

## 95. Synthesis and First Applications of a New Chiral Auxiliary (*tert*-Butyl 2-(*tert*-Butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate)

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Both enantiomers of *tert*-butyl 2-(*tert*-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate (**11**; Bbdmoic) were prepared from L-alanine (Schemes 1 and 2). The parent heterocycle, 2-*tert*-butyl-5,5-dimethylimidazolidin-4-one (**12**; from 2-aminoisobutyramide, H-Aib-NH<sub>2</sub>, and pivalaldehyde) was also available in both enantiomeric forms by resolution with *O,O'*-dibenzoyltartaric acid. The compound (*R*)- or (*S*)-**11** was used as an auxiliary, but also as a chiral Aib building block in a dipeptide synthesis. The 3-propanoyl derivative **13** of (*R*)-**11** was used for the preparation of enantiomerically pure 2-methyl-3-phenylpropanoic acid (enantiomer ratio (e.r.) 99.5:0.5), by benzylation of the Zn-enolate ( $\rightarrow$  **14**; Scheme 3). Oxidative coupling of the bis-enolate derived from heptanedioic acid and (*S*)-**11** ( $\rightarrow$  **23**) and methanolysis of the auxiliary gave dimethyl *trans*-cyclopentane-1,2-dicarboxylate (**26**) with an e.r. of 93:7 (Scheme 5, Fig. 5). The 3-(Boc-Gly)-Bbdmoic derivative **29** was doubly deprotonated and, after addition of ZnBr<sub>2</sub> alkylated with alkyl, benzyl, or allyl halides to give the higher amino-acid derivatives with excellent selectivities (e.r. > 99.5:0.5, Schemes 6 and 7). Michael additions of cuprates to [(*E*)-MeCH=CHCO]-Bbdmoic **36** occurred in high yields, but high diastereoselectivities were only observed with aryl cuprates (diastereoisomer ratio (d.r.) 99:1 for R = Ph, Scheme 8). Finally, 3-(Boc-CH<sub>2</sub>)-Bbdmoic **17** was alkylated through the ester Li-enolate with primary and secondary alkyl, allyl, and benzyl halides with diastereoselectivities (ds) ranging from 91 to 98%, giving acetals of Boc-Aib-Xxx-O(*t*-Bu) dipeptides (Scheme 4). The effectiveness of Bbdmoic is compared with that of other chiral auxiliaries previously used for the same types of transformations.

**1. Introduction.** – Since the first reports of chiral-auxiliary-induced stereoselective reactions in the early 20th century by McKenzie [1], many 'chiral inductors' have been developed and successfully applied in asymmetric synthesis. The chemistry of auxiliary-controlled stereoselective reactions (covalently bound) has been reviewed by several authors [2–8]. Normally, these chiral auxiliaries are derived from natural sources such as amino acids [2] [3], carbohydrates [4] [5], terpenes [6], and steroids [9]. Synthetic auxiliaries that can be recovered after a reaction have also been described [7] [8] [10–13]. In Fig. 1, a collection of successfully applied chiral auxiliaries is presented.

During the last ten years, we have developed various chiral building blocks, based on five-membered heterocycles, oxazolidinones [28], and imidazolidinones [29], for the preparation of enantiomerically pure natural and unnatural amino acids. In the present paper, we report the synthesis and some applications of a new chiral auxiliary which is based on the imidazolidinones.

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<sup>2</sup>) Part of the laboratory-course work of T. H., ETH Zürich, 1994.

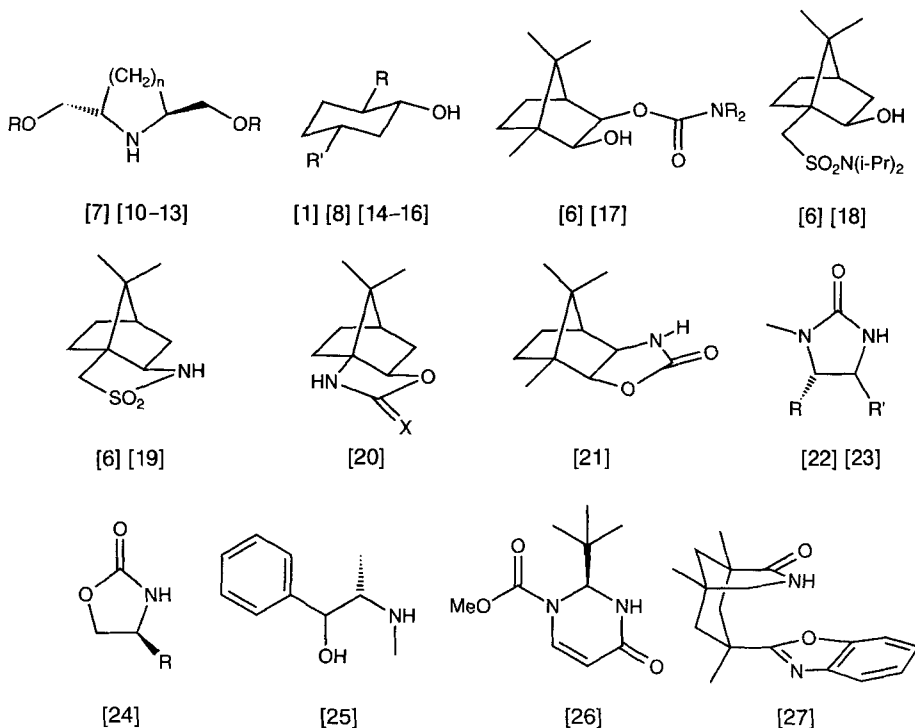
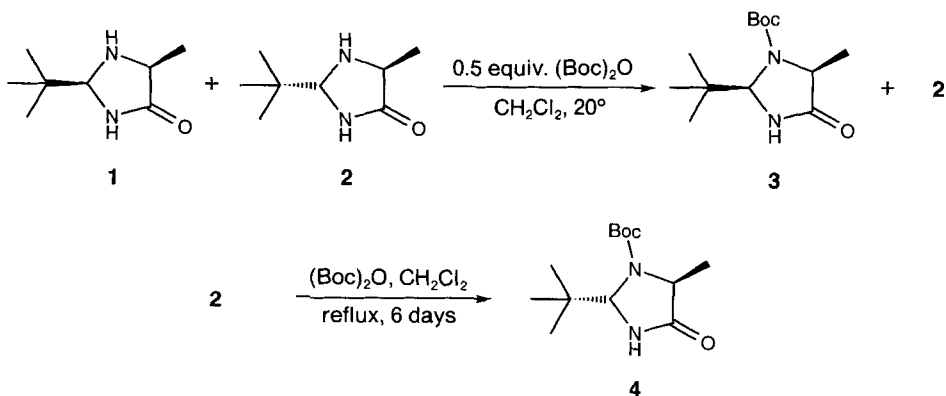


Fig. 1. Some chiral auxiliaries

**2. Synthesis of the Chiral Auxiliary.** – The *cis*-imidazolidinone **1** and the epimeric *trans*-derivative **2** were prepared according to the published procedure [30] in a *ca.* 1:1 ratio from *L*-alaninamide hydrochloride and pivalaldehyde (= 2,2-dimethylpropanal). Diastereoselective introduction of the (*tert*-butoxy)carbonyl (Boc) group using 1 equiv. of di(*tert*-butyl) dicarbonate ((Boc)<sub>2</sub>O) with respect to the *cis*-isomer **1** afforded the pro-

Scheme 1. Synthesis of the Boc-Protected *cis*- and *trans*-Imidazolidinones **3** and **4**

tected imidazolidinone **3** and the unreacted **2** both in high yield (*Scheme 1*)<sup>3</sup>. The *trans*-isomer **2** was transformed to the corresponding Boc-protected imidazolidinone **4** under more rigorous conditions (refluxing  $\text{CH}_2\text{Cl}_2$ , 6 days!).

The difference between the reactivity of the isomers **1** and **2** can be understood either by consideration of the structure of the unprotected imidazolidinones **1** and **2** or by analysis of the possible conformations of the corresponding products **3** and **4**. The first step of the transformation is the reaction of  $(\text{Boc})_2\text{O}$  with the secondary amino group leading to the intermediates **5** (from **1**) and **6** (from **2**; see *Fig. 2*). There is no doubt that the attack of the carbamoylating reagent occurs from the face opposite to the sterically demanding *t*-Bu group of the imidazolidinones **1** and **2**. In the case of the *trans*-isomer **2**, this face is shielded by the Me group in the 4-position of the heterocycle. We have

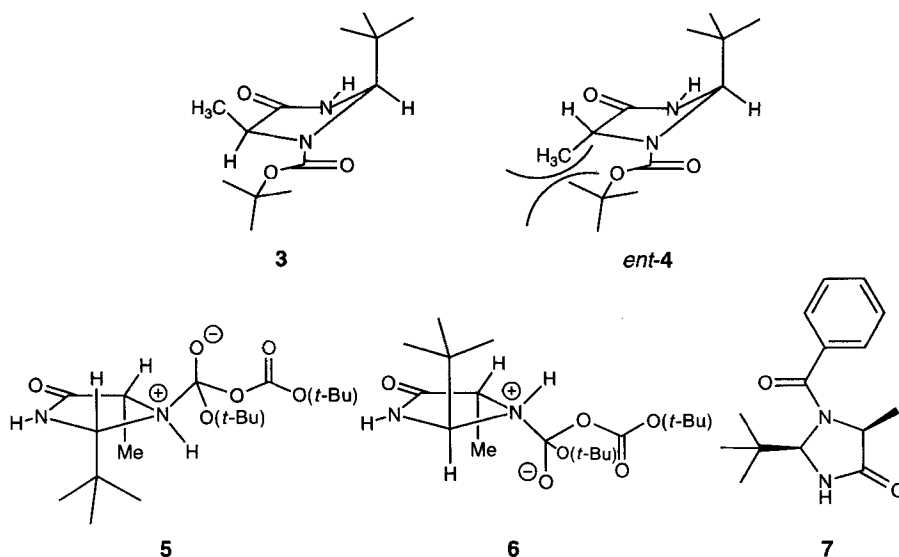


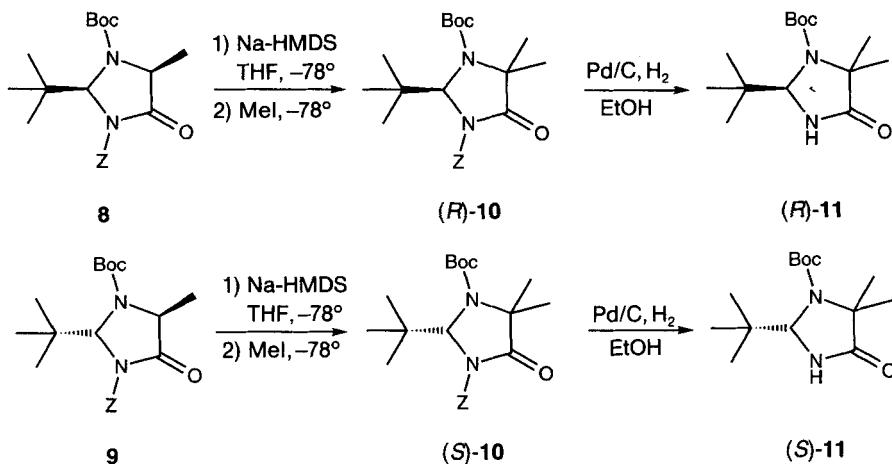
Fig. 2. Intermediates **5** (from **1**) and **6** (from **2**), possible conformations of imidazolidinones **3** and *ent*-**4** (for better comparison, the enantiomer of **4** is shown), and derivative **7** of *cis*-isomer **1**

previously shown that the conformation of *N*-acylated (or *N*-carbamoylated) oxazolidinones and imidazolidinones are quite similar with a quasixial *t*-Bu group ( $A^{1,3}$ -effect), pyramidalization of the N-atoms, and the *N*-acyl or (*N*-carbamoyl) carbonyl O-atom in a *s-cis*-conformation with respect to the *t*-Bu-substituted O, O- or N, O-acetal C-atom [32]. This explains that in the transformation of **1/2** with  $(\text{Boc})_2\text{O}$  the *trans*-isomer (see *ent*-**4** in *Fig. 2*) is the thermodynamically unfavored product compared to the *cis*-derivative **3** due to steric interaction between the Me group and the *t*-BuO of the Boc group. The assignment of the configuration at the N,N-acetal center is based on NOE experiments on the Boc-protected *trans*-isomer **4** and the *cis*-benzoyl-imidazolidinone **7** (from **1**).

<sup>3</sup>) This type of diastereoselective Boc protection has already been observed by Agami and coworkers on a related five-membered ring system [31].

The last step in the synthesis of the auxiliary is the introduction of a Me group at the 4-position of the imidazolidinone thus destroying the original stereogenic center derived from alanine<sup>4</sup>). Deprotonation of the amide H-atom with BuLi and carbamoylation with benzyloxycarbonyl chloride (Z-Cl) gave the doubly protected imidazolidinones **8** (from **3**) and **9** (from **4**) in high yields. Methylation (sodium hexamethyldisilazide (Na-HMDS), MeI;  $\rightarrow$ **10**) and hydrogenolysis ( $H_2$ , Pd/C) afforded the auxiliaries (*R*)-**11** (from **8**) and (*S*)-**11** (from **9**) in enantiomerically pure forms<sup>5</sup>) (Scheme 2).

Scheme 2. Transformation of the Diastereoisomeric Doubly Protected Imidazolidinones **8** and **9** to the Enantiomeric Chiral Auxiliaries **11**



We have also applied a resolution approach to the new auxiliaries **11**. Similar imidazolidinones such as **A** [29b], **B** [29b], and **C** [30] have been successfully resolved in our group (Fig. 3). Thus, the precursor *rac*-**12** of the auxiliaries **11** was prepared from 2-aminoisobutyramide (= 2-amino-2-methylpropanamide; H-Aib-NH<sub>2</sub>)<sup>6</sup>) and pivalalde-

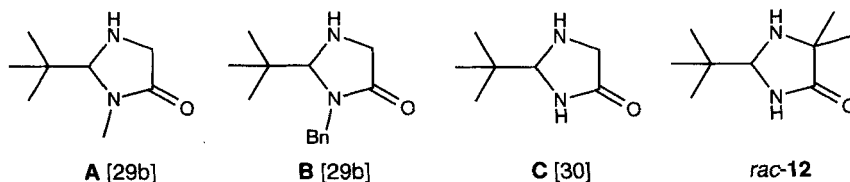


Fig. 3. Imidazolidinones **A–C** derived from glycine (resolution with mandelic acid (**A**), with the diacetonide of gulonic acid (**B**), and with camphorsulfonic acid (**C**)) and imidazolidinone *rac*-**12** derived from the achiral 2-aminoisobutyric acid (Aib; resolution with *O,O'*-dibenzoyltartaric acid)

<sup>4</sup>) Attempts to use the imidazolidinones **3** and **4** as chiral auxiliaries in the diastereoselective alkylation of their corresponding propanamides (see below) were unsuccessful. In addition, the presence of two Me groups protects the ring-bound carbonyl functionality of the auxiliary against nucleophilic attack.

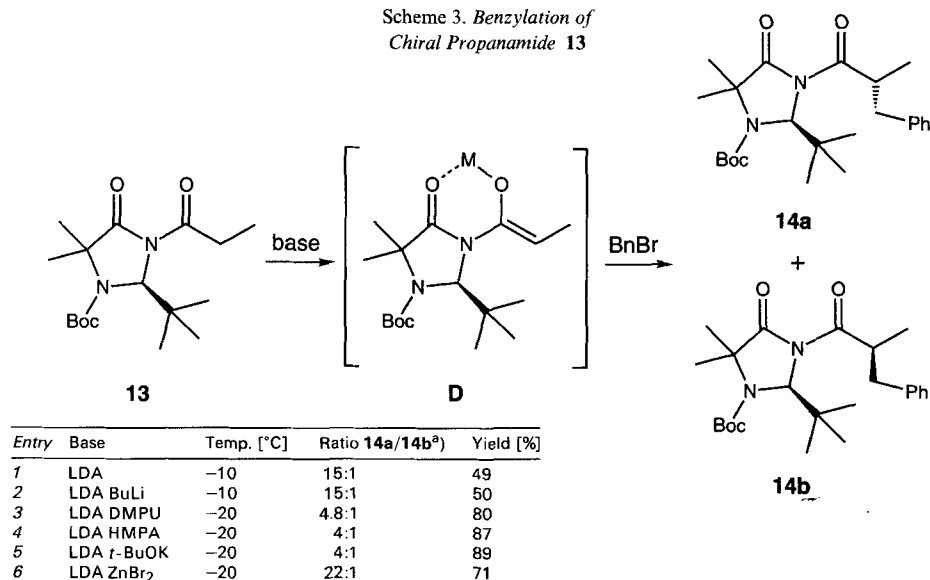
<sup>5</sup>) The enantiomer purity was checked by HPLC using a chiral column (*Chiracel OD*, see *Exper. Part*).

