H, H-N), 5.08 (s, 2 H, H-CPh), 3.74 (s, 3 H, H_3C-O), 2.15−2.11 (m, 1 H, H-CMe), 1.88−1.76 (m, 1 H, H-CMe), 1.57 (s, 3 H, H_3C-CN), 0.80 (t, *J* = 7 Hz, 3 H, H_3C-CH_2). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.7, 154.6, 136.6, 128.5, 128.1, 128.0, 66.4, 60.6, 52.6, 30.1, 23.0, 8.4. − MS (70 eV); *m*/*z* (%): 222 (2), 206 (13), 181 (3), 162 (20), 130 (3), 108 (11), 91 (100), 79 (6). − $C_{14}H_{19}NO_4$ (265.31): calcd. C 63.38, H 7.22, N 5.28; found C 63.33, H 7.42, N 5.57.

(2S)-Methyl 2-Benzyloxycarbonylamino-2-methyl-3-trimethylsilanylpropionate (**34**): The disubstituted dihydroimidazole **22** (0.75 g, 2.1 mmol) was, according to *GP4*, deprotected in 1 N TFA/CH_2Cl_2 (32 ml) and hydrolyzed in 2 N TFA/H_2O (8 ml) to give the free amino acid methylester (0.27 g, 69%). After protection of the amino group with benzylchloroformate (0.59 g, 3.5 mmol) in CH_2Cl_2 (11 ml) and 2 N NaOH (1.8 ml), the crude product was purified by FC (pentane/Et_2O, 5:1). The amino acid ester **34** (0.20 g, 30%) was isolated as a colorless oil. − IR ($CHCl_3$): 3072*w*, 2931*w*, 2859*m*, 2740*w*, 1693*s*, 1609*s*, 1472*w*, 1428*m*, 1391*w*, 1304*w*, 1165*w*, 1113*s*, 1092*s*, 1016*w*, 822*m*. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36−7.29 (m, 5 H, arom. H), 5.72−5.61 (br, 1 H, H-N), 5.07 (s, 2 H, H-CPh), 3.72 (s, 3 H, H_3C-O), 1.63 (s, 3 H, H_3C-CN), 1.61 (d, *J* = 15 Hz, 1 H, H-CSiMe_3), 1.24 (d, *J* = 15 Hz, 1 H, H-CSiMe_3), 0.03 (s, 9 H, Me_3Si). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.2, 155.3, 137.3, 129.2, 128.9, 128.8, 67.2, 59.5, 53.3, 27.8, 27.5. − MS (70 eV); *m*/*z* (%): 308 (6), 264 (24), 220 (33), 204 (4), 173 (10), 157 (5), 128 (2), 114 (6), 91 (100), 73 (11). − $C_{16}H_{25}NO_4Si$ (323.46): calcd. C 59.41, H 7.79, N 4.33; found C 59.27, H 7.76, N 4.47.

(2S)-Methyl 2-Benzyloxycarbonylamino-3-cyclopropyl-2-methylpropionate (**35**): The disubstituted dihydroimidazole **23** (0.68 g, 2.1 mmol) was, according to *GP4*, deprotected in 1 N TFA/CH_2Cl_2 (32 ml) and hydrolyzed in 2 N TFA/H_2O (8 ml) to give the free amino acid methylester (0.26 g, 79%). After protection of the amino group with benzylchloroformate (0.54 g, 3.1 mmol) in CH_2Cl_2 (10 ml) and 2 N NaOH (1.6 ml), the crude product was purified by FC (hexane/AcOEt, 10:1). The amino acid ester **35** (0.30 g, 49%) was isolated as a colorless oil. − $[\alpha]_D^{r.t.}$ = +15.06 (*c* = 0.83, $CHCl_3$). − IR ($CHCl_3$): 3417*w*, 3007*w*, 2954*w*, 1728*s*, 1502*s*, 1452*s*, 1374*w*, 1327*m*, 1062*s*, 1028*w*. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37−7.30 (m, 5 H, arom. H), 5.76−5.75 (br, 1 H, H-N), 5.09 (s, 2 H, H-C-Ph), 3.74 (s, 3 H, H_3C-O), 2.16−2.02 (m, 1 H), 1.68−1.61 (m, 4 H), 0.61−0.56 (m, 1 H), 0.46−0.38 (m, 2 H), 0.09−0.01 (m, 2 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.8, 154.7, 136.6, 128.5, 128.1, 66.5, 60.4, 52.5, 41.9, 23.4, 6.1, 4.0, 3.7, 1.0. − MS (70 eV); *m*/*z* (%): 232 (6), 200 (2), 192 (4), 188 (7), 184 (5), 181 (3), 169 (1), 156 (13), 140 (4), 129 (3), 108 (15), 91 (100), 81 (21). − $C_{16}H_{21}NO_4$ (290.34): calcd. C 66.19, H 6.94, N 4.82; found C 66.12, H 7.02, N 4.91.

