105. Peptide Enolates. *C*-Alkylation of Glycine Residues in Linear Tri-, Tetra-, and Pentapeptides *via* Dilithium Azadienediolates

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The Boc-protected tripeptides Boc-Val-Gly-Leu-OH (**1**), Boc-Leu-Sar-Leu-OH (**2**), Boc-Leu-Gly-MeLeu-OH (**3**), and Boc-Val-BzlGly-Leu-OMe (**64**), tetrapeptide Boc-Leu-Gly-Pro-Leu-OH (**9**), and pentapeptides Boc-Val-Leu-Gly-Abu-Ile-OH (**4**), Boc-Val-Leu-Sar-MeAbu-Ile-OH (**5**), Boc-Val-Leu-Gly-MeAbu-Ile-OH (**6**), Boc-Val-Leu-BzlGly-BzlAbu-Ile-OH (**7**), and Boc-Val-Leu-Gly-BzlAbu-Ile-OH (**8**) are prepared by conventional methods (*Schemes 4–7*) or by direct benzylation of the corresponding precursors (*Scheme 8*). Polylithiations in THF give up to Li_6 derivatives containing glycine, sarcosine, or *N*-benzylglycine Li enolate moieties (**A–H**). The polylithiated systems with a dilithium azadienediolate unit (**C**, **F–H**) are best generated by treatment with *t*-BuLi. The yields of alkylation of the glycine or sarcosine residues are up to 90%, with diastereoselectivities from nil to 9:1. Normally, the newly formed stereogenic center has (*R*)-configuration (*i.e.* a D-amino-acid residue is incorporated in the peptide chain). Electrophiles which can be employed with the highly reactive azadienediolate moiety are: MeI, EtI, i-PrI, allyl and benzyl bromide, ethyl bromoacetate, CO_2, and Me_2S_2 (*Schemes 11–13*). No epimerizations of the starting materials (racemization of the amino-acid residues) are observed under the strongly basic conditions. Selected conformations of the peptide precursors, generated by shock-freezing or by very slow cooling from room temperature to −75° before lithiation, give rise to different stereoselectivities (*Scheme 11*). The latter and the yields can also be influenced by tempering the lithiated species before (*Scheme 9*) or after addition of the electrophiles (*Scheme 12*). Besides the desired products, starting peptides are recovered in the chromatographic purification and isolation procedures (material balance 80–95%). The results described are yet another demonstration that peptides may be backbone-modified through Li enolates, and that whole series of analogous peptide derivatives with various side chains may thus be produced from a given precursor.

1. Introduction. – As an alternative of the classical modification of peptides by synthetic incorporation of proteinogenic or non-proteinogenic amino acids or other building blocks, we developed over the past ten years a methodology by which side chains can be attached through enolates of sarcosine residues [1–8]. Thus, a C-atom of the peptide backbone is rendered nucleophilic. Analogous modifications using electrophilic reactivity involving imine moieties generated within the peptide chain were also realized (through electrochemical decarboxylation [3] [9–11], through oxidative cleavage of serine residues [12], through *N*-bromosuccinimide bromination [13])[2]). Finally, introduction of didehydro-amino acid residues into the peptide backbone allowed nucleophilic and radical additions with modification of a given peptide [14] [15][3]).

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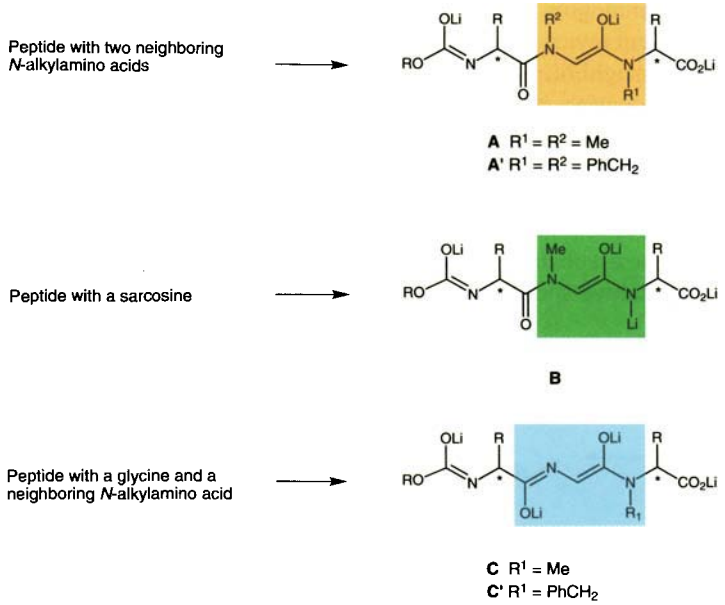
[1]) Part of the Ph. D. thesis of *H. G. B.*, Dissertation No. 10254, ETH-Zürich, 1993.

[2]) For a recent article describing generation of α-acetoxyglycine from serine moieties in peptides, with many leading references to iminoacetamide (= didehydroglycinamide) intermediates, see [12].

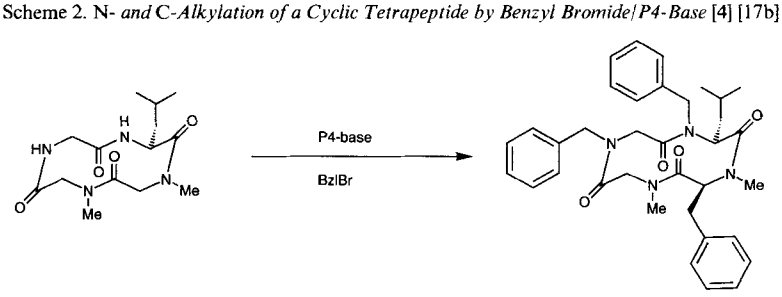
[3]) For a simple method of dehydrating serine to didehydroalanine residues within a peptide, with leading reference to the preparation of didehydropeptides and to their reactions, see [16].

Scheme 1. *Three Different Types of Peptide Lithium Enolate Derivatives for Backbone Modifications of Peptides*



In a previous paper on peptide enolates, we showed that Li enolates of sarcosine (= *N*-methylglycine) residues can be generated if another *N*-methylamino acid follows the sarcosine in the chain towards the C-terminus (see **A** in *Scheme 1*). Normally, the reactions of such peptide enolates with electrophiles lead to preferential formation of new stereogenic centers having (*R*)-configuration (D-amino-acid residues). The purpose of this paper is to describe our experiments aimed at alkylations of glycine and sarcosine residues within peptides. This was first attempted using *N*-benzyl analogues, the products of which could be debenzylated by Na/liq. NH_3 [17a] (see **A**, in *Scheme 1*, and also *Scheme 2*[4])). We then followed the philosophy 'the best protecting group is no protecting group' and tried to generate doubly lithiated sarcosine and glycine moieties of type **B** and **C** for the *C*-alkylation of peptides (*Scheme 1*).

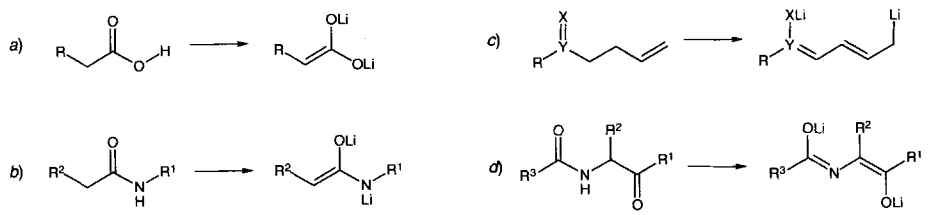
Scheme 2. N- *and* C-*Alkylation of a Cyclic Tetrapeptide by Benzyl Bromide/P4-Base* [4] [17b]



[4]) The cyclic *N*-benzylated peptide shown in *Scheme 2* [4] could not be successfully debenzylated under these conditions [17b].

Double deprotonations in α- and α′-position or in α- and β-position of carbonyl groups and their analogues are well documented in the literature (see *e.g.*, the rather comprehensive recent review article by *Thompson* and *Green* [18]). Particularly relevant to the dilithiation of neighboring positions in peptides are the four cases shown in *Scheme 3*: *a*) the α-deprotonation of Li carboxylates[5]) to geminal enediolates, *b*) the NH/CH dideprotonation in carboxyamides[6]) [20], *c*) the αβ-dideprotonation of ketones, thioesters [21] [22], and nitroalkanes [23] [24], and *d*) the vicinal NH/CH dideprotonation of simple *N*-acyl-substituted α-amino-acid derivatives [25–31][7]). Thus, there is ample precedence to the conversion planned with peptides – the question was whether stereogenic centers in these substrates would survive the strong bases (BuLi) necessary for generating such reactive species; so far we used only Li amides for deprotonations of peptides[8])[9])!

Scheme 3. *Double Deprotonations in the Vicinity of Carbonyl Groups*



2. *N*-Methyl- and *N*-Benzylpeptides – the Starting Materials for the Lithiations. – The peptides **1**–**9** containing three to five amino acids were chosen for the lithiation experiments. Rather lipophilic amino-acid components are present in these compounds to improve solubility in THF, also of their lithiated derivatives. Except for **2** and **9**, the peptides are built up from all different amino acids, so that we would be able to determine in which position, if any, epimerization may have occurred as a consequence of base treatment. In the case of pentapeptides **4**–**8**, β-branched amino-acid residues were avoided in the neighboring positions, since we knew that otherwise there would be problems with the coupling steps [35]. The glycine (Gly), sarcosine (Sar), or N-benzylglycine building block in **1**–**8** is positioned in the middle of the peptides built of an uneven number of amino acids.

The Boc-protected Me-Abu-OH **10** and Me-Leu-OH **11**, used for the synthesis of **3**, **5**, and **6**, were prepared following *Benoiton*'s procedure [36]. Me-Leu-OBzl·HCl (**12**) was made from **11** by esterification and removal of the Boc group by standard methods. Boc,Bzl > Abu-OH (**13**; for incorporation in **7** and **8**) was obtained by formation of the imine from 2-aminobutanoic acid and benzaldehyde and $NaBH_4$ reduction [37], followed by Boc-protection. Finally, Boc,Bzl > Gly-OH (**14**) was prepared by nucleophilic substi-

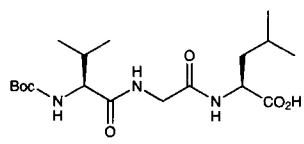
[5]) For a collection of early papers on this subject, see ref. in Table 4, line i, of [19].

[6]) For a list of references covering the literature up to 1976, see [19], p. 37, Table 4, line j.

[7]) For NH/CH dilithiation of Boc-protected allyl amine and additions to aldehydes and ketones, see [32].

[8]) In fact, when cyclosporin was treated with excess BuLi instead of lithium diisopropylamide, nucleophilic attack with cleavage of a peptide bond was observed as the main reaction (see Scheme 4 in [7]).

[9]) For polylithiated β-amino-acid and -ketone derivatives, see [33] [34].



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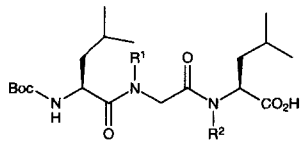
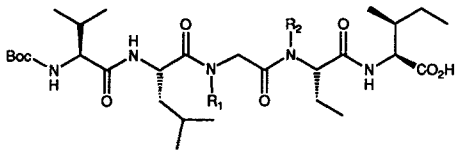
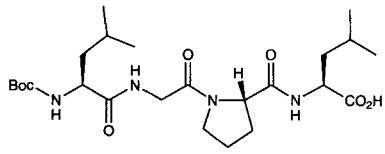


2 R^1 = Me, R^2 = H
3 R^1 = H, R^2 = Me



4 $R^1 = R^2$ = H
5 $R^1 = R^2$ = Me
6 R^1 = H, R^2 = Me
7 $R^1 = R^2 = PhCH_2$
8 R^1 = H, $R^2 = PhCH_2$



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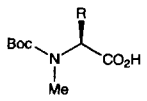
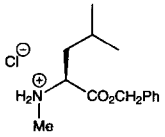


10 R = Et
11 R = i-Bu



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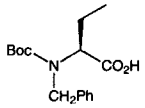

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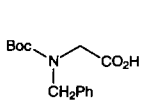

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tution from benzylamine and benzyl bromoacetate, followed by Boc-protection and hydrogenolytic ester cleavage.

The assembly of the peptides **1**–**9** is schematically presented in *Schemes 4–7* (intermediates **15**–**61**). The tripeptides **1**–**3** were built form N- to C-terminus[10]), all others from C- to N-terminus. We used exclusively Boc-protected amino acids which were activated by ethyl (in toluene) or isobutyl chlorocarbonate (in THF)/Et_3N or *N*-methylmorpholine (NMM); with *N*-benzyl and *N*-methylamino acids, we used preferably BOP-Cl/$(i\text{-}Pr)_2NEt$[11]) (in CH_2Cl_2) for activation. Dicyclohexylcarbodiimide (DCC)/BtOH[11]) was employed for coupling with the terminal valine residue of **4** and **7**. For details of the oligopeptide syntheses, see *Exper. Part* and the standard procedures [41–43].

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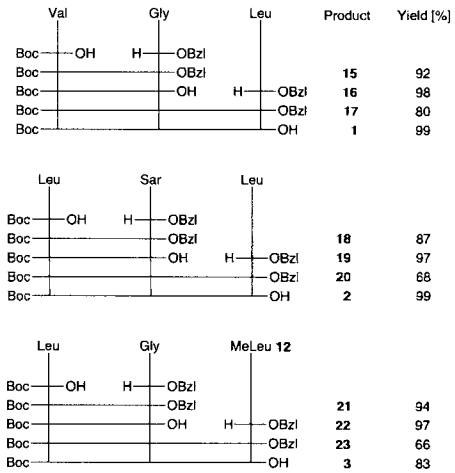
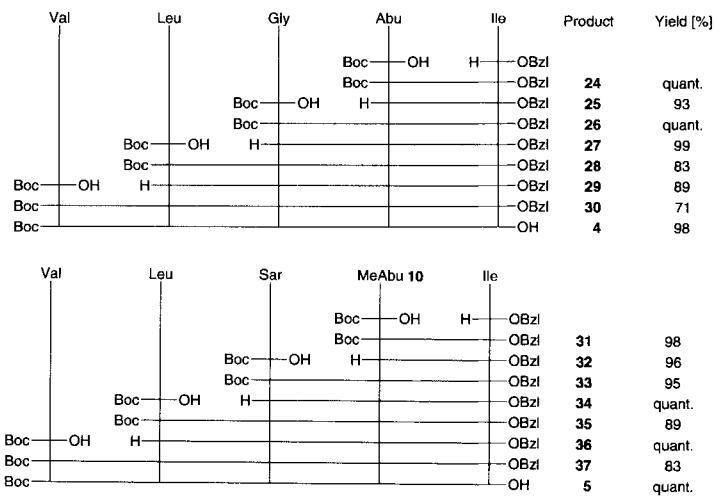
[10]) The different strategy with the tripeptides has 'historic reasons': in our previous peptide alkylations, we always used substrates containing sarcosine and a second *N*-methylamino acid in the C-terminal direction [2]; by this procedure, diketopiperazine formation (especially favorable with *N*-methylamino acids!) upon *N*-deprotection at the dipeptide stage is avoided.

[11]) BOP-Cl = bis(2-oxooxazolidin-3-yl)phosphinic chloride, the *Diago* reagent [38]; $(i\text{-}Pr)_2EtN$ = *Hünig*'s base [39]; BtOH = 1*H*-benzotriazol-1-ol [40].

Scheme 4. *Preparation of the Tripeptides* **1–3**



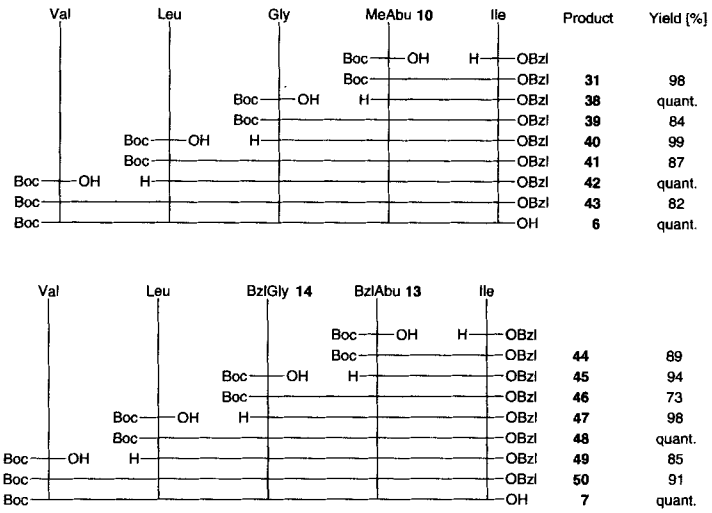
Scheme 5. *Preparation of the Pentapeptides* **4** *and* **5**



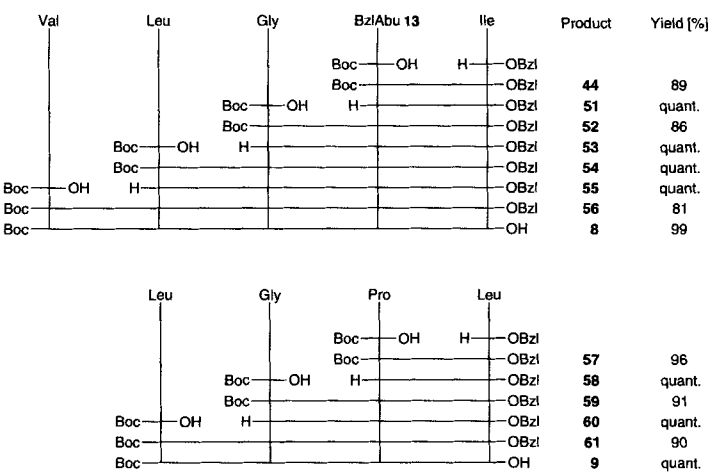
Besides the systematic syntheses of precursors for lithiations, we also did some experiments with the aim of protecting oligopeptides directly by introducing *N*-Boc or *N*-benzyl groups (see *Scheme 8*). Thus, we applied the conditions recommended by *Ragnarsson* and coworkers [44] for multiple Boc protection of amino acids and dipeptides to our tripeptide **17** to find that the $(Boc)_3$ derivative **62** and the cyclization product **63** were formed. Since preliminary experiments with the free acid of **62** indicated that base treatment led to massive destruction of the molecule, we did not further pursue this route.

We tested the *N*-benzylation with tripeptide **1** and pentapeptide **4**, using procedures which were previously applied for poly-*N*-methylation of peptides (NaH/THF [45],

Scheme 6. *Preparation of the Pentapeptides* **6** *and* **7**



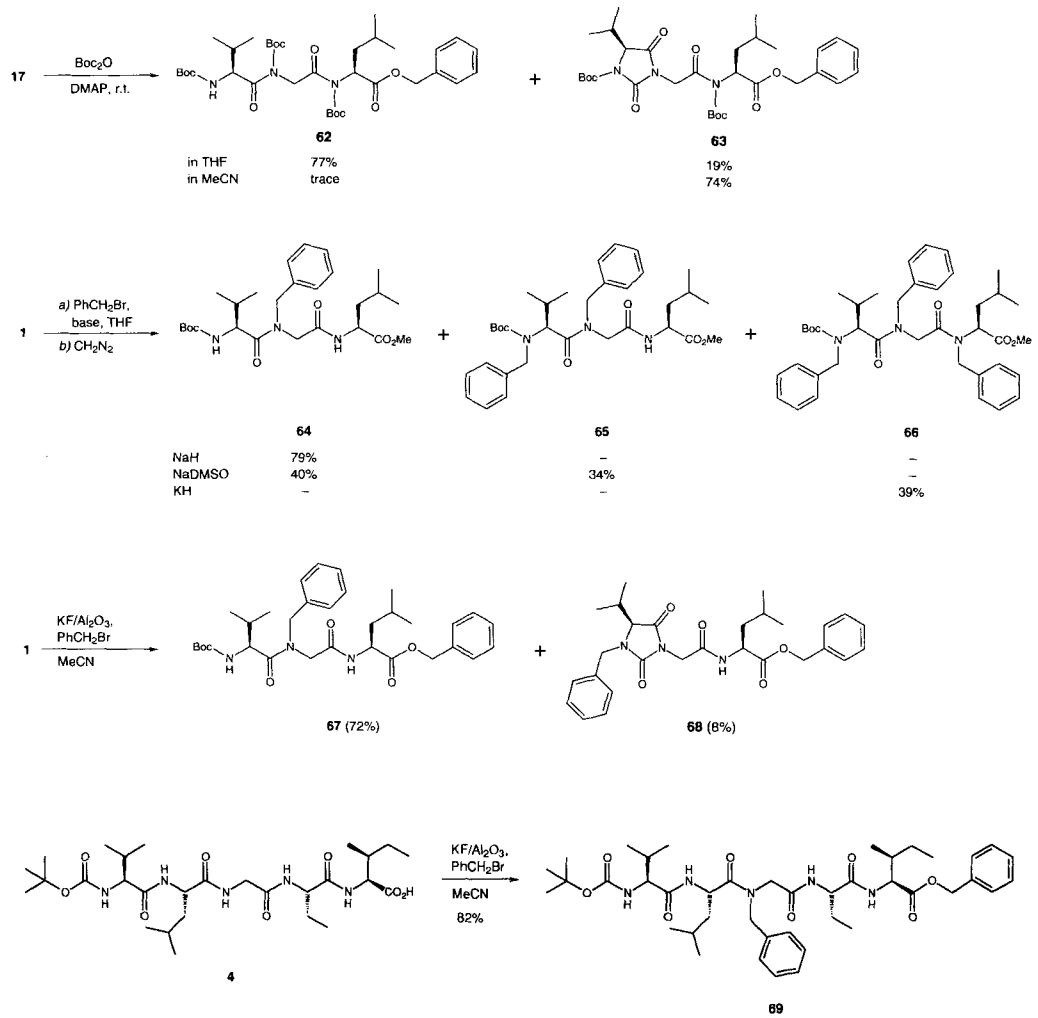
Scheme 7. *Preparation of the Pentapeptide* **8** *and of the Proline-Containing Tetrapeptide* **9**



NaH/DMSO [46], KH/THF, or KOH/DMSO [47][12]) and MeI) or for *N*-methylation and benzylation of simple amides and lactames (KF/Al_2O_3/MeCN and MeI or BzlBr) [48] [49][4]). A reasonable selectivity for monobenzylation of glycine NH groups was obtained (see products **64**, **67**, and **69**), depending on the method used; higher benzylated derivatives such as **65** and **66** were also formed, and cyclization to a hydantoin **68** was observed

[12]) When the *Johnstone* method (KOH/DMSO, large excess of BzlBr) was applied to **4**, a pentabenzyl (38%) and two hexabenzyl derivatives (56%) were isolated; one of the hexabenzylpeptides *must* be *C*-benzylated, just like *C*-methylations of glycine units were observed by *Johnstone* and *Rose* [47].

Scheme 8. *Preparation of* N-*Boc- and* N-*Benzyl-Protected Tripeptides and Selective* N-*Monobenzylation of a Pentapeptide*



as a side reaction (see *Scheme 8*)[13]). Note the remarkable conversion **4** → **69** in 82% yield, with one out of five NH groups being benzylated selectively[14])! Unfortunately, the *N*-benzylpeptides of the type thus accessible selectively did not lend themselves for lithiations, as will be outlined below. All products **62–69** were diastereoisomerically pure, with no epimerizations detectable by the analysis which we used throughout this work,

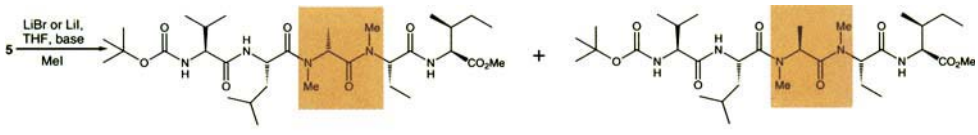
[13]) It is well known that peptides with a glycine residue in the next to N-terminal position form hydantoins of type **63** and **68** upon base treatment [50]; this sequence-specific reaction was not observed at all with pentapeptide **69**.