<sup>6</sup>) The 2-aminoisobutyramide was prepared according to the published procedure from acetone, KCN, NH<sub>4</sub>Cl, and H<sub>2</sub>SO<sub>4</sub> [33] [34].

hyde, using a procedure similar to that used for the synthesis of the isomers **1** and **2** (see above). The enantiomers of the Aib-derived imidazolidinone *rac*-**12** were separated by crystallization of their diastereoisomeric salts from ethyl methyl ketone as solvent. *O,O'*-Dibenzoyltartaric acid<sup>7)</sup> turned out to be the best resolving agent. A solution of *rac*-**12** and *O,O'*-dibenzoyl tartaric acid (1:0.5 molar ratio of base and acid) formed by dissolution in boiling ethyl methyl ketone (1 mmol/ml) was allowed to stand at room temperature for 24 h. The diastereoisomeric salt of *like*-configuration, containing the (*R,R*)-enantiomer of tartrate and the (*R*)-**12** crystallized preferentially (see *Exper. Part*). Thus, (*R*)-**12** was isolated with a 90:10 enantiomer ratio (e.r.)<sup>8)</sup> and in 33% yield (66% of theoretical yield). Enantiomer (*S*)-**12** was recovered from the mother liquor. After a second crystallization step (enriched (*R*)-**12** and (*R,R*)-diacid, or enriched (*S*)-**12** and (*S,S*)-diacid), the imidazolidinones (*R*)-**12** and (*S*)-**12** were obtained with an e.r. of 97:3. No further improvement of the enantiomer purity was observed on additional crystallization with or without chiral acid. Unfortunately, we did not succeed in protecting (by Boc) the secondary amino moiety of **12** without partial loss of enantiomer purity, but attempts to solve this problem are in progress.

**3. Diastereoselective Alkylations.** – A typical reaction for studying the potential of a new chiral auxiliary is the alkylation of its propanoic-acid derivative. For almost every auxiliary, the corresponding results were published [10] [12] [17] [24c] [25] [26]. We, therefore, decided to study this reaction first. Deprotonation (BuLi) of the auxiliary (*R*)-**11** and propanoylation (propanoyl chloride) afforded the chiral propanamide **13** in

Scheme 3. Benzylation of  
Chiral Propanamide **13**



<sup>a)</sup> The ratio was determined by HPLC (Entry 6) or by <sup>1</sup>H-NMR analysis of the crude product (Entries 1–5).

<sup>7)</sup> *O,O'*-Dibenzoyltartaric acid is commercially available in both enantiomeric forms.

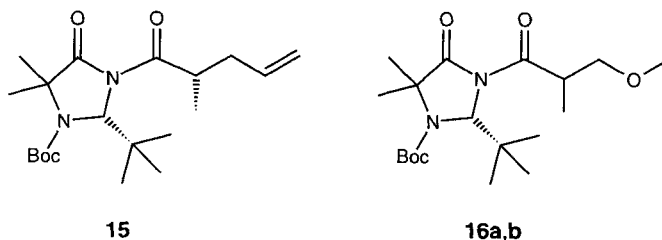
<sup>8)</sup> The e.r. was determined by HPLC using a chiral column (*Chiracel OD*).

high yield (*Scheme 3*). We first tried the benzylation of the propanoic-acid derivative **13** with different bases (see *Scheme 3*). It turned out that the enolates **D** ( $M = \text{Li}, \text{K}, \text{ZnBr}$ ) were very unreactive<sup>9</sup>). Alkylation ( $\text{PhCH}_2\text{Br}$ ) only occurred at temperatures above  $-20^\circ\text{C}$ <sup>10</sup>). With lithium diisopropylamide (LDA, *Entry 1*), the desired product **14a** was formed in 49% yield in high diastereoselectivity (94% ds, diastereoisomer ratio (d.r.) 15:1). In addition, more than 30% of the starting material was recovered. The addition of 1 equiv. of BuLi to the LDA-generated enolate [29d] [35] showed no significant effect (*Entry 2*). Better yields but lower selectivities were observed in the presence of cosolvents tetrahydro-1,3-dimethylpyrimidin-2(1*H*)-one (DMPU) [36] or hexamethylphosphoric triamide (HMPA, *Entries 3 and 4*) or by using the K-enolate (*Entry 5*). Best results were obtained by using the Zn-enolate generated by transmetallation of the Li-enolate (LDA) with  $\text{ZnBr}_2$  (96% ds, d.r. 22:1; 71% yield, *Entry 6*).

For determining the absolute configuration at the newly formed stereogenic center the main product of benzylation, **14a**, was transformed to 2-methyl-3-phenylpropanoic acid by applying a published procedure ( $\text{H}_2\text{O}_2/\text{LiOH}$ , 96% yield) [37]. The auxiliary (*R*)-**11** was recovered in enantiomerically pure form (88% yield). The (*R*)-enantiomer of the propanoic-acid derivative was obtained in 99% ee by comparison with the reported value of the optical rotation of (*S*)-2-methyl-3-phenylpropanoic acid [26].

Using the conditions optimized for the benzylation of **13**, we next investigated the alkylation of the propanamide *ent*-**13** via *ent*-**D** ( $M = \text{ZnBr}$ ) with various electrophiles (*Fig. 4*). Allylation (allyl bromide) gave the pentenoic-acid derivative **15** in 97% diastereoselectivity as determined by HPLC (76% yield)<sup>11</sup>), and the reaction with  $\text{MeOCH}_2\text{Cl}$  ( $\text{S}_\text{N}1$  reagent) afforded **16a/16b** in moderate selectivity (82% ds, 49% yield). The isomers **16a** and **16b** were separated and characterized, but we have not determined their configuration. With less reactive alkyl halides like EtI and PrI, no product was formed.

We previously showed that dipeptides can selectively be alkylated, if one amino acid is part of an imidazolidinone ring [38]<sup>12</sup>). Using the procedure described for the preparation of the propanoic-acid derivative **13** (see above), dipeptide derivative **17** was prepared by



*Fig. 4. Alkylation products 15 and 16a,b of the Zn-enolate ent-D (M = ZnBr) with allyl bromide and MeOCH<sub>2</sub>Cl, respectively*

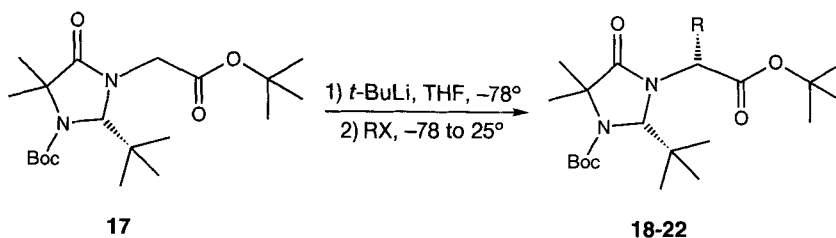
<sup>9</sup>) Compare also the low reactivity of the *Evans* Li-enolates [24c].

<sup>10</sup>) At  $0^\circ$ , the auxiliary was formed as the main product (decomposition of the enolate via ketene formation!).

<sup>11</sup>) The absolute configuration of the allylation product **15** was assigned by analogy with the benzylation product and was not experimentally proved.

<sup>12</sup>) For the alkylation of larger peptides and of cyclotetrapeptides, see [36b] [39].

treatment of the Li-amide of (*S*)-**11** with *tert*-butyl bromoacetate (94% yield). Ester-enolate formation with LDA ( $-78^{\circ}$ ) and treatment with benzyl bromide afforded the phenylalanine-containing dipeptide **18** ( $R = \text{PhCH}_2$ ) with 97% diastereoselectivity and in acceptable yield (56%). In addition to the benzylation product, more than 20% of starting material was recovered. The addition of DMPU [36] to the Li-enolate led to lower selectivity (83% ds). With Na-HMDS (97% ds), the yield decreased to 45%<sup>13</sup>). The highest yield (84%) was obtained with *t*-BuLi (96% ds, Scheme 4). Using these optimized conditions for enolate formation (*t*-BuLi), we also tested other electrophiles, *i.e.*, MeI ( $\rightarrow$  **19**),  $\text{CH}_2=\text{CHCH}_2\text{Br}$  ( $\rightarrow$  **20**), BuI ( $\rightarrow$  **21**), and *i*-PrI ( $\rightarrow$  **22**; Scheme 4).

Scheme 4. Diastereoselective Alkylation of the Chiral Dipeptide Derivative **17**

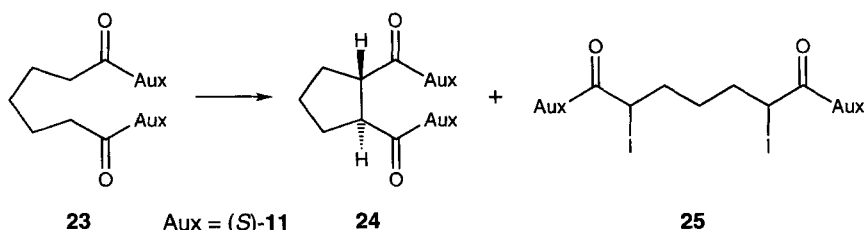
RX	Product	Selectivity [% ds]	Yield [%]
$\text{PhCH}_2\text{Br}$	<b>18</b>	96	84
MeI	<b>19</b>	95	93
$\text{CH}_2=\text{CHCH}_2\text{Br}$	<b>20</b>	94	90
BuI	<b>21</b>	91	81
<i>i</i> -PrI	<b>22</b>	98	40

For determination of the diastereoselectivity of the alkylations and for assignment of the absolute configurations, we hydrolyzed the alkylated dipeptides to the corresponding amino acids and analyzed them by gas chromatography on a chiral column (*Chirasil-Val*) after conversion to their *N*-pentafluoropropanoyl isopropyl esters<sup>14</sup>) [40].

**4. Intramolecular Oxidative Coupling of Chiral Bis-enolates.** – The oxidative coupling of enolates was first mentioned by *Ivanoff* and *Spasoff* in 1935 [41]. Besides  $\text{Br}_2$  [41],  $\text{I}_2$  [42] and  $\text{Cu}^{\text{II}}$  salts [43] were also used as oxidation reagents. Electrochemical oxidative coupling of enolates was only reported twice [42b] [44]. The intramolecular oxidative coupling of a bis-enolate is an attractive alternative to the well known *Dieckman* cyclization and to the acyloin condensation and was successfully applied for the construction of three-, four-, five-, and six-membered carbocycles [45]. To our knowledge, only two papers deal with the coupling of chiral enolates [42c,d]. We now present the first intramolecular oxidative coupling of a chiral bis-enolate. The Li-amide of the auxiliary, produced by the addition of BuLi, was treated with 0.5 equiv. of heptanedioyl dichloride providing the diamide **23** in 91% yield. The oxidative coupling of **23** was studied using different reaction conditions. If  $\text{I}_2$  was used as the oxidizing reagent, then the diiodo

<sup>13</sup>) Starting material was recovered (50%).

<sup>14</sup>) Details on the procedure for the synthesis of these derivatives are given in the *Exper. Part*.

Scheme 5. Oxidative Coupling of the Diamide **23**

Entry	Solvent	Base	Additive	Oxid. reagent	Temp. [°C]	Ratio <b>23/24/25<sup>a)</sup></b>	Yield [%]
1	THF	LDA	–	I <sub>2</sub>	–85 to 25	1:2:2	–
2	THF	LDA	–	I <sub>2</sub>	–20	1:0:1	–
3	THF	LDA	ZnBr <sub>2</sub>	I <sub>2</sub>	–78 to 25	1:0:1	80
4	THF	LDA	ZnBr <sub>2</sub>	I <sub>2</sub>	–85 to 20	1:0:1	–
5	THF	LDA	ZnBr <sub>2</sub>	I <sub>2</sub>	–20	1:7:2	70
6	THF	LDA	DMPU	I <sub>2</sub>	–85 to 25	0:1:1	– <sup>b)</sup>
7	Et <sub>2</sub> O	LDA	–	I <sub>2</sub>	–78 to 25	1:0:1	–
8	THF	LDA	–	CuCl <sub>2</sub>	–78	1:4:0	82
9	THF	LDA	BuLi	CuCl <sub>2</sub>	–78 to 25	1:0:0	– <sup>b)</sup>
10	THF	LDA	–	Cu(OTf) <sub>2</sub>	–78 to 25	1:0:0	– <sup>b)</sup>
11	THF	ArLi	–	CuCl <sub>2</sub>	–78	1:3:0	63

<sup>a)</sup> A zero in the ratio means that the amount of the corresponding compound was below detection limit of routine 200- or 300-MHz <sup>1</sup>H-NMR analysis.

<sup>b)</sup> Decomposition of the enolates was observed.

derivative **25** was observed as well as the five-membered carbocycle **24** (Scheme 5)<sup>15)</sup>. In the majority of cases, the undesired **25** was the main product; it was formed exclusively in Et<sub>2</sub>O (Entry 7). The best result was obtained with the LDA-generated bis-enolate using CuCl<sub>2</sub> as the oxidizing reagent (66%; Entry 8). With copper(II) trifluoromethanesulfonate, no product was observed (Entry 10). A satisfactory result was obtained with the amine-free base 2,4,6-tri(*tert*-butyl)phenyllithium (ArLi, Entry 11) [46]. In all experiments, the five-membered *trans*-carbocycle **24** was formed diastereoselectively as determined by <sup>1</sup>H-NMR analysis<sup>16)</sup>.

To determine the absolute configuration of the product, we transformed the diamide **24** to its diester **26** using the procedure mentioned before (H<sub>2</sub>O<sub>2</sub>/LiOH; CH<sub>2</sub>N<sub>2</sub>; see

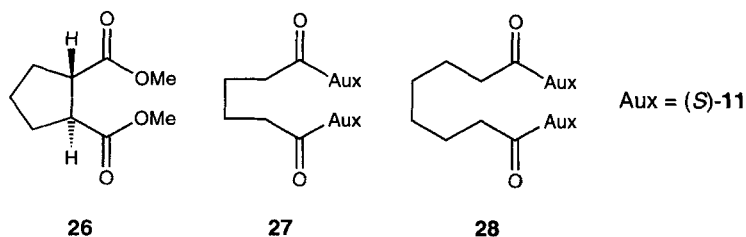


Fig. 5. (S,S)-Diester **26** (from **24**) and the 4- and 6-ring precursors **27** and **28** (from hexanedioyl and octanedioyl dichloride, resp.; cf. **23**)

<sup>15)</sup> The diamide **24** and the diiodo derivative **25** were not separable by flash chromatography.

<sup>16)</sup> In a first application, we successfully used this methodology for the synthesis of a chiral TADDOL-analogous ligand [47].