rac-Methyl 2-Benzyloxycarbonylamino-2-methyl-3-phenylpropionate (*rac*-**36**): The disubstituted dihydroimidazole *rac*-**24** (0.84 g, 2.6 mmol) was, according to *GP4*, deprotected in 1 N TFA/CH_2Cl_2 (39 ml) and hydrolyzed in 2 N TFA/H_2O (10 ml) to give the free amino acid methylester (0.45 g, 89%). After protection of the amino group with benzylchloroformate (0.66 g, 3.9 mmol) in CH_2Cl_2 (12 ml) and 2 N NaOH (2.0 ml), the crude product was purified by FC (hexane/AcOEt, 9:1). The amino acid ester *rac*-**36** (0.37 g, 44%) was isolated as a colorless oil. − IR ($CHCl_3$): 3415*w*, 3032*w*, 2954*w*, 1719*s*, 1504*s*, 1452*s*, 1375*w*, 1328*m*, 1280*m*, 1113*m*, 1078*s*, 1059*s*, 986*w*. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39−7.31 (m, 5 H, arom. H), 7.22−7.15 (m, 3 H, arom. H), 6.98−6.95 (m, 2 H, arom. H), 5.49−5.40 (br, 1 H, H-N), 5.17 (d, *J* = 12 Hz, 1 H), 5.08 (d, *J* = 12 Hz, 1 H), 3.74 (s, 3 H, H_3C-O), 3.40 (d, *J* = 13 Hz, 1 H), 3.17 (d, *J* = 13 Hz, 1 H), 1.63 (s, 3 H, H_3C-CN). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.1, 154.7, 136.7, 136.1, 129.9, 128.5, 128.3, 128.1, 127.0, 66.5, 60.9, 52.6, 41.9, 23.7. − MS (70 eV); *m*/*z* (%): 310 (2), 284 (5), 268 (2), 236 (12), 224 (4), 192 (20), 176 (12), 160 (2), 132 (2), 121 (3), 91 (100), 65 (9). − $C_{19}H_{21}NO_4$ (327.38): calcd. C 69.71, H 6.47, N 4.28; found C 69.85, H 6.54, N 4.18.

(2R)-Methyl 2-Amino-2-(4-methoxybenzyl)butyrate (**37**): The disubstituted dihydroimidazole **28** (0.62 g, 1.5 mmol) was, according to *GP4*, deprotected in 1 N TFA/CH_2Cl_2 (23 ml) and hydrolyzed in 2 N TFA/H_2O (6 ml) to give the free amino acid methylester, which was purified by FC (Et_2O/pentane, 2:1). The amino acid ester **37** (0.22 g, 60%) was isolated as a colorless oil. − IR ($CHCl_3$): 3414*w*, 3008*w*, 2957*m*, 2862*w*, 1717*s*, 1612*m*, 1512*s*, 1455*m*, 1346*m*, 1278*m*, 1108*m*, 1085*m*, 1024*s*, 909*w*. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.85 (d, *J* = 8 Hz, 2 H, arom. H), 6.70 (d, *J* = 8 Hz, 2 H, arom. H), 3.78 (s, 6 H, H_3C-O), 3.56 (d, *J* = 14 Hz, 1 H, H-CAr), 3.02 (d, *J* = 14 Hz, 1 H, H-CAr), 1.45−1.28 (m, 2 H, H_2C-CN), 0.89 (t, *J* = 7 Hz, 3 H, H_3C-CH_2). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 173.7, 158.5, 154.3, 136.9, 130.6, 128.5, 113.6, 66.1, 65.5, 55.1, 52.5, 40.2, 35.3, 29.6, 26.3, 22.4, 13.8. − MS (70 eV); *m*/*z* (%): 205 (1), 149 (2), 144 (3), 122 (13), 121 (100), 108 (6), 91 (37), 77 (3), 65 (2).