[14]) We did not check whether this selectivity may also be obtained with MeI instead of BzlBr, but we are quite confident that it might. This possibility should be tested by those who at present entertain a strong interest in *N*-methylpeptides (see, *e.g.*, the lit. cit. in progress reports [51]).

i.e. acid hydrolysis of the peptides to the amino acids, hydrogenolytic removal of *N*-benzyl groups, formation of derivatives with $(C_2F_5CO)_2O$/HCl/i-PrOH [52], and GC analysis on *Chirasil-Val* capillary columns [53].

3. Generation of Lithium Enolate Derivatives of Peptides and Their *C*-Alkylation. – As reported previously, the sarcosine enolate moieties present in linear polylithiated peptides of type **A** (*Scheme 1*) are usually alkylated to give preferentially D-amino-acid residues [2], while with cyclic peptides, the stereoselectivity may be reverse, depending on the position of the particular sarcosine moiety [6] and the reaction conditions [7]. We have now done a systematic investigation of the methylation of the pentalithiated derivative **D** of pentapeptide **5** under various conditions; the results are collected in *Scheme 9*. As can be seen, different bases (LTMP = lithium 2,2,6,6-tetramethylpiperidide, LDA = lithium diisopropylamide) lead to different stereoselectivities (up to 8.3:1 for Me-D-Ala forma-

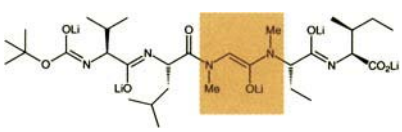
Scheme 9. Methylation of a Peptide Enolate of Type **A** *under Various Conditions*



70a **70b**

Entry	Base	Temp. before MeI addition	Yield of **70a** + **70b**	Ratio **70a**/**70b**	Recovery of ester **5**-OMe
1	LDA/BuLi	– 75°	32%	4.9:1	60%
2	*t*-BuLi	– 75°	31%	8.3:1	54%
3	LTMP/BuLi	– 75°	25%	2.5:1	59%
4	LTMP/BuLi	0°	50%	2.4:1	19%
5	LDA/BuLi	0°	50%	1:1.3	42%
6[a])	LDA/BuLi	0°	59%	1:1.5	18%

[a]) LiI used instead of LiBr.



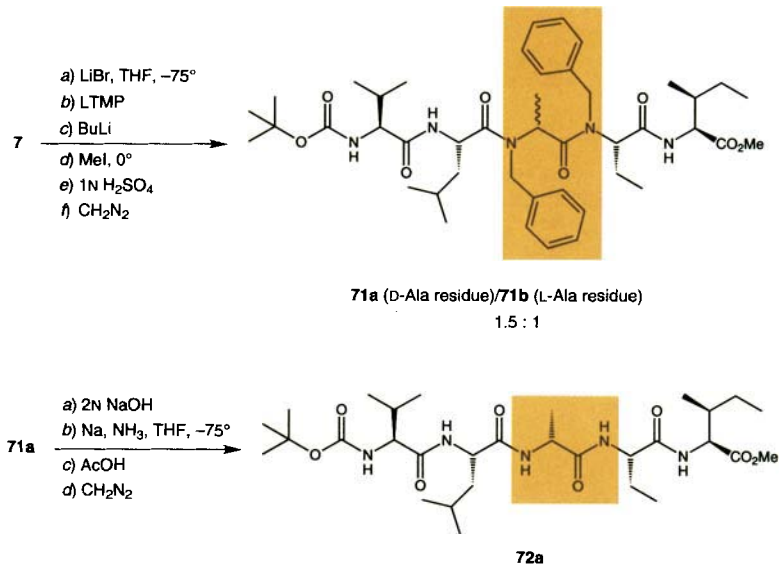
D (from pentapeptide **5**)

tion). We were surprized to find that warming of the enolate solution generated with LDA/BuLi to 0° before MeI addition not only led to a *ca.* twice as high yield of **70** but also produced preferentially a Me-Ala residue of L-configuration (see **70b**). Considering the structural complexity of the system (Li_5-peptide **D** + 5 LDA + 7 LiBr or LiI), it is impossible to rationalize this result[15]). It is appropriate at this point to emphasize that we do not know the structure of the lithiated peptides, and that the *Formulae* **A**–**H** drawn herein are deliberate (only crystal structures of simple lithiated carboxamides are known [54] [55], see also some recent review articles [1] [56]).

[15]) Possibilities are: *i*) a change of the aggregation of the various LiX species in the mixture, *ii*) (*E*/*Z*)-isomerization of the enolate double bond or *iii*) a conformational change of the entire Li_5-peptide by which the other diastereotopic face of the enolate trigonal center is being exposed to the electrophile.

We next tested the dibenzylated pentapeptide **7**: besides the expected products **71a**/**71b** (24%, ratio 1.5:1), which were formed under the optimum conditions found for the dimethyl analogue **5** (LTMP/BuLi/0°, *cf. Scheme 9*), we recovered half of the starting material, and there were several components in the crude product mixture in which benzylic CH_2 groups had been methylated (*Scheme 10*). After saponification of the C-terminal ester group of **71a**, debenzylation with Na in liq. NH_3/THF, and esterification, we isolated the desired pentapeptide **72a** containing a new D-Ala residue (*ca.* 60% from **71a**), in which the original stereogenic centers of the Ile, Abu, Leu, and Val residues were all unchanged[16]). Due to the poor yield of the desired reaction and due to the problems arising from benzylic methylations (**7** has *four* diastereotopic benzylic H-atoms!), we discontinued studying this route to enolate-modified non-*N*-alkylated peptides.

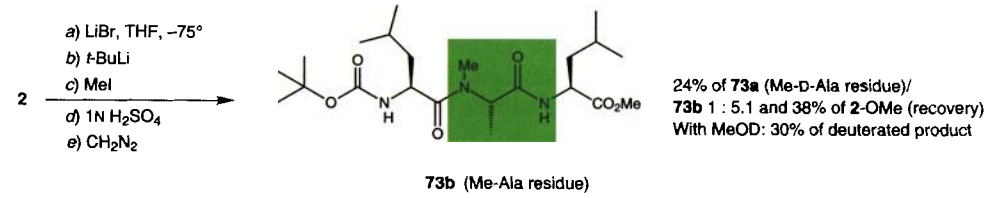
Scheme 10. *Methylation of Pentapeptide* **7** via *an Enolate of Type* **A'** (*cf.* **D** in *Scheme 9*) and *Debenzylation* (51% recovery of **7**-OMe in the first step)



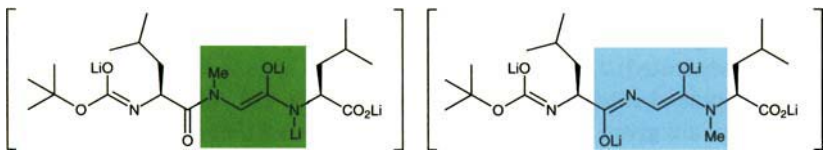
We then made a step backwards – considering the goal of eventually being able to prepare peptides without any *N*-methyl group *via* Li-enolates – and investigated reactions involving enolates of mono-*N*-methylpeptides. The tripeptide Boc-Leu-Sar-Leu-OH (**2**) was treated in THF in the presence of LiBr with 4 equiv. of *t*-BuLi at −75°. A yellow solution resulted which was treated with MeI or MeOD to give, after workup and CH_2N_2 esterification, the chromatographically separable tripeptides **73a**/**73b** (1:5.1), again only in 24% yield, or the deuterated product of peptide **2** (*Scheme 11*). Inspite of the strong lithiating conditions, there was no detectable racemization of the two leucine residues, neither in the two isolated products nor in the recovered starting material (for

[16]) See the analysis described in the last paragraph of *Section 2* and the *General Procedure* in the *Exper. Part.*

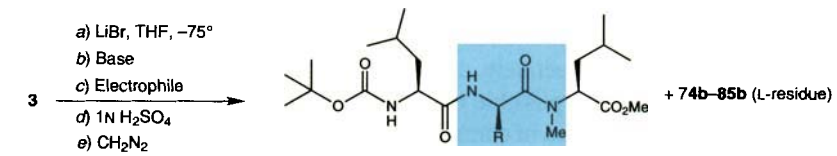
Scheme 11. *Generation of Enolates of Type* **B** *and* **C** *from Tripeptides and Reactions with Electrophiles*



73b (Me-Ala residue)



E **F**



74a–85a (D-residue)

Electrophile	Base	Product	R	Yield [%]	Ratio a/b
MeOD	LDA/BuLi	**74**	D	54	[a]
MeOD	*t*-BuLi	**74**	D	87	[a]
MeI	LDA/BuLi	**75**	Me	63	5.8:1
MeI	BuLi	**75**	Me	82	4.7:1
MeI	*t*-BuLi	**75**	Me	90	3.7:1
MeI	*t*-BuLi	**75**	Me	78	9.0:1[b]
EtI	*t*-BuLi	**76**	Et	64	2.8:1
i-PrI	*t*-BuLi	**77**	i-Pr	21	2.7:1
CH_2=$CHCH_2Br$	*t*-BuLi	**78**	CH_2=$CHCH_2$	82	3.4:1
CH_2=$CHCH_2Br$	*t*-BuLi	**78**	CH_2=$CHCH_2$	51	4.6:1[b]
BzlBr	*t*-BuLi	**79**	Bzl	73	4.1:1
$BrCH_2CO_2Et$	*t*-BuLi	**80**	CH_2CO_2Et	75	2.0:1
CO_2/CH_2N_2	*t*-BuLi	**81**	CO_2Me	66	—
MeSSMe	*t*-BuLi	**82**	MeS	84	—
MeCHO	*t*-BuLi	**83**	MeCH(OH)	89	[c]
PhCHO	*t*-BuLi	**84**	PhCH(OH)	93	—
Aceton	*t*-BuLi	**85**	Me_2C(OH)	81	—

[a] The ^{1}H-NMR chemical shifts of the two glycine H-atoms are very similar, therefore, it was not possible to determine the diastereoselectivity of the deuteration.

[b] The solution of the peptide and LiBr in THF was slowly cooled down to –75° with a rate of 5°/h.

[c] Ratio 1.0:2.0:1.8:1.3 of the peptide derivatives **83a/83b/83c/83d** containing D-Thr, Thr, D-aThr, and aThr, respectively.

N-methylamino acids, the analysis was performed using the (i-Pr)NCO method [57][17]). Thus, the first results obtained with the dilithium 1-(amidyl)enolate **E** were not encourag-

[17]) This analysis involves formation of (i-Pr)NH–CO–NR–CHR–CO–NH(i-Pr) which is investigated with the same chiral *Chirasil-Val* GC column [53] as are the derivatives C_2F_5CO–NH–CHR–CO_2(i-Pr).

ing; we did no further experiments with this type of peptide-derived nucleophiles, especially because the dilithium azadienediolates **F** gave much better results.

As can be seen from the lower part of *Scheme 11*, the peptide with an *N*-Me group next to glycine in C-terminal direction, Boc-Leu-Gly-MeLeu-OH (**3**), could be deuterated and methylated at the Gly residue when *t*-BuLi was employed as the base. The yield of methylation (→ **75**) reached 90%. Under the same conditions, all electrophiles gave the best yields we have encountered so far in our work on peptide-enolate alkylations: EtI (→ **76**, 64%), i-PrI (→ **77**, 21%!), allyl and benzyl bromide (→ **78** and **79**, 82 and 73% yield, resp.), and ethyl bromoacetate (→ **80**, 75%) all gave satisfactory results. The ratio of diastereoisomers **a**/**b** varied from 2:1 to 3.7:1, again with the newly formed stereogenic center having (*R*)-configuration in the main product[16]) (except for **76**, all diastereoisomers **a** and **b** could be separated). Other electrophiles such as CO_2, $(MeS)_2$, aldehydes, and a ketone were also employed successfully (see the products **81**–**85**). With one exception, no diastereoselectivities are given in *Scheme 11* for derivatives **81**–**85**, *i)* because NMR analysis of crude products and purified samples in this entire series of peptides was complicated by the presence of rotamers, *ii)* because analysis through the amines and components obtained by hydrolysis[16])[17]) was impossible for the carboxylated and thiolated products **81** and **82** (for obvious reasons!), and *iii)* because there were no reference samples available to us in the case of the hydroxyalkylation products **84** and **85** obtained with benzaldehyde and acetone, respectively. It is, on the other hand, clear from an analysis of tripeptide **83** that all four possible derivatives containing Thr, D-Thr, aThr (allothreonine), and D-aThr were formed in comparable amounts. In all experiments with tripeptide **3**, the sum of products and recovered starting material corresponded to > 90% of the material balance.

Different rotamers of a peptide to be deprotonated might lead to different Li enolate species, and hence to different diastereoisomeric product ratios. Therefore, the way of preparing the solution for lithiations may influence the selectivity. We tested this idea with tripeptide **3**[18]). Under standard conditions, the solution containing **3** and LiBr in THF was quickly cooled to dry-ice temperature and then treated with *t*-BuLi by dropwise addition of a pentane solution; this led to a selectivity of 3.7:1 with MeI (→ **75a**/**75b**) and 3.4:1 with allyl bromide (→**78a**/**78b**). When we cooled the solution of **3**/LiBr with a rate of 5°/min from +20 to −75° and then added the base and MeI, the selectivity rose to 9:1, the highest value recorded (see *Scheme 11*); the allylation was also somewhat more selective under these conditions, although the yields were smaller in both cases. These experiments demonstrate that the establishment of peptide conformational equilibria during slow cooling and the shock cooling from room temperature lead to different enolate species in the subsequent deprotonation step, under otherwise identical conditions (*cf.* the changes occurring by varying the temperature *after* lithiation mentioned above[15]) and [6]).

The results obtained with alkylations of dilithium azadienediolates of the pentapeptides **6** and **8** are collected in *Scheme 12*. For the generation of the hexalithio derivative **G**, we used the *t*-BuLi deprotonation conditions found to give best yields with tripeptide **3**

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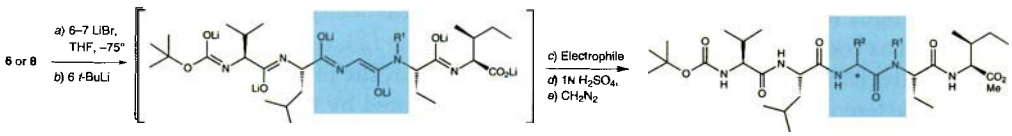
[18]) The methyl ester of **3**, **3**-OMe, consists of three rotamers in a ratio of 6:2:1 at room temperature in (D_8)THF (by ^{1}H-NMR analysis).

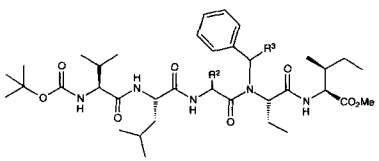
(*Scheme 11*)[19]). The *N*-methylpeptide **6** could be alkylated with MeI, EtI, and even with i-PrI (albeit in only 11% yield), allylated, and benzylated, and the yields could be improved by 15–20% when the reaction mixtures were allowed to warm from dry-ice to ice/salt temperature. Under optimum conditions, more than 70% of the desired product could be isolated, the diastereoselectivities being poor and varying from preferences of D- or of L-configuration on the newly formed center (see products **86–93** in *Scheme 12*). In

Scheme 12. Reactions of Enolates of Type **C** *and* **C'** *Derived from the Pentapeptides* **6** *and* **8** *with Electrophiles*



G R^1 = Me, Bzl

86a–93a (D-config. at C*)/**86b–93b** (L-config. at C*) R^1 = Me
94a–100a (D-config. at C*)/**94b–100b** (L-config. at C*) R^1 = Bzl



101 $R^2 = R^3 = Me$
102 $R^2 = H$, $R^3 = Et$
103 $R^2 = R^3 = CH_2{=}CHCH_2$
104 $R^2 = H$, $R^3 = CH_2CHCH_2$
105 $R^2 = H$, $R^3 = Bzl$
106 $R^2 = H$, $R^3 = CO_2Me$
107 $R^2 = H$, $R^3 = MeS$

Electrophile	Product	R^1	R^2	Yield [%] (recovered **6**-OMe or **8**-OMe)	Ratio **a**/**b**	By-product
MeI	**86**	Me	Me	32 (58)	1.2:1[a])	
MeI	**86**	Me	Me	49 (41)	1:1.2	
MeI	**86**	Me	Me	71 (9)	2.1:1[b])	
EtI	**87**	Me	Et	31 (35)	1:3.8	
EtI	**87**	Me	Et	47 (41)	1:2[b])	
i-PrI	**88**	Me	i-Pr	11 (81)	1:1.2	
$CH_2{=}CHCH_2Br$	**89**	Me	$CH_2{=}CHCH_2$	47 (39)	1:1.1	
BzlBr	**90**	Me	Bzl	44 (45)	1:1.5	
BzlBr	**90**	Me	Bzl	57 (36)	1.3:1[b])	
$BrCH_2CO_2Et$	**91**	Me	CH_2CO_2Et	48 (44)	1:2.2	
CO_2/CH_2N_2	**92**	Me	CO_2Me	30 (29)	—	
Me_2S_2	**93**	Me	MeS	48 (28)	1:1.4	
MeI	**94**	Bzl	Me	57 (20)	1:1	3% **101**
MeI	**94**	Bzl	Me	51 (34)	1:1.8[c])	—
EtI	**95**	Bzl	Et	47 (26)	1:2.8[b])	5% **102**
$CH_2{=}CHCH_2Br$	**96**	Bzl	$CH_2{=}CHCH_2$	47 (21)	1:1.4	2% **103**, 8% **104**
BzlBr	**97**	Bzl	Bzl	47 (21)	1:1.2	18% **105**
$BrCH_2CO_2Et$	**98**	Bzl	CH_2CO_2Et	31 (41)	1:1.7	—
CO_2/CH_2N_2	**99**	Bzl	CO_2Me	41 (41)	—	12% **106**
Me_2S_2	**100**	Bzl	MeS	41 (24)	1:4.0[b])	24% **107**

[a]) Base: LDA/BuLi.
[b]) After the addition of the electrophile, the mixture was allowed to warm to –18°.
[c]) DMPU (= *N*,*N'*-dimethylpropyleneurea = 1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1*H*)-one) was used as cosolvent.

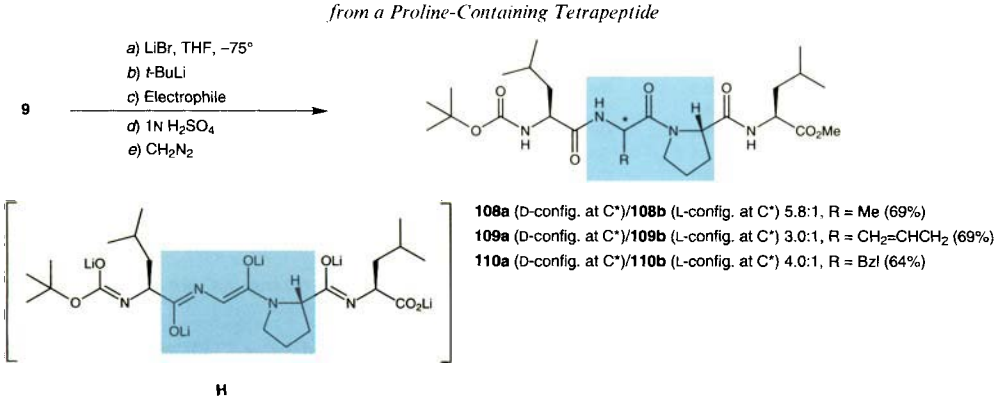
[19]) With LDA/BuLi/LiBr, the methylation of **6** gave 32% of **86** (D/L 1.2:1), and that of **8** 15% of **94** (D/L 1:1.1, *cf.* values in *Scheme 12*).

the methylation, ethylation, and benzylation, the D/L ratio increased somewhat when the reaction was carried out at higher temperatures. We also tested other electrophiles such as ethyl bromoacetate (→**91**), CO_2 with diazomethane treatment on workup (→**92**), and thiolation with Me_2S_2 (→**93**). Except for **92**, the diastereoisomeric products from the pentapeptide **6** could all be separated chromatographically and characterized by NMR and FAB mass spectroscopy, by their specific rotation, and by the usual[16]) hydrolysis to the components and GC analysis.

To prepare non-*N*-methylated products, we also studied the alkylations of the *N*-benzyl analogue **8** of **6**. The benzyl group in **8** did not drastically change the course of the reaction as compared to the Me analogue **6** (see *Scheme 12*), the yields (30–57%) and the selectivites (D/L 1:1 to 1:4) being comparable. However, the purification and isolation of pure diastereoisomeric products **94**–**100** was complicated by the fact that side products **101**–**107** resulting from benzylic alkylations were present (2–24%) in the reaction mixtures. Still, most of the derivatives in this series could be isolated in pure form. The peptides **95**, **96**, and **98** were debenzylated by treatment with Na in THF/liq. NH_3 [17a] (*cf.* **71a** →**72a** in *Scheme 10*), and the resulting products again identified by GC analysis[16]) [53]. It is interesting to note that with most electrophiles, either benzylic (5–24%) or enolate alkylation (31–57%) occurred, while we detected double alkylation products only with MeI (3% of **101**) and allyl bromide (2% of **103**). As with the tripeptide, the material balance in the alkylations of the pentapeptides **6** and **8** is excellent: if we include recovered (non-epimerized!) starting material, it amounts to 80–90% in most cases.

In all previous discussions, we have emphasized that a primary goal of this work is to show that we can *C*-alkylate peptides and prepare products containing only one or no *N*-methylamino acid residue. We should, however, not forget that there is a natural, proteinogenic *N*-alkylamino acid, namely proline. The tetrapeptide **9** was used to demonstrate that a glycine unit next to a proline in the *N*-terminal direction can in fact be *C*-alkylated (see *Scheme 13*). Solutions of the pentalithiated peptide **H** were generated in the usual way with *t*-BuLi and allowed to react with electrophiles to give the alkylation products **108**–**110** in *ca.* 60–70% and with the exceptional selectivities of 3:1 to 5.8:1 for formation of the D-amino-acid moiety. For isolation and full identification of these

Scheme 13. *Generation, Methylation, Allylation, and Benzylation of the Li_5 Derivative* **H** *from a Proline-Containing Tetrapeptide*



108a (D-config. at C*)/**108b** (L-config. at C*) 5.8:1, R = Me (69%)
109a (D-config. at C*)/**109b** (L-config. at C*) 3.0:1, R = CH_2=$CHCH_2$ (69%)
110a (D-config. at C*)/**110b** (L-config. at C*) 4.0:1, R = Bzl (64%)

products of methylation, allylation, and benzylation, see *Exper. Part.* We have no doubt that other electrophiles will react as well (*cf.* **3**, **6**, and **8**) and that further optimizations, especially of the reaction temperature, which was not varied by us in the case of this proline-containing peptide **9**, will lead to even better yields.

4. Conclusions. – The experiments described here show that linear oligopeptides containing a glycine residue and an *N*-alkylamino-acid building block (including proline) as a neighbor in the C-terminal direction, can be modified by reactions with electrophiles through Li-enolate derivatives. As compared to the simple Li enolates from sarcosine-containing peptides used previously, the dilithium azadienediolates of type **C** (see **F**, **G**, and **H**), described here for the first time, are highly reactive nucleophiles and furnish products of alkylation in much better yields. In those cases in which a comparison is possible, the diastereoselectivities observed with the azadienediolates are better than with the simple enolates. The extremely strong base and vigorous nucleophile *t*-BuLi is the best reagent for generating the polylithiated peptides containing an azadienediolate system. We have also demonstrated for the first time that the structure, and thus the reactivity of polylithiated peptides – and especially the diastereoselectivity of their reactions, may be modified through conformational equilibria established or prevented *before* the deprotonation step. We have provided further evidence for the influence of the base, of additives such as Li salts and DMPU cosolvent (see *Scheme 12*), and of the temperature chosen for enolate generation, for enolate 'tempering' or annealing, and for the subsequent reactions with electrophiles. Finally, we have found that certain *N*-benzylpeptides can be employed in polylithiations and *C*-alkylations, with only minor difficulties associated with the rather acidic benzyl CH_2 groups, for eventually preparing peptides containing no *N*-alkyl groups at all.

We thank *J. Müller* and *B. Seebass* for the performance of some alkylation reactions of the pentapeptide **8** and the tetrapeptide **9**.