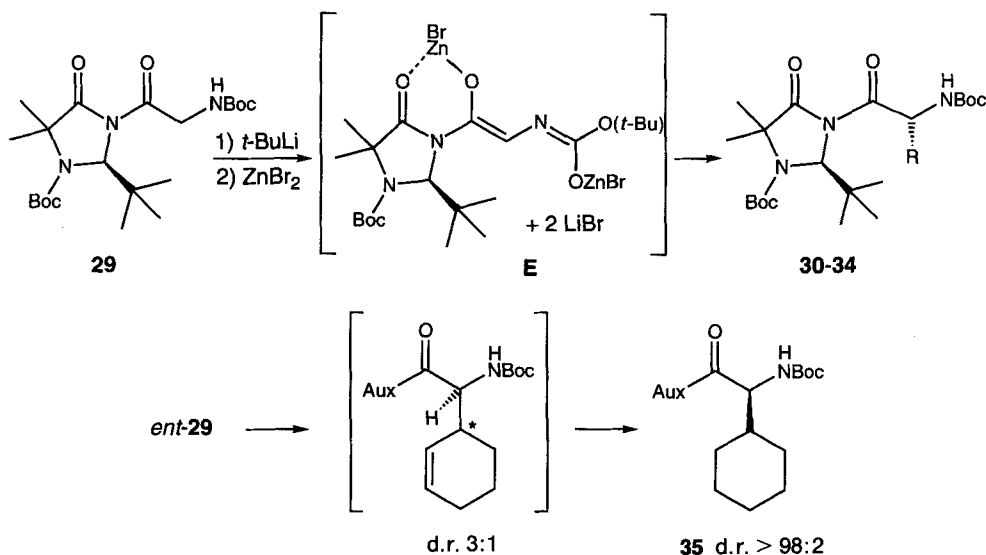


Fig. 5). The (*S,S*)-diester **26** was isolated in good yield (78 %) in 86 % ee<sup>17)</sup> [48]. We did not succeed in cyclizing the hexanedioic-acid derivative **27** and the C<sub>8</sub> derivative **28** to the corresponding four- and six-membered ring compounds under the conditions used for the preparation of **24**.

### 5. Diastereoselective Alkylations of a Chiral Dilithio-dianion Derivative of Glycine. –

In 1978, *Evans* and *Sidebottom* reported the *C*-alkylation of a doubly deprotonated *N*-benzoylglycine ethyl ester for the first time [49]. Later *Metcalf*, *Berkowitz*, and co-workers applied this methodology to the synthesis of racemic  $\alpha,\alpha$ -disubstituted  $\alpha$ -amino acids [50]. Chiral glycine-dianion moieties were generated and alkylated before [39b] [51]. In this section, we describe the diastereoselective alkylation of a chiral glycine derivative (containing auxiliary **11**) for the synthesis of enantiomerically pure  $\alpha$ -amino acids. The Li-amide of the auxiliary (*R*)-**11** was treated with *N*-[(*tert*-butoxy)carbonyl]glycyl fluoride (Boc-Gly-F)<sup>18)</sup> providing the amide **29** in 73 % yield. Dilithiodianion formation with

Scheme 6. Diastereoselective Alkylation of the Chiral Glycine Derivative **29**



Entry	R	Product	Temp. [°C]	Time [h]	Selectivity [% ds]	Yield [%]
1	Me	<b>30</b>	0	8	> 99	81
2	Et	<b>31</b>	25	12	> 98	70
3	CH <sub>2</sub> =CHCH <sub>2</sub>	<b>32</b>	0	8	> 98	76
4	PhCH <sub>2</sub>	<b>33</b>	25	12	> 99	73
5	Bu	<b>34</b>	25	48	> 98	51
6	Cyclohexyl	<b>35</b>	25	12	> 98	65 <sup>a)</sup>

<sup>a)</sup> The reaction was performed with *ent*-**29**; 3-bromocyclohex-1-ene was used as electrophile (see text).

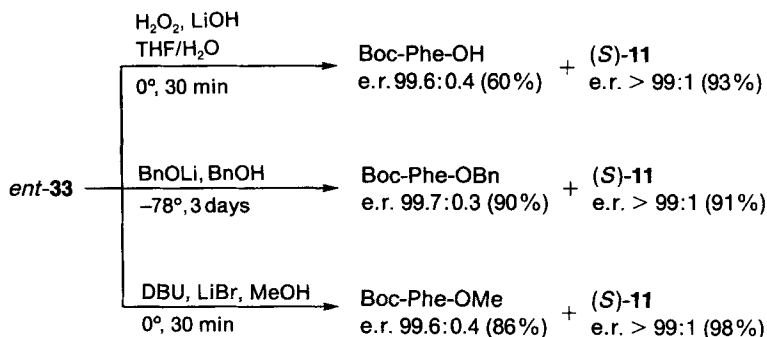
<sup>17)</sup> The conditions for this transformation (occurring with partial racemization) were not optimized.

<sup>18)</sup> Boc-Gly-F was prepared according to the published procedure from Boc-Gly-OH and cyanuric fluoride (2,4,6-trifluoro-1,3,5-triazine) [52].

2.2 equiv. of BuLi and transmetallation with  $\text{ZnBr}_2$ <sup>19)</sup> afforded a reagent (the dizinc derivative **E**?) which was successfully alkylated by various electrophiles ( $\rightarrow$ **30–35**) with high selectivity (*Scheme 6*). The selectivity was determined either by HPLC (*LiChrosorb 100*) or by  $^1\text{H-NMR}$  analysis of the crude product. The absolute configuration was determined, after hydrolysis of the alkylation products to the corresponding amino acids<sup>20)</sup> and transformation to a suitable derivative (see above), by GC or by analogy (**34** and **35**). With *i*-PrI, we did not observe any alkylation product. We, therefore, decided to introduce the cyclohexyl group by reaction of the Zn-enolate using the activated electrophile 3-bromocyclohex-1-ene, with subsequent hydrogenation of the double bond (65% overall yield, *Entry 6*). The primary reaction product with an additional stereogenic center at the  $\beta$ -position was formed as a 3:1 mixture of diastereoisomers (epimeric at the  $\beta$ -position). The observed topicity of the alkylations is compatible with a chelated *cis*-enolate conformation **E** as the reacting species (see *Scheme 6*).

For detachment of the auxiliary to yield the amino acid, three different methods<sup>21)</sup> were applied, as shown for the cleavage of the benzylation product *ent*-**33** to give Boc-L-phenylalanine or its esters (*Scheme 7*).

*Scheme 7. Cleavage of the Auxiliary from Product ent-33*



By using either of these different methods, we also synthesized *N*-[(*tert*-butoxy)-carbonyl]-L-alanine (Boc-Ala-OH; from *ent*-**30**,  $\text{H}_2\text{O}_2/\text{LiOH}$ ; e.r. > 99:1), methyl *N*-[(*tert*-butoxy)carbonyl]-L-2-aminobutanoate (Boc-Abu-OMe; from *ent*-**31**, DBU/LiBr, MeOH; e.r. > 99:1), and methyl *N*-[(*tert*-butoxy)carbonyl]-D-2-aminopent-4-enoate (from **32**, DBU/LiBr, MeOH, e.r. 98:2<sup>22)</sup>).

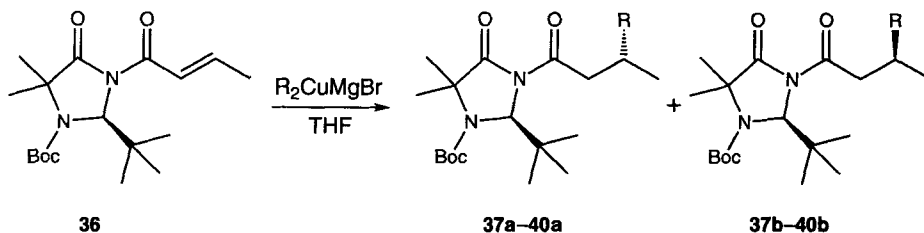
**6. Michael Additions.** – The chiral *Michael* acceptor **36** was prepared using crotonyl chloride ((*E*)-but-2-enoyl chloride) according to the procedure described for the synthesis of the propanoyl derivative **13**. Cuprates were prepared by transmetallation of the corresponding *Grignard* reagents with cuprous bromide ( $\text{CuBr} \cdot \text{SME}_2$ ) [54]. For the phenylated

<sup>19)</sup> With the dithio derivative, the results of alkylation were less satisfactory.

<sup>20)</sup> The allylated derivative **32** was hydrogenated ( $\text{Pd/C}$ ,  $\text{H}_2$ , EtOH) prior to hydrolysis.

<sup>21)</sup> The transesterification with the base system 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)/LiBr in MeOH (*Scheme 7*) was successfully used for the detachment of 'machine-built' peptides from the support resin [53]. See also section I.2.4 in [36b].

<sup>22)</sup> The chiral auxiliary used in this experiment was not enantiomerically pure.

Scheme 8. Cuprate Additions to the Chiral Michael Acceptor **36**

Entry	R	Product	Ratio a/b	Abs. configuration at C(β) of the a-series	Yield a/b [%]
1	Ph	<b>37</b>	99:1	( <i>R</i> )	80
2	Cyclohexyl	<b>38</b>	64:36	( <i>R</i> )	92
3	<i>i</i> -Pr	<b>39</b>	63:37	( <i>R</i> )	93
4	Bu	<b>40</b>	50:50	–	86

derivatives, the ratio **37a**/**37b** (99:1) was determined by HPLC (Scheme 8). The absolute configuration of the main product **37a** was assigned, after cleavage of the auxiliary ( $\text{H}_2\text{O}_2/\text{LiOH}$ ), by comparison of the optical rotation of the isolated acid with the reported value [55] for 3-phenylbutanoic acid. The isopropyl derivatives **39** and the butyl derivatives **40** were similarly transformed ( $\text{H}_2\text{O}_2/\text{LiOH}$ ) to 3,4-dimethylpentanoic acid (from **39**) and to 3-methylheptanoic acid (from **40**). The 3-methylheptanoic acid showed no optical rotation; the 3,4-dimethylpentanoic acid was obtained in 26% ee ((*R*)-enantiomer) [56]. The diastereoisomeric products **38** of the cyclohexyl addition were transformed to the auxiliary and to the corresponding primary alcohols by reduction with  $\text{LiBH}_4$ , yielding (*R*)-3-cyclohexylbutanol in 28% ee [57]. Thus the reaction of the crotonic-acid derivative **36** with alkyl cuprates proceeded only with poor selectivities and the produced diastereoisomers could not be separated.

**7. Conclusions.** – A major advantage of our chiral auxiliary **11** compared to other ‘chiral inductors’ is the availability of both enantiomeric forms from the same precursor (L-alanine). The resolution approach – provided that a suitable protection procedure for the last step can be found – also offers an economical way to both enantiomers of the auxiliary, since *O,O'*-dibenzoyltartaric acid, used in the resolution step, is commercially available (cheaply!) in both antipodes. A comparison of the properties of the new auxiliary in asymmetric synthesis with other related compounds shows some advantages but also some disadvantages. Thus, the application of **11** for the alkylation of its propanoic-acid derivative **13** is limited to reactive electrophiles, comparable with the situation reported by Evans and coworkers for alkylations of the Li-enolate of the corresponding oxazolidinone derivative [24c]. The *Michael* addition only works well with aryl cuprates leading to enantiomerically pure β-aryl-substituted carboxylic acids which also seems to be the case with the corresponding Evans chiral auxiliary [54b]. On the other hand, the high selectivities obtained for the alkylation of the dianion derivative of glycine **29** had not been previously observed. Also the hydrolysis of the dipeptide derivatives **18–22** (yet to be done) would lead to Aib-containing dipeptides, formation of which is sometimes difficult (coupling of an α,α-disubstituted amino acid!), especially if the

second amino acid used in the coupling procedure bears a sterically demanding substituent such as *i*-Pr (see **22**). In addition, these Aib-containing peptides are very interesting compounds since it is known that they adopt stable helical conformations in solution [58].

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### Experimental Part

1. *General*. THF used for alkylations was freshly distilled over Na under Ar. TLC: *Merck* silica gel 60  $F_{254}$  anal. plates; detection either with UV and by dipping into a soln. of anisaldehyde (9.2 ml), AcOH (3.75 ml), conc.  $H_2SO_4$  (12.5 ml), and EtOH (338 ml), followed by heating. LC: *Merck* silica gel 60 (40–63  $\mu$ m). GC: *Chirasil-Val*<sup>®</sup> column (*Macherey-Nagel*, 25 m, 0.4 mm); *Carlo-Erba-Fractovap 4160-HRGC*; temp. program: 3 min 85°, 4°/min. Anal. HPLC: *Kontron* HPLC system; UV detector *Uvikon LCD-75*, programmer 200, integrator *Shimadzu C-R 1B Chromatopak*; *Chiracel OD* (*Daicel Chemical Industries, Ltd.*; 4.6  $\times$  250 mm, 10  $\mu$ m), *Li-Chrosorb Si 100* (*Knauer*). Optical rotations: 10-cm, 1-ml cell, at r.t.; *Perkin-Elmer-241* polarimeter. IR Spectra: *Perkin-Elmer-782* spectrophotometer. <sup>1</sup>H-NMR: *Bruker-AMX-II-500* (500 MHz), *Bruker-AMX-400* (400 MHz), *Bruker-ARX-300* (300 MHz), or *Varian-Gem-200* (200 MHz) spectrometer. NOE:  $\delta$ (irrad. H)→modified signals. <sup>13</sup>C-NMR: *Bruker-AMX-II-500* (125 MHz), *Bruker-AMX-400* (100 MHz), or *Varian-XL-300* (75 MHz) spectrometer. MS: EI, electron ionization; FAB, fast-atom bombardment; 3-NOBA, 3-nitrobenzyl alcohol.

2. *General Procedure for GC Analysis*: In a screw-capped vial, 5–10 mg of the sample was hydrolyzed with conc. HCl soln. at 100–110° for 6–15 h. Then,  $H_2O$  was removed in an airflow, and ca. 1 ml of anh. 4M HCl in *i*-PrOH was added. The soln. was heated at 100° for 1 h, then the solvent removed in an airflow, and ca. 0.1 ml of  $CH_2Cl_2$  and 0.05 ml of pentafluoropropanoic anhydride were added. Heating at 100° for 15 min followed by removal of excess pentafluoropropanoic anhydride in an airflow gave the derivatives of the individual amino acids.

3. *General Procedure 1 (G.P.1): Acylation of the Auxiliary*. To a soln. of the auxiliary **11** (3.00 g, 11.1 mmol) in THF (15 ml), BuLi (8.14 ml, 12.1 mmol) was added at –78° under Ar. The resulting yellow soln. was stirred at –78° for 30 min. After addition of the acyl chloride (16.6 mmol), the mixture was allowed to warm to r.t. The reaction was monitored by TLC. The mixture was worked up by addition of sat.  $NH_4Cl$  soln. and  $Et_2O$ . The org. layer was washed twice with sat. aq. NaCl soln. All aq. layers were additionally extracted twice with  $Et_2O$ . The combined org. phases were dried ( $MgSO_4$ ) and evaporated.

4. *G.P.2: Removal of the Z Group or Hydrogenation*. To a soln. of the substrate in EtOH under Ar, 10% Pd/C was added. The Ar atmosphere was replaced by  $H_2$ , the suspension stirred for 10–16 h (TLC), the catalyst removed by filtration over *Celite*, and the filtrate evaporated.

5. *G.P.3: Alkylation of the Chiral Propanamide 13*. To a soln. of **13** (1.00 g, 3.07 mmol) in THF (10 ml), a precooled soln. of LDA (4.6 mmol) in THF (10 ml) was added under Ar at –78°. The LDA soln. was prepared by treating a soln. of (*i*-Pr)<sub>2</sub>NH (0.67 ml, 4.60 mmol) in THF (10 ml) with BuLi (3.1 ml, 4.6 mmol) at –78° (30 min). After stirring for 30 min at –78°, a soln. of  $ZnBr_2$  (1.04 g, 4.60 mmol) in THF (10 ml) was added. The resulting Zn-enolate was stirred for additional 30 min at –78° and then treated with the electrophile. The mixture was allowed to warm to –20° and maintained at –20° for 16 h. Workup according to *G.P.1*.

6. *G.P.4: Cleavage of the Auxiliary with  $H_2O_2/LiOH$* . A soln. of the acylated auxiliary (0.24 mmol) in THF/ $H_2O$  3:1 (5 ml) was cooled to 0° and treated with  $H_2O_2$  (1.92 mmol) and LiOH (0.48 mmol). The mixture was stirred at 0° for 30 min, and after complete reaction (TLC), 1.2M  $NaHSO_3$  (2.12 mmol) was added. After careful addition of 1N HCl (until pH 2), the mixture was extracted with AcOEt (3 $\times$ ). The combined org. phases were dried ( $MgSO_4$ ) and evaporated.

7. *G.P.5: Alkylation of Dipeptide 17*. To a soln. of dipeptide **17** (100 mg, 0.26 mmol) in THF (2 ml), *t*-BuLi (0.19 ml, 0.29 mmol) was added at –78° under Ar. The resulting yellow soln. was stirred at –78° for 30 min. After addition of the electrophile, the mixture was allowed to warm to r.t. The reaction was monitored by TLC. Workup according to *G.P.1*.