(2R)-Methyl 2-Benzyloxycarbonylamino-2-(3,5-dimethoxybenzyl)pent-4-encarboxylate (**38**): The disubstituted dihydroimidazole **29** (0.15 g, 0.3 mmol) was, according to *GP4*, deprotected in 1 N TFA/CH_2Cl_2 (5 ml) and hydrolyzed in 2 N TFA/H_2O (2 ml) to give the free amino acid methylester (0.09 g, 98%). After protection of the amino group with benzylchloroformate (85 mg, 0.5 mmol) in CH_2Cl_2 (2 ml) and 2 N NaOH (0.3 ml), the crude product was purified by FC (pentane/Et_2O, 2:1). The amino acid ester **38** (86 mg, 69%) was isolated as a colorless oil. − IR ($CHCl_3$): 3690*w*, 3413*w*, 3008*w*, 2955*w*, 2839*w*, 1716*s*, 1597*s*, 1503*s*, 1457*m*, 1431*m*, 1345*m*, 1153*s*, 1068*s*, 1027*m*, 994*w*, 928*w*, 836*w*. − ^{1}H NMR (300 MHz, [D_6]DMSO, 94.5°C): δ = 7.50 (s, 1 H, H-N), 7.41−7.31 (m, 5 H, arom. H), 6.37 (s, 1 H, arom. H), 6.20 (s, 2 H, arom. H), 5.83−5.69 (m, 1 H, H-C=C), 5.14−5.02 (m, 4 H), 3.66 (s, 6 H, H_3CO-Ar), 3.60 (s, 3 H, H_3CO-CO), 3.15 (d, *J* = 13 Hz, 1 H, H-CAr), 2.95 (d, *J* = 13 Hz, 1 H, H-CAr), 2.44 (dd, *J* = 10 und 7 Hz, 1 H, H_2C-C=C), 2.33 (dd, *J* = 10 und 7 Hz, 1 H, H_2C-C=C). − ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 172.4, 160.0, 154.6, 137.9, 136.9, 132.5, 128.3, 127.8, 127.7, 119.0, 108.2, 98.6, 65.3, 62.5, 54.9, 51.8. − MS (70 eV); *m*/*z* (%): 413 (1) [M^+], 305 (9), 289 (13), 262 (6), 249 (7), 218 (4), 195 (12), 177 (4), 152 (90), 139 (22), 108 (23), 91 (100), 79 (24). − $C_{23}H_{27}NO_6$ (413.47): calcd. C 66.81, H 6.58, N 3.39; found C 66.98, H 6.82, N 3.45.

rac-2-(Cyclohexylmethyl)phenylalanine (*rac*-**39**): The disubstituted dihydroimidazole *rac*-**32** (0.94 g, 2.1 mmol) was heated in 6 N HCl (25 ml) at reflux for 14 h. After evaporation of the solvent using a rotary evaporator and crystallization of the crude product from MeOH/H_2O, the hydrochloride of *rac*-**39** (0.57 g, 91%) was isolated as an amorphous solid. The analytical data were identical to those published in ref.[43].

Michael Additions of BDI to α,β-Unsaturated Phenol Esters

rac-tert-Butyl 2-tert-Butyl-5-[2-(2,6-di-tert-butyl-4-methoxyphenoxycarbonyl)-1-methylethyl]-4-methoxy-2,5-dihydroimidazole-1-carboxylate (*rac*-**40**): After the reaction of *rac*-BDI (1.49 g, 5.8 mmol) with 2,6-di-*tert*-butyl-4-methoxyphenylbut-2-encarboxylate[19] (2.65 g, 8.7 mmol) according to *GP5*, the crude product

(diastereoisomer ratio of 94:6 with respect to the exocyclic stereocenter as determined by ^{1}H-NMR spectroscopy) was purified by FC (pentane/Et_2O, 6:1) giving *rac*-**40** (2.61 g, 80%) as an amorphous solid, m.p. 150.8−152.2°C. − IR ($CHCl_3$): 2964*s*, 1754*m*, 1692*s*, 1595*m*, 1456*m*, 1395*m*, 1364*s*, 1303*m*, 1277*m*, 1149*s*, 1062*m*, 995*w*. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.88 (s, 2 H, arom. H), 5.40−5.39 [br, 1 H, H-C(2)], 4.37−4.34 [br, 1 H, H-C(5)], 3.93 (s, 3 H, H_3C-O), 3.81 (s, 3 H, H_3C-O), 3.52−3.36 (br, 1 H), 2.98−2.63 (m, 2 H), 1.45 (s, 9 H, Me_3C-O), 1.34 (s, 18 H, Me_3C-Ar), 0.94 [s, 9 H, Me_3C-C(2)], 0.82 (d, *J* = 7 Hz, 3 H, H_3C-CH). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.2, 166.7, 156.3, 153.9, 143.5, 143.4, 141.7, 111.7, 88.5, 80.2, 65.5, 55.3, 39.5, 39.2, 35.5, 31.4, 31.3, 28.2, 26.2, 13.5. − MS (70 eV); *m*/*z* (%): 503 (10), 487 (3), 445 (2), 403 (94), 347 (32), 269 (21), 225 (100), 205 (4), 181 (13), 167 (54), 125 (36), 99 (21), 57 (17). − $C_{32}H_{52}N_2O_6$ (560.77): calcd. C 68.54, H 9.35, N 5.00; found C 68.67, H 9.32, N 5.05.