Experimental Part

1. *General.* THF used for alkylation reactions was freshly distilled over K under Ar. TLC: *Merck* silica gel *60* F_{254} anal. plates; detection either with UV and by placing in a Cl_2 tank for 5 min, then staining with a soln. of *N,N,N′,N′*-tetramethyl-4,4′-methylenebis(aniline). LC: *Merck* silica gel *60* (40–63 μm). Optical rotations: 10-cm, 1-ml cell; *Perkin-Elmer-241* polarimeter. IR Spectra: *Perkin-Elmer-782* spectrophotometer. ^{1}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; chemical-shift values in italics refer to a conformer. ^{13}C-NMR: *Bruker-AMX-II-500* (125 MHz), *Bruker-AMX-400* (100 MHz), or *Varian XL-300* (75 MHz) spectrometer.

2. *General Procedures GC Analysis.* 2.1. *Peptides Alkylated on a Glycine Residue.* In a screw-capped vial, the peptide (10–20 mg) was hydrolyzed with conc. HCl soln. at 100–110° for 6–15 h. Then, H_2O was removed in an airflow and anh. 4M HCl in i-PrOH (*ca.* 1 ml) added. The soln. was heated at 100° for 1 h and then the solvent removed in an airflow. CH_2Cl_2 (*ca.* 0.1 ml) and pentafluoropropionic anhydride (0.05 ml) were added. Heating at 100° for 15 min followed by removal of excess pentafluoropropionic anhydride in an airflow gave the derivatives of the individual amino acids. The residue was taken up in Et_2O, the mixture filtered, and the filtrate submitted to GC. Peptides containing an allylic group were hydrogenated (H_2, 10% Pd/C in MeOH) prior to hydrolysis. The hydrolysate of peptides with *N*-benzyl groups were also hydrogenated to remove the *N*-benzyl group.

2.2. *Peptides Alkylated on Sarcosine Residue.* The hydrolysis was performed as described in *2.1.* The dry hydrolysate was taken up in CH_2Cl_2 (0.3 ml) and isopropyl isocyanate (0.3 ml) added. After 15 min of heating at 100°, the mixture was evaporated in an airflow.

2.3. *GC Analysis. Chirasil-Val* (*Macherey-Nagel*, 25 m, 0.4 mm) column; *Carlo Erba-Fractovap 4160-HRGC*. Temp. program for derivatives from *Exper. 2.1*: 3 min 85°, 4°/min. Temp. program for derivatives from *Exper. 2.2*: 5 min 160°, 2°/min, 10 min 200°.

3. *Starting Materials. General Procedure 1* (*G.P.1*): *Coupling with Isobutyl Chloroformate*. To a soln. of the carboxyl component in THF at −15°, NMM and isobutyl chloroformate were added. Then a cold soln. of the salt of the amino component and NMM in DMF was added dropwise. After 30–60 min, the soln. was warmed to r.t., stirred for 1–2 h, and then evaporated. The residue was taken up in AcOEt and washed with 5% citric acid, sat aq. $NaHCO_3$, and sat. aq. NaCl soln. All aq. layers were additionally extracted twice with AcOEt. The combined org. layers were dried ($MgSO_4$) and evaporated.

General Procedure 2 (*G.P.2*): *Coupling with Bis[2-oxooxazolidin-3-yl]phosphinic Chloride* (BOP-Cl). To the suspension of the acid component, $(i\text{-}Pr)_2EtN$, and BOP-Cl in CH_2Cl_2, the amino component and $(i\text{-}Pr)_2EtN$ in CH_2Cl_2 were added at 0° and warmed to r.t. overnight. Workup according to *G.P.1*.

General Procedure 3 (*G.P.3*): *Cleavage of the Boc Group with CF_3COOH*. The Boc-protected peptide was stirred at r.t. in CH_2Cl_2 and CF_3COOH. Then the soln. was evaporated, the residue taken up in AcOEt, and the soln. washed with sat. aq. $NaHCO_3$ and sat. aq. NaCl soln. and further worked up according to *G.P.1*.

General Procedure 4 (*G.P.4*): *Cleavage of the Boc Group with Sat. HCl/Et_2O Solution*. At r.t., the peptide was dissolved in Et_2O and a sat. HCl soln. in Et_2O added. After the reaction, the solvent was evaporated.

Boc-MeAbu-OH (**10**). To a soln. of Boc-Abu-OH (29.9 g, 147 mmol) and MeI (75 ml, 1.2 mol) in THF (500 ml), NaH dispersion (55–60%; 18 g, *ca.* 0.45 mol) was added slowly at 0°. Then the mixture was warmed to r.t. and after 24 h hydrolyzed with ice. THF was evaporated, the residue dissolved in H_2O and washed with Et_2O, and the aq. layer acidified with sat. $KHSO_4$ soln. to pH 2 at 0° and extracted 3 times with Et_2O. After washing all org. layers twice with sat. aq. NaCl soln., the combined org. layer was dried ($MgSO_4$) and evaporated. The residue was recrystallized from hexane/AcOEt: 27.83 g (87%) of **10**. $[\alpha]_D^{r.t.} = -39.9$ ($c = 0.99$, EtOH). ^{1}H-NMR (200 MHz, $CDCl_3$): 0.95 (*t*, $J = 7.5$, 3 H); 1.46 (*s*, 9 H); 1.75 (*m*, 1 H); 1.99 (*m*, 1 H); 2.82 (*s*, 3 H); 4.38, 4.60 (2*m*, 1 H); 8.9 (br., 1 H). FAB-MS: 240.1 (84, $[M + 23]^+$), 218.1 (49, $[M + 1]^+$), 162.1 (100), 118.0 (79), 116.0 (60), 72.0 (57), 56.9 (71).

Boc-MeLeu-OH (**11**). The H_2O of Boc-Leu-OH·H_2O (19.5 g, 78.3 mmol) was removed azeotropically with CH_2Cl_2. Then the solvent was evaporated and the residue methylated according to the procedure for **10** with MeI (39.2 ml, 0.63 mol), THF (240 ml), and NaH dispersion (60–65%; 9.4 g, *ca.* 0.24 mol): 18.2 g (96%) of **11**. $[\alpha]_D^{r.t.} = -30.3$ ($c = 0.5$, EtOH). ^{1}H-NMR (200 MHz, $CDCl_3$): 0.78–0.98 (*m*, 6 H); 1.45 (*s*, 9 H); 1.50–1.79 (*m*, 3 H); 2.79, 2.82 (2*s*, 3 H); 4.61, 4.83 (2*m*, 1 H); 7.8 (br., 1 H).

MeLeu-OBzl·HCl (**12**). In the presence of KF/Al_2O_3 (30 g, 0.17 mol; 5.5 mmol F^-/g), and benzyl bromide (13.2 ml, 0.11 mol), **11** (18.2 g, 74.3 mmol) in MeCN (100 ml) was stirred 2 d at r.t. The suspension was filtered through *Celite*, the filtrate evaporated, and the residue treated with sat. HCl/Et_2O soln. After 2 h, the solvent was removed and the crude product suspended in pentane, filtered, and dried: 19.8 g (98%) of **12**. M.p. 115–116°. ^{1}H-NMR (200 MHz, (D_6)acetone): 0.88–1.00 (2*d*, $J = 9$, 6 H); 1.80–2.15 (*m*, 3 H); 2.70 (*s*, 3 H); 4.00–4.10 (*m*, 1 H); 5.31 (*s*, 2 H); 7.31–7.55 (*m*, 5 H).

Boc-BzlAbu-OH (**13**). In 2N NaOH (150 ml), (*S*)-2-aminobutanoic acid (30.95 g, 0.3 mol) was dissolved. Then benzaldehyde (30.3 ml, 0.3 mol) was added and after 15 min $NaBH_4$ (3.44 g, 91 mmol) at 10°. After 1 h, again benzaldehyde (30.3 ml) and $NaBH_4$ (3.44 g) were added. The mixture was washed with Et_2O after 1 h. The aq. layer was saturated with NaCl and acidified to pH 7 in an ice-bath with 2N HCl. The precipitated product was separated (*Büchner* funnel) and dried: 60.0 g (quant.) of *(S)-2-(benzylamino)butanoic acid*. The crude product was dissolved in dioxane (500 ml) 1N NaOH (300 ml). To the cold (3°) soln., Boc_2O (65.4 g, 0.3 mol) was added. The mixture was warmed to r.t. and after 2 d, more Boc_2O (48 g, 0.22 mol) was added. After 2 d, the mixture was acified with 1N $KHSO_4$ to pH 2 and extracted with CH_2Cl_2. The org. layer was extracted with aq. NaOH soln. Then, the aq. layer was acified with 1N H_2SO_4 and extracted with CH_2Cl_2. The org. layer was washed with NaCl soln., dried ($MgSO_4$), and evaporated: 45.1 g (51%) of **13**. $[\alpha]_D^{r.t.} = -195.3$ ($c = 0.95$, EtOH). ^{1}H-NMR (200 MHz, $CDCl_3$): 0.82 (*m*, 3 H); 1.47 (*s*, 3 H); 1.80 (*m*, 1 H); 1.99 (*m*, 1 H); 3.79, 4.12 (2*m*, 1 H); 4.28–4.73 (*m*, 2 H); 7.28 (*m*, 5 H). FAB-MS: 316.1 (27, $[M + 23]^+$), 294.1 (27, $[M + 1]^+$), 238.1 (59), 194.1 (59), 192.1 (43), 148.1 (31), 91.0 (100), 56.9 (67).

Boc-BzlGly-OH (**14**). To a soln. of benzylamine (65.5 ml, 0.6 mol) in THF (300 ml), benzyl bromoacetate (48.6 ml, 0.31 mol) was added slowly at 0°. After 4 h, the mixture was filtered, the filtrate evaporated, the residue dissolved in Et_2O, and the soln. washed with sat. aq. $NaHCO_3$ and sat. aq. NaCl soln. After drying ($MgSO_4$) and evaporation, the free amine was treated with sat. HCl/Et_2O soln. and the resulting salt recrystallized from i-PrOH: 52.2 g (58%) of *benzyl N-benzylglycinate hydrochloride*. To a soln. of this product (57.25 g 0.196 mol) in MeCN (500 ml), Et_3N (27.4 ml, 0.2 mol), 4-(dimethylamino)pyridine (492 mg, 4.03 mmol) and Boc_2O (43.7 g, 0.2 mol) were added. After 30 min, the mixture was filtered, the filtrate evaporated, the residue dissolved in AcOEt, the soln.

washed with 5% citric acid, sat. aq. $NaHCO_3$, and sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated, and the product chromatographed (pentane/Et_2O 3:1): 63.9 g (92%) of *benzyl N-benzyl-N-[(tert-butoxy)carbonyl]glycinate*. The latter was hydrogenated in the presence of 10% Pd/C (0.88 g) in EtOH (600 ml) for 18 h: 48.4 g (quant.) of **14**. ^{1}H-NMR (200 MHz, $CDCl_3$): 1.49 (*s*, 9 H); 3.81, 3.96 (2*s*, 2 H); 4.52 (*s*, 2 H); 7.17–7.37 (*m*, 5 H). FAB-MS: 288.1 (64, $[M + 23]^+$), 266.1 (22, $[M + 1]^+$), 210.1 (76), 166.1 (43), 154.0 (27), 137.0 (24), 120.0 (26), 91.0 (100), 56.9 (75).

Boc-Val-Gly-OBzl (**15**). At −17°, ethyl chloroformate (7.8 ml, 82.4 mmol) was added dropwise to a soln. of Boc-Val-OH (17.83 g, 82.1 mmol) and Et_3N (11.5 ml, 82.1 mmol) in toluene (85 ml) and $CHCl_3$ (70 ml). After 25 min stirring, a cooled soln. of benzyl glycinate·TsOH (29.2 g, 86.5 mmol) and Et_3N (12 ml, 86.5 mmol) in $CHCl_3$ (165 ml) was added. After 60 min, the mixture was warmed to 13° (60 min), then heated to 40° for 30 min. Workup according to *G.P.1* and LC (pentane/Et_2O 1:4) gave 27.61 g (92%) of **15**. $[\alpha]_D^{r.t.} = -25.0$ ($c = 1.5$, EtOH). ^{1}H-NMR (200 MHz, $CDCl_3$): 0.91 (*d*, $J = 7$, 3 H); 0.97 (*d*, $J = 7$, 3 H); 1.44 (*s*, 9 H); 2.20 (*m*, 1 H); 3.94–4.12 (*m*, 3 H); 5.00 (br. *d*, $J = 9$, 1 H); 5.11 (*s*, 2 H); 6.47 (br. *t*, $J = 4$, 1 H); 7.36 (*s*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 17.62 (Me); 19.23 (Me); 28.29 (3 Me); 30.85 (CH); 41.26 (CH_2); 59.78 (CH_2); 67.20 (CH_2); 79.99 (C); 128.42 (CH); 128.55 (CH); 128.64 (CH); 135.15 (C); 155.87 (C); 169.56 (C); 171.98 (C). FAB-MS: 497.1 (86, $[M + 133]^+$), 387.1 (8, $[M + 23]^+$), 365.2 (30, $[M + 1]^+$), 309.1 (59), 265.1 (59), 201.1 (12), 166.1 (17), 132.9 (70), 166.0 (31), 91.0 (100).

Boc-Val-Gly-OH (**16**). In EtOH (500 ml), **15** (27.48 g, 75.4 mmol) and 10% Pd/C (0.8 g) were stirred under H_2. After 17 h, the soln. was filtered through *Celite* and evaporated: 20.35 g (98%) of **16**. $[\alpha]_D^{r.t.} = -21.8$ ($c = 1.06$, EtOH). ^{1}H-NMR (200 MHz, $CDCl_3$): 0.93 (*d*, $J = 6$, 3 H); 0.96 (*d*, $J = 7$, 3 H); 1.42 (*s*, 9 H); 2.05 (*m*, 1 H); 3.99–4.18 (*m*, 3 H); 5.52 (br. *d*, $J = 8$, 1 H); 6.47 (br. *s*, 1 H); 9.45 (br. *s*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 18.01 (Me); 19.21 (Me); 28.31 (3 Me); 31.21 (CH); 41.33 (CH_2); 59.77 (CH); 67.20 (CH_2); 80.60 (C); 156.48 (C); 172.36 (C); 172.62 (C). FAB-MS: 407.1 (68, $[M + 133]^+$), 297.1 (22, $[M + 23]^+$), 275.1 (9, $[M + 1]^+$), 219.1 (33), 175.1 (31), 116.0 (15), 71.9 (37).

Boc-Val-Gly-Leu-OBzl (**17**). As described for **15**, with **16** (20.25 g, 73.8 mmol), toluene (80 ml) $CHCl_3$ (65 ml) Et_3N (10.3 ml, 73.8 mmol) ethyl chloroformate (7.0 ml, 73.8 mmol; 25 min); benzyl L = leucinate·TsOH (30.81 g, 78.3 mmol), Et_3N (10.9 ml, 78.3 mmol), and $CHCl_3$ (200 ml, 2 h). LC (hexane/AcOEt 1:2) gave 28.36 g (80 %) of **17**. $[\alpha]_D^{r.t.} = -26.4$ ($c = 1.13$, EtOH). IR ($CHCl_3$): 3430*m*, 3325*w*, 3010*m*, 2965*s*, 2930*m*, 2875*m*, 1735*s*, 1675*s*, 1500*s*, 1455*m*, 1390*m*, 1370, 1335*w*, 1275*m*, 1235*s*, 1160*s*, 1010*w*, 870*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.89–0.97 (*m*, 12 H); 1.44 (*s*, 9 H); 1.55–1.70 (*m*, 3 H); 2.15 (*m*, 1 H); 3.91–4.07 (*m*, 3 H); 4.64 (*m*, 1 H); 5.09 (br. *d*, $J = 8$, 1 H); 5.14, 5.17 (*AB*, $J = 12$, 2 H); 6.81 (br. *m*, 2 H); 7.34 (*m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 17.74 (Me); 19.30 (Me); 21.88 (Me); 22.72 (Me); 24.77 (CH); 28.33 (3 Me); 30.78 (CH); 41.24 (CH_2); 43.09 (CH_2); 50.99 (CH); 60.10 (CH); 67.05 (CH_2); 80.07 (C); 128.22 (CH); 128.38 (CH); 128.58 (CH); 135.41 (C); 155.94 (C); 168.62 (C); 172.31 (C); 172.54 (C). FAB-MS: 610.3 (63, $[M + 133]^+$), 478.4 (24, $[M + 1]^+$), 422.3 (29), 378.3 (69), 279.2 (55), 222.2 (47), 162.1 (23), 120.1 (12), 91.0 (100).

Boc-Val-Gly-Leu-OH (**1**). As described for **16**, with **17** (20.0 g, 41.9 mmol), EtOH (300 ml), and 10% Pd/C (0.54 g, 15 h): 17.64 g (99%) of **1**. $[\alpha]_D^{r.t.} = -13.2$ ($c = 1.17$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.90–0.98 (*m*, 12 H); 1.43 (*s*, 9 H); 1.60–1.74 (*m*, 3 H); 2.05 (*m*, 1 H); 3.94–4.07 (*m*, 3 H); 4.48 (*m*, 1 H); 5.53 (*d*, $J = 8$, 1 H); 7.44 (*d*, $J = 7$, 1 H); 7.63 (*t*, $J = 5$, 1 H); 9.74 (br. *s*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 17.93 (Me); 19.26 (Me); 21.57 (Me); 22.85 (Me); 24.83 (CH); 28.35 (3 Me); 31.33 (CH); 40.29 (CH_2); 42.95 (CH_2); 51.30 (CH); 59.88 (CH); 80.35 (C); 156.45 (C); 170.22 (C); 172.84 (C); 175.50 (C). FAB-MS: 410.1 (12, $[M + 23]^+$), 388.2 (6, $[M + 1]^+$), 332.1 (7), 288.1 (14), 201.0 (13), 189.1 (34), 157.0 (13), 132.0 (29), 116.0 (20), 98.0 (15), 71.9 (100).

Boc-Leu-Sar-OBzl (**18**). According to *G.P.1*, with Boc-Leu-OH·H_2O (19.95 g, 80 mmol), THF (400 ml), NMM (8.8 ml, 80 mmol), isobutyl chloroformate (10.5 ml, 80 mmol), benzyl sarcosinate·HCl (17.25 g, 80 mmol), NMM (8.8 ml), and DMF (160 ml; 1 h at −15°, 3 h at r.t.). Chromatographic purification (pentane/Et_2O 3:2) gave 27.23 g (87%) of **18**. $[\alpha]_D^{r.t.} = -33.0$ ($c = 1.0$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.92 (*d*, $J = 6.7$, 3 H); 0.99 (*d*, $J = 6.5$, 3 H); 1.41, *1.43* (2*s*, 9 H); 1.40–1.54 (*m*, 2 H); 1.75 (*m*, 1 H); 2.98, *3.14* (2*s*, 3 H); 3.81 (*d*, $J = 17.3$, 1 H); 4.52 (*d*, $J = 17.3$, 1 H); 4.69 (*m*, 1 H); 5.16 (*s*, 2 H); 5.18–5.21 (*m*, 1 H); 7.35 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.79 (Me); 23.40 (Me); 24.62 (CH); 28.36 (3 Me); 35.22, *38.61* (Me); 42.41 (CH_2); 48.68 (CH); 49.79 (CH_2); 67.04 (CH_2); 79.57 (C); 128.55 (2 CH_2); 128.49 (CH); 128.67 (2 CH_2); 135.32 (C); 155.67 (C); 168.38 (C); 173.74 (C). FAB-MS: 415.1 (6, $[M + 23]^+$), 393.2 (47, $[M + 1]^+$), 337.1 (46), 293.1 (76), 299.1 (14), 180.1 (41), 130.1 (21), 91.0 (100), 86.0 (35), 56.9 (58).

Boc-Leu-Sar-OH (**19**). In EtOH (400 ml) **18** (27.00 g, 68.8 mmol) and 10% Pd/C (1/g) were stirred under H_2. After 16 h, the soln. was filtered through *Celite* and evaporated: 20.1 g (97%) of **19**. $[\alpha]_D^{r.t.} = -29.1$ ($c = 1.0$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.89–1.00 (*m*, 6 H); 1.37–1.56 (*m*, 2 H); 1.41, *1.43* (2*s*, 9 H); 1.74 (*m*, 1 H); 2.99, *3.17* (2*s*, 3 H); 3.84 (*d*, $J = 17.5$, 1 H); 4.44 (*d*, $J = 17.5$, 1 H); 4.70 (*m*, 1 H); *5.49*, 5.55 (2*d*, $J = 9.0, 9.1$, 1 H); 7.76 (br. *s*,

1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.75 (Me); 23.34 (Me); 24.63 (CH); 28.35 (3 Me); 35.28, *36.48* (Me); *41.79*, 42.24 (CH_2); 48.83 (CH); 49.77 (CH_2); *79.81*, 80.15 (C); 155.92 (C); 172.05 (C); 174.48 (C). FAB-MS: 325.1 (100, $[M + 23]^+$), 303.1 (50, $[M + 1]^+$), 247.1 (70), 225.1 (29), 203.1 (60), 130.1 (22), 86.0 (60), 56.9 (49).

Boc-Leu-Sar-Leu-OBzl (**20**). According to *G.P.1*, with **19** (20.02 g, 66.2 mmol), THF (330 ml), NMM (7.3 ml, 66.2 mmol), isobutyl chloroformate (8.65 ml, 66.2 mmol), benzyl L-leucinate·TsOH (25.0 g, 63.5 mmol), NMM (7.3 ml), and DMF (140 ml; 2 h at −15°, 2 h at r.t.). LC (pentane/Et_2O 1:5) gave 22.6 g (68%) of **20**. $[\alpha]_D^{r.t.} = -45.1$ ($c = 0.97$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.86–1.00 (*m*, 12 H); 1.38–1.77 (*m*, 6 H); 1.41, *1.43* (2*s*, 9 H); 2.95, *3.10* (2*s*, 3 H); 3.81–3.87 (*m*, 1 H); 4.20–4.31 (*m*, 1 H); 4.52–4.68 (*m*, 2 H); 5.10 (*d*, $J = 10$, 1 H); 5.13, 5.17 (*AB*, $J = 12.3$, 2 H); *6.67*, 7.93 (2*d*, $J = 7.9$, 7.7, 1 H); 7.35 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.69 (Me); 21.89 (Me); 22.73 (Me); 23.37 (Me); 24.70 (CH); 24.80 (CH); 28.39 (3 Me); 36.22 (Me), 41.04 (CH_2); 41.53 (CH_2); 49.01 (CH); 50.88 (CH); 52.28 (CH_2); 67.01 (CH_2); 79.86 (C); 127.93 (CH); 128.32 (2 CH); 128.57 (2 CH); 135.51 (C); 155.97 (C); 168.43 (C); 172.47 (C); 173.86 (C). FAB-MS: 528.3 (28, $[M + 23]^+$), 506.3 (20, $[M + 1]^+$), 406.3 (85), 293.2 (70), 229.1 (70), 130.1 (21), 91.0 (100), 86.0 (39), 56.9 (79).

Boc-Leu-Sar-Leu-OH (**2**). As described for **16**, with **20** (22.7 g, 44.9 mmol), EtOH (300 ml), and 10% Pd/C (1.0 g; 16 h): 18.47 g (99%) of **2**. M.p. 69–73°. $[\alpha]_D^{r.t.} = -34.3$ ($c = 1.05$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.91–1.00 (*m*, 12 H); 1.33–1.79 (*m*, 6 H); 1.41, *1.43* (2*s*, 9 H); 2.98, *3.17* (2*s*, 3 H); 3.89 (*d*, $J = 15.8$, 1 H); 4.28 (*d*, $J = 15.8$, 1 H); 4.62 (*m*, 2 H); 4.88 (br. *s*, 1 H); 5.25, *5.33* (2*d*, $J = 7.6$, 8.1, 1 H); *6.89*, 7.87 (2*d*, $J = 8.0$, 7.8, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.62 (Me); 21.82 (Me); 22.83 (Me); 23.38 (Me); 24.70 (CH); 24.80 (CH); 28.36 (3 Me); 36.60 (Me); 40.79 (CH_2); 41.53 (CH_2); 49.16 (CH); 50.87 (CH); 52.38 (CH_2); 80.18 (C); 156.23 (C); 168.81 (C); 174.16 (C); 175.31 (C). FAB-MS: 438.2 (65, $[M + 23]^+$), 416.2 (42, $[M + 1]^+$), 360.1 (9), 316.2 (88), 285.1 (19), 229.1 (86), 203.1 (100), 185.1 (21), 130.1 (28), 100.0 (18), 86.0 (77), 56.9 (77).