8. *G.P.6: Alkylation of the Chiral Glycine Derivative 29*. To a soln. of **29** (400 mg, 0.94 mmol) in THF (8 ml), *t*-BuLi (0.19 ml, 0.29 mmol) was added at –78° under Ar. The resulting yellow soln. was stirred at –78° for 30 min,

and a soln. of  $\text{ZnBr}_2$  (529 mg, 2.34 mmol) in THF (8 ml) was added. The Zn-enolate was stirred at  $-78^\circ$  for additional 30 min and then treated with the electrophile. The mixture was allowed to warm to  $0^\circ$  or to r.t. and stirred for 8–48 h at that temp. Workup according to *G.P.I.*

9. *G.P.7: Transesterification with DBU/LiBr in MeOH.* A soln. of the acylated auxiliary (0.43 mmol) in MeOH (7 ml) was cooled to  $0^\circ$ , and LiBr (dried under h.v. at  $180^\circ$ , 16 h; 185 mg, 2.14 mmol) and DBU (0.13 ml, 0.86 mmol) were added. The mixture was stirred for 30–60 min at  $0^\circ$  (TLC). Workup according to *G.P.I.*

10. *G.P.8: Michael Addition.* A suspension of Mg (47 mg, 1.9 mmol) in THF (1.5 ml) was treated at r.t. with the halide (1.9 mmol). The formed soln. (if a precipitation is formed, short heating is necessary to obtain the soln.) was cooled to  $-30^\circ$ . A suspension of  $\text{CuBr} \cdot \text{SMe}_2$  (197 mg, 1.00 mmol) in THF (1.5 ml) was treated at  $-30^\circ$  with the Grignard soln. The resulting mixture was allowed to warm to  $-10^\circ$  (alkyl cuprates) or  $0^\circ$  (phenyl cuprate) and stirred at that temp. for 16 h. Workup according to *G.P.I.* and purification by FC ( $\text{Et}_2\text{O}$ /pentane 1:15) yielded the products as diastereoisomer mixture.

*tert-Butyl (2R,5S)-2-(tert-Butyl)-5-methyl-4-oxoimidazolidine-1-carboxylate (3).* A suspension of L-alaninamide hydrochloride (0.02 kg, 161 mmol) and  $\text{NEt}_3$  (26.4 ml, 194 mmol) in  $\text{CH}_2\text{Cl}_2$  (200 ml) was refluxed (Dean-Stark) for 16 h. The resulting soln. was cooled to  $0^\circ$ , and  $\text{NEt}_3 \cdot \text{HCl}$  was filtered off. The filtrate was treated with  $\text{CF}_3\text{COOH}$  (18.5 ml, 242 mmol) at  $0^\circ$ . The suspension thus formed was allowed to warm to r.t. and stirred for 4 h. After addition of 2N KOH (until pH 11), the mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (5 $\times$ ). The combined org. phases were dried ( $\text{MgSO}_4$ ) and evaporated: 17.98 g (71 %) of 1/2 1:1.2. The mixture was dissolved in  $\text{CH}_2\text{Cl}_2$  (200 ml), treated slowly at r.t. with a soln. of  $(\text{Boc})_2\text{O}$  (12 g, 55 mmol) in  $\text{CH}_2\text{Cl}_2$  (50 ml), and stirred for 3 h at r.t. Evaporation yielded a colorless oil which was purified (without aq. workup!) by FC ( $\text{EtO}$ /pentane 2:1): 13.3 g (97 % rel. to 1) of 3. The unreacted 2 (8.26 g (86 %)) was eluted with  $\text{Et}_2\text{O}$ . 3: Colorless solid. M.p.  $122\text{--}123^\circ$ .  $[\alpha]_D^{25} = +44.6$  ( $c = 1.01$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 3444w, 2977m, 1707s, 1479w, 1455w, 1424w, 1368s, 1298m, 1260w, 1167m, 1128w, 1061w, 1033w, 1016w.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 0.94 (s, *t*-Bu); 1.46 (*d*,  $J = 7$ , Me); 1.48 (s, *t*-Bu); 4.1–4.3 (br. s, H–C(5)); 4.99 (s, H–C(2)); 8.00 (br. s, NH).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ): 17.68 (Me); 25.57 (Me); 28.33 (Me); 36.77 (C); 56.46 (CH); 77.28 (CH); 81.06 (C); 155.83 (C); 175.09 (C). EI-MS: 257.2 ( $< 1$ ,  $[M + H]^+$ ), 199.1 (35), 183.1 (15), 143.1 (100), 99.1 (52), 71.1 (9), 57.1 (100), 41.0 (21), 29.0 (8). Anal. calc. for  $\text{C}_{13}\text{H}_{24}\text{N}_2\text{O}_3$  (256.4): C 60.91, H 9.44, N 10.93; found: C 61.21, H 9.52, N 10.91.

*tert-Butyl (2S,5S)-2-(tert-Butyl)-5-methyl-4-oxoimidazolidine-1-carboxylate (4).* A soln. of 2 (3000 mg, 19.23 mmol) and  $(\text{Boc})_2\text{O}$  (5.15 g, 23.1 mmol) in  $\text{CH}_2\text{Cl}_2$  (35 ml) was refluxed for 6 days. Evaporation and recrystallization ( $\text{Et}_2\text{O}$ /pentane) gave 4.58 g (93 %) of 4. Colorless solid. M.p.  $167\text{--}168^\circ$ .  $[\alpha]_D^{25} = -9.9$  ( $c = 1.14$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 3447w, 2970m, 1712s, 1700s, 1478w, 1449w, 1385s, 1369s, 1316w, 1295m, 1261m, 1171m, 1138m, 1056w, 1010w.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 0.93 (s, *t*-Bu); 1.49 (s, *t*-Bu); 1.57 (*d*,  $J = 6.6$ , Me); 3.96 (*q*,  $J = 6.2$ , H–C(5)); 5.08 (br. s, H–C(2)); 8.00 (br. s, NH); NOE: 3.96 (H–C(5))  $\rightarrow$  0.93 (*t*-Bu); 1.57 (Me)  $\rightarrow$  5.08 (weak; H–C(2)); 0.93 (*t*-Bu)  $\rightarrow$  3.96 (H–C(5)).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ): 17.87 (Me); 25.28 (Me); 28.30 (Me); 39.50 (C); 55.55 (CH); 76.06 (CH); 80.73 (C); 153.56 (C); 175.86 (C). EI-MS: 257.0 ( $< 1$ ,  $[M + H]^+$ ), 199.1 (20), 183.1 (9), 143.0 (83), 99.0 (51), 57.0 (100), 41.0 (19), 29.0 (9). Anal. calc. for  $\text{C}_{13}\text{H}_{24}\text{N}_2\text{O}_3$  (256.4): C 60.91, H 9.44, N 10.93; found: C 61.01, H 9.23, N 10.90.

*(2R,5S)-Benzoyl-2-(tert-Butyl)-5-methylimidazolidin-4-one (7).* A soln. of 1/2 (680 mg, 4.36 mmol) in  $\text{CH}_2\text{Cl}_2$  (10 ml) was cooled to  $0^\circ$  and treated with benzoyl chloride (0.76 ml, 6.54 mmol) and  $\text{NEt}_3$  (0.91 ml, 6.54 mmol). The mixture was allowed to warm to r.t., and stirring was continued for 7 h. After evaporation, the residue was taken up in  $\text{Et}_2\text{O}$  and worked up according to *G.P.I.* Purification by FC ( $\text{Et}_2\text{O}$ /pentane 6:1) yielded 7 (420 mg, 37 %) and its epimer (484 mg, 43 %). 7: Colorless solid. M.p.  $154\text{--}155^\circ$ .  $[\alpha]_D^{25} = -39.2$  ( $c = 1.09$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 3446m, 3210 (br.), 2974s, 1713s, 1656s, 1360s, 1298s, 1261m, 1150w, 1077w, 1014m, 875w.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 1.01 (s, *t*-Bu); 1.41 (*d*,  $J = 7$ , Me); 3.91 (*q*,  $J = 7$ , H–C(5)); 5.63 (*d*,  $J = 0.5$ , H–C(2)); 7.38–7.47 (m, arom. H); 8.26 (br. s, NH); NOE: 5.63 (H–C(2))  $\rightarrow$  3.91 (weak; H–C(5)); 1.41 (Me)  $\rightarrow$  1.01 (*t*-Bu); 1.01 (*t*-Bu)  $\rightarrow$  1.41 (Me).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ): 19.52 (Me); 25.77 (Me); 36.62 (C); 57.16 (CH); 76.38 (CH); 126.89 (CH); 128.51 (CH); 130.29 (CH); 136.51 (C); 174.25 (C); 174.82 (C). EI-MS: 260.1 ( $< 1$ ,  $M^+$ ), 203.1 (69), 105.0 (100), 77.1 (36). Anal. calc. for  $\text{C}_{15}\text{H}_{20}\text{N}_2\text{O}_2$  (260.3): C 69.20, H 7.74, N 10.76; found: C 69.07, H 7.60, N 10.77.

*tert-Butyl (2R,5S)-3-(Benzyloxycarbonyl)-2-(tert-butyl)-5-methyl-4-oxoimidazolidine-1-carboxylate (8).* To a soln. of 3 (13.3 g, 51.8 mmol) in THF (150 ml), BuLi (37.9 ml, 56.9 mmol) was added at  $-78^\circ$  under Ar. The resulting yellow soln. was stirred at  $-78^\circ$  for 30 min. After addition of Z-Cl (16.6 mmol), the mixture was allowed to warm to r.t. The reaction was monitored by TLC. Workup according to *G.P.I.* and purification by FC ( $\text{Et}_2\text{O}$ /pentane 1:8) gave 18.9 g (94 %) of 8. Colorless solid. M.p.  $75\text{--}76.5^\circ$ .  $[\alpha]_D^{25} = +70.3$  ( $c = 1.11$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 2977m, 1792s, 1732s, 1705s, 1480w, 1456w, 1369s, 1355s, 1332w, 1277s, 1157s, 1042w, 1020w, 907w.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 0.92 (s, *t*-Bu); 1.49 (s, *t*-Bu); 1.53 (*d*,  $J = 7$ , Me); 4.2–4.5 (br. s, H–C(5)); 5.30 (s,

PhCH<sub>2</sub>); 5.6–5.75 (br., H–C(2)); 7.3–7.5 (*m*, arom. H). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 17.00 (Me); 26.45 (Me); 28.26 (Me); 38.62 (C); 56.87 (CH); 68.81 (CH<sub>2</sub>); 78.02 (C); 81.58 (CH); 128.41 (CH); 128.64 (CH); 134.78 (C); 150.56 (C); 155.02 (C); 171.63 (C). EI-MS: 333.2 (23), 277.1 (38), 189.1 (27), 90.1 (99), 57.1 (100), 41.0 (13). Anal. calc. for C<sub>21</sub>H<sub>30</sub>N<sub>2</sub>O<sub>5</sub> (390.5): C 64.60, H 7.74, N 7.17; found: C 64.81, H 7.47, N 7.16.

*tert*-Butyl (2*S*,5*S*)-3-(Benzyloxycarbonyl)-2-(*tert*-butyl)-5-methyl-4-oxoimidazolidine-1-carboxylate (**9**). As described for **8**, with **4** (16.0 g, 62.5 mmol), THF (150 ml), BuLi (42.0 ml, 62.5 mmol), and Z-Cl (11.8 ml, 75.0 mmol): 23 g (94%) of **9**. Colorless solid. M.p. 88.5–89.5°. [ $\alpha$ ]<sub>D</sub><sup>25</sup> = –50.5 (*c* = 1.0, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 2974*m*, 1789*s*, 1764*w*, 1733*s*, 1697*s*, 1477*w*, 1451*w*, 1393*s*, 1367*s*, 1312*w*, 1277*s*, 1164*s*, 1133*m*, 1010*w*. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.91 (*s*, *t*-Bu); 1.44 (*s*, *t*-Bu); 1.62 (*d*, *J* = 7, Me); 4.09 (*q*, *J* = 7, H–C(5)); 5.30 (*s*, PhCH<sub>2</sub>); 5.80 (*s*, H–C(2)); 7.31–7.46 (*m*, arom. H). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 18.16 (Me); 26.20 (Me); 28.29 (Me); 41.44 (C); 56.95 (CH); 68.79 (CH<sub>2</sub>); 76.97 (C); 81.32 (CH); 128.43 (CH); 128.61 (CH); 134.76 (C); 150.29 (C); 152.56 (C); 172.38 (C). EI-MS: 333.3 (63), 277.2 (100), 233.2 (97), 189.2 (51), 91.1 (55), 57.1 (21). Anal. calc. for C<sub>21</sub>H<sub>30</sub>N<sub>2</sub>O<sub>5</sub> (390.5): C 64.60, H 7.74, N 7.17; found: C 64.84, H 7.83, N 7.14.

*tert*-Butyl (R)-3-(Benzyloxycarbonyl)-2-(*tert*-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate ((R)-**10**). A soln. of **8** (10.8 g, 27.6 mmol) in THF (70 ml) was cooled under Ar to –78° and treated with a precooled soln. of Na-HMDS (7.0 g, 36 mmol) in THF (70 ml). The resulting pale yellow soln. was stirred at –78° for 30 min, and MeI (3.36 ml, 55.1 mmol) was added. The mixture was stirred at –78° for 6 h (TLC). Workup according to *G.P.1* and purification by FC (Et<sub>2</sub>O/pentane 1:5) gave 8.48 g (76%) of (R)-**10**. Colorless solid. M.p. 62–63°. [ $\alpha$ ]<sub>D</sub><sup>25</sup> = +84.3 (*c* = 1.09, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 2974*s*, 1790*s*, 1760*m*, 1733*s*, 1697*s*, 1477*w*, 1456*w*, 1390*s*, 1364*s*, 1349*s*, 1282*s*, 1077*w*, 1026*w*, 1000*m*, 892*w*. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.90, 0.93 (2*s*, *t*-Bu); 1.50 (*s*, *t*-Bu, rotamers); 1.56, 1.57 (2*s*, Me, rotamers); 1.62, 1.64 (2*s*, Me, rotamers); 5.29, 5.32 (2*s*, PhCH<sub>2</sub>, rotamers); 5.68, 5.84 (2*s*, H–C(2), rotamers); 7.30–7.42 (*m*, arom. H). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 23.08, 23.40 (Me, rotamers); 26.67, 26.97 (Me, rotamers); 27.77 (Me); 28.32 (Me); 39.91 (C); 62.20 (C); 68.76 (CH<sub>2</sub>); 76.21 (CH); 81.09 (C); 128.01 (CH); 128.40 (CH); 128.56 (CH); 128.64 (CH); 134.74 (C); 150.36 (C); 154.47 (C); 174.73 (C). EI-MS: 405.3 (*c* < 1, [M + H]<sup>+</sup>), 347.2 (25), 291.2 (40), 247.1 (48), 203.2 (28), 91.1 (100), 57.1 (62), 41.1 (14).

*tert*-Butyl (S)-3-(Benzyloxycarbonyl)-2-(*tert*-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate ((S)-**10**). As described for (R)-**10**, with **9** (23 g, 59 mmol), THF (100 ml), Na-HMDS (13.7 g, 70.8 mmol) in THF (100 ml), and MeI (7.20 ml, 118 mmol): 20.9 g (88%) of (S)-**10** [ $\alpha$ ]<sub>D</sub><sup>25</sup> = –85.1 (*c* = 1.0, CHCl<sub>3</sub>).