rac-tert-Butyl 2-tert-Butyl-5-[1-(2,6-di-tert-butyl-4-methoxyphenoxycarbonylmethyl)-2-methylpropyl]-4-methoxy-2,5-dihydroimidazole-1-carboxylate (*rac*-**41**): After the reaction of *rac*-BDI (1.38 g, 5.4 mmol) with 2,6-di-*tert*-butyl-4-methoxyphenyl 4-methylpent-2-encarboxylate[19] (2.69 g, 8.1 mmol) according to *GP5*, the crude product (diastereoisomer ratio of 83:17 with respect to the exocyclic stereocenter as determined by ^{1}H-NMR spectroscopy) was purified by FC (hexane/AcOEt, 15:1) giving *rac*-**41** (2.16 g, 68%) as an amorphous solid, m.p. 52.6−53.8°C. − IR ($CHCl_3$): 2964*s*, 1754*m*, 1692*s*, 1590*m*, 1446*m*, 1395*m*, 1364*s*, 1297*m*, 1139*s*, 1062*m*, 1000*m*, 954*w*, 928*w*, 903*w*, 872*w*. − ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 6.81 (s, 2 H, arom. H), 5.18 [d, *J* = 3 Hz, 1 H, H-C(2)], 4.45−4.42 [m, 1 H, H-C(5)], 3.81 (s, 3 H, H_3C-O), 3.73 (s, 3 H, H_3C-O), 2.66−2.60 (m, 1 H), 1.67−1.60 (m, 1 H), 1.39 (s, 9 H, Me_3C-O), 1.27 (s, 18 H, Me_3C-Ar), 0.87 (d, *J* = 7 Hz, 3 H, H_3C-CH), 0.84 [s, 9 H, Me_3C-C(2)], 0.74 (d, *J* = 7 Hz, 3 H, H_3C-CH). − ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 173.1, 167.4, 167.1, 155.8, 152.9, 143.0, 141.1, 111.4, 87.4, 79.3, 62.4, 55.1, 54.9, 37.7, 35.1, 35.0, 31.0, 30.8, 27.8, 26.0, 25.8, 22.0, 17.4. − MS (70 eV); *m*/*z* (%): 531 (10), 515 (3), 487 (3), 473 (2), 431 (100), 375 (43), 297 (16), 253 (88), 236 (37), 221 (16), 195 (51), 181 (8), 153 (44), 126 (7), 99 (15), 57 (18). − $C_{34}H_{56}N_2O_6$ (588.83): calcd. C 69.35, H 9.59, N 4.76; found C 69.44, H 9.70, N 4.89.

rac-tert-Butyl 2-tert-Butyl-5-[2-(2,6-di-tert-butyl-4-methoxyphenoxycarbonyl)-1-phenylethyl]-4-methoxy-2,5-dihydroimidazole-1-carboxylate (*rac*-**42**): After the reaction of *rac*-BDI (1.70 g, 6.6 mmol) with 2,6-di-*tert*-butyl-4-methoxyphenyl 3-phenylacrylate[44] (3.65 g, 10.0 mmol) according to *GP5*, the crude product (diastereoisomer ratio of >98:2 with respect to the exocyclic stereocenter as determined by ^{1}H-NMR spectroscopy) was purified by FC (hexane/AcOEt, 17:1) giving *rac*-**42** (2.90 g, 70%) as an amorphous solid, m.p. 89.6−90.8°C. − IR ($CHCl_3$): 3680*w*, 2968*s*, 1756*m*, 1672*s*, 1591*m*, 1479*m*, 1447*m*, 1416*m*, 1395*m*, 1367*s*, 1298*w*, 1262*w*, 1177*m*, 1136*s*, 1105*m*, 1062*m*, 1024*w*, 990*w*, 960*w*, 872*w*. − ^{1}H NMR (300 MHz, [D_6]DMSO, 94.0°C): δ = 7.27−7.22 (m, 3 H, arom. H), 7.13−7.11 (m, 2 H, arom. H), 6.80 (s, 1 H, arom. H), 6.77 (s, 1 H, arom. H), 4.72−4.68 (br, 1 H), 4.56 (s, 1 H), 3.86 (s, 3 H, H_3C-O), 3.74 (s, 3 H, H_3C-O), 3.31 (d, *J* = 7 Hz, 2 H), 1.48 (s, 9 H, Me_3C-O), 1.28 (s, 9 H, Me_3C-Ar), 1.07 (s, 9 H, Me_3C-Ar), 0.81 [s, 9 H, Me_3C-C(2)]. − ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 172.0, 171.9, 166.2, 165.4, 155.7, 152.7, 152.2, 143.0, 142.9, 141.1, 137.8, 137.5, 128.7, 128.2, 127.9, 127.8, 127.1, 111.2, 87.4, 87.1, 79.5, 65.7, 65.3, 55.2, 54.9, 37.3, 36.8, 36.3, 35.0, 34.7, 31.0, 30.8, 27.9, 27.8, 26.2, 26.0. − MS (70 eV); *m*/*z* (%): 623 (3) [M^+], 565 (11), 549 (3), 523 (10), 465 (77), 409 (24), 331 (21), 311 (7), 287 (100), 255 (9), 236 (57), 205 (10), 187 (43), 155 (31), 131 (64), 99 (48), 57 (13). − $C_{37}H_{54}N_2O_6$ (622.85): calcd. C 71.35, H 8.74, N 4.50; found C 71.31, H 8.66, N 4.41.