Boc-Leu-Gly-OBzl (**21**). According to *G.P.1*, with Boc-Leu-OH·H_2O (22.41 g, 90 mmol) THF (400 ml), NMM (10.1 ml, 90 mmol), isobutyl chloroformate (12.1 ml, 90 mmol), benzyl glycinate·TsOH (30.37 g, 90 mmol), NMM (10.1 ml, 90 mmol), and DMF (180 ml; 30 min at −15°, 1.5 h at r.t.): 32.1 g (95%) of **21**. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.85–0.97 (*m*, 6 H); 1.42 (*s*, 9 H); 1.4–1.57 (*m*, 1 H); 1.60–1.77 (*m*, 2 H); 4.02–4.25 (*m*, 3 H); 4.98 (*d*, $J = 11$, 1 H); 5.17 (*s*, 2 H); 6.78 (*t*, $J = 9$, 1 H); 7.35 (*m*, 5 H).

Boc-Leu-Gly-OH (**22**). As described for **16**, with **21** (32.1 g, 84.9 mmol), MeOH (180 ml), and 10% Pd/C (1.08 g; 18 h): 23.7 g (97%) of **22**. M.p. 110–112°. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.82–1.00 (*m*, 6 H); 1.42 (*s*, 9 H); 1.35–1.78 (*m*, 3 H); 4.00 (*m*, 1 H); 4.28–4.45 (*m*, 2 H); 4.65 (br., 1 H); 5.19 (*d*, $J = 9$, 1 H); 7.06 (*t*, $J = 3$, 1 H).

Boc-Leu-Gly-MeLeu-OBzl (**23**). According to *G.P.2*, with **22** (22.75 g, 79 mmol), (i-Pr)$_2$EtN (29.5 ml, 0.17 mol), BOP-Cl (21.94 g, 82.2 mmol), CH_2Cl_2 (400 ml), **12** (19.5 g, 71.8 mmol), (i-Pr$_2$)EtN (12.3 ml, 71.8 mmol), and CH_2Cl_2 (400 ml; 22 h). LC (pentane/AcOEt 3:1) gave 23.8 g (66%) of **23**. M.p. 110–112°. $[\alpha]_D^{r.t.} = -52.1$ ($c = 1.05$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.89–0.96 (*m*, 12 H); 1.44 (*s*, 9 H); 1.46–1.54 (*m*, 2 H); 1.65–1.77 (*m*, 4 H); 2.59 (*s*, 3 H); 4.06–4.08 (*m*, 2 H); 4.16–4.23 (*m*, 1 H); 4.86–4.90 (*d*, $J = 6$, 1 H); 5.09, 5.14 (*AB*, $J = 12$, 2 H); 5.32 (*dd*, $J = 5.6$, 5.6, 1 H); 6.99–7.04 (*m*, 1 H); 7.30–7.40 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.40 (Me); 21.79 (Me); 23.08 (2 Me); 24.83 (CH); 25.02 (CH); 28.33 (3 Me); 30.20 (Me); 37.16 (CH_2); 41.63 (CH_2); 41.85 (CH_2); 53.29 (CH); 54.99 (CH); 67.04 (CH_2); 80.09 (C); 128.21 (CH); 128.45 (CH); 128.67 (CH); 135.51 (C); 155.52 (C); 168.91 (C); 171.26 (C); 172.63 (C). FAB-MS: 528.3 (14, $[M + 23]^+$), 506.3 (37, $[M + 1]^+$), 450.3 (36), 406.3 (21), 342.2 (9), 293.2 (29), 236.2 (38), 215.1 (12), 146.1 (13), 130.1 (22), 100.0 (95), 98.0 (13), 91.0 (100), 86.0 (38), 56.9 (67).

Boc-Leu-Gly-MeLeu-OH (**3**). As described for **16**, with **23** (23.8 g, 47.1 mmol), EtOH (200 ml), and 10% Pd/C (0.60 g; 16 h): 16.5 g (83%) of **3**. M.p. 160–161°. $[\alpha]_D^{r.t.} = -42.2$ ($c = 1.0$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.90–0.99 (*m*, 12 H); *1.43*, 1.44 (2*s*, 9 H); 1.47–1.90 (*m*, 6 H); 2.89, *2.92* (2*s*, 3 H); 4.04–4.23 (*m*, 2 H); 4.23–4.37 (*m*, 1 H); 5.19–5.30 (*m*, 2 H); 7.28–7.41 (*m*, 1 H); COOH. ^{13}C-NMR (75 MHz, $CDCl_3$): 21.37 (Me); 21.82 (Me); 23.08 (Me); 23.18 (Me); 24.80 (CH); 25.05 (CH); 28.33 (3 Me); 30.77 (Me); 37.06 (CH_2); 41.58 (CH_2); 41.76 (CH_2); 53.11 (CH); 55.13 (CH); 80.20 (C); 155.81 (C); 169.30 (C); 173.31 (C); 174.06 (C). FAB-MS: 438.2 (82, $[M + 23]^+$), 416.3 (19, $[M + 1]^+$), 360.2 (29), 316.2 (27), 203.2 (39), 146.2 (40), 130.1 (15), 100.1 (58), 56.9 (100).

Boc-Abu-Ile-OBzl (**24**). According to *G.P.1*, with Boc-Abu-OH (20.32 g, 0.10 mol), THF (500 ml), NMM (11.0 ml, 0.10 mol) isobutyl chloroformate (13.1 ml, 0.10 mol), H-Ile-OBzl·TsOH (39.32 g, 0.10 mol), NMM (11.0 ml, 0.1 mol), and DMF (200 ml; 40 min at −15°, 1 h at r.t.): 40.6 g (quant.) of **24**. $[\alpha]_D^{r.t.} = -35.8$ ($c = 1.26$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.83–0.94 (*m*, 9 H); 1.16 (*m*, 1 H); 1.39 (*m*, 1 H); 1.43 (*s*, 9 H); 1.64 (*m*, 1 H); 1.84 (*m*, 1 H); 1.91 (*m*, 1 H); 4.01 (*m*, 1 H); 4.62 (*dd*, $J = 5$, $J = 9$, 1 H); 5.06 (*d*, $J = 8$, 1 H); 5.11, 5.19 (*AB*, $J = 12$, 2 H); 6.56 (*d*, $J = 9$, 1 H); 7.34 (*s*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 9.96 (Me); 11.50 (Me); 15.46 (Me); 24.92 (CH_2); 25.45 (CH_2); 28.92 (Me); 37.91 (CH); 55.81 (CH); 56.46 (CH); 66.98 (CH_2); 79.96 (C); 128.38 (2 CH); 128.38 (C); 128.57 (CH); 135.34 (C); 155.69 (C); 171.57 (C); 171.86 (C). FAB-MS: 429.2 (24, $[M + 23]^+$), 407.2 (45, $[M + 1]^+$), 351.1 (73), 307.1 (8), 243.1 (13), 222.1 (14), 215.1 (12), 149.0 (17), 102.0 (24), 91 (100), 86.0 (57).

H-Abu-Ile-OBzl·CF$_3$COOH·CF$_3$COOH (**25**). According to *G.P.3*, with **24** (39.1 g, 96.2 mmol), CH_2Cl_2 (50 ml), and CF_3COOH (50 ml; 30 min): 27.49 g (93%) of **25**·CF_3COOH. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.79–0.92 (*m*, 9 H); 1.15 (*m*, 1 H); 1.34 (*m*, 1 H); 1.76–1.93 (*m*, 3 H); 4.13 (*m*, 1 H); 4.43 (*dd*, *J* = 5, 7, 1 H); 5.08, 5.19 (*AB*, *J* = 12, 2 H); 7.33 (*m*, 6 H); 8.12 (br. *m*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 8.74 (Me); 1.27 (Me); 15.17 (Me); 24.98 (2 CH_2); 37.13 (CH); 54.64 (CH); 57.81 (CH); 67.30 (CH_2); 116.06 (*q*, ^1J(C,F) = 291); 128.54 (2 CH); 128.61 (3 CH); 135.08 (C); 161.84 (*q*, ^2J(C,F) = 36); 169.23 (C); 171.02 (C). FAB-MS: 329.2 (54, $[M + 23]^+$), 307.2 (100, $[M + 1]^+$), 222.1 (19), 148.1 (33), 91.0 (86).

Boc-Gly-Abu-Ile-OBzl (**26**). According to *G.P.1*, with Boc-Gly-OH (16.95 g, 96.8 mmol), THF (500 ml), NMM (10.6 ml, 96.2 mmol), isobutyl chloroformate (12.6 ml, 96.2 mmol), **25** (containing CF_3COOH; 27.49 g), and DMF (200 ml; 1 h at −15°, 2 h at r.t.). Flash chromatography (hexane/AcOEt 1:2) yielded 41.65 g (quant.) of **26**. $[\alpha]_D^{r.t.} = -37.2$ (*c* = 1.03, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.84–0.93 (*m*, 9 H); 1.14 (*m*, 1 H); 1.35 (*m*, 1 H); 1.46 (*s*, 9 H); 1.67 (*m*, 1 H); 1.86 (*m*, 1 H); 1.91 (*m*, 1 H); 3.82 (*m*, 2 H); 4.46 (*m*, 1 H); 4.62 (*dd*, *J* = 5, 9, 1 H); 5.13, 4.22 (*AB*, *J* = 12, 2 H); 5.2 (*m*, 1 H); 6.68 (*m*, 1 H); 6.81 (*m*, 1 H); 7.36 (*s*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 9.66 (Me); 11.54 (Me); 15.51 (Me); 24.99 (CH_2); 25.75 (CH_2); 28.26 (3 Me); 37.78 (CH); 44.32 (CH_2); 54.28 (CH); 56.26 (CH); 67.07 (CH_2); 80.35 (C); 128.42 (CH); 128.58 (CH); 135.28 (C); 155.93 (C); 169.46 (C); 171.15 (C); 171.44 (C). FAB-MS: 596.1 (1, $[M + 133]^+$), 486.2 (8, $[M + 23]^+$), 464.2 (8, $[M + 1]^+$), 408.2 (21), 364.2 (2), 307.2 (3), 222.1 (21), 187.1 (6), 159.1 (11), 132.9 (9), 115.0 (5), 91.0 (100), 86.0 (40).

H-Gly-Abu-Ile-OBzl (**27**). According to *G.P.3*, with **26** (41.65 g, 89.9 mmol), CH_2Cl_2 (80 ml), CF_3COOH (60 ml; 10 h): 32.35 (99%) of **27**. $[\alpha]_D^{r.t.} = -43.8$ (*c* = 0.95, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.81–0.94 (*m*, 9 H); 1.15 (*m*, 1 H); 1.33 (*m*, 1 H); 1.68 (*m*, 1 H); 1.84 (*m*, 1 H); 1.89 (*m*, 1 H); 3.49 (*s*, 2 H); 3.58 (br. *s*, 2 H); 4.47 (*m*, 1 H); 4.59 (*dd*, *J* = 5, 8, 1 H); 5.10, 5.20 (*AB*, *J* = 12, 1 H); 7.01 (*d*, *J* = 8, 1 H); 7.92 (*d*, *J* = 8, 1 H); 7.34 (*s*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 9.61 (Me); 11.51 (Me); 15.46 (Me); 25.02 (CH_2); 25.59 (CH_2); 37.65 (CH); 43.57 (CH_2); 54.35 (CH); 56.71 (CH); 67.00 (CH_2); 128.39 (CH); 128.57 (CH); 135.34 (C); 171.20 (C); 171.57 (C); 171.73 (C). FAB-MS: 386.2 (25, $[M + 23]^+$), 364.2 (79, $[M + 1]^+$), 307.2 (10), 222.2 (42), 154.1 (14), 149.0 (18), 143.1 (13), 137.1 (14), 136.0 (13), 120.1 (10), 115.1 (25), 91.0 (100), 86.0 (42).

Boc-Leu-Gly-Abu-Ile-OBzl (**28**). According to *G.P.1*, with Boc-Leu-OH·H_2O (22.4 g, 89.9 mmol), THF (250 ml), NMM (9.9 ml, 89.9 mmol), isobutyl chloroformate (11.7 ml, 89.8 mmol), **27** (32.35, 89 mmol), and DMF (160 ml; 1 h at −15°, 2 h at r.t.). Purification by chromatography (CH_2Cl_2/EtOH 19:1) gave 42.87 g (83%) of **28**. $[\alpha]_D^{r.t.} = -34.2$ (*c* = 1.02, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.81–0.95 (*m*, 15 H); 1.13 (*m*, 1 H); 1.35–1.70 (*m*, 5 H); 1.42 (*s*, 9 H); 1.89–1.95 (*m*, 2 H); 4.00 (*m*, 2 H); 4.17 (*m*, 1 H); 4.56 (*m*, 1 H); 4.62 (*dd*, *J* = 5, 9, 1 H); 5.10, 5.23 (*AB*, *J* = 12, 2 H); 5.34 (*m*, 1 H); 7.04–7.07 (*m*, 2 H); 7.21 (*m*, 1 H); 7.34 (*s*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 9.98 (Me); 11.56 (Me); 15.47 (Me); 21.81 (Me); 22.96 (Me); 24.73 (CH); 24.96 (CH_2); 25.74 (CH_2); 28.31 (3 Me); 37.87 (CH); 41.30 (CH_2); 43.05 (CH_2); 53.44 (CH); 54.75 (CH); 56.52 (CH); 67.07 (CH_2); 80.15 (C); 128.38 (CH); 128.45 (CH); 128.58 (CH); 135.28 (C); 155.95 (C); 168.94 (C); 171.41 (C); 171.89 (C); 173.40 (C). FAB-MS: 599.3 (100, $[M + 23]^+$), 477.3 (33, $[M + 1]^+$), 521.2 (8), 499.2 (11), 477.3 (25), 391.2 (8), 300.1 (12), 222.1 (22), 149.0 (28), 91.0 (78), 86.0 (46).

H-Leu-Gly-Abu-Ile-OBzl (**29**). According to *G.P.3*, with **28** (41.17 g, 71.4 mmol) CH_2Cl_2 (80 ml), and CF_3COOH (60 ml; 20 h): 30.45 g (89%) of **29**. $[\alpha]_D^{r.t.} = -41.6$ (*c* = 1.0, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.82–0.95 (*m*, 15 H); 1.15 (*m*, 1 H); 1.26–1.94 (*m*, 7 H); 2.72 (br. *s*, 2 H); 3.55 (*m*, 1 H); 3.97 (*m*, 2 H); 4.46 (*m*, 1 H); 4.60 (*dd*, *J* = 5, 8, 1 H); 5.10, 5.23 (*AB*, *J* = 12, 2 H); 6.88, 7.16 (2 br. *m*, 2 H); 7.34 (*s*, 5 H); 8.11 (br. *m*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 9.84 (Me); 11.58 (Me); 15.54 (Me); 21.56 (Me); 23.18 (Me); 24.80 (CH); 25.06 (CH_2); 25.74 (CH_2); 37.80 (CH); 43.00 (CH_2); 43.53 (CH_2); 53.26 (CH); 54.60 (CH); 56.61 (CH); 67.10 (CH_2); 128.41 (CH); 128.61 (CH); 128.84 (CH); 135.71 (C); 169.24 (C); 171.48 (C); 171.60 (C); 175.69 (C). FAB-MS: 499.3 (25, $[M + 23]^+$), 477.3 (100, $[M + 1]^+$), 391.3 (23), 222.2 (14), 149.0 (91), 129.1 (31), 91.0 (80), 86.0 (85).

Boc-Val-Leu-Gly-Abu-Ile-OBzl (**30**). To a soln. of **29** (30.45 g, 63.9 mmol) Boc-Val-OH (13.88 g, 63.9 mmol), and BtOH (8.63 g, 63.9 mmol) in THF (250 ml), DCC (13.18 g, 63.9 mmol) was added at 0°. After 4 h, the precipitated urea was filtered off and the filtrate evaporated. The residue was worked up with CH_2Cl_2 according to *G.P.1*. Chromatographical purification (hexane/AcOEt 1:5) provided 30.72 g (71%) of **30**. $[\alpha]_D^{r.t.} = -43.5$ (*c* = 1.04, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.82–0.93 (*m*, 21 H); 1.16 (*m*, 1 H); 1.35 (*m*, 1 H); 1.42 (*s*, 9 H); 1.51–1.70 (*m*, 4 H); 1.76–1.92 (*m*, 2 H); 2.04 (*m*, 1 H); 3.85 (*dd*, *J* = 4.2, 16.6, 1 H); 4.03 (*m*, 1 H); 4.30 (*dd*, *J* = 5.6, 16.6, 1 H); 4.65–4.75 (*m*, 3 H); 5.11, 5.26 (*AB*, *J* = 12.3, 2 H); 5.47 (*d*, *J* = 5, 1 H); 7.34 (*m*, 5 H); 7.47 (*d*, *J* = 8.6, 1 H); 7.80 (*m*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 9.97 (Me); 11.59 (Me); 15.45 (Me); 18.23 (Me); 19.35 (Me); 22.05 (Me); 22.95 (Me); 24.76 (CH); 25.06 (CH_2); 26.17 (CH_2); 28.36 (3 Me); 30.98 (CH); 37.98 (CH); 41.57 (CH_2); 42.91 (CH_2); 51.89 (CH); 54.37 (CH); 56.58 (CH); 60.35 (CH); 67.01 (CH_2); 79.89 (C); 128.73 (3 CH); 128.55 (2 CH); 135.47 (C); 156.22 (C); 168.83 (C); 171.66 (C); 171.94 (C); 172.18 (C); 172.75 (C). FAB-MS: 698.4 (43, $[M + 23]^+$),

676.4 (33, $[M + 1]^+$), 599.3 (14), 576.4 (19), 455.3 (11), 399.2 (18), 314.2 (34), 257.1 (17), 222.2 (28), 116.1 (17), 91.0 (94), 86.0 (100).

Boc-Val-Leu-Gly-Abu-Ile-OH (**4**). As described for **16**, with **30** (30.72 g, 45.5 mmol), EtOH (300 ml), and 10% Pd/C (0.53 g; 16 h): 26.06 g (96%) of **4**. $[\alpha]_D^{r.t.} = -30.9$ ($c = 1.03$, EtOH). ^{1}H-NMR (300 MHz, (D_6)DMSO): 0.79–0.92 (*m*, 21 H); 1.22 (*m*, 1 H); 1.38 (*s*, 9 H); 1.37–1.58 (*m*, 4 H); 1.58–1.73 (*m*, 2 H); 1.76 (*m*, 1 H); 1.91 (*m*, 1 H); 3.33 (br. *s*, 1 H); 3.62–3.79 (*m*, 3 H); 4.14 (*m*, 1 H); 4.31 (*m*, 2 H); 6.72 (*d*, $J = 8.7$, 1 H); 7.73 (*d*, $J = 8.1$, 1 H); 7.84 (*d*, $J = 7.7$, 1 H); 7.98 (*d*, $J = 8.2$, 1 H); 8.15 (*t*, $J = 4.1$, 1 H). ^{13}C-NMR (75 MHz, (D_6)DMSO): 9.87 (Me); 11.23 (Me); 15.46 (Me); 18.12 (Me); 19.17 (Me); 21.46 (Me); 22.95 (Me); 23.89 (CH); 24.64 (CH_2); 25.54 (CH_2); 28.06 (3 Me); *30.14* (CH); *36.16* (CH); *40.88* (CH_2); *41.84* (CH_2); 50.93 (CH); 53.21 (CH); 56.20 (CH); 59.84 (CH); 77.99 (C); 155.37 (C); 168.23 (C); 171.21 (C); 171.37 (C); 172.17 (C); 172.73 (C). FAB-MS: 608.3 (66, $[M + 23]^+$), 586.3 (15, $[M + 1]^+$), 486.3 (26), 455.3 (10), 399.2 (21), 314.1 (38), 270.2 (17), 257.1 (22), 217.1 (17), 132.1 (19), 116.0 (21), 86.0 (100), 71.9 (46), 56.9 (63).

Boc-MeAbu-Ile-OBzl (**31**). According to *G.P.1*, with **10** (22.8 g, 105 mmol), THF (500 ml), NMM (11.6 ml, 105 mmol), isobutyl chloroformate (13.7 ml, 105 mmol), benzyl L-isoleucinate·TsOH (41.7 g, 106 mmol), NMM (11.7 ml), DMF (200 ml; 30 min at −15° and 45 min at r.t.): 43.42 (98%) of **31**. $[\alpha]_D^{r.t.} = -60.9$ ($c = 1.24$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.83–0.93 (*m*, 9 H); 1.09 (*m*, 1 H); 1.33 (*m*, 1 H); 1.48 (*s*, 9 H); 1.68 (*m*, 1 H); 1.91 (*m*, 2 H); 2.76 (*s*, 3 H); 4.45 (*m*, 1 H); 4.61 (*dd*, $J = 4.8$, 8.8, 1 H); 5.13, 5.19 (*AB*, $J = 12.2$, 2 H); 6.68 (*m*, 1 H); 7.35 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.46 (Me); 11.46 (Me); 15.54 (Me); 20.82 (CH_2); 24.87 (CH_2); 28.36 (3 Me); 29.75 (Me); 37.81 (CH); 56.29 (CH); 59.57 (CH); 66.91 (CH_2); 80.45 (C); 128.32 (2 CH); 128.58 (3 CH); 135.39 (C); 156.4 (C); 170.88 (C); 171.50 (C). FAB-MS: 443.0 (6, $[M + 23]^+$), 421.1 (32, $[M + 1]^+$), 365.0 (23), 321.1 (90), 222.1 (19), 172.2 (21), 144.0 (16), 116.0 (71), 91.0 (100), 72.0 (96), 56.9 (72).

MeAbu-Ile-OBzl (**32**). According to *G.P.3*, with **31** (43.34 g, 103 mmol), CH_2Cl_2 (40 ml), CF_3COOH (75 ml; 4 h): 30.7 g (96%) of **32**. $[\alpha]_D^{r.t.} = -36.2$ ($c = 0.97$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.85–0.98 (*m*, 9 H); 1.16 (*m*, 1 H); 1.36 (*m*, 1 H); 1.64 (*m*, 1 H); 1.75 (*m*, 1 H); 1.95 (*m*, 1 H); 2.35 (br. *m*, 1 H); 2.39 (*s*, 3 H); 3.00 (*m*, 1 H); 4.64 (*dd*, $J = 4.8$, 9.3, 1 H); 5.12, 5.21 (*AB*, $J = 12.2$, 2 H); 7.35 (*m*, 5 H); 7.67 (*d*, $J = 9.3$, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.13 (Me); 11.52 (Me); 15.71 (Me); 24.92 (CH_2); 26.49 (CH_2); 35.03 (Me); 37.71 (CH); 56.07 (CH); 66.30 (CH); 66.88 (CH_2); 128.17 (3 CH); 128.55 (2 CH); 135.44 (C); 171.82 (C); 173.61 (C). FAB-MS: 343.0 (6, $[M + 23]^+$), 321.1 (98.7, $[M + 1]^+$), 162.1 (7), 91.0 (50), 72.0 (100).

Boc-Sar-MeAbu-Ile-OBzl (**33**). According to *G.P.2*, with Boc-Sar-OH (19.96 g, 106 mmol), $(i\text{-Pr})_2$EtN (36 ml, 0.21 mol), **32** (30.7 g, 95.8 mmol), BOP-Cl (28.05 g, 0.11 mol), and CH_2Cl_2 (1 l; 16 h). LC (hexane/AcOEt 1:1) gave 44.74 g (95%) of **33**. $[\alpha]_D^{r.t.} = -70.6$ ($c = 1.01$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$; 2 conformations): 0.82–0.90 (*m*, 9 H); 1.12 (*m*, 1 H); 1.30 (*m*, 1 H); 1.42, 1.44, *1.46* (3*s*, 9 H); 1.70 (*m*, 1 H); 1.92 (*m*, 2 H); 2.82, 2.90, 2.92 (3*s*, 3 H); 3.86–4.13 (*m*, 2 H); 4.56 (*dd*, $J = 5.0$, 8.8, 1 H); 4.89 (*m*, 1 H); 5.11, 5.20 (*AB*, $J = 12$, 2 H); 6.55, *6.62* (2*d*, $J = 8.6$, 1 H); 7.34 (*m*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.39 (Me); 11.46 (Me); 15.61 (Me); 20.53 (CH_2); 24.83 (CH_2); 28.31 (3 Me); *29.75*, 35.60 (Me); 37.45 (CH); 50.48 (CH_2); 56.45 (CH); 58.18 (CH); 66.85 (CH_2); 79.99 (C); 128.34 (2 CH); 128.55 (3 CH); 135.46 (C); 156.13 (C); 169.88 (C); 170.23 (C); 171.31 (C). FAB-MS: 514.3 (24, $[M + 23]^+$), 492.3 (38, $[M + 1]^+$), 418.2 (12), 392.2 (52), 321.2 (14), 305.1 (6), 271.1 (35), 215.1 (100), 171.1 (30), 90.9 (70), 71.9 (81), 56.9 (60).