*tert*-Butyl (R)-2-(*tert*-Butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate ((R)-**11**). According to *G.P.2*, with (R)-**10** (7.56 g, 18.7 mmol), EtOH (100 ml), and Pd/C (200 mg): 4.86 g (96%) of (R)-**11**; > 99% ee by HPLC (Chiracel OD, hexane/*i*-PrOH 93:7, flow 1 ml/min; UV detection 214 nm; 1 mg/ml; (S)-enantiomer was first eluted). Colorless solid. M.p. 138–140°. [ $\alpha$ ]<sub>D</sub><sup>25</sup> = +40.0 (*c* = 1.0, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 3446*m*, 3211*w*, 3007*m*, 2978*s*, 1710*s*, 1479*m*, 1425*w*, 1368*s*, 1300*s*, 1259*m*, 1196*s*, 1102*s*, 1078*s*, 958*w*, 900*w*, 858*w*. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.92 (*s*, *t*-Bu); 1.50 (*s*, *t*-Bu); 1.54 (*s*, Me); 1.62 (*s*, Me); 5.07 (br. *s*, H–C(2)); 6.62 (br. *s*, NH). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 23.95 (Me); 25.77 (Me); 26.10 (Me); 28.31 (Me); 37.94 (C); 61.55 (CH); 75.10 (C); 80.67 (C); 177.26 (C). EI-MS: 271.2 (*c* < 1, [M + H]<sup>+</sup>), 213.1 (16), 157.1 (90), 113.1 (40), 57.1 (100), 41.0 (15). Anal. calc. for C<sub>14</sub>H<sub>26</sub>N<sub>2</sub>O<sub>3</sub> (270.4): C 62.19, H 9.69, N 10.36; found: C 62.29, H 9.40, N 10.40.

*tert*-Butyl (S)-2-(*tert*-Butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate ((S)-**11**). According to *G.P.2*, with (S)-**10** (0.02 kg, 49.5 mmol), EtOH (200 ml), and Pd/C (400 mg): 13.4 g (99%) of (S)-**11**. [ $\alpha$ ]<sub>D</sub><sup>25</sup> = –41.7 (*c* = 1.0, CHCl<sub>3</sub>).

*rac*-2-(*tert*-Butyl)-5,5-dimethylimidazolidin-4-one (*rac*-**12**). A soln. of H-Aib-NH<sub>2</sub> (7.7 g, 75 mmol) and pivalaldehyde (9.8 ml, 90 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (100 ml) was refluxed (Dean-Stark) for 16 h. The soln. was cooled to 0° and treated with CF<sub>3</sub>COOH (8.63 ml, 113 mmol). The suspension thus formed was allowed to warm to r.t. and stirred for 5 h. After addition of 2*N* KOH (until pH 11), the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5×). The combined org. phases were dried (MgSO<sub>4</sub>) and evaporated: 10.2 g (80%) of *rac*-**12**. <sup>1</sup>H-NMR (200 MHz, CDCl<sub>3</sub>): 0.91 (*s*, *t*-Bu); 1.29 (*s*, Me); 1.31 (*s*, Me); 1.68 (br. *s*, NH(1)); 4.28 (*s*, H–C(2)); 6.26 (br. *s*, NH(3)).

1. *Crystallization*: *rac*-**12** (1 equiv.) and *O,O'*-dibenzoyltartaric acid (0.5 equiv.) were dissolved in boiling ethyl methyl ketone (1 mmol/ml) and allowed to stand at r.t. for 24 h. The (R,R)-acid crystallized with (R)-**12**. The crystals were isolated and washed with cold Et<sub>2</sub>O and then dissolved in 2*N* KOH. The soln. was extracted with CH<sub>2</sub>Cl<sub>2</sub> (5×). The combined org. phases were dried (MgSO<sub>4</sub>) and evaporated: 65% (theoretical yield) of (R)-**12** in 75–80% ee. Analogous workup of the mother liquor yielded the other enantiomer in 64–75% ee. The ee was determined by HPLC (Chiracel OD, hexane/*i*-PrOH 93:7, flow 1 ml/min; UV detection 214 nm; 1 mg/ml; (S)-enantiomer was first eluted).

2. *Crystallization*: the enriched (79% ee) (R)-**12** (1 equiv.) and *O,O'*-dibenzoyltartaric acid (0.5 equiv.) were dissolved at r.t. in ethyl methyl ketone (0.08 mmol/ml) and allowed to stand at –20° for 24 h. Workup as described before: 45–65% of (R)-**12** (93–94% ee).

tert-Butyl (R)-2-(tert-Butyl)-5,5-dimethyl-4-oxo-3-propanoylimidazolidine-1-carboxylate (**13**). According to G.P.1, with propanoyl chloride (1.46 ml, 16.6 mmol). Purification by FC (Et<sub>2</sub>O/pentane 1:10): 3.07 g (85%) of **13**. Colorless solid. M.p. 85–86°.  $[\alpha]_D^{25} = +132.7$  ( $c = 1.04$ , CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 2920s, 1748s, 1712s, 1702s, 1692m, 1477m, 1456s, 1384s, 1359s, 1272m, 1149w, 1087w, 953w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.92, 0.94 (2s, *t*-Bu, rotamers); 1.18 (*t*,  $J = 7.3$ , Me–C(2')); 1.50 (*s*, *t*-Bu); 1.54, 1.58, 1.59, 1.64 (4s, 2 Me–C(5), rotamers); 2.70–3.00 (*m*, 2 H–C(2')); 5.88, 6.06 (2s, H–C(2), rotamers). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 8.65 (Me); 22.86, 23.08, 23.24 (Me, rotamers); 25.93, 27.06, 27.31, 27.55 (Me, rotamers); 27.80, 28.10, 28.35 (Me, rotamers); 30.32 (CH<sub>2</sub>); 39.53, 39.87 (C, rotamers); 62.63 (C); 75.05, 75.26, 75.49 (CH, rotamers); 80.97, 81.37 (C, rotamers); 154.36 (C); 172.90 (C); 176.89 (C). EI-MS: 327.3 ( $< 1$ ,  $[M + H]^+$ ), 213.1 (22), 169.1 (14), 157.1 (20), 113.1 (23), 57.1 (100), 41.0 (13). Anal. calc. for C<sub>17</sub>H<sub>30</sub>N<sub>2</sub>O<sub>4</sub> (326.4): C 62.55, H 9.26, N 8.58; found: C 62.83, H 8.76, N 8.55.

tert-Butyl (2R,2'R)-2-(tert-Butyl)-5,5-dimethyl-3-(2'-methyl-3'-phenylpropanoyl)-4-oxoimidazolidine-1-carboxylate (**14a**). According to G.P.3, with benzyl bromide (3.60 ml, 30.7 mmol). Purification by FC (Et<sub>2</sub>O/pentane 1:8): 907 mg (71%) of **14a**; 96% ds by HPLC (LiChrosorb Si 100, flow 1 ml/min; UV detection at 254 nm; hexane/*i*-PrOH 99.84:0.16). M.p. 68–70°.  $[\alpha]_D^{25} = +92.3$  ( $c = 1.0$ , CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 2980s, 1751s, 1707s, 1604w, 1496w, 1479m, 1456m, 1388s, 1367s, 1270s, 1151s, 1097m, 1082m, 960w, 887w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.81, 0.83 (2s, *t*-Bu, rotamers); 1.07 (*t*,  $J = 5.3$ , Me–C(2')); 1.50 (*s*, *t*-Bu); 1.57, 1.60, 1.61, 1.64, 1.67 (5s, 2 Me–C(5), rotamers); 2.54 (*dd*,  $J = 9.0$ , 13.1, 1 H, PhCH<sub>2</sub>); 3.26 (*dd*,  $J = 6.0$ , 13.1, 1 H, PhCH<sub>2</sub>); 3.8–4.0 (br. *m*, H–C(2')); 6.07, 7.19 (2s, H–C(2), rotamers); 7.17–7.34 (*m*, arom. H). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 15.75 (Me); 22.86, 23.27, 26.09, 27.96 (2 Me, rotamers); 26.81, 27.06 (Me, rotamers); 28.33 (Me); 39.42, 39.78 (C, rotamers); 40.16 (CH<sub>2</sub>); 40.81 (CH); 62.80, 63.37 (C, rotamers); 75.02, 75.43 (CH, rotamers); 80.97, 81.40 (C, rotamers); 126.37 (CH); 128.37 (CH); 129.29 (CH); 139.24 (C); 154.36 (C); 174.81, 175.16 (C, rotamers); 176.80 (C). EI-MS: 417.2 ( $< 1$ ,  $[M + H]^+$ ), 359.2 (30), 303.1 (48), 259.1 (25), 157.0 (58), 147.1 (33), 126.1 (13), 119.1 (30), 118.1 (11), 113.1 (80), 91.0 (46), 57.1 (100), 41.0 (15). Anal. calc. for C<sub>24</sub>H<sub>36</sub>N<sub>2</sub>O<sub>4</sub> (416.7): C 69.20, H 8.71, N 6.72; found: C 69.13, H 8.60, N 6.64.

tert-Butyl (2S,2'S)-2-(tert-Butyl)-5,5-dimethyl-3-(2'-methylpent-4'-enoyl)-4-oxoimidazolidine-1-carboxylate (**15**). According to G.P.3, with *ent*-**13** (500 mg, 1.54 mmol) in THF (5 ml), LDA (2.3 mmol) in THF (5 ml), ZnBr<sub>2</sub> (520 mg, 2.30 mmol) in THF (5 ml), and allyl bromide (1.09 ml, 15.4 mmol). Purification by FC (Et<sub>2</sub>O/pentane 1:15): 425 mg (76%) of **15**; 97% ds by HPLC (LiChrosorb Si 100, flow 1 ml/min; UV detection at 254 nm; hexane/*i*-PrOH 99.9:0.1). M.p. 52–52.5°.  $[\alpha]_D^{25} = -134.7$  ( $c = 1.02$ , CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 2980s, 1749s, 1708s, 1641w, 1477m, 1456m, 1385s, 1364s, 1267s, 1169s, 1149s, 1082m, 920w, 885w, 850w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.91, 0.93 (*t*-Bu, rotamers); 1.10 (*t*,  $J = 4.9$ , Me–C(2')); 1.50 (*s*, *t*-Bu); 1.54, 1.58, 1.60, 1.62, 1.66 (5s, 2 Me–C(5), rotamers); 2.05–2.20 (*m*, H–C(3')); 2.55–2.70 (*m*, H–C(3')); 3.50–3.70 (*m*, H–C(2')); 5.05–5.15 (*m*, CH<sub>2</sub>=CHCH<sub>2</sub>); 5.76–5.88 (*m*, CH<sub>2</sub>=CHCH<sub>2</sub>); 5.89, 6.06 (2s, H–C(2), rotamers). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 15.74 (Me); 22.89, 23.28 (Me, rotamers); 26.09, 26.97, 27.22 (Me, rotamers); 27.96, 28.35 (Me, rotamers); 38.33 (CH<sub>2</sub>); 38.51 (CH); 39.53, 39.88 (C, rotamers); 62.78, 63.36 (C, rotamers); 75.06, 75.48 (CH, rotamers); 80.99, 81.44 (C, rotamers); 117.25 (CH<sub>2</sub>); 135.46 (CH); 154.40 (C); 174.88, 175.22 (C); 176.81 (C). EI-MS: 366.3 ( $< 1$ ,  $M^+$ ), 309.2 (21), 253.1 (70), 209.1 (26), 181.2 (11), 157.1 (74), 113.1 (76), 97.1 (21), 69.1 (22), 57.1 (100), 41.0 (21). Anal. calc. for C<sub>20</sub>H<sub>34</sub>N<sub>2</sub>O<sub>4</sub> (366.5): C 65.54, H 9.35, N 7.64; found: C 65.77, H 9.10, N 7.70.

tert-Butyl (2S,2'R)- and (2S,2'S)-2-(tert-Butyl)-3-(3'-methoxy-2'-methylpropanoyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate (**16**). According to G.P.3, with *ent*-**13** (500 mg, 1.54 mmol) in THF (5 ml), LDA (2.3 mmol) in THF (5 ml), ZnBr<sub>2</sub> (520 mg, 2.30 mmol) in THF (5 ml), and MeOCH<sub>2</sub>Cl (1.33 ml, 15.4 mmol). Purification by FC (Et<sub>2</sub>O/pentane 1:8): 225 mg (40%) of **16a** (first eluted) and 52 mg (9%) of **16b**.

**16a**: M.p. 58–59°.  $[\alpha]_D^{25} = -114.8$  ( $c = 1.0$ , CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 2981s, 1751s, 1708s, 1480w, 1457w, 1388s, 1367s, 1262s, 1153s, 1098m, 960w, 887w, 855w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.91, 0.93 (2s, *t*-Bu, rotamers); 1.12, 1.14 (2d,  $J = 6.6$ , 6.2, Me–C(2'), rotamers); 1.50 (*s*, *t*-Bu); 1.55, 1.58, 1.60, 1.63, 1.66 (5s, 2 Me–C(5), rotamers); 3.33 (*s*, MeO); 3.52–3.59 (*m*, H–C(3')); 3.67 (*dd*,  $J = 6.6$ , 9.1, H–C(3')); 3.87–3.99 (*m*, H–C(2')); 5.94, 6.11 (2s, H–C(2), rotamers). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 13.30 (Me); 22.96, 23.21, 23.34 (Me, rotamers); 26.54, 27.95 (Me, rotamers); 26.74, 27.00 (Me, rotamers); 28.32 (Me); 39.56, 39.76, 39.91 (CH, rotamers); 58.71 (Me); 62.81, 63.40 (C, rotamers); 74.94 (CH<sub>2</sub>); 75.38, 75.48 (CH, rotamers); 80.93, 81.41 (C, rotamers); 152.83, 154.41 (C, rotamers); 173.74, 174.02 (C, rotamers); 176.61 (C). EI-MS: 371.2 ( $< 1$ ,  $[M + H]^+$ ), 313.1 (57), 257.1 (100), 225.1 (12), 213.1 (23), 185.1 (15), 181.1 (10), 157.0 (17), 113.1 (18), 101.0 (11), 73.1 (12), 57.1 (83); 45.0 (25), 41.0 (43), 29.0 (18). Anal. calc. for C<sub>19</sub>H<sub>34</sub>N<sub>2</sub>O<sub>5</sub> (370.5): C 61.60, H 9.25, N 7.56; found: C 61.97, H 8.94, N 7.56.

**16b**:  $[\alpha]_D^{25} = -134.2$  ( $c = 0.98$ , CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 2974s, 1749s, 1703s, 1600w, 1477m, 1451m, 1385s, 1364s, 1333m, 1262s, 1164m, 1149s, 1103m, 1082m, 954w, 887w, 851w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.92, 0.94 (2s, *t*-Bu, rotamers); 1.22 (d,  $J = 7.0$ , Me–C(2')); 1.50 (*s*, *t*-Bu); 1.54, 1.58, 1.60, 1.61, 1.66 (5s, 2 Me, rotamers); 3.29–3.35 (*m*, H–C(3'), MeO, rotamers); 3.62–3.75 (*m*, H–C(3')); 3.83–3.98 (*m*, H–C(2')); 5.92, 6.08 (2s, H–C(2), rotamers).

$^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ): 13.50, 14.73 (Me, rotamers); 22.84, 23.21 (Me, rotamers); 26.90, 27.19 (Me, rotamers); 25.67, 27.54 (Me, rotamers); 28.35 (Me); 39.01, 39.60, 39.77, 39.93 (CH, rotamers); 58.92 (Me); 62.72, 63.27 (C, rotamers); 74.24, 74.37 ( $\text{CH}_2$ , rotamers); 74.81, 75.07, 75.27 (CH, rotamers); 80.93, 81.41 (C, rotamers); 152.76, 154.36 (C, rotamers); 173.81, 174.08 (C, rotamers); 176.73, 176.83 (C, rotamers). EI-MS: 257.2 (18), 157.2 (18), 113.2 (28), 101.1 (16), 73.1 (13), 69.1 (11), 57.1 (100), 41.1 (11).