Aldol Additions of BDI to Aldehydes

Preparation of erythro Adducts

rac-tert-Butyl 2-tert-Butyl-5-(1-hydroxy-2-methylpropyl)-4-methoxy-2,5-dihydroimidazole-1-carboxylate (*rac*-**43**): The aldol addition of *rac*-BDI (2.06 g, 8.0 mmol) to isobutyric aldehyde (1.45 g, 20.0 mmol) according to *GP6* and purification of the crude product (*erythro*/*threo* = 86:14 according to ^{1}H-NMR spectroscopy) by FC (hexane/AcOEt, 6:1) gave *rac*-**43** (1.14 g, 61%) as an amorphous solid, m.p. 87.8−88.6°C. − IR ($CHCl_3$): 3573*w*, 2978*s*, 1691*s*, 1478*m*, 1445*m*, 1395*s*, 1368*s*, 1265*m*, 1164*m*, 1131*s*, 1076*w*, 993*m*, 943*w*, 888*w*, 854*w*. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.27 [d, *J* = 3 Hz, 1 H, H-C(2)], 4.45−4.34 (m, 2 H), 3.90 (s, 3 H, H_3C-O), 2.55 (d, *J* = 11 Hz, 1 H, *H*O-CH), 1.69−1.56 (m, 1 H, H-CMe_2), 1.48 (s, 9 H, Me_3C-O), 0.99−0.79 (m, 15 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.4, 153.6, 88.5, 80.6, 73.2, 64.5, 55.5, 39.4, 30.0, 28.4, 26.3, 20.3, 17.5. − MS (70 eV); *m*/*z* (%): 271 (8), 255 (5), 229 (4), 215 (8), 197 (48), 171 (8), 153 (59), 143 (80), 111 (8), 99 (100), 84 (9), 57 (17). − $C_{17}H_{32}N_2O_4$ (328.45): calcd. C 62.17, H 9.82, N 8.53; found C 61.93, H 9.67, N 8.43.

rac-tert-Butyl 2-tert-Butyl-5-(1-hydroxy-2,2-dimethylpropyl)-4-methoxy-2,5-dihydroimidazole-1-carboxylate (*rac*-**44**): The aldol addition of *rac*-BDI (1.28 g, 5.0 mmol) to pivalaldehyde (1.08 g, 12.5 mmol) according to *GP6* and purification of the crude product (*erythro*/*threo* = >98:2 according to ^{1}H-NMR spectroscopy) by FC (hexane/AcOEt, 10:1) gave *rac*-**44** (0.14 g, 8%) as an amorphous solid, m.p. 86.2−87.2°C. − IR ($CHCl_3$): 3676*w*, 3485*w*, 2976*s*, 1703*m*, 1662*s*, 1479*m*, 1394*s*, 1367*s*, 1334*s*, 1165*m*, 1122*m*, 1080*m*, 997*s*, 926*w*, 878*w*. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 5.23 [s, 1 H, H-C(2)], 4.48 [d, *J* = 7 Hz, 1 H, H-C(5)], 3.83 (s, 3 H, H_3C-O), 3.25−3.14 (m, 1 H), 3.12−3.02 (m, 1 H), 1.48 (s, 9 H, Me_3C-O), 1.02 (s, 9 H, Me_3C-COH), 0.96 [s, 9 H, Me_3C-C(2)]. − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.7, 157.6, 89.7, 81.7, 63.1, 55.5, 36.6, 35.8, 28.4, 26.3, 26.1. − MS (70 eV); *m*/*z* (%): 285 (7), 269 (3), 229 (35), 211 (4), 199 (23), 185 (18), 155 (5), 143 (100), 99 (46), 84 (7), 57 (7). − $C_{18}H_{34}N_2O_4$ (342.48): calcd. C 63.13, H 10.01, N 8.18; found C 63.16, H 9.92, N 8.12.

rac-tert-Butyl 2-tert-Butyl-5-(cyclohexylhydroxymethyl)-4-methoxy-2,5-dihydroimidazole-1-carboxylate (*rac*-**45**): The aldol addition of *rac*-BDI (2.19 g, 8.5 mmol) to cyclohexane carbaldehyde (2.39 g, 21.3 mmol) according to *GP6* and purification of the crude product (*erythro*/*threo* = 67:33 according to ^{1}H-NMR spectroscopy) by FC (pentane/Et_2O, 2:1) gave *rac*-**45** (1.07 g, 62%) as an amorphous solid, m.p. 143.2−145.0°C. − IR ($CHCl_3$): 3675*w*, 3569*w*, 2930*s*, 2856*m*, 1694*s*, 1672*s*, 1479*w*, 1447*m*, 1395*m*, 1368*s*, 1263*m*, 1168*m*, 1131*m*, 1077*w*, 991*m*, 949*w*, 930*w*, 890*w*, 856*w*. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.28 [d, *J* = 3 Hz, 1 H, H-C(2)], 4.43−4.41 (m, 2 H), 3.91 (s, 3 H, H_3C-O), 2.57 (d, *J* = 11 Hz, 1 H, *H*O-CH), 1.72−1.65 (m, 5 H), 1.48 (s, 9 H, Me_3C-O), 1.21−1.15 (m, 6 H), 0.92 [s, 9 H, Me_3C-C(2)]. − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.6, 153.5, 88.5, 80.5, 72.8, 64.2, 55.5, 39.9, 39.4, 30.3, 28.3, 27.4, 26.9, 26.5, 26.2. − MS (70 eV); *m*/*z* (%): 311 (9), 295 (3), 255 (7), 237 (100), 211 (6), 193 (35), 155 (11), 143 (86), 111 (9), 99 (99), 84 (13). − $C_{20}H_{36}N_2O_4$ (368.52): calcd. C 65.19, H 9.85, N 7.60; found C 65.05, H 9.81, N 7.63.