Sar-MeAbu-Ile-OBzl (**34**). According to *G.P.3*, with **33** (44.7 g, 91 mmol), CH_2Cl_2 (40 ml), CF_3COOH (70 ml; 3 h): 35.6 g (quant.) of **34**. $[\alpha]_D^{r.t.} = -67.1$ ($c = 1.09$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$; 2 conformations): 0.82–0.90 (*m*, 9 H); 1.07 (*m*, 1 H); 1.32 (*m*, 1 H); 1.68 (*m*, 1 H); 1.91 (*m*, 2 H); 2.11 (br. *m*, 1 H); *2.46*, 2.47 (2*s*, 3 H); 2.78, *2.89* (2*s*, 3 H); 3.33–3.66 (*m*, 2 H); 4.26 (*dd*, $J = 5.4$, 9.8, 0.3 H); *4.56*, 4.64 (2*dd*, $J = 5.0$, 8.7, 5.1, 8.8, 1 H); 4.95 (*dd*, $J = 6.9$, 8.7, 0.7 H); 5.10–5.23 (*m*, 2 H); 6.62 (*d*, $J = 8.8$, 0.6 H); 7.35 (*m*, 5 H); 8.62 (*d*, $J = 8.1$, 0.4 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.43 (Me); 11.47 (Me); 15.60 (Me); 20.76 (CH_2); 25.00 (CH_2); 29.64 (Me); 36.61 (Me); 37.61 (CH); 52.64 (CH_2); 56.42 (CH); 58.20 (CH); 61.79 (CH); 66.98 (CH_2); 128.43 (3 CH); 128.61 (2 CH); 135.41 (C); 170.34 (C); 171.40 (C); 172.31 (C). FAB-MS: 414.1 (10, $[M + 23]^+$), 392.1 (100, $[M + 1]^+$), 321.1 (13), 171.1 (44), 90.9 (43), 71.9 (39).

Boc-Leu-Sar-MeAbu-Ile-OBzl (**35**). According to *G.P.2*, with **34** (37.3 g, 91 mmol), CH_2Cl_2 (1 l), Boc-Leu-OH·H_2O (29.26 g, 117 mmol), $(i\text{-Pr})_2$EtN (40.0 ml, 0.23 mol), and BOP-Cl (28.00 g, 110 mmol; 36 h). LC (hexane/AcOEt 1:3) gave 49.2 g (89%) of **35**. $[\alpha]_D^{r.t.} = -86.8$ ($c = 1.1$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.83–1.02 (*m*, 15 H); 1.13 (*m*, 1 H); 1.30–1.51 (*m*, 3 H); 1.43 (*s*, 9 H); 1.67 (*m*, 1 H); 1.75 (*m*, 1 H); 1.93 (*m*, 2 H); 2.76, *2.94* (2*s*, 3 H); *3.16*, 3.32 (2*s*, 3 H); 3.82 (*d*, $J = 16.0$, 0.5 H); 4.48–4.60 (*m*, 2.5 H); 4.70–4.75 (*m*, 1 H); 4.89 (*m*, 1 H); 5.11, 5.20 (*AB*, $J = 12$, 2 H); 5.24 (*m*, 1 H); 6.59 (*d*, $J = 8.6$, 0.7 H); 7.34 (*m*, 5 H); 7.90 (*d*, $J = 8.3$, 0.3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.47 (Me); 11.50 (Me); 15.60 (Me); 20.78 (CH_2); 21.82 (Me); 23.44 (Me); 24.67 (CH); 24.94 (CH_2); 28.39 (3 Me); 30.07 (Me); 36.67 (CH); 37.61 (Me); 42.35 (CH_2); 48.75 (CH); 49.78 (CH_2); 56.42 (CH); 58.37 (CH); 66.94 (CH_2); 79.60 (C); 128.41 (3 Me); 128.57 (2 CH); 135.42 (C); 155.68 (C); 169.18 (C); 170.15 (C); 171.40

(C); 173.57 (C). FAB-MS: 627.3 (27, $[M + 23]^+$), 605.3 (78, $[M + 1]^+$), 505.2 (87), 392.1 (26), 384.1 (54), 328.1 (98), 321.1 (38), 285.1 (43), 229.0 (100), 154.0 (35), 130.0 (33), 90.9 (76), 86.0 (38), 71.9 (54), 56.9 (67).

H-Leu-Sar-MeAbu-Ile-OBzl (**36**). According to *G.P.3*, with **35** (49.2 g, 81.4 mmol), CH_2Cl_2 (50 ml), and CF_3COOH (70 ml; 15 h): 40.95 g (quant.) of **36**. $[\alpha]_D^{r.t.} = -69.6$ ($c = 0.91$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$; 2 conformations): 0.82–0.98 (*m*, 15 H); 1.15 (*m*, 1 H); 1.29–1.50 (*m*, 3 H); 1.66 (*m*, 1 H); 1.85–2.05 (*m*, 3 H); 1.95 (br. *s*, 2 H); 2.77, *2.95* (2*s*, 3 H); *3.13*, 3.27 (2*s*, 3 H); 3.78 (*m*, 1 H); 4.15, 4.18 (*AB*, $J = 15.9$, 2 H); 4.56 (*m*, 1 H); 4.92 (*dd*, $J = 6.9$, 8.6, 1 H); 5.08–5.23 (*m*, 1 H); 6.66 (*d*, $J = 8.6$, 0.8 H); 7.34 (*m*, 5 H); 7.88 (*d*, $J = 8.6$, 0.2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.43 (Me); 11.46 (Me); 15.57 (Me); 20.71 (CH_2); 21.50 (Me); 23.57 (Me); 24.70 (CH); 24.96 (CH_2); 30.14 (Me); 36.52 (CH); 37.52 (Me); 43.88 (CH_2); 49.43 (CH); 49.90 (CH_2); 56.50 (CH); 58.39 (CH); 66.88 (CH_2); 128.25 (3 CH); 128.55 (2 CH); 135.42 (C); 169.59 (C); 170.14 (C); 171.43 (C); 171.67 (C); 176.75 (C). FAB-MS: 527.2 (16, $[M + 23]^+$), 505.2 (100, $[M + 1]^+$), 392.1 (6), 321.1 (9), 284.1 (21), 185.1 (24), 171.1 (19), 99.9 (27), 90.9 (33), 86.0 (37), 71.9 (28).

Boc-Val-Leu-Sar-MeAbu-Ile-OBzl (**37**). According to *G.P.1*, with Boc-Val-OH (19.4 g, 89.3 mmol), THF (450 ml), NMM (9.85 ml, 89.4 mmol), isobutyl chloroformate (11.7 ml, 89.3 mmol), **36** (40.94 g, 81.1 mmol), and DMF (150 ml; 30 min at −11°, 1 h at r.t.). LC (CH_2Cl_2/AcOEt 2:3) gave 47.4 g (83%) of **37**. $[\alpha]_D^{r.t.} = -91.8$ ($c = 1.02$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.83–1.02 (*m*, 21 H); 1.16 (*m*, 1 H); 1.37 (*m*, 1 H); 1.43 (*s*, 9 H); 1.50–1.80 (*m*, 4 H); 1.91–2.10 (*m*, 3 H); 2.77, *2.95* (2*s*, 3 H); *3.19*, 3.32 (2*s*, 3 H); 3.90 (*d*, $J = 15.8$, 1 H); 4.00 (*m*, 1 H); 4.35 (*d*, $J = 15.8$, 1 H); 4.62 (*dd*, $J = 5.1$, 8.8, 1 H); 4.93 (*dd*, $J = 6.8$, 8.8, 1 H); 5.05–5.27 (*m*, 4 H); 6.72 (*m*, 2 H); 7.35 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.42 (Me); 11.47 (Me); 15.57 (Me); 17.77 (Me); 19.26 (Me); 20.75 (CH_2); 21.93 (Me); 23.24 (Me); 24.66 (CH); 25.02 (CH_2); 28.29 (3 Me); 30.15 (Me); 31.24 (CH); 37.00 (Me); 37.73 (CH); 42.05 (CH_2); 47.13 (CH); 49.76 (CH_2); 56.37 (CH); 58.34 (CH); 59.82 (CH); 61.99 (CH); 67.05 (CH_2); 79.60 (C); 128.32 (3 CH); 128.55 (2 CH); 135.38 (C); 155.71 (C); 169.17 (C); 170.14 (C); 171.28 (C); 171.67 (C); 172.76 (C). FAB-MS: 726.3 (37, $[M + 23]^+$), 704.3 (13, $[M + 1]^+$), 604.3 (5), 505.2 (3), 483.2 (29), 427.1 (53), 392.1 (64), 384.1 (57), 328.0 (52), 284.1 (10), 257.0 (12), 171.1 (38), 116.0 (19), 90.9 (54), 86.0 (100), 71.9 (58), 56.9 (57).

BocVal-Leu-Sar-MeAbu-Ile-OH (**5**). As described for **16**, with **37** (24.1 g, 34.2 mmol), EtOH (200 ml), and 10% Pd/C (0.40 g; 16 h): 16.79 g (quant.) of **5**. M.p. 92–97°. $[\alpha]_D^{r.t.} = -84.7$ ($c = 1.0$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$; 4 conformations): 0.84–1.03 (*m*, 21 H); 1.23 (*m*, 1 H); 1.43 (*s*, 9 H); 1.47–1.85 (*m*, 5 H); 1.99 (*m*, 2 H); 2.14 (*m*, 1 H); 2.76, 2.79, 2.94, *3.04* (4*s*, 3 H); *3.26*, 3.32, 3.35 (3*s*, 3 H); 3.85–4.32 (3*m*, 2 H); 4.52–4.68 (br. *m*, 2 H); 4.84–5.08 (2*m*, 2 H); 5.24 (*m*, 1 H); 7.03 (*d*, $J = 8.7$, 1 H); 7.29 (*d*, $J = 9.7$, 1 H); COOH not visible. ^{13}C-NMR (75 MHz, $CDCl_3$): 10.56 (Me); 11.75 (Me); 15.58 (Me); 18.01 (Me); 19.23 (Me); 20.79 (CH_2); 22.42 (Me); 22.99 (Me); 24.73 (CH); 25.25 (CH_2); 28.31 (3 Me); 30.72 (CH); 31.04 (Me); 37.74 (Me); 37.51 (CH); 41.80 (CH_2), 47.31 (CH); 49.88 (CH_2); 56.69 (CH); 58.72 (CH); 59.85 (CH); 80.28 (C); 156.13 (C); 169.06 (C); 170.11 (C); 171.46 (C); 172.67 (C); 174.00 (C). FAB-MS: 636.3 (75, $[M + 23]^+$), 614.3 (39, $[M + 1]^+$), 483.2 (21), 427.1 (44), 384.1 (47), 328.0 (57), 302.1 (83), 257.0 (12), 232.1 (19), 171.1 (32), 116.0 (21), 86.0 (100), 71.9 (59), 56.9 (61). GC: 8.36 (Val), 9.18 (MeAbu), 10.4 (Sar), 10.68 (Ile), 11.14 (Leu).

MeAbu-Ile-OBzl·HCl (**38**·HCl). According to *G.P.4*, with **31** (30.1 g, 71.6 mmol), and sat. HCl/Et_2O soln. (200 ml; 2 h): 25.8 g (quant.) of **38**·HCl. $[\alpha]_D^{r.t.} = -19.7$ ($c = 1.0$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.87 (*t*, $J = 7.3$, 3 H); 0.95–1.03 (*m*, 6 H); 1.32–1.49 (*m*, 2 H); 2.01–2.20 (*m*, 3 H); 2.70 (*s*, 3 H); 4.05 (*dd*, $J = 5.1$, 9.0, 1 H); 4.53 (*dd*, $J = 5.0$, 7.4, 1 H); 5.11, 5.21 (*AB*, $J = 12.1$, 2 H); 7.34 (*m*, 5 H); 8.19 (*d*, $J = 7.4$, 1 H); 9.46 (br. *s*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 9.5 (Me); 11.6 (Me); 15.8 (Me); 23.9 (CH_2); 25.3 (CH_2); 31.5 (Me); 36.8 (CH); 57.9 (CH); 64.0 (CH); 67.1 (CH_2); 128.5 (5 CH); 135.3 (C); 167.5 (C); 171.0 (C). FAB-MS: 321.3 (100, $[M + 1]^+$), 107.1 (6), 91.0 (38), 72.0 (63).

Boc-Gly-MeAbu-Ile-OBzl (**39**). According to *G.P.1*, with Boc-Gly-OH (12.67 g, 72 mmol), THF (360 ml), NMM (7.97 ml, 72 mmol), isobutyl chloroformate (9.45 ml, 72 mmol), **38** (25.8 g, 72 mmol), NMM (7.97 ml), and DMF (145 ml; 20 min at −15°, 2 h at r.t.). LC (hexane/AcOEt 2:1) gave 29.0 g (84%) of **39**. $[\alpha]_D^{r.t.} = -73.9$ ($c = 1.0$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.81–0.89 (*m*, 9 H); 1.00–1.14 (*m*, 1 H); 1.24–1.35 (*m*, 1 H); 1.46 (*s*, 9 H); 1.61–1.76 (*m*, 1 H); 1.84–2.00 (*m*, 2 H); 2.90 (*s*, 3 H); 3.98 (*dd*, $J = 2.6$, 4.2, 2 H); 4.57 (*dd*, $J = 4.9$, 8.7, 1 H); 4.93 (*dd*, $J = 7.0$, 8.7, 1 H); 5.12, 5.21 (*AB*, $J = 12.2$, 2 H); 5.52 (br. *m*, 1 H); 6.55 (*d*, $J = 8.6$, 1 H); 7.35 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.4 (Me); 11.5 (Me); 15.6 (Me); 20.8 (CH_2); 25.0 (CH_2); 28.4 (3 Me); 29.5 (Me); 37.7 (CH); 42.7 (CH_2); 56.4 (CH); 58.3 (CH); 67.0 (CH_2); 79.8 (C); 128.4 (3 CH); 128.6 (2 CH); 135.8 (C); 155.8 (C); 170.0 (2 C); 171.4 (C). FAB-MS: 499.9 (6, $[M + 23]^+$), 477.9 (17, $[M + 1]^+$), 421.9 (8), 319.0 (5), 291.0 (7), 257.0 (22), 222.1 (9), 201.0 (100), 173.0 (12), 157.0 (16), 129.0 (14), 106.9 (11), 90.9 (88), 71.9 (86), 56.8 (73).

H-Gly-MeAbu-Ile-OBzl·HCl (**40**·HCl). According to *G.P.4*, with **39** (29.0 g, 60.7 mmol), and sat. HCl/Et_2O soln. (200 ml; 2 h): 24.9 g (99%) of **40**. $[\alpha]_D^{r.t.} = -51.2$ ($c = 1.0$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$; 2 conformations): 0.81–1.00 (*m*, 9 H); 1.15–1.31 (*m*, 1 H); 1.32–1.48 (*m*, 1 H); 1.56–1.73 (*m*, 1 H); 1.91–2.03 (*m*, 2 H); 2.91, *2.96* (2*s*, 3 H); 4.07–4.20 (*m*, 2 H); 4.41 (*m*, 0.25 H); 4.46 (*dd*, $J = 6.1$, 7.8, 0.75 H); 5.07, 5.17 (*AB*, $J = 12.3$, 2 H);

5.04–5.14 (*m*, 1 H); 7.32 (*m*, 5 H); 7.57 (*d*, *J* = 7.9, 0.75 H); 8.05 (*d*, *J* = 7.5, 0.25 H); 8.18 (br. *s*, 1 H); 8.33 (br. *s*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.6 (Me); 11.2 (Me); 15.7 (Me); 22.0 (CH_2); 25.6 (CH_2); 30.2 (Me); 36.7 (CH); 41.0 (CH_2); 57.1 (CH); 58.2 (CH); 66.9 (CH_2); 128.3 (3 CH); 128.5 (2 CH); 135.4 (C); 167.9 (C); 170.6 (C); 172.3 (C). FAB-MS: 421.2 (14, $[M + 23]^+$), 378.1 (100, $[M + 1]^+$), 321.1 (9), 307.0 (8), 289.0 (6), 222.1 (32), 172.1 (12), 76.9 (27), 71.9 (44).

Boc-Leu-Gly-MeAbu-Ile-OBzl (**41**). According to *G.P. 1*, with Boc-Leu-OH·H_2O (14.96 g, 60 mmol), THF (300 ml), NMM (6.61 ml, 60 mmol), isobutyl chloroformate (7.84 ml, 60 mmol), **40** (24.8 g, 60 mmol) NMM (6.61 ml), and DMF (120 ml; 15 min at −15°, 2 h at r.t.): 30.3 g (87%) of **41** $[\alpha]_D^{r.t.} = -73.4$ (*c* = 0.98, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.81–0.95 (*m*, 15 H); 1.00–1.17 (*m*, 1 H); 1.22–1.39 (*m*, 1 H); 1.44 (*s*, 9 H); 1.49 (*m*, 1 H); 1.60–1.77 (*m*, 3 H); 1.84–2.06 (*m*, 2 H); 2.96 (*s*, 3 H); 4.01, 4.17 (*ABX*, $J_{AB} = 17.9$, $J_{AX} = 2.8$, $J_{BX} = 4.3$, 2 H); 4.29 (*m*, 1 H); 4.58 (*dd*, *J* = 4.9, 8.6, 1 H); 5.02 (*dd*, *J* = 6.6, 8.9, 1 H); 5.10–5.23 (*m*, 1 H); 5.12, 5.22 (*AB*, *J* = 12.2, 2 H); 6.76 (br. *d*, *J* = 7.9, 1 H); 7.26 (br. *m*, 1 H); 7.35 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.5 (Me); 11.5 (Me); 15.6 (Me); 21.3 (CH_2); 21.8 (Me); 23.1 (Me); 24.8 (CH); 25.1 (CH_2); 28.3 (Me); 29.7 (Me); 37.7 (CH); 41.6 (CH_2); 42.0 (CH_2); 53.1 (CH); 56.4 (CH); 58.3 (CH); 67.0 (CH_2); 79.9 (C); 128.4 (2 CH); 128.6 (3 CH); 135.4 (C); 155.6 (C); 169.4 (C); 170.2 (C); 171.5 (C); 172.9 (C). FAB-MS: 613.3 (20, $[M + 23]^+$), 591.3 (11, $[M + 1]^+$), 370.2 (46), 335.2 (6), 321.2 (9), 314.2 (97), 270.2 (15), 215.1 (6), 157.1 (6), 130.1 (12), 91.0 (65), 86.0 (33), 72.0 (100), 56.9 (47).

H-Leu-Gly-MeAbu-Ile-OBzl·HCl (**42**·HCl). According to *G.P. 4*, with **41** (30.3 g, 51.3 mmol) and sat. HCl/Et_2O soln. (150 ml; 45 min): 27.6 g (quant.) of **42** $[\alpha]_D^{r.t.} = -32.7$ (*c* = 1.01, EtOH). ^{1}H-NMR (500 MHz, $CDCl_3$; 3 conformations): 0.81–1.03 (*m*, 15 H); 1.18, 1.28 (2*m*, 1 H); 1.36 (*m*, 1 H); 1.62 (*m*, 1 H); 1.70–1.86 (*m*, 2 H); 1.86–2.10 (*m*, 3 H); 2.97, 2.98, *3.00* (3*s*, 3 H); 3.89–4.43 (*m*, 2 H); 4.43–4.75 (*m*, 2 H); 5.09, 5.19 (*AB*, *J* = 12.2, 2 H); 5.06–5.22 (*m*, 1 H); 7.33 (*m*, 6 H); 8.22–8.77 (br. *m*, 4 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 10.6 (Me); 11.4 (Me); 15.6 (Me); 22.1 (CH_2); 22.5 (Me); 22.7 (Me); 24.5 (CH); 25.5 (CH_2); 30.3 (Me); 37.3 (CH); 40.4 (CH_2); 41.9 (CH_2); 52.4 (CH); 56.7 (CH); 58.1 (CH); 67.0 (CH_2); 128.3 (2 CH); 128.6 (3 CH); 135.4 (C); 169.7 (C); 169.8 (C); 170.6 (C); 172.0 (C). FAB-MS: 513.2 (17, $[M + 23]^+$), 491.3 (68, $[M + 1]^+$), 335.2 (21), 321.2 (15), 288.2 (8), 270.2 (100), 222.2 (14), 176.2 (13), 157.1 (18), 91.0 (81), 86.0 (62), 72.0 (86).

Boc-Val-Leu-Gly-MeAbu-Ile-OBzl (**43**). According to *G.P. 1*, with Boc-Val-OH (11.38 g, 52.4 mmol), THF (250 ml), NMM (5.8 ml, 52.4 mmol), isobutyl chloroformate (6.8 ml, 52.4 mmol), **42** (27.6 g, 52.4 mmol), NMM (5.8 ml), and DMF (100 ml; 1 h at −15°, 2 h at r.t.): 29.5 g (82%) of **43**. $[\alpha]_D^{r.t.} = -91.4$ (*c* = 1.0, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.72–1.00 (*m*, 21 H); 1.00–1.15 (*m*, 1 H); 1.20–1.37 (*m*, 1 H); 1.43 (*s*, 9 H); 1.50–1.78 (*m*, 4 H); 1.78–1.97 (*m*, 2 H); 1.98–2.10 (*m*, 1 H); 2.98, 3.02 (2*s*, 3 H); 3.91 (*dd*, *J* = 2.6, 17.8, 1 H); 4.01 (*t*, *J* = 7.9, 1 H); 4.32 (*dd*, *J* = 5.7, 17.8, 1 H); 4.58 (*dd*, *J* = 5.0, 8.7, 1 H); 4.78 (*dd*, *J* = 8.2, 14.4, 1 H); 5.08–5.22 (*m*, 1 H); 5.10, 5.23 (*AB*, *J* = 12.2, 2 H); 5.38 (*d*, *J* = 8.8, 1 H); 6.91 (*d*, *J* = 8.0, 1 H); 7.29 (*m*, 1 H); 7.35 (*m*, 5 H); 7.64 (br. *s*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.6 (Me); 11.5 (Me); 15.6 (Me); 17.9 (Me); 19.4 (Me); 21.9 (Me); 21.9 (CH_2); 23.0 (Me); 24.7 (CH); 25.2 (CH_2); 28.4 (3 Me); 29.9 (Me); 31.0 (CH); 37.7 (CH); 41.7 (CH_2); 41.9 (CH_2); 51.4 (CH); 56.4 (CH); 57.9 (CH); 59.9 (CH); 67.0 (CH_2); 79.7 (C); 128.4 (3 CH); 128.6 (2 CH); 135.4 (C); 156.0 (C); 169.2 (C); 170.8 (C); 171.7 (C); 171.9 (C); 172.3 (C). FAB-MS: 712.6 (20, $[M + 23]^+$), 690.6 (3, $[M + 1]^+$), 612.5 (2), 590.5 (2), 469.4 (39), 413.3 (45), 369.3 (5), 321.3 (11), 314.2 (7), 257.2 (10), 157.1 (19), 116.1 (9), 91.0 (41), 86.0 (59), 72.0 (100), 56.9 (43).