*tert*-Butyl (*S*)-3-{[(*tert*-Butoxy)carbonyl]methyl}-2-{(*tert*-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate} (17). To a soln. of (*S*)-11 (1.0 g, 3.7 mmol) in THF (20 ml), BuLi (2.46 ml, 4.92 mmol) was added at  $-78^\circ$  under Ar. The resulting yellow soln. was stirred at  $-78^\circ$  for 30 min. After addition of *tert*-butyl bromoacetate (0.59 ml, 4.00 mmol), the mixture was allowed to warm to r.t. Workup according to G.P.1 and purification by FC ( $\text{Et}_2\text{O}$ /pentane 2:3) gave 1.27 g (90%) of 17. Colorless solid. M.p. 61.5–62.5°.  $[\alpha]_D^{25} = -26.1$  ( $c = 1.13$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 3007w, 2978m, 1740m, 1697s, 1456w, 1394w, 1381m, 1369s, 1285m, 1153s, 1105m, 952w, 846w.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ): 0.96, 0.98 (2s, *t*-Bu, rotamers); 1.47 (s, *t*-Bu); 1.50 (s, *t*-Bu); 1.52 (s, Me–C(5)); 1.57 (s, Me–C(5)); 3.69 (d,  $J = 17.6$ , H–C(1')); 4.61 (d,  $J = 17.6$ , H–C(1')); 5.10, 5.26 (2s, H–C(2), rotamers).  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ): 24.10, 24.21 (Me, rotamers); 26.76, 27.23 (Me, rotamers); 26.87 (Me); 28.03 (Me); 28.30 (Me); 38.30, 38.63 (C, rotamers); 45.80 ( $\text{CH}_2$ , rotamers); 45.80 ( $\text{CH}_2$ ); 61.22 (CH); 77.96, 78.42 (C, rotamers); 80.51 (C); 82.49 (C); 155.31 (C); 166.68 (C); 175.87 (C). FAB-MS (3-NOBA): 385.2 (14,  $[M + H]^+$ ), 329.2 (69), 327.1 (49), 271.1 (80), 229.1 (36), 227.1 (13), 215.1 (47), 171.1 (37), 126.1 (19), 56.9 (100). Anal. calc. for  $\text{C}_{20}\text{H}_{36}\text{N}_2\text{O}_5$  (384.5): C 62.47, H 9.44, N 7.29; found: C 62.48, H 9.33, N 7.03.

*tert*-Butyl (1*R*,2*S*)-3-{1'-[(*tert*-Butoxy)carbonyl]-2'-phenylethyl}-2-{(*tert*-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate} (18). According to G.P.5, with 17 (100 mg, 0.26 mmol), THF (2 ml), *t*-BuLi (0.19 ml, 0.29 mmol), and benzyl bromide (0.06 ml, 0.52 mmol). Purification by FC (AcOEt/hexane 1:4): 104 mg (84%) of 18 (d.r. 25:1). Colorless solid. M.p. 117–118°.  $[\alpha]_D^{25} = +35.8$  ( $c = 1.25$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 3007w, 2980m, 1699s, 1455m, 1393w, 1369s, 1359s, 1288s, 1152s, 1103w, 1065w, 847w.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ): 0.92, 0.93 (2s, *t*-Bu, rotamers); 1.30 (s, Me–C(5)); 1.41, 1.43 (2s, *t*-Bu, rotamers); 1.49 (Me–C(5)); 1.51, 1.53 (2s, *t*-Bu, rotamers); 3.21, 3.24 (2d,  $J = 14.2$ , 1 H,  $\text{PhCH}_2$ , rotamers); 3.40, 3.41 (2d,  $J = 14.2$ , 1 H,  $\text{PhCH}_2$ , rotamers); 4.02, 4.31 (2s, H–C(2), rotamers); 4.25–4.32 (m, H–C(1')); 7.17–7.34 (m, arom. H).  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ): 23.86, 24.13 (Me, rotamers); 26.00, 27.81 (Me, rotamers); 26.84, 27.13 (Me, rotamers); 27.98 (Me); 28.09 (Me); 35.05, 35.15 ( $\text{CH}_2$ , rotamers); 39.07, 39.32 (C, rotamers); 60.83 (CH); 61.09, 61.63 (C, rotamers); 79.79, 80.36 (CH, rotamers); 80.14, 80.48 (C, rotamers); 82.38, 82.54 (C, rotamers); 127.06 (CH); 128.71 (CH); 129.16, 129.28 (CH, rotamers); 137.44, 137.91 (C, rotamers); 153.01, 154.64 (C, rotamers); 168.22 (C); 174.74 (C). FAB-MS (3-NOBA): 475.3 (26,  $[M + H]^+$ ), 419.2 (84), 417.2 (70), 363.1 (12), 361.1 (81), 319.2 (27), 317.1 (11), 305.1 (61), 261.1 (34), 126.1 (31), 68.9 (11), 56.9 (100). Anal. calc. for  $\text{C}_{27}\text{H}_{42}\text{N}_2\text{O}_5$  (474.6): C 68.32, H 8.92, N 5.90; found: C 68.56, H 8.70, N 5.84.

*tert*-Butyl (1*R*,2*S*)-3-{1'-[(*tert*-Butoxy)carbonyl]ethyl}-2-{(*tert*-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate} (19). According to G.P.5, with 17 (100 mg, 0.26 mmol), THF (2 ml), *t*-BuLi (0.19 ml, 0.29 mmol), and MeI (0.032 ml, 0.520 mmol). Purification by FC ( $\text{Et}_2\text{O}$ /pentane 1:9): 97 mg (93%) of 19 (d.r. 19:1). Colorless oil.  $[\alpha]_D^{25} = -73.3$  ( $c = 0.99$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 3008w, 2980m, 1732m, 1696s, 1456w, 1382m, 1368s, 1357s, 1290m, 1159s, 1114m, 960w, 882w.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ): 1.02 (s, *t*-Bu); 1.40 (d,  $J = 6.9$ , Me(2')); 1.46 (s, Me–C(5)); 1.49 (s, *t*-Bu); 1.50, 1.56 (2s, Me–C(5), rotamers); 4.00 (q,  $J = 6.9$ , H–C(1')); 4.86, 5.06 (2s, H–C(2), rotamers).  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ): 14.08 (Me); 23.24, 23.38 (Me, rotamers); 26.61 (Me); 26.96 (Me); 28.03 (Me); 28.32 (Me); 39.69 (C); 55.17 (CH); 61.37 (C); 78.35 (CH); 80.58 (C); 81.93 (C); 155.42 (C); 168.98, 169.07 (C, rotamers); 174.82 (C). FAB-MS (3-NOBA): 399.2 (52,  $[M + H]^+$ ), 343.2 (100), 341.2 (62), 285.1 (83), 243.1 (31), 241.1 (13), 229.1 (55), 185.1 (34), 154.0 (16), 136.0 (11), 126.1 (25), 112.1 (10), 56.9 (93). Anal. calc. for  $\text{C}_{21}\text{H}_{38}\text{N}_2\text{O}_5$  (398.5): C 63.29, H 9.61, N 7.03; found: C 63.17, H 9.87, N 7.05.

*tert*-Butyl (1*R*,2*S*)-3-{1'-[(*tert*-Butoxy)carbonyl]but-3'-enyl}-2-{(*tert*-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate} (20). According to G.P.5, with 17 (300 mg, 0.78 mmol), THF (6 ml), *t*-BuLi (0.58 ml, 0.86 mmol), and allyl bromide (0.20 ml, 2.34 mmol). Purification by FC (AcOEt/hexane 1:4): 298 mg (90%) of 20 (d.r. 17:1). M.p. 97–98°.  $[\alpha]_D^{25} = -45.8$  ( $c = 0.75$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 3007w, 2980m, 1699s, 1393w, 1382m, 1368s, 1358s, 1292m, 1157s, 1103m, 845w.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ): 1.02 (s, *t*-Bu); 1.46–1.54 (m, 2 *t*-Bu, 2 Me–C(5)); 2.73–2.78 (m, 2 H–C(2')), 4.90, 5.08 (2s, H–C(2), rotamers); 5.05–5.13 (m, 2 H–C(4')); 5.73–5.86 (m, H–C(3')).  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ): 23.67 (Me); 26.76, 26.93 (Me, rotamers); 27.90 (Me); 28.06 (Me); 28.27 (Me); 33.92 ( $\text{CH}_2$ ); 39.27, 39.67 (C, rotamers); 59.35 (CH); 61.31 (C); 80.09 (CH); 80.45, 80.76 (C, rotamers); 82.28 (C); 118.55, 118.77 ( $\text{CH}_2$ , rotamers); 134.18, 134.33 (CH, rotamers); 155.28 (C); 168.07 (C); 174.87 (C). FAB-MS (3-NOBA): 425.2 (28,  $[M + H]^+$ ), 369.2 (73), 367.2 (57), 313.1 (13), 311.1 (74), 269.1 (39), 267.1 (14), 255.1 (59), 211.1 (39), 138.1 (10), 126.1 (30), 68.9 (13), 56.9 (100). Anal. calc. for  $\text{C}_{23}\text{H}_{40}\text{N}_2\text{O}_5$  (424.6): C 65.06, H 9.50, N 6.60; found: C 65.21, H 9.46, N 6.72.



*tert*-Butyl (1'*R*,2*S*)-3-{1'-[*t*-(*tert*-Butoxy)carbonyl]pentyl}-2-(*tert*-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate (**21**). According to *G.P.5*, with **17** (200 mg, 0.52 mmol), THF (4 ml), *t*-BuLi (0.4 ml, 0.6 mmol), and BuI (0.3 ml, 2.6 mmol). Purification by FC (Et<sub>2</sub>O/pentane 1:6): 186 mg (81%) of **21** (d.r. 10:1). Colorless solid. M.p. 86–87°.  $[\alpha]_D^{25} = -45.1$  ( $c = 0.87$ , CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 3009w, 2978m, 1699s, 1393w, 1382m, 1368s, 1358s, 1290m, 1157s, 1101w, 952w, 848w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.80–1.00 (*m*, *t*-Bu); 1.02 (*s*, *t*-Bu); 1.20–1.50 (*m*, 2 Me); 1.45 (*s*, Me–C(5)); 1.49, 1.50 (2*s*, *t*-Bu, rotamers); 1.90–2.10 (*m*, CH<sub>2</sub>); 3.81–3.86 (*m*, H–C(1')); 4.89, 5.06 (2*s*, H–C(2), rotamers). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 13.92 (Me); 22.52 (CH<sub>2</sub>); 23.53 (Me); 26.64, 26.87 (Me, rotamers); 27.51 (Me); 28.07 (Me); 28.29 (Me); 28.98 (Me); 39.72 (C); 59.96 (CH); 61.40 (C); 80.09 (CH<sub>2</sub>); 80.51 (C); 81.97 (C); 155.34 (C); 168.75 (C); 174.75 (C). FAB-MS (3-NOBA): 441.3 (35, [*M* + H]<sup>+</sup>), 385.2 (93), 383.2 (62), 329.1 (11), 327.1 (78), 285.2 (21), 283.1 (12), 271.1 (60), 227.1 (33), 154.1 (14), 126.1 (27), 69.0 (11), 56.9 (100). Anal. calc. for C<sub>24</sub>H<sub>44</sub>N<sub>2</sub>O<sub>5</sub> (440.6): C 65.42, H 10.07, N 6.36; found: C 65.58, H 10.17, N 6.13.

*tert*-Butyl (1'*R*,2*S*)-3-{1'-[*t*-(*tert*-Butoxy)carbonyl]-2'-methylpropyl}-2-(*tert*-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate (**22**). According to *G.P.5*, with **17** (100 mg, 0.26 mmol), THF (2 ml), *t*-BuLi (10.19 ml, 0.29 mmol), and *i*-PrI (0.1 ml, 1.0 mmol). Purification by FC (Et<sub>2</sub>O/pentane 1:7): 44 mg (40%) of **22** (d.r. 43:1) and 37 mg (37%) of **17**. **22**: Colorless solid. M.p. 146–147°.  $[\alpha]_D^{25} = -50.6$  ( $c = 0.82$ , CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 3008w, 2979m, 1697s, 1382m, 1368s, 1358m, 1288m, 1159s, 1100m, 949w, 847w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.95 (*d*, *J* = 6.9, Me–C(2')); 1.03 (*s*, *t*-Bu); 1.07 (*d*, *J* = 6.7, Me–C(2')); 1.49 (br. *s*, 2 *t*-Bu, Me–C(5)); 1.56 (*s*, Me–C(5)); 2.57–2.69 (*m*, H–C(2')); 3.59 (*d*, *J* = 8.0, H–C(1')); 4.95, 5.12 (2*s*, H–C(2), rotamers). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 19.25, 19.64 (Me, rotamers); 21.07 (Me); 23.72, 23.92 (Me, rotamers); 26.93 (Me); 27.84, 28.10 (Me, rotamers); 28.32 (Me); 29.18, 29.36 (CH, rotamers); 39.67 (C); 61.28 (C); 65.26 (CH); 80.51, 80.79 (CH, rotamers); 81.93 (2 C); 155.30 (C); 167.92 (C); 174.89 (C). FAB-MS (3-NOBA): 427.3 (38, [*M* + H]<sup>+</sup>), 371.2 (88), 369.2 (54), 315.1 (14), 313.1 (68), 271.2 (29), 269.1 (15), 257.1 (67), 213.1 (39), 154.0 (12), 140.1 (13), 126.1 (32), 68.9 (13), 56.9 (100), 54.9 (11). Anal. calc. for C<sub>24</sub>H<sub>42</sub>N<sub>2</sub>O<sub>5</sub> (426.6): C 64.76, H 9.92, N 6.57; found: C 64.57, H 10.08, N 6.39.

3,3'-Heptanedioylbis[*tert*-butyl 2-(*tert*-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate] (**23**). According to *G.P.1*, with (*S*)-**11** (1.0 g, 3.7 mmol), THF (20 ml), BuLi (2.53 ml, 3.80 mmol), and heptanedioyl dichloride (0.31 ml, 1.85 mmol). Purification by FC (Et<sub>2</sub>O/pentane 1:3): 1.12 g (91%) of **23**. M.p. 41.5–43°.  $[\alpha]_D^{25} = -136.4$  ( $c = 0.8$ , CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 2979s, 1750s, 1709s, 1480w, 1456w, 1389s, 1368s, 1273m, 1152m, 1100w, 1080m, 965w, 887w, 858w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.91, 0.93 (2*s*, *t*-Bu, rotamers); 1.40–1.85 (*m*, 3 CH<sub>2</sub>); 1.50 (*s*, *t*-Bu); 1.54, 1.58, 1.64, 1.65 (4*s*, 2 Me–C(5), rotamers); 2.70–3.00 (*m*, 2 CH<sub>2</sub>–C(1')); 5.87, 6.04 (2*s*, H–C(2), rotamers). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 22.82, 23.21 (Me, rotamers); 24.21 (CH<sub>2</sub>); 25.92, 27.79 (Me, rotamers); 27.03, 27.31 (Me, rotamers); 28.33 (Me); 28.65 (CH<sub>2</sub>); 36.55 (CH<sub>2</sub>); 39.50, 39.86 (C, rotamers); 62.61, 63.18 (C, rotamers); 74.96, 75.41 (CH, rotamers); 80.96, 81.41 (C, rotamers); 152.71, 154.34 (C, rotamers); 171.82, 172.15 (C, rotamers); 176.86 (C). FAB-MS (3-NOBA): 666.4 (2, [*M* + H]<sup>+</sup>), 607.3 (18), 553.3 (26), 509.3 (11), 507.3 (25), 339.1 (11), 215.1 (27), 213.1 (14), 197.1 (35), 171.1 (16), 157.0 (30), 154.0 (13), 125.0 (40), 113.0 (84), 86.0 (21), 68.9 (16), 57.9 (100). Anal. calc. for C<sub>35</sub>H<sub>60</sub>N<sub>4</sub>O<sub>8</sub> (664.9): C 63.23, H 9.10, N 8.43; found: C 63.25, H 8.99, N 8.21.

3,3'-(Cyclopentane-1,2-dicarbonyl)bis[*tert*-butyl 2-(*tert*-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate] (**24**). To a soln. of **23** (500 mg, 0.73 mmol) in THF (2 ml), a precooled soln. of LDA (1.58 mmol) in THF (3 ml), prepared according to *G.P.3*, was added under Ar at –78°. The resulting pale yellow soln. was stirred for 60 min and treated with CuCl<sub>2</sub> (dried under h.v. at 180°, 16 h; 215 mg, 0.73 mmol). The resulting suspension was stirred at –78° for 24 h. Workup according to *G.P.1*, and purification by FC (AcOEt/hexane 1:4): 327 mg (66%) of **24**. Colorless solid. M.p. 139.5–141°.  $[\alpha]_D^{25} = -94.9$  ( $c = 0.84$ , CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 2975s, 1755s, 1704s, 1480w, 1456w, 1388s, 1368s, 1271m, 1150s, 1082m, 964w, 886w, 853w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.94, 0.95 (2*s*, *t*-Bu, rotamers); 1.49 (*s*, *t*-Bu); 1.53, 1.56, 1.57, 1.61, 1.64, 1.65 (Me–C(5), rotamers); 1.60–2.10 (*m*, 3 CH<sub>2</sub> (cyclopentane)); 4.14–4.35 (*m*, 2 H–C(2')); 5.86, 6.03 (2*s*, H–C(2), rotamers). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 22.70, 23.11 (Me, rotamers); 25.22 (CH); 26.06, 27.91 (Me, rotamers); 26.91, 27.18 (Me, rotamers); 28.35 (Me); 28.61, 28.80 (CH<sub>2</sub>, rotamers); 39.67, 40.01 (C, rotamers); 48.23 (CH); 62.61, 63.19 (CH, rotamers); 75.33, 75.77 (C, rotamers); 80.93, 81.38 (C, rotamers); 152.75, 154.34 (C, rotamers); 173.13, 173.47 (C, rotamers); 176.70, 176.86 (C, rotamers). FAB-MS (3-NOBA): 663.4 (6, [*M* + H]<sup>+</sup>), 605.3 (11), 393.2 (67), 337.1 (25), 293.1 (18), 235.1 (11), 197.1 (17), 157.0 (19), 126.1 (45), 113.0 (31), 95.0 (34), 56.9 (100). Anal. calc. for C<sub>35</sub>H<sub>58</sub>N<sub>4</sub>O<sub>8</sub> (662.9): C 63.42, H 8.82, N 8.45; found: C 63.23, H 8.55, N 8.27.