The bicyclic compound *rac*-**49** (0.21 g, 15%) with a diastereoisomer ratio of >98:2 was also formed during this reaction.

rac-tert-Butyl 2-tert-Butyl-5-(hydroxyphenylmethyl)-4-methoxy-2,5-dihydroimidazole-1-carboxylate (*rac*-**46**): The aldol addition of

rac-BDI (2.05 g, 8.0 mmol) to benzaldehyde (2.13 g, 20.0 mmol) according to *GP6* and purification of the crude product (*erythro*/*threo* = 91:9 according to ^{1}H-NMR spectroscopy) by FC (pentane/Et_2O, 3:1) gave *rac*-**46** (2.54 g, 88%) as an amorphous solid. All analytical data were identical to those published in ref.[11].

Preparation of Bicyclic Carbamates

rac-5-tert-Butyl-1-isopropyl-7-methoxy-5,7a-dihydro-1H-imidazo-[1,5-c]oxazol-3-one (*rac*-**47**): The reaction of *rac*-BDI (2.01 g, 7.9 mmol) and isobutyric aldehyde (1.42 g, 19.6 mmol) according to *GP7* and purification of the crude product (diastereoisomer ratio of >98:2 with respect to the stereocenter at C(1) as determined by ^{1}H-NMR spectroscopy) by FC (pentane/Et_2O, 3:1) gave *rac*-**47** (0.72 g, 36%) as a colorless oil. − IR ($CHCl_3$): 2968*m*, 2873*w*, 1755*s*, 1651*s*, 1464*w*, 1444*w*, 1366*m*, 1341*m*, 1319*m*, 1276*m*, 1135*w*, 1087*w*, 1061*w*, 1028*m*, 986*m*, 954*w*, 920*w*, 882*w*. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.10 (s, 1 H), 4.50 (s, 2 H), 3.92 (s, 3 H, H_3C-O), 2.15−2.02 (m, 1 H, *H*-CMe_2), 1.08 (d, *J* = 8 Hz, 3 H, H_3C-CH), 0.95 (s, 9 H, Me_3C-C), 0.93 (d, *J* = 8 Hz, 3 H, H_3C-CH). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 167.1, 162.5, 92.8, 82.7, 63.9, 56.5, 36.7, 29.4, 25.1, 19.9, 16.3. − MS (70 eV); *m*/*z* (%): 239 (1), 211 (3), 197 (100), 153 (94), 138 (9), 125 (5), 111 (13), 99 (27), 57 (4).

The aldol adduct *rac*-**43** (0.12 g, 5%) with *erythro*:*threo* > 98:2 was also formed during this reaction.

rac-1,5-Di-tert-butyl-7-methoxy-5,7a-dihydro-1H-imidazo[1,5-c]-oxazol-3-one (*rac*-**48**): The reaction of *rac*-BDI (2.27 g, 8.8 mmol) and pivalaldehyde (1.91 g, 22.1 mmol) according to *GP7* and purification of the crude product (diastereoisomer ratio of >98:2 with respect to the stereocenter at C(1) as determined by ^{1}H-NMR spectroscopy) by FC (pentane/Et_2O, 5:1) gave *rac*-**48** (1.87 g, 79%) as a colorless solid, m.p. 86.6−87.4°C. − IR (KBr): 2966*m*, 1749*s*, 1648*s*, 1438*w*, 1364*m*, 1331*m*, 1317*m*, 1277*m*, 1238*m*, 1157*w*, 1104*w*, 1028*w*, 1007*w*, 984*m*, 881*w*, 795*w*, 758*w*. − ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 4.93 (d, *J* = 3 Hz, 1 H), 4.79 (dd, *J* = 9 und 3 Hz, 1 H), 4.63 (d, *J* = 9 Hz, 1 H), 3.87 (s, 3 H, H_3C-O), 0.96 (s, 9 H, Me_3C-C), 0.88 (s, 9 H, Me_3C-C). − ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 167.0, 161.3, 91.3, 85.4, 63.1, 56.3, 36.3, 33.4, 24.8, 24.6. − MS (70 eV); *m*/*z* (%): 253 (1), 211 (50), 155 (6), 99 (100), 84 (4), 69 (14), 57 (12), 41 (17), 29 (7). − $C_{14}H_{24}N_2O_3$ (268.36): calcd. C 62.66, H 9.01, N 10.44; found C 62.89, H 8.89, N 10.35.