Boc-Val-Leu-Gly-MeAbu-Ile-OH (**6**). As described for **16**, with **43** (15.2 g, 22 mmol), EtOH (300 ml), and 10% Pd/C (0.3 g; 24 h): 13.2 g (quant.) of **6**. $[\alpha]_D^{r.t.} = -85.5$ (*c* = 1.01, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.78–0.98 (*m*, 21 H); 1.01–1.15 (*m*, 1 H); 1.24–1.38 (*m*, 1 H); 1.42 (*s*, 9 H); 1.49–1.66 (*m*, 3 H); 1.66–1.85 (*m*, 1 H); 1.85–2.10 (*m*, 3 H); 3.05, 3.16 (2*s*, 3 H); 4.07–4.25 (*m*, 3 H); 4.71 (*dd*, *J* = 3.5, 9.0, 1 H); 5.15–5.29 (*m*, 2 H); 5.41 (*dd*, *J* = 6.5, 9.1, 1 H); 7.60 (*d*, *J* = 9.7, 1 H); 7.87–7.94 (br. *m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.8 (Me); 11.8 (Me); 15.6 (Me); 17.9 (Me); 19.2 (Me); 22.2 (Me); 22.7 (Me); 23.1 (CH); 25.1 (CH_2); 28.3 (3 Me); 30.2 (Me); 31.1 (CH); 38.2 (CH); 42.3 (CH_2); 42.9 (CH_2); 51.1 (CH); 55.9 (CH); 57.5 (CH); 59.9 (CH); 80.1 (C); 155.8 (C); 168.9 (C); 171.5 (C); 172.2 (C); 172.3 (C); 174.6 (C). FAB-MS: 622.4 (35, $[M + 23]^+$), 469.3 (25), 413.2 (45), 369.2 (6), 314.1 (10), 257.1 (15), 231.2 (24), 157.1 (35), 116.0 (17), 98.0 (12), 86.0 (80), 71.9 (100), 56.9 (51). GC: 5.29 (Val), 5.61 (MeAbu), 6.03 (Gly), 7.21 (Ile), 8.75 (Leu).

Boc-BzlAbu-Ile-OBzl (**44**). According to *G.P. 1*, with **13** (43.4 g, 148 mmol), THF (0.7 l), NMM (16.3 ml, 148 mmol), isobutyl chloroformate (19.3 ml, 148 mmol), benzyl L-isoleucinate·TsOH (58.2 g, 148 mmol), NMM (16.3 ml), and DMF (300 ml; 15 min at −12°, 30 min at r.t.). LC (hexane/AcOEt 4:1) gave 65.4 g (89%) of **44**. $[\alpha]_D^{r.t.} = -54.6$ (*c* = 1.15, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.78–0.86 (*m*, 9 H); 1.05 (*m*, 1 H); 1.25–1.50 (*m*, 2 H); 1.43 (*s*, 9 H); 1.66 (*m*, 1 H); 1.96 (*m*, 1 H); 4.35 (*m*, 1 H); 4.51 (*m*, 1 H); 5.11, 5.18 (*AB*, *J* = 12.3, 2 H); 6.93 (br. *m*, 1 H); 7.21–7.35 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.95 (Me); 11.49 (Me); 15.51 (Me); 22.17 (CH_2); 24.96 (CH_2); 28.31 (3 Me); 37.55 (CH); 49.20 (CH_2); 56.49 (CH); 61.83 (CH); 66.78 (CH_2); 81.00 (C); 127.08 (CH);

127.45 (CH); 128.33 (CH); 128.55 (CH); 135.52 (C); 138.90 (C); 156.3 (C); 171.12 (C); 171.44 (C). FAB-MS: 519.3 (7, $[M + 23]^+$), 497.3 (37, $[M + 1]^+$), 441.2 (11), 397.3 (49), 248.2 (12); 222.2 (10), 220.2 (11), 192.1 (37), 148.1 (48), 91.0 (100), 56.9 (42).

BzlAbu-Ile-OBzl (**45**). According to *G.P.3*, with **44** (52.0 g, 131 mmol), CH_2Cl_2 (50 ml), CF_3COOH (57 ml; 9 h): 39.0 g (94%) of **45**. $[\alpha]_D^{r.t.} = -42.9$ ($c = 1.02$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.86–0.96 (*m*, 9 H); 1.18 (*m*, 1 H); 1.40 (*m*, 1 H); 1.60 (br. *s*, 1 H); 1.65 (*m*, 1 H); 1.97 (*m*, 1 H); 3.12 (*dd*, $J = 5.2, 7.2$, 1 H); 3.60, 3.81 (*AB*, $J = 12.7, 2$ H); 4.67 (*dd*, $J = 4.7, 9.4$, 1 H); 5.14, 5.20 (*AB*, $J = 12.2$, 2 H); 7.28–7.34 (*m*, 5 H); 7.82 (*d*, $J = 9.2$, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.23 (Me); 11.59 (Me); 15.80 (Me); 25.02 (CH_2); 26.96 (CH_2); 37.90 (CH); 52.90 (CH_2); 56.05 (CH); 63.97 (CH); 66.93 (CH_2); 127.31 (CH); 128.43 (CH); 128.48 (CH); 135.48 (C); 139.65 (C); 171.89 (C); 174.09 (C). FAB-MS: 419.0 (7, $[M + 23]^+$), 397.1 (100, $[M + 1]^+$); 148.1 (72), 90.9 (85).

Boc-BzlGly-BzlAbu-Ile-OBzl (**46**). According to *G.P.2*, with **45** (39.0 g, 98.4 mmol), CH_2Cl_2 (1 l), $(i\text{-Pr})_2EtN$ (40.4 ml, 0.24 mol), **14** (31.31 g, 118 mmol), and BOP-Cl (30.04 g, 118 mmol; 1.5 d). LC (hexane/AcOEt 3:1) gave 46.0 g (73%) of **46**. $[\alpha]_D^{r.t.} = -46.0$ ($c = 0.91$, EtOH). ^{1}H-NMR (300 MHz, (D_6)DMSO, 180°): 0.73–0.85 (*m*, 9 H); 1.19 (*m*, 2 H); 1.40 (*s*, 9 H); 1.61 (*m*, 1 H); 2.50 (*m*, 2 H); 4.03 (br. *s*, 2 H); 4.23 (*dd*, $J = 6.0, 7.9$, 1 H); 4.41 (br. *s*, 2 H); 4.54, 4.71 (*AB*, $J = 17$, 2 H); 4.59 (*m*, 1 H); 5.11, 5.14 (*AB*, $J = 12$, 2 H); 7.18–7.36 (*m*, 15 H); 7.80 (*d*, $J = 6.0$, 1 H). ^{13}C-NMR (75 MHz, broad-band decoupling, (D_6)DMSO, 180°): 10.27; 10.84; 15.31; 23.05; 25.01; 28.04; 36.33; 47.28; 48.65; 51.19; 56.71; 60.18; 65.92; 79.27; 126.46; 126.66; 126.84; 127.45; 127.64; 127.87; 127.93; 128.15; 135.87; 138.15; 138.66; 155.36; 169.62; 170.17; 170.69. FAB-MS: 666.1 (5, $[M + 23]^+$), 644.1 (4, $[M + 1]^+$), 544.1 (21), 423.1 (23), 397.1 (15), 395.1 (11), 367.0 (57), 323.0 (10), 148.1 (71), 120.0 (23), 90.9 (100), 56.9 (52).

BzlGly-BzlAbu-Ile-OBzl (**47**). According to *G.P.2*, with **46** (46.0 g, 71.4 mmol), CH_2Cl_2 (50 ml), and CF_3COOH (40 ml; 21 h): 38.05 g (98%) of **47**. $[\alpha]_D^{r.t.} = -61.0$ ($c = 0.97$, EtOH). ^{1}H-NMR (300 MHz, (D_6)DMSO, 180°): 0.73–0.85 (*m*, 9 H); 1.20 (*m*, 1 H); 1.40 (*m*, 1 H); 1.60 (*m*, 1 H); 1.79 (*m*, 2 H); 2.87 (br. *m*, 1H + H_2O); 3.40, 3.45 (*AB*, $J = 16$, 2 H); 4.69 (*s*, 2 H); 4.23 (*m*, 1 H); 4.51, 4.71 (*AB*, $J = 17,2$ H); 4.59 (*m*, 1 H); 5.12, 5.15 (*AB*, $J = 12$, 2 H); 7.19–7.36 (*m*, 15 H); 7.85 (br. *m*, 1 H). ^{13}C-NMR (75 MHz, broad-band decoupling, (D_6)DMSO, 180°): 10.33; 10.84; 15.31; 22.89; 25,01; 36.36; 47.24; 50.36; 52.84; 56.71; 60.36; 65.93; 126.46; 126.74; 127.87; 127.96; 128.20; 135.89; 138.77, 140.31; 170.23; 170.72; 172.44. FAB-MS: 566.1 (8, $[M + 23]^+$), 544.1 (93, $[M + 1]^+$), 397.1 (20), 323.0 (23), 176.1 (13), 148.1 (48), 120.0 (45), 90.9 (100).

Boc-Leu-BzlGly-BzlAbu-Ile-OBzl (**48**). According to *G.P.2*, with **47** (38.05 g, 70 mmol), CH_2Cl_2 (0.8 l), Boc-Leu-OH · H_2O (21.0 g, 84.2 mmol), $(i\text{-Pr})_2EtN$ (28.8 ml, 168 mmol), and BOP-Cl (21.45 g, 84.3 mmol; 18 h): 55.7 g (quant.) of **48**. ^{1}H-NMR (300 MHz, (D_6)DMSO; several conformations): 0.6–0.9 (*m*, 15 H); 0.9–1.86 (*m*, 8 H); 1.32, 1.35, 1.41 (3*s*, 9 H); 3.8–4.95 (*m*, 9 H); 5.06, 5.12 (*AB*, $J = 12.4$, 2 H); 6.98 (*m*, 1 H); 7.05–7.45 (*m*, 15 H); 8.3–8.5 (*m*, 1 H). ^{13}C-NMR (75 MHz, broad-band decoupling, (D_6)DMSO, 180°): 10.28; 10.86; 15.31; 21.59; 22.86; 23.05; 23.12; 24.18; 25.02; 28.16; 36.33; 47.50; 47.63; 49.18; 56.73; 60.33; 65.90; 78.36; 126.47; 126.67; 127.04; 127.35; 127.87; 127.98; 128.18; 135.90; 136.98; 138.46; 155.04; 169.09; 170.07; 170.68; 173.17. FAB-MS: 779.4 (8, $[M + 23]^+$), 757.3 (8, $[M + 1]^+$), 657.3 (12), 544.2 (4), 536.2 (24), 480.2 (28), 436.2 (5), 397.2 (12), 361.2 (14), 305.1 (35), 261.1 (7), 148.1 (30), 120.0 (62), 91.0 (100), 86.0 (26), 56.9 (47).

H-Leu-BzlGly-BzlAbu-Ile-OBzl (**49**). According to *G.P.3*, with **48** (55.7 g, 70 mmol), CH_2Cl_2 (50 ml), and CF_3COOH (40 ml; 15 h). LC (CH_2Cl_2/MeOH 19:1) gave 39.16 g (85%) of **49**. $[\alpha]_D^{r.t.} = -51.4$ ($c = 0.93$, EtOH). ^{1}H-NMR (300 MHz, (D_6)DMSO; several conformations): 0.6–0.9 (15 H); 1.0–1.8 (8 H); 3.5–5.0 (*m*, 9 H); 5.06, 5.12 (*AB*, $J = 12.5$, 2 H); 7.03–7.42 (*m*, 15 H); 8.25–8.50 (*m*, 1 H). FAB-MS: 679.3 (10, $[M + 23]^+$), 657.4 (67, $[M + 1]^+$), 544.3 (3), 436.2 (14), 397.2 (8), 261.1 (19), 176.1 (34), 148.1 (41), 120.1 (27), 91.0 (100), 86.0 (69).

Boc-Val-Leu-BzlGly-BzlAbu-Ile-OBzl (**50**). To a soln. of Boc-Val-OH (12.90 g, 59.4 mmol), **49** (38.98 g, 59.3 mmol), and BtOH (8.02 g, 59.4 mmol) in THF (110 ml), DCC (12.83 g, 62.2 mmol) was added at 0°. After 90 min, the mixture was warmed to r.t., stirred 1 h, filtered, the filtrate evaporated, and the residue worked up with CH_2Cl_2 according to *G.P.1*. LC (pentane/Et_2O 1:2) gave 46.5 g (91%) of **50**. $[\alpha]_D^{r.t.} = -64.7$ ($c = 0.99$, EtOH). ^{1}H-NMR (200 MHz, $CDCl_3$; several conformations): 0.75–0.98 (*m*, 21 H); 1.20–1.78 (*m*, 6 H); *1.42*, 1.44 (2*s*, 9 H); 2.04 (*m*, 3 H); 2.75–5.33 (*m*, 13 H); 6.80 (*d*, $J = 9.1$, 1 H); 7.0–7.4 (*m*, 16 H). ^{13}C-NMR (75 MHz, broad-band decoupling, (D_6)DMSO, 200°): 10.29; 10.82; 15.31; 17.86; 19.01; 19.14; 21.51; 21.60; 21.69; 22.89; 23.09; 24.03; 25.04; 28.19; 30.46; 36.37; 47.12; 47.70; 56.76; 59.97; 60.06; 60.63; 65.93; 78.32; 126.49; 126.74; 127.01; 127.42; 127.85; 127.98; 128.17; 135.90; 137; 138.41; 155.22; 169.13; 170.08; 170.68; 170.86; 172.75; 172.95. FAB-MS: 878.6 (10, $[M + 23]^+$), 856.6 (4, $[M + 1]^+$), 635.4 (15), 579.3 (13), 544.3 (16), 460.3 (19), 404.2 (14), 257.2 (5), 148.1 (22), 120.1 (33), 91.0 (100), 86.0 (80), 56.9 (37).

Boc-Val-Leu-BzlGly-BzlAbu-Ile-OH (**7**). As described for **16**, with **50** (43.3 g, 50.6 mmol), EtOH (300 ml), and 10% Pd/C (0.6 g; 24 h): 38.74 g (quant.) of **7**. $[\alpha]_D^{r.t.} = -61.2$ ($c = 0.95$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.71–1.02 (*m*, 21 H); 1.1–2.15 (*m*, 9 H); 1.43 (*s*, 3 H); 3.65–5.27 (8*m*, 9 H); 6.9–7.4 (*m*, 12 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 11.70 (Me); 11.85 (Me); 15.66 (Me); 18.05 (Me); 19.26 (Me); 21.80 (CH_2); 22.35 (Me); 22.84 (Me); 24.69

(CH); 25.46 (CH_2); 28.30 (3 Me); 30.92 (CH); 37.90 (CH); 41.86 (CH_2); 47.46 (CH); 48.13 (CH_2); 49.42 (CH_2); 53.07 (CH_2); 56.65 (CH); 59.92 (CH); 60.96 (CH); 80.30 (C); 125.88 (CH); 127.18 (CH); 127.48 (CH); 128.01 (CH); 128.90 (CH); 128.98 (CH); 135.87 (C); 137.27 (C); 156.15 (C); 170.43 (C); 171.27 (C); 171.41 (C); 173.11 (C); 174.12 (C). FAB-MS: 788.4 (36, $[M + 23]^+$), 766.4 (10, $[M + 1]^+$), 635.3 (20), 579.3 (28), 460.2 (31), 454.2 (57), 404.2 (37), 307.2 (23), 257.1 (13), 148.1 (41), 120.1 (54), 91.0 (100), 86.0 (93), 72.0 (33), 56.9 (87).

BzlAbu-Ile-OBzl·HCl (**51**·HCl). According to *G.P. 4*, with **44** (30.6 g, 61.6 mmol) and sat. HCl/Et_2O soln. (200 ml; 13 h): 26.7 g (quant.) of **51**. $[\alpha]_D^{r.t.} = -27.3$ ($c = 1.2$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.90–0.93 (*m*, 6 H); 1.01 (*d*, $J = 6.8$, 2 H); 1.48 (*m*, 2 H); 2.01–2.16 (*m*, 3 H); 3.75 (br. *m*, 1 H); 4.04 (*m*, 2 H); 4.51 (*m*, 1 H); 5.15, 5.23 (*AB*, $J = 12.2$, 2 H); 7.32–7.37 (*m*, 8 H); 7.56 (*m*, 2 H); 8.27 (*m*, 1 H); 9.50 (br. *m*, 1 H); 10.07 (br. *m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 9.69 (Me); 11.66 (Me); 15.91 (Me); 23.70 (CH_2); 25.44 (CH_2); 36.53 (CH); 49.79 (CH_2); 57.92 (CH); 62.96 (CH); 67.06 (CH_2); 128.40 (CH); 128.43 (CH); 128.56 (CH); 128.96 (CH); 129.54 (CH); 130.06 (C); 130.78 (CH); 135,37 (C); 167.28 (C); 171.21 (C). FAB-MS: 397.3 (100, $[M + 1]^+$), 289.1 (2), 148.2 (20), 91.0 (22).

Boc-Gly-BzlAbu-Ile-OBzl (**52**). According to *G.P. 1*, with Boc-Gly-OH (10.8 g, 61.6 mmol), THF (300 ml), NMM (6.8 ml, 61.7 mmol), isobutyl chloroformate (8.05 ml, 61.6 mmol), **51** (26.7 g, 61.6 mmol), NMM (6.8 ml), and DMF (120 ml; 20 min at −15°, 17 h at r.t.). LC (pentane/Et_2O 1:1) gave 29.4 g (86%) of **52**. $[\alpha]_D^{r.t.} = -63.5$ ($c = 0.96$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.82–0.89 (*m*, 9 H); 1.15 (*m*, 1 H); 1.34 (*m*, 1 H); 1.42 (*s*, 9 H); 1.63 (*m*, 1 H); 1.99 (*m*, 2 H); 3.84, 3.96 (*ABX*, $J_{AB} = 17.4$, $J_{AX} = 4.4$, $J_{BX} = 4.6$, 2 H); 4.51–4.59 (*m*, 3 H); 4.74 (*m*, 1 H); 5.12, 5.21 (*AB*, $J = 12.2$, 2 H); 5.42 (*m*, 1 H); 6.89 (*d*, $J = 8.5$, 1 H); 7.15–7.37 (*m*, 10 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.82 (Me); 11.55 (Me); 15.60 (Me); 21.85 (CH_2); 25.09 (CH_2); 28.33 (3 Me); 37.49 (CH); 42.94 (CH_2); 48.41 (CH_2); 56.57 (CH); 60.91 (CH); 66.94 (CH_2); 79.72 (C); 126.10 (CH); 127.64 (CH); 128.39 (CH); 128.58 (CH); 128.94 (CH); 135.41 (C); 136.45 (C); 155.59 (C); 170.13 (C); 171.04 (C); 171.31 (C). FAB-MS: 576.3 (7, $[M + 23]^+$), 554.3 (35, $[M + 1]^+$), 397.2 (21), 395.2 (19), 333.1 (17), 277.1 (57), 148.1 (33), 91.0 (100), 56.9 (60).

H-Gly-Bzl-Abu-Ile-OBzl (**53**). According to *G.P. 4*, with **52** (22.9 g, 41.4 mmol) and sat. HCl/Et_2O soln. (400 ml; 40 min): 20.27 g (quant.) of **53**. $[\alpha]_D^{r.t.} = -59.9$ ($c = 0.99$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$; 2 conformations): 0.73–0.82 (*m*, 9 H); 1.15 (*m*, 1 H); 1.32 (*m*, 1 H); 1.51 (*m*, 1 H); 1.63–1.90 (*m*, 2 H); 2.8 (br. *m*, 1 H); 3.80 (*m*, 2 H); 4.15–4.20 (*m*, 1 H); 4.38, 4.51 (2*m*, 1 H); 5.02, 5.13 and 5.04, 5.15 (2*AB*, each $J = 12.3$, 2 H); 7.07–7.35 (*m*, 10 H); 7.54, 8.12 (*d*, $J = 7.9$, 6.7, 1 H); 8.40 (br. *m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.69 (Me); 11.52 (Me); 15.64 (Me); 22.94 (CH_2); 25.57 (CH_2); 36.99 (CH); 40.87 (CH_2); 47.89 (CH_2); 57.00 (CH); 59.49 (CH); 66.91 (CH_2); 126.19 (CH); 127.18 (CH); 128.25 (CH); 128.35 (CH); 128.54 (CH); 129.04 (CH); 135.42 (C); 136.08 (C); 167.97 (C); 170.14 (C); 171.92 (C). FAB-MS: 454.1 (49, $[M + 1]^+$), 397.2 (38), 307.1 (5), 233.1 (21), 149.0 (48), 91.0 (100), 76.9 (55).

Boc-Leu-Gly-BzlAbu-Ile-OBzl (**54**). According to *G.P. 1*, with Boc-Leu-OH·H_2O (10.6 g, 42.5 mmol), THF (200 ml), NMM (4.7 ml, 42.7 mmol), isobutyl chloroformate (5.56 ml, 42.5 mmol), **53** (20.3 g, 41.4 mmol), NMM (4.7 ml), and DMF (85 ml; 30 min at −15°, 2.5 h at r.t.): 27.58 g (quant.) of **54**. $[\alpha]_D^{r.t.} = -72.6$ ($c = 1.03$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.82–0.94 (*m*, 15 H); 1.15 (*m*, 1 H); 1.34 (*m*, 1 H); 1.42 (*s*, 19 H); 1.46 (1 H); 1.58–1.69 (*m*, 3 H); 1.85–1.98 (*m*, 2 H); 4.01 (*m*, 2 H); 4.25 (*m*, 1 H); 4.53 (*dd*, $J = 4.8$, 1 H); 4.65 (*s*, 2 H); 4.82 (*m*, 1 H); 5.04 (*d*, $J = 8.2$, 1 H); 5.10, 5.21 (*AB*, $J = 12.2$, 2 H); 6.99 (*d*, $J = 8.0$, 1 H); 7.15–7.36 (*m*, 11 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.84 (Me); 11.59 (Me); 15.64 (Me); 21.84 (Me); 22.18 (CH_2); 23.05 (Me); 24.77 (CH); 25.34 (CH_2); 28.34 (3 Me); 37.45 (CH); 41.89 (2 CH_2); 48.36 (CH_2); 52.98 (CH); 56.60 (CH); 60.66 (CH); 66.98 (CH_2); 126.10 (CH); 127.70 (CH); 128.43 (CH); 128.60 (CH); 128.99 (CH); 135.44 (C); 136.48 (C); 155.60 (C); 170.21 (C); 170.44 (C); 171.45 (C); 172.67 (C). FAB-MS: 689.5 (10, $[M + 23]^+$), 667.5 (15, $[M + 1]^+$), 446.3 (63), 390.3 (67), 346.3 (12), 305.2 (7), 215.2 (8), 148.2 (80), 91.0 (100), 86.1 (29), 56.9 (42).

H-Leu-Gly-Bzl-Abu-Ile-OBzl·HCl (**55**). According to *G.P. 4*, with **54** (27.58 g, 41.4 mmol) and 200 ml of sat. HCl/Et_2O soln. (20 min): 25.18 g (quant.) of **55**. $[\alpha]_D^{r.t.} = -36.8$ ($c = 0.9$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.77–0.98 (*m*, 15 H); 1.17 (*m*, 1 H); 1.35 (*m*, 1 H); 1.57 (*m*, 1 H); 1.62–1.95 (*m*, 5); 4.02 (*m*, 1.5 H); 4.31 (*m*, 0.9 H); 4.45 (*m*, 1.9 H); 4.64–4.75 (*m*, 1.1 H); 4.77–5.00 (*m*, 1 H); 5.00–5.28 (*m*, 2.6 H); 7.14–7.33 (*m*, 11 H); 7.51 (*d*, $J = 7.4$, 0.7 H); 8.01 (*m*, 0.3 H); 8.33–8.50 (br. *m*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.81 (Me); 11.54 (Me); 15.63 (Me); 22.38 (Me); 22.70 (Me); 22.89 (CH_2); 24.44 (CH); 25.45 (CH_2); 37.19 (CH); 40.40 (CH_2); 42.08 (CH_2); 48.22 (CH_2); 52.38 (CH); 56.80 (CH); 59.65 (CH); 66.90 (CH_2); 126.02 (CH); 127.08 (CH); 127.52 (CH); 128.29 (CH); 128.52 (CH); 58.80 (CH); 135.39 (C); 136.77 (C); 169.63 (C); 170.35 (C); 170.48 (C); 171.80 (C). FAB-MS: 589.4 (14, $[M + 23]^+$), 567.5 (35), 397.3 (20), 346.3 (72), 233.2 (11), 176.2 (14), 148.2 (72), 91.0 (100), 86.1 (54).