3,3'-(2,5-Diiodoheptanedioyl)bis[*tert*-butyl 2-(*tert*-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate] (**25**). To a soln. of **23** (0.150 g, 0.226 mmol) in Et<sub>2</sub>O (1 ml), a precooled soln. of LDA (0.474 mmol) in Et<sub>2</sub>O (1 ml), prepared according to *G.P.3*, was added under Ar at –78°. The resulting pale yellow soln. was stirred for 60 min, treated with a soln. of I<sub>2</sub> (127 mg, 0.50 mmol) in THF (0.5 ml), and allowed to warm to r.t. overnight. Workup according to *G.P.1*, and purification by FC (Et<sub>2</sub>O/pentane 1:8) gave 99 mg (48%) of **25**. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.92–0.99 (*m*, *t*-Bu, rotamers); 1.20–1.60 (*m*, CH<sub>2</sub>, rotamers); 1.51 (*s*, *t*-Bu); 1.55, 1.58, 1.60, 1.62, 1.65,

1.67 (5s, Me); 2.00–2.20 (br. *m*, 2  $\text{CH}_2\text{CHI}$ ); 5.55–5.59 (*m*, 2  $\text{CH}_2\text{CHI}$ ); 5.84, 5.92, 6.01, 6.10 (4s, H–C(2), rotamers).  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ): 21.26, 21.58, 21.68, 21.98 (Me, rotamers); 23.03, 23.24, 23.42 (Me, rotamers); 25.93, 26.35, 26.57, 26.84, 27.07, 27.33, 27.81 (Me, rotamers); 28.33, 28.60 (Me, rotamers); 28.88, 29.08 ( $\text{CH}_2$ , rotamers); 34.13, 34.83 ( $\text{CH}_2$ , rotamers); 39.90, 40.86, 41.17 (C, rotamers); 62.62, 62.93, 63.52 (C, rotamers); 75.01, 75.48, 75.60, 76.08 (CH, rotamers); 81.15, 81.69 (C, rotamers); 152.74, 154.34 (C, rotamers); 168.93, 169.18 (C, rotamers); 176.23 (C). FAB-MS (3-NOBA): 917.3 (2,  $[M + H]^+$ ), 805.2 (13), 197.2 (10), 157.1 (12), 154.1 (12), 126.1 (26), 113.0 (70), 68.9 (10), 56.9 (100).

*Dimethyl (1S,2S)-Cyclopentane-1,2-dicarboxylate (26)*. Transformation to the diacid according to *G.P.4*, with **24** (160 mg, 0.24 mmol), THF/ $\text{H}_2\text{O}$  (6 ml),  $\text{H}_2\text{O}_2$  (0.44 ml, 3.87 mmol), LiOH (23.2 mg, 0.97 mmol; 75 min), and 1*M*  $\text{NaHSO}_3$  (4.1 ml, 4.1 mmol). The diacid was dissolved in  $\text{Et}_2\text{O}$  and esterified with diazomethane. Purification by bulb-to-bulb distillation (100°/0.5 Torr): 35 mg (78%) of **26** (86% ee). Physical data: in agreement with data in [48].  $[\alpha]_D^{25} = +61.8$  ( $c = 0.60$ ,  $\text{CCl}_4$ , [48]);  $+71.9$  ( $c = 1.1$ ,  $\text{CCl}_4$ ).

*tert-Butyl (R)-3-{[(tert-Butoxy)carbonylamino]acetyl}-2-(tert-butyl)-5,5-dimethyl-4-oximidazolidine-1-carboxylate (29)*. According to *G.P.1*, with (*R*)-**11** (1.0 g, 3.7 mmol) in THF (20 ml), BuLi (2.71 ml, 4.1 mmol), and Boc-Gly-F (prepared according to [52]; 786 mg, 4.44 mmol) in THF (10 ml). Purification by FC ( $\text{Et}_2\text{O}$ /pentane 1:3): 1.15 g (73%) of **29**. Colorless solid. M.p. 47.5–48.5°.  $[\alpha]_D^{25} = +89.9$  ( $c = 1.05$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 3451*w*, 2981*s*, 1755*s*, 1702*s*, 1504*s*, 1456*w*, 1392*s*, 1368*s*, 1154*s*, 1082*m*, 965*w*, 887*w*, 856*w*.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ): 0.93, 0.95 (Me, *t*-Bu, rotamers); 1.46 (Me, *t*-Bu); 1.50 (Me, *t*-Bu); 1.56, 1.69, 1.65, 1.68 (4s, 2 Me–C(5), rotamers); 4.32, 4.38, 4.42, 4.49 (4*d*,  $J = 5.2, 5.3, 6.0, 5.8$ , 2 H–C(2'), rotamers); 5.10–5.30 (br. *s*, NH); 5.85, 6.03 (2*s*, H–C(2), rotamers).  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ): 22.86, 23.21 (Me, rotamers); 25.94 (Me); 26.96, 27.26 (Me, rotamers); 27.80 (Me); 27.95, 28.04 (Me, rotamers); 28.32 (Me); 39.53, 39.89 (C, rotamers); 45.86 ( $\text{CH}_2$ ); 62.42 (C); 75.13, 75.65 (CH, rotamers); 79.96 (C); 81.19, 81.60 (C, rotamers); 154.27 (C); 155.75 (C); 168.82 (C); 176.94 (C). FAB-MS (3-NOBA): 855.4 (6,  $[2 M + H]^+$ ), 428.1 (7,  $[M + H]^+$ ), 372.1 (23), 316.1 (52), 272.1 (42), 213.1 (58), 157.1 (48), 154.1 (13), 137.0 (10), 126.1 (20), 113.0 (24), 86.0 (11), 56.9 (100). Anal. calc. for  $\text{C}_{21}\text{H}_{37}\text{N}_3\text{O}_6$  (427.5): C 59.00, H 8.72, N 9.83; found: C 59.05, H 8.73, N 9.59.

*tert-Butyl (2R,2'R)-3-{2'-[(tert-Butoxy)carbonylamino]propanoyl}-2-(tert-butyl)-5,5-dimethyl-4-oximidazolidine-1-carboxylate (30)*. According to *G.P.6*, with **29** (400 mg, 0.94 mmol) in THF (8 ml), *t*-BuLi (0.19 ml, 0.29 mmol),  $\text{ZnBr}_2$  (529 mg, 2.34 mmol) in THF (8 ml), and MeI (0.44 ml, 7.50 mmol). Purification by FC ( $\text{Et}_2\text{O}$ /pentane 1:3): 333 mg (81%) of **30**; > 99% ds by HPLC (*LiChrosorb Si 100*, flow 1 ml/min; UV detection at 254 nm; hexane/*i*-PrOH 99:1). Colorless solid. M.p. 118–119°.  $[\alpha]_D^{25} = +101.0$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 3440*w*, 2974*s*, 1754*s*, 1708*s*, 1497*s*, 1456*m*, 1390*s*, 1364*s*, 1262*m*, 1164*s*, 1087*m*, 1015*w*, 959*w*, 887*w*, 851*w*.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ): 0.90, 0.92 (2*s*, *t*-Bu, rotamers); 1.43 (*s*, *t*-Bu); 1.47 (*d*,  $J = 6.7$ , Me–C(2')); 1.50 (*s*, *t*-Bu); 1.58, 1.61, 1.65, 1.66 (4*s*, 2 Me–C(5), rotamers); 5.12–5.29 (*m*, NH, H–C(2')); 5.89, 6.08 (2*s*, H–C(2), rotamers).  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ): 19.22 (Me); 22.97, 23.30 (Me, rotamers); 25.94 (Me); 26.74 (Me); 27.03 (Me); 27.82 (Me); 28.09 (Me); 28.35 (Me); 39.67, 40.02 (C, rotamers); 50.05 (CH); 62.68, 63.22 (C, rotamers); 74.75, 75.26 (CH, rotamers); 79.74 (C); 81.14, 81.58 (C, rotamers); 154.42 (C); 155.00 (C); 172.39 (C); 176.32 (C). FAB-MS (3-NOBA): 883.4 (3,  $[2 M + H]^+$ ), 442.2 (10,  $[M + H]^+$ ), 386.1 (11), 330.1 (56), 286.1 (45), 215.1 (17), 213.1 (59), 157.1 (58), 126.1 (18), 113.0 (28), 87.9 (11), 86.0 (13), 56.9 (100). Anal. calc. for  $\text{C}_{22}\text{H}_{39}\text{N}_3\text{O}_6$  (441.6): C 59.84, H 8.90, N 9.52; found: C 59.92, H 8.83, N 9.43.

*tert-Butyl (2R,2'R)-3-{2'-[(tert-Butoxy)carbonylamino]butanoyl}-2-(tert-butyl)-5,5-dimethyl-4-oximidazolidine-1-carboxylate (31)*. According to *G.P.6*, with **29** (200 mg, 0.47 mmol) in THF (4 ml), *t*-BuLi (0.69 ml, 1.03 mmol),  $\text{ZnBr}_2$  (276 mg, 1.22 mmol) in THF (4 ml), and EtI (0.30 ml, 3.74 mmol). Purification by FC ( $\text{Et}_2\text{O}$ /pentane 1:7): 150 mg (70%) of **31**; > 98% ds by  $^1\text{H}$ -NMR. Colorless solid. M.p. 142–142.5°.  $[\alpha]_D^{25} = +89.6$  ( $c = 1.04$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 3436*w*, 2974*s*, 1754*s*, 1708*s*, 1497*s*, 1477*m*, 1456*w*, 1385*s*, 1364*s*, 1267*s*, 1164*s*, 1077*m*, 887*w*, 851*w*.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ): 0.90, 0.92 (2*s*, *t*-Bu, rotamers); 1.08 (*t*,  $J = 7.3$ , Me–C(3')); 1.43 (*s*, *t*-Bu); 1.50 (*s*, *t*-Bu); 1.58, 1.61, 1.65, 1.67 (4*s*, 2 Me, rotamers); 1.90–2.10 (*m*,  $\text{CH}_2$ –C(2')); 4.90–5.10 (*m*, H–C(2'), NH); 5.88, 6.06 (2*s*, H–C(2), rotamers).  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ): 10.29 (Me); 23.01, 23.34 (Me, rotamers); 25.93 (Me); 26.82, 27.11 (Me, rotamers); 39.61, 39.97 (C, rotamers); 55.26 (CH); 62.68, 63.23 (C, rotamers); 74.84, 75.36 (CH, rotamers); 79.71 (C); 81.14, 81.56 (C, rotamers); 154.43 (C); 155.61 (C); 171.98 (C); 176.45, 176.59 (C, rotamers). FAB-MS (3-NOBA): 911.4 (4,  $[2 M + H]^+$ ), 456.2 (19,  $[M + H]^+$ ), 400.1 (18), 356.2 (15), 344.1 (90), 300.1 (59), 269.1 (19), 213.1 (100), 197.1 (10), 171.1 (12), 157.0 (96), 154.0 (14), 136.0 (12), 126.1 (24), 113.0 (49), 102.0 (29), 86.0 (24), 74.0 (24), 69.0 (13), 56.9 (95), 54.8 (11). Anal. calc. for  $\text{C}_{23}\text{H}_{41}\text{N}_3\text{O}_6$  (455.6): C 60.64, H 9.07, N 9.22; found: C 60.85, H 8.89, N 9.27.

*tert-Butyl (2R,2'R)-3-{2'-[(tert-Butoxy)carbonylamino]pent-4'-enoyl}-2-(tert-butyl)-5,5-dimethyl-4-oximidazolidine-1-carboxylate (32)*. According to *G.P.6*, with **29** (200 mg, 0.47 mmol) in THF (4 ml), *t*-BuLi (0.69 ml,

1.03 mmol),  $\text{ZnBr}_2$  (276 mg, 1.22 mmol) in THF (4 ml), and allyl bromide (0.32 ml, 3.74 mmol). Purification by FC ( $\text{Et}_2\text{O}$ /pentane 1:8): 166 mg (70%) of **32**; > 98% ds by  $^1\text{H-NMR}$ . Colorless solid. M.p.  $38-41^\circ$ .  $[\alpha]_D^{25} = +87.8$  ( $c = 1.11$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 3436w, 2974s, 1754s, 1708s, 1497s, 1477m, 1456w, 1390s, 1369s, 1272s, 1159s, 1082m, 928w, 887w, 856w.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 0.90, 0.93 (2s, *t*-Bu, rotamers); 1.42 (s, *t*-Bu); 1.51 (s, *t*-Bu); 1.59, 1.62, 1.66, 1.67 (4s, 2 Me, rotamers); 2.30–2.50 (*m*,  $\text{H-C}(3'')$ ); 2.70–2.90 (*m*,  $\text{H-C}(3'')$ ); 5.08–5.22 (*m*,  $\text{H-C}(2'')$ , NH, 2  $\text{H-C}(5'')$ ); 5.75–5.88 (*m*,  $\text{H-C}(4'')$ ); 5.88, 6.06 (2s,  $\text{H-C}(2)$ , rotamers).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ): 22.99, 23.31 (Me, rotamers); 25.90 (Me); 26.80, 27.10 (Me, rotamers); 27.80 (Me); 28.33 (Me); 37.17 ( $\text{CH}_2$ ); 39.59, 39.94 (C); 53.11 (CH); 62.65, 63.18 (C); 74.87, 75.40 (CH); 79.77 (C); 81.15, 81.60 (C); 119.15 ( $\text{CH}_2$ ); 132.54 (CH); 154.39 (C); 155.26 (C); 171.16, 171.35 (C, rotamers); 176.80 (C). FAB-MS (3-NOBA): 468.2 (6,  $[\text{M} + \text{H}]^+$ ), 368.2 (14), 356.1 (38), 312.1 (42), 269.1 (15), 213.1 (62), 171.1 (12), 157.0 (64), 126.1 (27), 113.0 (45), 86.0 (25), 69.9 (53), 56.9 (100). Anal. calc. for  $\text{C}_{24}\text{H}_{41}\text{N}_3\text{O}_6$  (467.6): C 61.65, H 8.84, N 8.99; found: C 61.35, H 8.61, N 8.86.