The aldol adduct *rac*-**44** (0.11 g, 5%) with *erythro*/*threo* > 98:2 was also formed during this reaction.

rac-5-tert-Butyl-1-cyclohexyl-7-methoxy-5,7a-dihydro-1H-imidazo[1,5-c]oxazol-3-one (*rac*-**49**): The reaction of *rac*-BDI (2.27 g, 8.8 mmol) and cyclohexane carbaldehyde (2.49 g, 22.2 mmol) according to *GP7* and purification of the crude product (diastereoisomer ratio of 67:33 with respect to the stereocenter at C(1) as determined by ^{1}H-NMR spectroscopy) by FC (hexane/AcOEt, 7:1) gave *rac*-**49** (1.10 g, 78%) as a colorless solid, m.p. 125.2−126.4°C. − IR ($CHCl_3$): 3682*w*, 3026*w*, 2933*m*, 2862*w*, 1754*s*, 1651*s*, 1600*w*, 1446*w*, 1380*w*, 1364*w*, 1344*m*, 1323*m*, 1277*m*, 1139*w*, 1062*w*, 1010*w*, 990*m*, 928*w*. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.09 (s, 1 H), 4.50 (s, 2 H), 3.92 (s, 3 H, H_3C-O), 1.80−1.60 (m, 6 H), 1.26−1.13 (m, 5 H), 0.96 (s, 9 H, Me_3C-C). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.2, 162.4, 92.8, 82.0, 63.8, 56.5, 39.1, 36.7, 30.4, 26.7, 26.1, 25.9, 25.5, 25.2. − MS (70 eV); *m*/*z* (%): 237 (100), 193 (44), 166 (4), 155 (10), 111 (9), 99 (41). − $C_{16}H_{26}N_2O_3$ (294.39): calcd. C 65.28, H 8.90, N 9.52; found C 65.43, H 9.00, N 9.60.

rac-5-tert-Butyl-7-methoxy-1-phenyl-5,7a-dihydro-1H-imidazo-[1,5-c]oxazol-3-one (*rac*-**50**): The reaction of *rac*-BDI (2.21 g, 8.6 mmol) and benzaldehyde (2.29 g, 21.6 mmol) according to *GP7* and purification of the crude product (diastereoisomer ratio of >98:2 with respect to the stereocenter at C(1) as determined by ^{1}H-NMR spectroscopy) by FC (hexane/AcOEt, 9:1) gave *rac*-**50** (0.65 g, 26%) as a colorless solid, m.p. 135.4−135.8°C. − IR (KBr): 2968*m*, 1747*s*, 1653*s*, 1459*m*, 1445*m*, 1385*m*, 1363*m*, 1331*m*, 1303*m*, 1255*w*, 1236*m*, 1213*w*, 1160*m*, 1065*m*, 1001*m*, 983*m*, 926*m*, 887*w*, 795*w*, 770*w*, 758*m*, 740*m*, 695*m*. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36−7.34 (m, 3 H, arom. H), 7.18−7.15 (m, 2 H, arom. H), 5.71 (d, *J* = 9 Hz, 1 H), 5.17 (d, *J* = 3 Hz, 1 H), 4.82 (dd, *J* = 9 und 3 Hz, 1 H), 3.35 (s, 3 H, H_3C-O), 0.97 (s, 9 H, Me_3C-C). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.4, 162.2, 135.4, 129.1, 128.5, 125.9, 93.3, 79.3, 66.1, 55.8, 36.9, 25.2. − MS (70 eV); *m*/*z* (%): 231 (73), 187 (100), 155 (10), 130 (52), 117 (5), 103 (19), 90 (7), 77 (12), 70 (4), 57 (12), 41 (14), 29 (9). − $C_{16}H_{20}N_2O_3$ (288.35): calcd. C 66.65, H 6.99, N 9.72; found C 66.90, H 7.08, N 9.54.

The aldol adduct *rac*-**46** (1.63 g, 52%) with *erythro*/*threo* > 98:2 was also formed during this reaction.

Preparation of erythro-α-Amino-β-hydroxy Acids

erythro-2-Amino-3-hydroxy-4-methylpentanoic Acid (*rac*-**51**): The aldol adduct *rac*-**43** (0.13 g, 0.4 mmol) was hydrolyzed in 6 N HCl (10 ml) according to *GP8*. After purification of the crude product by ion exchange chromatography (Dowex 50Wx8) the amino acid *rac*-**51** (57 mg, 97%) was isolated as an amorphous solid. All analytical data were identical to those published in ref.[32].

erythro-2-Amino-3-hydroxy-3-phenylpropionic Acid (*rac*-**52**): The aldol adduct *rac*-**46** (0.54 g, 1.5 mmol) was hydrolyzed in 6 N HCl (15 ml) according to *GP8*. After purification of the crude product by ion exchange chromatography (Dowex 50Wx8) the amino acid *rac*-**52** (0.25 g, 92%) was isolated as an amorphous solid. All analytical data were identical to those published in ref.[33].