Boc-Val-Leu-Gly-BzlAbu-Ile-OBzl (**56**). According to *G.P. 1*, with Boc-Val-OH (9.2 g, 42.3 mmol), NMM (4.7 ml, 42.6 mmol), isobutyl chloroformate (5.53 ml, 42.3 mmol), **5** (25.18 g, 41.3 mmol), NMM (4.6 ml), and DMF (100 ml; 30 min at −15°, 3 h at r.t.). LC (hexane/AcOEt 3:2) gave 25.57 g (81%) of **56**. $[\alpha]_D^{r.t.} = -86.3$ ($c = 1.2$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.76–0.92 (*m*, 21 H); 1.11 (*m*, 1 H); 1.32 (*m*, 1 H); 1.42 (*s*, 9 H); 1.52–1.69 (*m*,

4 H); 1.81–1.96 (*m*, 2 H); 2.06 (*m*, 1 H); 3.83, 4.15 (*ABX*, J_{AB} = 17.6, J_{AX} = 3.0, J_{BX} = 5.5, 2 H); 3.92 (*m*, 1 H); 4.52 (*dd*, *J* = 5.0, 8.5, 1 H); 4.67 (*m*, 1 H); 4.72 (*m*, 2 H); 4.97 (*dd*, *J* = 6.1, 8.7, 1 H); 5.09, 5.21 (*AB*, *J* = 12.2, 2 H); 5.25 (*d*, *J* = 9.8, 1 H); 6.65 (*d*, *J* = 8.1, 1 H); 7.15–7.36 (*m*, 11 H); 7.44 (*m*, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.78 (Me); 11.59 (Me); 15.64 (Me); 17.88 (Me); 19.36 (Me); 21.90 (Me); 22.56 (CH_2); 23.05 (Me); 24.68 (CH); 25.19 (CH_2); 28.33 (3 Me); 30.82 (CH); 37.40 (CH); 41.66 (CH_2); 41.94 (CH_2); 48.10 (CH_2); 51.37 (CH); 56.62 (CH); 60.09 (2 CH); 66.94 (CH_2); 79.86 (C); 125.95 (CH); 127.57 (CH); 128.39 (CH); 128.58 (CH); 128.93 (CH); 135.47 (C); 136.79 (C); 155.97 (C); 170.33 (C); 170.50 (C); 171.60 (C); 171.78(C); 172.04 (C). FAB-MS: 788.5 (36, $[M + 23]^+$), 766.5 (4, $[M + 1]^+$), 545.4 (74), 489.3 (52), 445.3 (7), 397.3 (20), 395.2 (16), 370.2 (3), 314.2 (13), 257.2 (16), 233.2 (15), 48.2 (81), 91.0 (100), 86.1 (81), 72.0 (31), 56.9 (52).

Boc-Val-Leu-Gly-BzlAbu-Ile-OH (**8**). As described for **16**, with **56** (22.55 g, 29.4 mmol), MeOH (200 ml), and 10% Pd/C (0.4 g; 6 h): 19.6 g (99%) of **8**. $[\alpha]_D^{r.t.} = -80.4$ (*c* = 1.1, EtOH). ^{1}H-NMR (500 MHz, $CDCl_3$; 2 conformations): 0.71 (*m*, 1 H); 0.85 (*m*, 20 H); 1.18 (*m*, 1 H); 1.41, 1.44 (2*s*, 9 H); 1.47 (*m*, 1 H); 1.53 (*m*, 2 H); 1.83 (*m*, 1 H); 1.93 (*m*, 1 H); 2.05 (*m*, 1 H); 3.7–4.24 (4*m*, 3 H); 4.40–5.30 (9*m*, 6 H); 6.72 (br. *m*, 0.3 H); 7.06–7.31 (*m*, 6 H); 7.61 (br. *m*, 0.8 H); 7.73 (*d*, *J* = 8.8, 0.9 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 10.78 (Me); 11.86 (Me); 15.68 (Me); 17.81 (Me); 19.18 (Me); 22.04 (Me); 22.75 (Me); 23.28 (CH_2); 24.70 (CH); 25.15 (CH_2); 28.28 (3 Me); 30.72 (CH); 37.68 (CH); 42.23 (CH_2); 42.37 (CH_2); 47.78 (CH_2); 51.17 (CH); 56.10 (CH); 59.17 (CH); 60.11 (CH); 80.20 (C); 125.67 (CH); 127.44 (CH); 128.88 (CH); 137.11 (C); 155.92 (C); 170.24 (C); 170.89 (C); 172.03 (C); 172.17 (C); 174.50 (C). FAB-MS: 698.5 (46, $[M + 23]^+$), 576.4 (2, $[M + 1]^+$), 545.4 (48), 489.3 (50), 445.3 (6), 314.2 (11), 307.2 (24), 305.2 (15), 257.2 (15), 233.2 (18), 148.2 (82), 86.1 (100), 72.0 (38), 56.9 (70).

Boc-Pro-Leu-OBzl (**57**). According to *G.P. 1*, with Boc-Pro-OH (17.81 g, 82.8 mmol), THF (300 ml), NMM (9.2 ml, 83.5 mmol), isobutyl chloroformate (11.5 ml, 83.6 mmol), benzyl L-leucinate·TsOH (32.54 g, 82.7 mmol), NMM (9.2 ml), and DMF (110 ml; 40 at −12°, 1 h at r.t.). LC (hexane/AcOEt 4:1) gave 33.17 g (96%) of **57**. $[\alpha]_D^{r.t.} = -72.5$ (*c* = 1.04, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.89 (*m*, 6 H); 1.46 (*s*, 9 H); 1.53–1.67 (*m*, *ca.* 3 H); 1.87 (*m*, *ca.* 3 H); 2.12 (br. *m*, 1 H); 3.25–3.45 (*m*, 2 H); 4.25–4.35 (*m*, 2 H); 4.58–4.69 (*m*, 1 H); 5.15 (*s*, 2 H); 6.45 (br. *m*, 0.5 H); 7.28–7.41 (*m*, 5.5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.9 (Me); 22.9 (Me); 23.8 (br., *ca.* 0.5 CH_2); 24.6 (br., *ca.* 0.5 CH_2); 24.9 (CH); 27.6 (br., *ca.* 0.5 CH_2); 28.3 (3 Me); 30.9 (br., *ca.* 0.5 CH_2); 41.4 (br. CH_2); 47.0 (CH_2); 50.9 (br. CH); 59.7 (br. 0.5 CH); 61.0 (br. 0.5 CH); 66.9 (CH_2); 80.5 (br. C); 128.2 (CH); 128.3 (CH); 128.6 (CH); 135.6 (C); *ca.* 155 (C, CH); *ca.* 172 (C, CH); 172.5 (C). FAB-MS: 441.3 (17, $[M + 23]^+$), 419.3 (58, $[M + 1]^+$), 363.3 (38), 319.3 (92), 227.2 (17), 170.2 (37), 91.0 (100), 70.0 (42).

Pro-Leu-OBzl·HCl (**58**·HCl). According to *G.P. 4*, with **57** (33.08 g, 79.0 mmol) and sat. HCl/Et_2O soln. (200 ml; 45 min): 28.37 g (quant.) of **58**. $[\alpha]_D^{r.t.} = -64.2$ (*c* = 0.95, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.89 (*d*, *J* = 6.1, 3 H); 0.93 (*d*, *J* = 6.0, 3 H); 1.63–1.90 (*m*, 4 H); 1.90–2.08 (*m*, 2 H); 2.44–2.56 (*m*, 1 H); 3.32–3.49 (*m*, 2 H); 4.42–4.49 (*m*, 1 H); 4.82 (*dd*, $J_{AX} \approx J_{BX} \approx 7.2$, 1 H); 5.06 (*d*, *J* = 12.2, 1 H); 5.19 (*d*, *J* = 12.2, 1 H); 7.30–7.38 (*m*, 5 H); *ca.* 7.6 (br. *m*, 0.6 H); 8.71 (*d*, *J* = 6.8, 1 H); *ca.* 10.67 (br. *m*, 0.6 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.7 (Me); 22.8 (Me); 24.4 (CH_2); 24.9 (CH); 30.7 (CH_2); 39.7 (CH_2); 46.9 (CH_2); 52.2 (CH); 59.6 (CH); 67.1 (CH_2); 128.3 (CH); 128.4 (CH); 128.6 (C); 135.4 (C); 168.9 (C); 171.9 (C). FAB-MS: 341.3 (2, $[M + 23]^+$), 319.3 (100, $[M + 1]^+$), 160.2 (12), 136.1 (8), 91.0 (36), 70.0 (52).

Boc-Gly-Pro-Leu-OBzl (**59**). According to *G.P. 1*, with Boc-Gly-OH (13.36 g, 76.2 mmol), THF (350 ml), NMM (8.4 ml, 76.2 mmol), isobutyl chloroformate (10 ml, 72.7 mmol), **5** (27.36 g, 76.2 mmol), NMM (8.4 ml), and DMF (100 ml; 30 min at −15°, 45 min at r.t.): 32.93 g (91%) of **59**. $[\alpha]_D^{r.t.} = -89.2$ (*c* = 0.98, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.82–0.96 (*m*, 6 H); 1.45 (*s*, 9 H); 1.5–1.7 (*m*, 3 H); 1.75–1.95 (*m*, 1 H); 1.95–2.05 (*m*, 1 H); 2.05–2.2 (*m*, 1 H); 2.32–2.39 (*m*, 1 H); 3.34–3.43 (*m*, 1 H); 3.47–3.54 (*m*, 1 H); 3.88, 3.98 (*ABX*, J_{AB} = 17.4, J_{AX} = 4.4, J_{BX} = 4.8, 2 H); 4.50–4.60 (*m*, 2 H); 5.14, 5.18 (*AB*, J_{AB} = 12.3, 2 H); 5.42 (*m*, 1 H); 7.10 (*d*, *J* = 7.7, 1 H); 7.32–7.40 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 22.0 (Me); 22.7 (Me); 24.9 (CH_2); 25.0 (CH); 27.3 (CH_2); 28.4 (3 Me); 41.1 (CH_2); 43.1 (CH_2); 46.3 (CH_2); 51.3 (CH); 60.0 (CH); 67.0 (CH_2); 79.8 (C); 128.2 (CH); 128.4 (CH); 128.6 (CH); 135.5 (C); 155.8 (C); 168.7 (C); 170.6 (C); 172.5 (C). FAB-MS: 498.3 (12, $[M + 23]^+$), 476.3 (53, $[M + 1]^+$), 420.2 (35), 376.2 (52), 317.2 (25), 199.1 (21), 91.0 (98), 91.0 (98), 70.0 (100).

H-Gly-Pro-Leu-OBzl·HCl (**60**·HCl). According to *G.P. 4*, with **59** (32.89 g, 69.2 mmol) and sat. HCl/Et_2O soln. (200 ml; 20 min): 29.08 g (77.5 mmol) of **60**. $[\alpha]_D^{r.t.} = -86.2$ (*c* = 1.11, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.84 (*d*, *J* = 6.3, 3 H); 0.90 (*d*, *J* = 6.3, 3 H); 1.53–1.72 (*m*, 2 H); 1.72–2.21 (*m*, 5 H); 3.37–3.47 (*m*, 1 H); 3.57–3.65 (*m*, 1 H); 3.83–4.02 (*m*, 1 H); 4.02–4.19 (*m*, 1 H); 4.42–4.48 (*m*, 1 H); 4.62 (*m*, 1 H); 5.03–5.16 (*m*, 2 H); 7.26–7.35 (*m*, 5 H); 8.03 (*d*, *J* = 6.9, 1 H); 8.14 (br. *s*, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 21.5 (Me); 22.9 (Me); 24.2 (CH_2); 25.0 (CH); 29.9 (CH_2); 39.3 (CH_2); 41.7 (CH_2); 46.8 (CH_2); 51.7 (CH); 60.8 (CH); 66.9 (CH_2); 128.0 (CH); 128.2 (CH); 128.6 (CH); 135.7 (C); 166.8 (C); 172.3 (C); 173.5 (C). FAB-MS: 398.3 (7, $[M + 23]^+$), 376.3 (100, $[M + 1]^+$), 319.3 (10), 317.3 (6), 229.2 (10), 91.0 (58), 70.0 (48).

Boc-Leu-Gly-Pro-Leu-OBzl (**61**). According to *G.P. 1*, with Boc-Leu-OH·H_2O (17.26 g, 69.2 mmol), THF (300 ml), NMM (7.7 ml, 69.9 mmol), isobutyl chloroformate (9.5 ml, 69.1 mmol), **60** (29.08 g, 69.2 mmol), NMM (7.7 ml), and DMF (80 ml; 30 min at −15°, 40 min at r.t.). LC (hexane/AcOEt 1:4) gave 36.73 g (90%) of **61**. $[\alpha]_D^{r.t.} = -83.3$ ($c = 0.91$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.87–0.93 (*m*, 12 H); 1.43 (*s*, 9 H); 1.48–1.73 (*m*, 5 H); 1.85–2.05 (*m*, 3 H); 2.05–2.2 (*m*, 1 H); 2.2–2.3 (*m*, 1 H); 3.38–3.47 (*m*, 1 H); 3.56–3.60 (*m*, 1 H); 3.97; 4.13 (*ABX*, $J_{AB} = 17.8$, $J_{AX} \approx 2$, $J_{BX} = 5$, 2 H); 4.25–4.35 (*m*, 1 H); 4.53–4.65 (*m*, 2 H); 5.03 (*d*, $J = 8.4$, 1 H); 5.13, 5.18 (*AB*, $J = 12.3$, 2 H); 6.65 (*d*, $J = 5.7$, 0.25 H); 6.93 (*m*, 0.25 H); 7.09 (br. *d*, $J = 7.2$, 1 H); 7.24–7.40 (*m*, 5.5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.8 (Me); 21.9 (Me); 22.7 (Me); 23.0 (Me); 24.8 (CH); 24.8 (CH_2); 24.9 (CH); 27.9 (CH_2); 28.3 (3 Me); 41.0 (CH_2); 42.0 (CH_2); 42.1 (CH_2); 46.5 (CH_2); 51.1 (CH); 52.9 (CH); 60.0 (CH); 66.9 (CH_2); 80.0 (C); 128.2 (CH); 128.3 (CH); 128.5 (CH); 135.5 (C); 155.6 (C); 167.7 (C); 170.8 (C); 172.6 (C); 172.8 (C). FAB-MS: 611.4 (26, $[M + 23]^+$), 589.4 (9, $[M + 1]^+$), 533.3 (3), 511.3 (6), 489.3 (35), 376.2 (22), 319.2 (57), 317.2 (36), 229.2 (23), 91.0 (86), 69.9 (100).

Boc-Leu-Gly-Pro-Leu-OH (**9**). As described for **16**, with **61** (29.77 g, 50.6 mmol), EtOH (400 ml), and 10% Pd/C (0.9 g; 23 h): 25.44 g (quant.) of **9** $[\alpha]_D^{r.t.} = -80.2$ ($c = 1.03$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.90–0.93 (*m*, 12 H); 1.42, *1.43* (2*s*, 9 H); 1.45–1.55 (*m*, 1 H); 1.55–1.78 (*m*, 5 H); 1.83–1.98 (*m*, 1 H); 1.98–2.11 (*m*, 2 H); 2.2–2.3 (*m*, 1 H); 3.46–3.72 (*m*, 2 H); 3.89–4.11 (*m*, 2 H); 4.30–4.76 (5*m*, 3 H); 5.26, 5.32 (2*d*, $J = 7.8, 9.3$, 1 H); 7.18 (br. *m*, 0.25 H); 7.24 (*d*, $J = 7.1$, 0.5 H); 7.40 (br. *m*, 0.5 H); 7.45 (*d*, $J = 7.9$, 0.25 H); 7.53 (br. *m*, 0.75 H); *ca.* 8 (1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 21.9 (Me); 22.3 (CH_2); 22.9 (Me); 23.0 (Me); 23.2 (Me); 24.7 (CH); 25.0 (CH); 28.3 (3 Me); 28.6 (CH_2); 32.0 (CH_2); 40.8 (CH_2); 42.1 (CH_2); 46.8 (CH_2); 51.1 (CH); 52.8 (CH); 60.5 (CH); 80.1 (C); 155.8 (C); 168.4 (C); 171.5 (C); 173.5 (C); 174.9 (C). FAB-MS: 521.2 (100, $[M + 23]^+$), 499.2 (10, $[M + 1]^+$), 443.2 (7), 421.2 (7), 399.2 (27), 286.1 (17), 229.1 (44), 70.0 (83).

4. *Introduction of* N-*Protective Groups. Boc-Val-Boc-Gly-Boc-Leu-OBzl* (**62**) *and Benzyl* N-{*[3-(*tert-*Butyloxycarbonyl)-4-isopropyl-2,5-dioxoimidazolidin-1-yl]acetyl*}-N-(tert-*butyloxycarbonyl)*-L-*leucinate* (**63**). To a soln. of **17** (118 mg, 0.25 mmol) and 4-(dimethylamino)pyridine (60 mg, 0.49 mmol) in THF (1 ml), Boc_2O (180 mg, 0.82 mmol) in THF (0.5 ml) was added. After 40 min, the soln. was diluted with Et_2O, washed with 1M $KHSO_4$, sat. $NaHCO_3$, and sat. NaCl soln., dried ($MgSO_4$), and evaporated and the residue chromatographed (pentane/Et_2O 3:1): 130 mg (77%) of **62** and 28 mg (19%) of **63**.

62: ^{1}H-NMR (200 MHz, $CDCl_3$): 0.75 (*d*, $J = 7$, 3 H); 0.86 (*d*, $J = 6$, 3 H); 0.90 (*d*, $J = 7$, 3 H); 1.04 (*d*, $J = 7$, 3 H); 1.40 (*s*, 9 H); 1.43 (*s*, 9 H); 1.47 (*s*, 9 H); 1.65–2.05 (*m*, 3 H); 2.22 (*m*, 1 H); 4.87, 5.11 (*AB*, $J = 20$, 2 H); 5.09, 5.14 (*AB*, $J = 13$, 2 H); 5.23 (br. *d*, $J = 9$, 1 H); 5.37 (*dd*, $J = 8, 8$, 1 H); 5.62 (*dd*, $J = 3, 9$, 1 H); 7.33 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 15.73 (Me); 19.94 (Me); 21.96 (Me); 23.25 (Me); 25.08 (CH); 27.81 (Me); 28.36 (Me); 31.14 (CH); 38.90 (CH_2); 50.20 (CH_2); 54.45 (CH); 58.54 (CH); 66.85 (CH_2); 79.21 (C); 84.01 (C); 84.59 (C); 128.16 (CH); 128.55 (CH); 135.57 (C); 151.66 (C); 151.98 (C); 155.83(C); 170.56(C); 170.72 (C); 175.29 (C). FAB-MS: 700.2 (3, $[M + 23]^+$), 676.2 (1, $[M + 1]^+$), 578.2 (7), 522.1 (5), 422.1 (10), 378.1 (38), 323.1 (13), 279.1 (32), 222.1 (25), 201.1 (16), 162.1 (14), 116.0 (26), 91.0 (89), 86.0 (45), 72.0 (57), 56.9 (100).

63: ^{1}H-NMR (200 MHz, $CDCl_3$): 0.86–0.97 (*m*, 9 H); 1.20 (*d*, $J = 7$, 3 H); 1.38 (*s*, H); 1.55 (*s*, H); 1.3–2.03 (*m*, 3 H); 2.53 (*m*, 1 H); 4.40 (*d*, $J = 3$, 1 H); 4.81 (*s*, 2 H); 5.13 (*s*, 2 H); 5.29 (*dd*, $J = 5, 8$, 1 H); 7.35 (*m*, 5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 15.93 (Me); 18.20 (Me); 22.01 (Me); 23.18 (Me); 25.25 (Me); 27.75 (Me); 28.03 (Me); 29.98 (CH); 38.74 (CH_2); 44.03 (CH_2); 54.93 (CH); 64.48 (CH); 66.97 (CH_2); 84.20 (C); 85.10 (C); 128.29 (CH); 128.38 (CH); 128.59 (CH); 135.57 (C); 148.65 (C); 152.01 (C); 168.46 (C); 169.81 (C); 170.30 (C). FAB-MS: 626.1 (17, $[M + 23]^+$), 448.1 (20), 426.1 (16), 404.1 (55), 222.1 (10), 154.0 (25), 150.0 (14), 137.0 (26), 107.0 (18), 91.0 (100).

Boc-Val-BzlGly-Leu-OMe (**64**), *Boc-BzlVal-BzlGly-Leu-OMe* (**65**), *and Boc-BzlVal-BzlGly-BzlLeu-OMe* (**66**). With NaH: At 0°, to a soln. of **1** (521 mg, 1.34 mmol) and benzyl bromide (1.5 ml, 12.6 mmol) in THF (5 ml), 60–65% NaH dispersion (260 mg, 6.77 mmol) was added and warmed to r.t. After 24 h, the mixture was worked up as described for **62**/**63**. FC (hexane/AcOEt 2:1) gave 521 mg (79%) of **64** and 49 mg (6%) of *Boc-Val-BzlGly-Leu-OBzl* (**67**).

With KH: As described for NaH above, with **1** (348 mg, 0.9 mmol), benzyl bromide (1.1 ml, 9.25 mmol), THF (4 ml), and 20% KH in oil (0.8 ml, 4 mmol, 6 h at 0°, 16 h at r.t.). Workup and chromatography (hexane/AcOEt 4:1) gave 238 mg (39%) of **66**.

With NaDMSO: To **1** (361 mg, 0.93 mmol) in THF (10 ml), NaH (158 mg, 3.95 mmol) in DMSO (1.5 ml) [46] was added dropwise, and the soln. became solid portionally. After 30 min, the mixture was warmed to −20° and stirred for 2 h. Then benzyl bromide (0.55 ml, 4.63 mmol) was added. After 23 h of stirring at r.t., the mixture was worked up as usual. Chromatography (hexane/AcOEt 3:1) gave 185 mg (40%) of **64** and 182 mg (34%) of **65**.

64: ^{1}H-NMR (400 MHz, $CDCl_3$): 0.90–1.05 (*m*, 12 H); 1.44 (*s*, 9 H); 1.49–1.67 (*m*, 23 H); 2.03 (*m*, 1 H); 3.71, 3.72 (2*s*, 3 H); 3.71–4.94 (*m*, 6H); 5.08, 5.25 (2 br. *d*, $J = 8$, 1 H); 6.54, 7.65 (2 br. *d*, $J = 8$, 1 H); 7.26–7.36 (*m*, 5 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 17.32 (Me); 19.63 (Me); 21.91 (Me); 22.79 (Me); 24.79 (CH); 28.28 (Me); 30.56

(CH); 41.47 (CH_2); 49.87 (CH_2); 50.71 (CH); 50.79 (CH_2); 52.25 (Me); 56.10 (CH); 80.32 (C); 128.22–128.95 (several CH); 135.11 (C); 156.71 (C); 168.33 (C); 172.59–173.55 (several C). FAB-MS: 514.2 (25, $[M + 23]^+$), 492.2 (36, $[M + 1]^+$), 392.1 (41), 347.1 (10), 293.1 (75), 291.1 (69), 247.1 (10), 146.1 (10), 120.0 (52), 91.0 (100), 71.9 (33).

65: ^{1}H-NMR (400 MHz, $CDCl_3$): 0.83–0.97 (*m*, 12 H); 1.25, 1.31 (2*s*, 9 H); 1.4–1.63 (*m*, 3 H); 2.47 (*m*, 1 H); 3.39–5.19 (2*m*, 11 H); 6.6 (br. *m*, 1 H); 7.02–7.38 (*m*, 10 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 18.08 (Me); 19.49 (Me); 21.92 (Me); 22.70 (Me); 4.63 (CH); 28.13 (Me); 28.32 (CH); 41.53 (CH_2); 46.81 (CH_2); 48.43 (CH_2); 50.57 (CH); 50.87 (CH_2); 52.12 (Me); 61.58 (CH); 80.83 (C); 126.51–129.42 (mehrere CH); 139.29 (C); 156 (C); 168.40–172.83 (several C). FAB-MS: 604.3 (4, $[M + 23]^+$), 582.3 (2, $[M + 1]^+$), 482.3 (11), 381.1 (8), 293.2 (58), 206.1 (22), 162.1 (49), 120.1 (28), 91.0 (100).