tert-Butyl (2*R*,2'*R*)-3-{2'-[(tert-Butoxy)carbonylamino]-3'-phenylpropanoyl}-2-(tert-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate (**33**). According to *G.P.6*, with **29** (200 mg, 0.47 mmol) in THF (4 ml), *t*-BuLi (0.69 ml, 1.03 mmol),  $\text{ZnBr}_2$  (276 mg, 1.22 mmol) in THF (4 ml), and benzyl bromide (0.44 ml, 3.74 mmol). Purification by FC ( $\text{Et}_2\text{O}$ /pentane 1:7): 176 mg (73%) of **33**; > 99% ds by HPLC (*LiChrosorb Si 100*, flow 1 ml/min; UV detection at 254 nm, hexane/*i*-PrOH 99:1). Colorless solid. M.p.  $169-174^\circ$ .  $[\alpha]_D^{25} = +68.0$  ( $c = 1.08$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 3443w, 2980m, 1757m, 1709s, 1497m, 1456w, 1391m, 1368s, 1269m, 1168s, 1080m, 887w, 853w.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 0.92, 0.94 (2s, *t*-Bu, rotamers); 1.16, 1.31 (2 br. s, *t*-Bu); 1.51 (s, *t*-Bu); 1.61, 1.62, 1.65, 1.70 (4s, 2 Me, rotamers); 2.50–2.70 (*m*,  $\text{H-C}(3'')$ ); 3.30–3.50 (*m*,  $\text{H-C}(3'')$ ); 4.98 (*d*,  $J = 8$ , NH); 5.38–5.46 (*m*,  $\text{H-C}(2'')$ ); 5.91–6.08 (2s,  $\text{H-C}(2)$ , rotamers); 7.24–7.38 (*m*, arom. H).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ): 23.00, 23.34 (Me, rotamers); 25.94 (Me); 26.83, 27.13 (Me); 27.84 (Me); 28.22, 28.35 (Me, rotamers); 38.99 ( $\text{CH}_2$ ); 39.65, 40.00 (C, rotamers); 55.00 (CH); 62.72, 63.27 (C, rotamers); 74.96, 75.23 (CH, rotamers); 79.71 (C); 81.17, 81.61 (C, rotamers); 126.93 (CH); 128.51 (CH); 129.41 (CH); 136.39 (C); 152.66 (C); 155.15 (C, rotamers); 171.42 (C); 176.81, 176.96 (C, rotamers). FAB-MS (3-NOBA): 518.3 (6,  $[\text{M} + \text{H}]^+$ ), 418.2 (21), 406.1 (24), 362.1 (51), 269.1 (10), 213.1 (54), 171.1 (15), 164.0 (23), 157.0 (62), 154.0 (11), 136.0 (10), 126.1 (28), 120.0 (59), 113.0 (42), 91.0 (15), 86.0 (25), 68.9 (10), 56.9 (100). Anal. calc. for  $\text{C}_{28}\text{H}_{43}\text{N}_3\text{O}_6$  (517.7): C 64.97, H 8.37, N 8.12; found: C 65.18, H 8.25, N 8.13.

tert-Butyl (2*R*,2'*R*)-3-{2'-[(tert-Butoxy)carbonylamino]hexanoyl}-2-(tert-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate (**34**). According to *G.P.6*, with **29** (200 mg, 0.47 mmol) in THF (4 ml), *t*-BuLi (0.69 ml, 1.03 mmol),  $\text{ZnBr}_2$  (276 mg, 1.22 mmol) in THF (4 ml), and BuI (0.43 ml, 3.74 mmol). Purification by FC ( $\text{Et}_2\text{O}$ /pentane 1:8): 115 mg (51%) of **34**; > 98% ds by  $^1\text{H-NMR}$ . Colorless solid. M.p.  $210-211^\circ$ .  $[\alpha]_D^{25} = +94.0$  ( $c = 1.03$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 3436w, 2974m, 1754m, 1703s, 1497m, 1456w, 1385s, 1364s, 1267m, 1164s, 856w.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 0.90–0.93 (*m*, *t*-Bu, rotamers); 1.25–1.50 (*m*, Bu); 1.43 (s, *t*-Bu); 1.50 (s, *t*-Bu); 1.58, 1.61, 1.65, 1.67 (4s, 2 Me–C(5)); 1.71–1.95 (*m*, 2  $\text{H-C}(3'')$ ); 5.06–5.15 (*m*, NH,  $\text{H-C}(2'')$ ); 5.88, 6.05 (2s,  $\text{H-C}(2)$ , rotamers).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ): 13.95 (Me); 22.28 ( $\text{CH}_2$ ); 22.97, 23.30 (Me, rotamers); 25.92, 27.81 (Me, rotamers); 26.79, 27.08 (Me, rotamers); 27.96 ( $\text{CH}_2$ ); 28.58 (Me); 33.11 ( $\text{CH}_2$ ); 39.63, 39.98 (C); 54.07 (CH); 62.67, 63.20 (C, rotamers); 74.78, 75.30 (CH, rotamers); 79.67 (C); 81.11, 81.56 (C); 152.68, 154.41 (C, rotamers); 155.48, 155.57 (C, rotamers); 172.18 (C); 176.48, 176.56 (C, rotamers). FAB-MS (3-NOBA): 484.2 (3,  $[\text{M} + \text{H}]^+$ ), 372.2 (17), 328.2 (40), 171.2 (12), 157.1 (14), 126.1 (12), 86.0 (24), 56.9 (100). Anal. calc. for  $\text{C}_{25}\text{H}_{45}\text{N}_3\text{O}_6$  (483.7): C 62.09, H 9.38, N 8.69; found: C 62.31, H 9.23, N 8.54.

tert-Butyl (2*R*,2'*R*)-3-{2'-[(tert-Butoxy)carbonylamino]-2'-cyclohexylacetyl}-2-(tert-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate (**35**). According to *G.P.6*, with *ent*-**29** (100 mg, 0.234 mmol) in THF (2 ml), *t*-BuLi (0.35 ml, 0.52 mmol),  $\text{ZnBr}_2$  (138 mg, 0.61 mmol) in THF (2 ml), and 3-bromocyclohexene (0.11 ml, 0.94 mmol). Purification by FC ( $\text{Et}_2\text{O}$ /pentane 1:3) yielded the primary alkylation product as a 3:1 diastereoisomer mixture. Hydrogenation according to *G.P.2*, with EtOH (5 ml) and Pd/C (10 mg): 94 mg (79%) of **35**; > 98% ds by  $^1\text{H-NMR}$ . Colorless solid. M.p.  $149-151^\circ$ .  $[\alpha]_D^{25} = -72.1$  ( $c = 1.22$ ,  $\text{CHCl}_3$ ). IR ( $\text{CHCl}_3$ ): 3445w, 2979s, 2932s, 2857w, 1755s, 1707s, 1500s, 1452m, 1392s, 1368s, 1303w, 1266s, 1167s, 1082m, 887w, 859w.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 0.92, 0.94 (2s, *t*-Bu, rotamers); 1.00–2.00 (*m*,  $\text{C}_6\text{H}_{11}$ ); 1.42 (s, *t*-Bu); 1.50 (s, *t*-Bu); 1.58, 1.60, 1.62, 1.67 (4s, 2 Me, rotamers); 5.02–5.05 (*m*,  $\text{H-C}(2'')$ ); 5.14–5.17 (*m*, NH); 5.88, 6.06 (2s,  $\text{H-C}(2)$ , rotamers).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ): 23.04, 23.41 (Me, rotamers); 26.02 ( $\text{CH}_2$ ); 26.32 ( $\text{CH}_2$ ); 26.81 (Me); 27.12, 27.77 (Me, rotamers); 28.26, 28.35 (Me, rotamers); 30.40 ( $\text{CH}_2$ ); 39.45, 39.82 (C, rotamers); 40.90 (CH); 57.86 (CH); 62.61, 63.14 (C, rotamers); 74.85, 75.36 (CH, rotamers); 79.62 (C); 81.10, 81.52 (C, rotamers); 152.64 (C); 154.39, 155.72 (C, rotamers); 171.30 (C); 176.72 (C). FAB-MS (3-NOBA): 510.1 (12,  $[\text{M} + \text{H}]^+$ ), 410.1 (12), 354.1 (17), 215.0 (27), 213.0 (20), 171.1 (19), 157.0 (19), 126.0 (24), 112.0 (54), 85.9 (16), 56.9 (100). Anal. calc. for  $\text{C}_{27}\text{H}_{47}\text{N}_3\text{O}_6$  (509.7): C 63.63, H 9.29, N 8.24; found: C 63.48, H 9.31, N 8.09.

tert-Butyl (R,E)-3-(But-2'-enoyl)-2-(tert-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate (**36**). According to *G.P.1*, with (*R*)-**11** (3.96 g, 14.7 mmol) in THF (15 ml), BuLi (10.1 ml, 16.1 mmol), and crotonyl chloride (1.89 ml, 19.5 mmol). Purification by FC (Et<sub>2</sub>O/pentane 1:9): 4.27 g (86%) of **36**. Colorless oil.  $[\alpha]_D^{25} = +133.8$  (*c* = 1.02, CHCl<sub>3</sub>). IR (CHCl<sub>3</sub>): 2980m, 1750m, 1700s, 1640w, 1480w, 1440w, 1390m, 1370m, 1340m, 1270w, 1150m, 1100w, 1080w, 970w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.93, 0.95 (2s, *t*-Bu, rotamers); 1.50 (s, *t*-Bu); 1.54, 1.58, 1.59, 1.65 (4s, 2 Me-C(5), rotamers); 1.97 (*d*, *J* = 5.5, Me-C(3')); 5.95, 6.11 (2s, H-C(2), rotamers); 7.15–7.19 (*m*, H-C(3'), H-C(2')). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 18.60 (Me); 22.87, 23.25 (Me, rotamers); 25.87, 27.75 (Me, rotamers); 27.26, 27.00 (Me, rotamers); 28.33 (Me); 39.69, 40.06 (C, rotamers); 62.83, 63.42 (C, rotamers); 75.13, 75.56 (CH, rotamers); 80.91, 81.38 (C, rotamers); 123.13 (CH); 147.45, 147.57 (CH, rotamers); 152.78, 154.38 (C, rotamers); 164.12, 164.34 (C, rotamers); 176.91 (C). FAB-MS (3-NOBA): 677.4 (2, [2 *M* + H]<sup>+</sup>), 339.2 (61, [*M* + H]<sup>+</sup>), 283.1 (47), 281.1 (59), 239.1 (23), 225.1 (74), 197.1 (18), 181.1 (42), 157.0 (16), 154.0 (13), 126.1 (16), 113.0 (17), 68.9 (78), 56.9 (100). Anal. calc. for C<sub>18</sub>H<sub>30</sub>N<sub>2</sub>O<sub>4</sub> (338.5): C 63.88, H 8.93, N 8.28; found: C 63.86, H 8.99, N 8.33.

tert-Butyl (2*R*,3'*R*)-2-(tert-Butyl)-5,5-dimethyl-4-oxo-3-(3'-phenylbutanoyl)imidazolidine-1-carboxylate (**37a**). According to *G.P.8*, with **36** (509 mg, 1.50 mmol) in THF (3 ml), Mg (110 mg, 4.50 mmol), bromobenzene (0.47 ml, 4.50 mmol), and CuBr·SMe<sub>2</sub> (463 mg, 2.30 mmol) in THF (6 ml): 80% of **37a**; 99% ds by HPLC (*Chiracel OD*, flow 1 ml/min; UV detection at 250 nm; hexane/*i*-PrOH 99.7:0.3). Colorless oil. IR (CHCl<sub>3</sub>): 2980m, 1750m, 1700s, 1480w, 1450w, 1390m, 1370m, 1270m, 1150m, 1080w, 970w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 0.77 (s, *t*-Bu); 1.31–1.34 (*m*, Me-C(3')); 1.48, 1.49 (2s, *t*-Bu, rotamers); 1.54, 1.58, 1.61, 1.64 (4s, 2 Me-C(5)); 2.93–3.04 (*m*, H-C(3')); 3.34–3.49 (*m*, 2 H-C(2')); 5.84, 6.02 (2s, H-C(2), rotamers); 7.10–7.35 (*m*, arom. H). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): 22.08 (Me); 22.86, 25.93 (Me, rotamers); 23.24, 27.77 (Me, rotamers); 26.80, 27.04 (Me, rotamers); 28.31 (Me); 35.96 (CH<sub>2</sub>); 39.33, 39.69 (C, rotamers); 44.42 (CH<sub>2</sub>); 62.61, 63.21 (C, rotamers); 74.96, 75.36 (CH, rotamers); 80.96, 81.38 (C, rotamers); 126.34 (CH); 127.02 (CH); 128.45 (CH); 145.83 (C); 154.29 (C); 170.53, 170.84 (C, rotamers); 176.94 (C). FAB-MS (3-NOBA): 417.2 (26, [*M* + H]<sup>+</sup>), 361.1 (34), 359.1 (25), 303.1 (18), 259.1 (12), 215.1 (12), 197.1 (12), 157.0 (30), 154.0 (13), 147.0 (15), 126.1 (13), 113.0 (40), 105.0 (71), 90.0 (14), 56.9 (100). Anal. calc. for C<sub>24</sub>H<sub>36</sub>N<sub>2</sub>O<sub>4</sub> (416.6): C 69.20, H 8.71, N 6.72; found: C 69.28, H 8.63, N 6.79.

tert-Butyl (2*R*,3'*R*)- and (2*R*,3'*S*)-2-(tert-Butyl)-3-(3'-cyclohexylbutanoyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate (**38**). According to *G.P.8*, with **36** (214 mg, 0.64 mmol) in THF (2 ml), Mg (47 mg, 1.9 mmol), cyclohexyl bromide (0.24 ml, 2.00 mmol), and CuBr·SMe<sub>2</sub> (197 mg, 0.69 mmol) in THF (3 ml): 247 mg (92%) of **38a/38b** 64:36 (ratio determined after LiBH<sub>4</sub> reduction of the crude mixture). The isomers **38a/38b** were inseparable. FAB-MS (3-NOBA): 423.3 (57, [*M* + H]<sup>+</sup>), 412.2 (24), 367.2 (59), 365.2 (62), 309.1 (32), 271.2 (23), 265.1 (22), 215.1 (21), 213.1 (40), 197.1 (29), 171.1 (17), 157.0 (80), 153.1 (38), 151.1 (22), 135.1 (18), 126.1 (29), 113.0 (81), 111.0 (12), 109.0 (30), 86.0 (24), 83.0 (13), 80.9 (13), 68.9 (40), 66.9 (14), 56.9 (100), 54.9 (25). Anal. calc. for C<sub>24</sub>H<sub>42</sub>N<sub>2</sub>O<sub>4</sub> (422.6): C 68.21, H 10.02, N 6.63; found: C 68.29, H 10.31, N 6.36.

tert-Butyl (2*R*,3'*R*)- and (2*R*,3'*S*)-2-(tert-Butyl)-3-(3',4'-dimethylpentanoyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate (**39**). According to *G.P.8*, with **36** (207 mg, 0.64 mmol) in THF (2 ml), Mg (47 mg, 1.9 mmol), *i*-PrBr (0.18 ml, 1.83 mmol), and CuBr·SMe<sub>2</sub> (197 mg, 0.96 mmol) in THF (5 ml): 217 mg (93%) of **39a/39b** 63:37 (ratio determined after cleavage of the auxiliary according to *G.P.4*). The isomers **39a/39b** were inseparable. FAB-MS (3-NOBA): 383.2 (39, [*M* + H]<sup>+</sup>), 327.2 (51), 325.2 (52), 271.2 (15), 269.1 (33), 225.1 (18), 215.1 (13), 213.1 (20), 197.1 (21), 171.1 (11), 157.1 (52), 126.1 (21), 113.0 (71), 111.0 (14), 85.0 (17), 69.0 (18), 56.9 (100). Anal. calc. for C<sub>21</sub>H<sub>38</sub>N<sub>2</sub>O<sub>4</sub> (382.6): C 65.94, H 10.01, N 7.32; found: C 66.07, H 9.78, N 7.25.

tert-Butyl (2*R*,3'*R*)- and (2*R*,3'*S*)-2-(tert-Butyl)-5,5-dimethyl-3-(3'-methylheptanoyl)-4-oxoimidazolidine-1-carboxylate (**40**). According to *G.P.8*, with **36** (200 mg, 0.59 mmol) in THF (2 ml), Mg (44 mg, 1.8 mmol), BuBr (0.19 ml, 1.8 mmol), and CuBr·SMe<sub>2</sub> (185 mg, 0.90 mmol) in THF (5 ml): 201 mg (86%) of **40a/40b** 1:1 (ratio determined after cleavage of the auxiliary according to *G.P.4*). The isomers **40a/40b** were inseparable. FAB-MS (3-NOBA): 397.3 (38, [*M* + H]<sup>+</sup>), 341.2 (50), 339.2 (49), 283.1 (28), 271.2 (13), 239.2 (18), 215.1 (12), 213.1 (20), 197.1 (17), 157.1 (53), 127.1 (33), 125.1 (20), 113.0 (55), 86.0 (12), 69.0 (15), 56.9 (100), 54.9 (14). Anal. calc. for C<sub>22</sub>H<sub>40</sub>N<sub>2</sub>O<sub>4</sub> (396.6): C 66.63, H 10.17, N 7.06; found: C 66.52, H 9.95, N 7.26.

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