☆ Dedicated to Professor *Wolfgang Steglich* on the occasion of his 65th birthday.

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[12] ...mainly due to the fact that it was difficult to exceed enantiomer ratios above 97:3.

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[14] The absolute configuration of (*R*)- and (*S*)-**1** was determined from the X-ray crystal structure of the salt **3** (P. Seiler, X-ray service of our laboratory)[11]. It also follows from the compari-

son of amino acid esters, synthesized from BDI, with authentic enantiopure samples of known configuration.
[15] For the isolation and characterization of the racemic as well as of the enantiopure (*Z*)-analogs of **2** and of BDI see ref.[10].
[16] Most mono- and dialkylated BDI derivatives are oils which may partially decompose upon distillation. The yields given in Scheme 3 and 5 refer to analytically pure chromatographed samples.
[17] The structure of enantiopure **14** (Scheme 3) with *p*-nitrobenzyl instead of *p*-methoxybenzyl as the substituent was determined by *B. Rheiner*, as part of the requirements in a crystallography course at ETH Zürich, **1992**.
[18] With Li-Boc-BMI, *Fitzi* had obtained the product of alkylation with *rac*-1-phenylethylbromide in 68% yield and with a diastereoisomer ratio of 92.5:7.5[4]; see the mechanistic discussion in footnote 43 of [19]. For another enantiomer differentiation of an alkyl halide by a chiral oxazoline see: A. I. Meyers, K. Kamata, *J. Am. Chem. Soc.* **1976**, *98*, 2290−2294.
[19] K. Suzuki, D. Seebach, *Liebigs Ann. Chem.* **1992**, 51−61.
[20] Various amounts and concentrations of hydrochloric acid, trifluoro acetic acid (TFA) and acidic ion exchange resin in aqueous methanol, aqueous THF and water were tested.
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[22] The amino acid methyl ester obtained after hydrolysis of dihydroimidazole derivative **9** was Boc-protected in order to avoid possible loss of the acetylenic Me_3Si-protection under the conditions of introducing the (*Z*) group. Only the amino acid ester *rac*-**16** could be obtained in analytically pure form as such (bulb-to-bulb destillation at high vacuum). A protection of the amino functionality followed by flash chromatography was therefore not necessary in this case. In all other cases (also with the α-branched amino acid esters shown in Scheme 6) the (*Z*) protecting group was introduced in order to obtain analytically pure samples of the esters **F** and **H**.
[23] Formation of diketopiperazines by dimerization of amino acid methyl esters **F** was not observed. The poor overall yields of (*Z*)-protected esters (see Experimental Part) is partially due to losses caused by water-solubility of the esters **F**.
[24] L-Alanine, L-valine, and L-phenylalanine methyl ester (as obtained from (*S*)-(+)-BDI) were characterized by gas chromatography following the literature procedure: S. Abdalla, E. Bayer, H. Frank, *Chromatographia* **1987**, *23*, 83−85.
[25] The crystal structure of the product with $R^1 = CH_2C_6H_5$, $R^2 = CH_3$ (5-*epi*-**24**) was determined by *B. Rheiner*, as part of the requirements in a crystallography course at ETH Zürich, **1992**.
[26] The methodology of using BDI as a chiral building block in amino acid synthesis clearly employs milder hydrolysis conditions than all the other methods developed in our group, so far, and also than many other synthetic methods found in the literature (for an overview see ref.[1][5]).
[27] D. Seebach, E. Pfammatter, V. Gramlich, T. Bremi, F. Kühnle, S. Portmann, I. Tironi, *Liebigs. Ann. Chem.* **1992**, 1145−1151.
[28] For results and a detailed mechanistic discussion of *Michael* additions to di-*tert*-butylphenol esters see ref.[19] and references to *Heathcock'*s and *Cooke'*s work therein.
[29] See also our other papers on carbonyl derivatives with "sterically protected but electronically active" CO groups, reference 10 in ref.[19].
[30] At this temperature pivalaldehyde reacted very slowly with enaminate **E**, giving rise to the product *rac*-**44** in only 8% yield.
[31] For *erythro*-hydroxyleucine see ref.[32] and for *erythro*-hydroxyphenylalanine see ref.[33].
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[33] A. Saeed, D. W. Young, *Tetrahedron* **1992**, *48*, 2507−2514.
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[35] The two diastereomeric Li-alkoxides formed in the original addition step are expected to cyclize with different rates, and, indeed, the ratios of epimers detected in the two types of products **43**−**46** and **47**−**50** are different.
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