66: ^{1}H-NMR (200 MHz, $CDCl_3$): 0.69–0.98 (*m*, 12 H); 1.26, 1.27 (2*s*, 9 H); 1.4–1.92 (*m*, 3 H); 2.4 (*m*, 1 H); 3.43–5.28 (2*m*, 13 H); 6.9–7.27 (*m*, 15 H). FAB-MS: 694.4 (2, $[M + 23]^+$), 672.4 (7, $[M + 1]^+$), 572.3 (6), 383.2 (51), 236.1 (13), 206.1 (21), 162.1 (28), 120.0 (16), 91.0 (100).

Boc-Val-BzlGly-Leu-OBzl (**67**) *and Benzyl* N-*[(3-Benzyl-4-isopropyl-2,5-dioxoimidazolidin-1-yl)acetyl]*-L-*leucinate* (**68**). A soln. of **1** (274 mg, 0.71 mmol) in MeCN (2.5 ml) was treated with KF/Al_2O_3 (1.29 g, 7.09 mmol F^-) and benzyl bromide (0.5 ml, 4.21 mmol). After 15 h, the suspension was filtered through *Celite* and chromatographed (hexane/AcOEt 2:1): 290 mg (72%) of **67** and 30 mg (8%) of **68**.

67: ^{1}H-NMR (200 MHz, $CDCl_3$): 0.87–0.98 (*m*, 12 H); 1.43 (*s*, 9 H); 1.43–1.67 (*m*, 3 H); 2.00 (*m*, 1 H); 3.83–5.25 (*m*, 6 H); 5.15, 5.16 (2*s*, 3 H); 6.54, 7.77 (2 br. *d*, *J* = 8, 1 H); 7.26–7.39 (*m*, 10 H). FAB-MS: 590.1 (24, $[M + 23]^+$), 568.1 (23, $[M + 1]^+$), 468.1 (32), 369.0 (42), 347.0 (10), 290.9 (40), 120.0 (36), 90.9 (100).

68: ^{1}H-NMR (200 MHz, $CDCl_3$): 0.89–94 (*m*, 9 H); 1.11 (*d*, *J* = 7, 1, 3 H); 1.50–1.70 (*m*, 3 H); 2.12 (*m*, 1 H); 3.72 (*m*, 1 H); 4.10, 5.10 (*AB*, *J* = 15.2 H); 4.21 (*m*, 2 H); 4.71 (*m*, 1 H); 6.34 (*d*, *J* = 6, 1 H); 7.22–7.37 (*m*, 10 H). FAB-MS: 516.2 (13, $[M + 23]^+$), 494.2 (31, $[M + 1]^+$), 291.1 (10), 273.1 (7), 245.1 (7), 120.0 (9), 91.0 (100).

Boc-Val-Leu-BzlGly-Abu-Ile-OBzl (**69**). To a slurry of **4** in (161 mg, 0.28 mmol) in MeCN (5 ml), KF/Al_2O_3 (750 mg, 4.12 mmol F^-) and benzyl bromide (0.24 ml, 2 mmol) were added. After 7 d, filtration through *Celite* and chromatography (hexane/AcOEt 2:3) gave 173 mg (82%) of **69**. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.67–0.97 (*m*, 21 H); 1.08–2.17 (*m*, 9 H); 1.41 (*s*, 9 H); 3.80–5.28 (*m*, 1 H); 6.62–6.85 (*m*, 2H); 7.18–7.42 (*m*, 11 H). FAB-MS: 788.3 (7, $[M + 23]^+$), 766.3 (6, $[M + 1]^+$), 666.3 (3), 545.2 (3), 489.2 (6), 460.2 (14), 454.2 (36), 404.1 (29), 360.1 (8), 257.1 (7), 205.1 (11), 120.0 (32), 90.9 (100), 86.0 (93); 71.9 (26), 56.9 (64).

5. *Alkylations. General Procedure 5* (*G. P. 5*). Dried LiCl or LiBr (10 h at 160°/0.03 Torr) and the peptide were dissolved in THF and cooled to −75° under Ar. The base (*t*-BuLi or freshly prepared LDA soln. in THF) was added dropwise. After *ca.* 1 h stirring, BuLi (only in the case of LDA as base) and the appropriate electrophile were added. The mixture was worked up by addition of 1N H_2SO_4 and with AcOEt. The org. layer was washed twice with sat. aq. NaCl soln. All aq. layers were extracted twice with AcOEt. The combined org. phases were dried ($MgSO_4$) and evaporated. To the crude product in Et_2O (*ca.* 10 ml), diazomethane in Et_2O was added dropwise. The excess diazomethane was destroyed by some drops of AcOH. Washing with sat. $NaHCO_3$ and sat. NaCl soln., drying ($MgSO_4$), and evaporation gave the product which then was purified.

*Boc-Val-Leu-Me-*D*-Ala-MeAbu-Ile-OMe* (**70a**), *Boc-Val-Leu-MeAla-MeAbu-Ile-OMe* (**70b**), *and Boc-Val-Leu-Sar-MeAbu-Ile-OMe* (**5**-OMe). According to *G.P.5*, with **5** (344 mg, 0.56 mmol), LiBr (298 mg, 3.43 mmol), THF (6 ml), LDA soln. (6 ml, 2.67 mmol; 2 h). BuLi (1.8 ml, 2.67 mmol), and MeI (0.17 ml, 2.73 mmol; LiI precipitated, 2 h); then LDA soln. (6 ml) and MeI (0.17 ml; 18 h); then LDA soln. (6 ml) and MeI (0.17 ml). After a total of 45 h reaction time at −75°, the mixture was worked up. LC (hexane/AcOEt 1:1) gave 96 mg (27%) of **70a**, 19.5 mg (5%) of **70b**, and 212 mg (60%) of **5**-OMe.

According to *G.P. 5*, with **5** (329 mg, 0.54 mmol), LiBr (350 mg, 4.03 mmol), THF (11 ml), *t*-BuLi (2.11 ml, 3.36 mmol; 1 h), MeI (0.33 ml, 5.30 mmol, LiI precipitated). After 18 h (−75°) workup as usual. LC (hexane/AcOEt 1:2) provided 108 mg (31%) of **70a**/**70b** 8.3:1 (by ^{1}H-NMR) and 182 mg (54%) of **5**-OMe.

According to *G.P. 5*, **5** (205 mg, 0.33 mmol), LiBr (293 mg, 3.57 mmol), THF (5 ml), LTMP soln. (5.3 ml, 1.85 mmol; 2 h), BuLi (1.2 ml, 1.67 mmol; 1 h), MeI (0.15 ml, 2.41 mmol; 5 h); then LTMP soln. (4.8 ml, 1.67 mmol) and MeI (0.15 ml; 17 h); then LTMP soln. (6.7 ml, 1.82 mmol) and MeI (0.15 ml; 22 h); then LTMP soln. (6.6 ml, 1.83 mmol) and MeI (0.3 ml, 4.82 mmol). After a total of 68 h at −75°, the mixture was worked up. LC (hexane/AcOEt 1:1) gave 38 mg (18%) of **70a**, 15.5 mg (7%) of **70b**, and 124 mg (59%) of **5**-OMe.

According to *G.P. 5*, with **5** (211 mg, 0.34 mmol), LiBr (220 mg, 2.53 mmol), THF (6 ml), LDA soln. (8.5 ml, 1.90 mmol; 2.5 h), BuLi (1.2 ml, 1.9 mmol; −75°), and MeI (0.25 ml, 4.02 mmol; 14.5 h at 0°). LC (hexane/AcOEt 1:2) gave 15 mg of **70a**, 95 mg of **70b** (containing 35% of **70a**) and 91 mg (42%) of **5**-OMe. Yield 50%, D/L 1:1.3.

According to *G.P. 5*, with **5** (186 mg, 0.30 mmol), LiI (236 mg, 1.76 mmol), THF (6 ml), further addition of THF (10 ml), LDA soln. (1.67 mmol; 2 h), BuLi (1.1 ml, 1.67 mmol; −75°, then warmed up to 0°), MeI (0.2 ml, 3.21

mmol; 5 h); then LDA soln. (1.67 mmol), and MeI (0.2 ml). After 12 h, workup with CH_2Cl_2. LC (hexane/AcOEt 1:2) gave 11 mg (5%) of Boc-Val-MeLeu-MeAla-MeAbu-MeIle-OMe, 24 mg of **70a**, 89 mg of **70b** (containing 25% of **70a**), and 34 mg (18%) of **5**-OMe. Yield 59%, D/L 1:1.5.

70a: $[\alpha]_D^{r.t.} = -31.2$ ($c = 1.0$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.83–1.00 (*m*, 21 H); 1.21–1.33 (*m*, 2 H); 1.38 (*d*, $J = 7.2$, 3 H); 1.42 (*s*, 9 H); 1.47–1.67 (*m*, 4 H); 1.97 (*m*, 2 H); 2.16 (*m*, 1 H); 2.98 (*s*, 3 H); 3.15 (*s*, 3 H); 3.73, 3.77 (2*s*, 3 H); 4.06 (*m*, 1 H); 4.60 (*dd*, $J = 6.0$, 8.9, 1 H); 5.01–5.17 (*m*, 4 H); 7.03–7.11 (*m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.39 (Me); 11.40 (Me); 14.40 (Me); 15.51 (Me); 17.71 (Me); 19.26 (Me); 20.62 (CH_2); 22.47 (Me); 22.97 (Me); 24.67 (CH); 25.38 (CH_2); 28.33 (3 Me); 30.46 (Me); 30.88 (Me); 31.59 (CH); 37.77 (CH); 41.11 (CH_2); 47.42 (CH); 50.50 (CH); 52.47 (Me); 56.42 (CH); 58.41 (CH); 59.49 (CH); 79.31 (C); 155.67 (C); 170.27 (C); 171.34 (C); 172.93 (C); 173.21 (C); 173.92 (C). FAB-MS: 664.4 (33, $[M + 23]^+$), 642.4 (18, $[M + 1]^+$), 497.3 (25), 441.2 (28), 398.2 (100), 342.2 (64), 330.2 (34), 298.2 (13), 257.1 (10), 245.2 (13), 116.0 (17), 86.0 (81), 72.0 (45), 57.9 (100). GC: 9.40 (Val, MeAla), 10.26 (MeAbu), 11.80 (Ile), 12.38 (Leu).

70b: $[\alpha]_D^{r.t.} = -52.7$ ($c = 0.73$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$; 2 conformations): 0.83–1.02 (*m*, 21 H); 1.11 (*m*, 1 H); 1.29 (*d*, $J = 6.9$, 2 H); 1.33–1.43 (*m*, 2 H); 1.43, 1.44 (2*s*, 9 H); 1.47–1.55 (*m*, 1 H); 1.62–1.82 (*m*, 2 H); 1.84–2.02 (3 H); 2.06–2.14 (*m*, 1 H); 2.73, *2.88* (2*s*, 3 H); *3.02*, 3.21 (2*s*, 3 H); *3.73*, 3.79 (2*s*, 3 H); *3.93*, 4.05 (2*m*, 1 H); *4.52*, 4.61 (2*dd*, $J = 5.0$, 8.7, 5.3, 7.9, 1 H); 4.76, *4.87* (2*dd*, $J = 5.8$, 8.9, 6.4, 9.4, 1 H); 4.94–5.08 (*m*, 1.7 H); 5.24 (*m*, 0.3 H); 5.31, 5.35 (*AB*, $J = 7.1$, 0.4 H); 5.48, 5.52 (*AB*, $J = 6.8$, 0.6 H); 6.54, *6.61* (2*d*, $J = 8.4$, 8.7, 1 H); *7.01*, 8.21 (2*d*, $J = 8.8$, 8.1, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.29 (Me); 10.68 (Me); 11.43 (Me); 14.25 (Me); 15.57 (Me); 17.61 (Me); 19.25 (Me); 20.43 (CH_2); 21.69 (Me); 23.37 (Me); 24.73 (CH_2); 24.99 (CH); 28.29 (3 Me); 30.23 (Me); 30.36 (Me); 37.65 (CH); 42.49 (CH_2); 47.65 (CH); 49.56 (CH); 52.09 (Me); 56.26 (CH); 58.60 (CH); 61.60 (CH); 79.90 (C); 155.78 (C); 169.98 (C); 171.40 (C); 172.20 (C); 172.76 (C); 173.06 (C). FAB-MS: 664.4 (14, $[M + 23]^+$), 642.5 (4, $[M + 1]^+$), 564.4 (1), 497.3 (31), 441.3 (8), 398.3 (100), 342.2 (23), 257.2 (7), 116.0 (10), 86.0 (68), 72.0 (32), 57.9 (82). GC: 8.97 (Val), 9.24 (Me-D-Ala), 9.79 (MeAbu), 11.36 (Ile), 11.84 (Leu).

5-OMe: $[\alpha]_D^{r.t.} = -84.1$ ($c = 1.17$, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.87–1.02 (*m*, 21 H); 1.19 (*m*, 1 H); 1.37–1.50 (*m*, 1 H); 1.44 (*s*, 9 H); 1.52–1.81 (*m*, 3 H); 1.88–2.10 (*m*, 3 H); 2.77, *2.95*, 2.99 (3*s*, 3 H); 3.20, 3.34 (2*s*, 3 H); 3.72, *3.74*, 3.74 (3*s*, 3 H); 3.92, 4.35 (*AB*, $J = 15.7$, 2 H); 3.99 (*m*, 1 H); 4.52–4.60 (*m*, 1 H); 4.94 (*m*, 1 H); 5.06–5.24 (*m*, 2 H); 6.70–6.82 (*m*, 2 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 10.46 (Me); 11.46 (Me); 15.53 (Me); 17.71 (Me); 19.30 (Me); 20.75 (CH_2); 21.95 (Me); 23.28 (Me); 24.67 (CH); 25.15 (CH_2); 28.32 (3 Me); 30.14 (Me); 31.24 (CH); 37.03 (Me); 37.64 (CH); 42.08 (CH_2); 47.16 (CH); 49.79 (CH_2); 52.20 (Me); 56.33 (CH); 58.33 (CH); 59.78 (CH); 79.60 (C); 155.75 (C); 169.21 (C); 170.14 (C); 171.31 (C); 172.38 (C); 172.80 (C). FAB-MS: 650.3 (18, $[M + 23]^+$), 628.4 (6, $[M + 1]^+$), 483.3 (15), 427.2 (31), 384.2 (33), 328.1 (38), 316.2 (48), 284.1 (8), 257.1 (10), 245.2 (15), 171.1 (33), 116.0 (17), 86.0 (100), 72.0 (65), 56.9 (58).

*Boc-Val-Leu-Bzl-*D*-Ala-BzlAbu-Ile-OMe* (**71a**), *Boc-Val-Leu-BzlAla-BzlAbu-Ile-OMe* (**71b**), *and Boc-Val-Leu-BzlGly-BzlAbu-Ile-OMe* (**7**-OMe). According to *G.P. 5*, with **7** (237 mg, 0.31 mmol), LiBr (207 mg, 2.38 mmol), THF (15 ml), LDA soln. (8.3 ml, 2.37 mmol; 2 h), BuLi (1.5 ml, 2.36 mmol), and MeI (0.23 ml, 3.69 mmol, 6 h at −75°, 13 h at 0°). LC (hexane/AcOEt 2:1) gave 22 mg (9%) of **71a/71b** and 155 mg (64%) of **7**-OMe.

According to *G.P. 5*, with **7** (273 mg, 0.36 mmol), LiBr (222 mg, 2.56 mmol), THF (7 ml), LTMP soln. (6.8 ml, 1.88 mmol; 2 h), BuLi (1.48 ml, 1.88 mmol), and MeI (0.3 ml, 4.82 mmol; 6 hat −75°, 13 h at 0°). LC gave 39 mg (14%) of **71a**, 28 mg (10%) of **71b**, and 141 mg (51%) of **7**-OMe.

According to *G.P. 5*, with **7** (231 mg, 0.30 mmol), LiBr (337 mg, 3.88 mmol), THF (6 ml), LTMP soln. (6.3 ml, 1.65 mmol; 2 h), BuLi (1.0 ml, 1.55 mmol), and MeI (0.2 ml, 3.21 mmol; 2 h at −75°, 40 h at −20°). LC gave 31 mg (13%) of **71a**, 29 mg (12%) of **71b**, 32 mg of by-product, and 123 mg (52%) of **7**-OMe.

According to *G.P. 5*, with **7** (214 mg, 0.28 mmol), LiBr (221 mg, 2.54 mmol), THF (7 ml), LHMDS soln. (5.3 ml, 1.49 mmol; 2 h), BuLi (0.97 ml, 1.49 mmol), and MeI (0.20 ml, 3.21 mmol; warmed to 0°, 13 h). LC gave 15 mg (7%) of **71**, 18 mg (8%) of **71b**, and 141 mg (72%) of **7**-OMe (slightly contaminated with a by-product).

71a: ^{1}H-NMR (400 MHz, $CDCl_3$): 0.55 (*d*, $J = 6.0$, 2 H); 0.63 (*d*, $J = 6.1$, 2 H); 0.81–1.01 (*m*, 18 H); 1.10 (*t*, $J = 7.3$, 2 H); 1.34–1.56 (*m*, 3 H); 1.40 (*s*, 9 H); 1.59–1.70 (*m*, 2 H); 1.74 (*m*, 1 H); 1.94 (*m*, 1 H); 2.04 (*m*, 1 H); 2.40 (*m*, 1 H); 3.72, 3.75, *4.10* (3*s*, 3 H); 4.10 (*m*, 1 H); 4.29 (*d*, $J = 17.0$, 1 H); 4.67–4.73, 4.82–4.86 (2*m*, 3 H); 5.05–5.26 (*m*, 3 H); 7.10–7.40 (*m*, 11.4 H); 7.61 (*d*, $J = 9.3$, 0.6 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.38 (Me); 11.97 (Me); 14.13 (Me); 15.62 (Me); 17.94 (Me); 19.32 (Me); 21.95 (CH_2); 21.99 (Me); 22.89 (Me); 24.24 (CH); 25.73 (CH_2); 28.32 (3 Me); 31.89 (CH); 37.90 (CH); 42.07 (CH_2); 47.28 (CH_2); 47.65 (CH); 50.94 (CH_2); 52.26 (CH); 52.57 (Me); 56.71 (CH); 59.29 (CH); 61.23 (CH); 79.09 (C); 125.73 (CH); 127.24 (CH); 127.36 (CH); 127.89 (CH); 128.83 (CH); 128.99 (CH); 137.92 (C); 139.06 (C); 155.65 (C); 170.33 (C); 171.49 (C); 173.91 (C); 175.14 (C); 176.07 (C). FAB-MS: 816.4 (14, $[M + 23]^+$), 649.3 (16), 474.2 (78), 418.2 (22), 321.2 (129), 257.1 (12), 91.0 (97), 56.9 (100). GC: 3.56 (D-Ala), 5.00 (Abu), 5.15 (Val); 7.07 (Ile), 8.61 (Leu).

71b: ^{1}H-NMR (400 MHz, $CDCl_3$; several conformations): 0.42–1.14 (*m*, 24 H); 1.18–1.83 (*m*, 16 H); 1.89–2.13 (*m*, 2 H); 2.75–5.52 (*m*, 10 H); 3.70, 3.72, 3.75, 3.76 (4*s*, 3 H); 6.26–6.93 (*m*, 1 H); 7.10–7.41 (*m*, 10.5 H); 8.14–8.39 (*m*, 0.5 H). FAB-MS: 816.4 (21, $[M + 23]^+$), 649.3 (31), 482.2 (22), 474.2 (55); 460.2 (17), 404.2 (24), 404.2 (24), 378.2 (10), 257.2 (12), 231.1 (13), 105.0 (43), 91.0 (69), 86.0 (60), 56.9 (100). GC: 4.10 (Ala), 5.41 (Abu), 5.61 (Val), 7.53 (Ile), 9.10 (Leu).

7-OMe: $[\alpha]_D^{r.t.} = -60.8$ (*c* = 1.58, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.73–0.98 (*m*, 21 H); 1.27 (*m*, 1 H); *1.43*, 1.44 (2*s*, 9 H); 1.48–1.66 (*m*, 4 H); 1.82 (*m*, 1 H); 1.93–2.13 (*m*, 3 H); 3.74, *3.76* (2*s*, 3 H); 3.86–4.04 (*m*, 2 H); 4.28–5.18 (*m*, 9 H); 6.83 (*d*, *J* = 8.9, 1 H); 7.00–7.45 (*m*, 11 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.30 (Me); 11.55 (Me); 15.63 (Me); 17.69 (Me); 19.34 (Me); 21.73 (CH_2); 21.96 (Me); 23.15 (Me); 24.61 (CH); 25.36 (CH_2); 28.31 (3 Me); 31.34 (Me); 37.54 (CH); 42.26 (CH_2); 47.14 (CH); 47.89 (CH_2); 48.88 (CH_2); 52.25 (Me); 52.78 (CH_2); 56.57 (CH); 59.66 (CH); 60.65 (CH); 79.54 (C); 125.98 (CH); 127.23 (CH); 127.50 (CH); 128.00 (CH); 128.89 (CH); 128.98 (CH); 135.91 (C); 136.99 (C); 155.75 (C); 170.38 (C); 170.48 (C); 171.31 (C); 172.64 (C); 173.30 (C). FAB-MS: 802.3 (16, $[M + 23]^+$), 780.3 (11, $[M + 1]^+$), 635.2 (24), 579.1 (22), 468.2 (40), 460.1 (29), 404.2 (26), 321.1 (16), 257.1 (10), 148.1 (31), 120.0 (43), 90.9 (95), 86.0 (100), 71.9 (22), 56.9 (47).

*Boc-Val-Leu-*D*-Ala-Abu-Ile-OMe* (**72a**). At −75°, Na (12 mg, 0.56 mmol) was dissolved in NH_3 (*ca.* 3 ml). Then, educt (**71a** after saponification; 25 mg, 0.03 mmol) in THF (2 ml) was added dropwise. After 10 min, AcOH (0.1 ml) was added and warmed to r.t. The residue was taken up in AcOEt and 1N H_2SO_4. The aq. phase extracted twice with AcOEt. All org. layers were washed with sat. NaCl soln., the combined extract was dried ($MgSO_4$), and evaporated and the residue esterified according *G.P. 5*. Chromatography (hexane/AcOEt 1.5:8.5) gave 12 mg (61%) of **72a**. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.81–1.02 (*m*, 21 H); 1.10–2.36 (*m*, 18 H); 1.42 (*s*, 9 H); 1.66 (*d*, *J* = 6, 3 H); 3.75 (*m*, 3 H); 3.87 (*m*, H); 4.21–4.63 (*m*, 4 H); 4.93 (*d*, *J* = 7.5, 1 H); 6.78 (*m*, 2 H); 6.96 (*d*, *J* = 8, 1 H); 7.08 (*d*, *J* = 7.5, 1 H). FAB-MS: 636.3 (27, $[M + 23]^+$), 614.3 (50, $[M + 1]^+$), 514.3 (10), 469.2 (9), 413.2 (15), 384.2 (7), 328.1 (25), 257.1 (22), 231.2 (16), 146.1 (20), 86.0 (100), 56.9 (56). GC: 3.72 (D-Ala), 5.18 (Abu), 5.33 (Val), 7.25 (Ile), 8.79 (Leu).

*Boc-Leu-Me-*D*-Ala-Leu-OMe* (**73a**), *Boc-Leu-MeAla-Leu-OMe* (**73b**), *and Boc-Leu-Sar-Leu-OMe* (**2**-OMe). According to *G.P. 5*, with **2** (268 mg, 0.645 mmol), LiBr (296 mg, 3.41 mmol), THF (7 ml), *t*-BuLi (2.2 ml, 2.88 mmol; 1 h), MeI (0.4 ml, 6.43 mmol; 6.5 h at −75°). LC (pentane/Et_2O 1:1) gave 11 mg (5%) of **73a**, 58 mg (20%) of **73b**, 12 mg of by-product, and 106 mg (38%) of **2**-OMe.

73a: ^{1}H-NMR (300 MHz, $CDCl_3$): 0.89–1.02 (*m*, 12 H); 1.33 (*d*, *J* = 7.1, 3 H); 1.38–1.82 (*m*, 6 H); 1.43 (*s*, 9 H); 3.01 (*s*, 3 H); 3.70 (*s*, 3 H); 4.51–4.60 (*m*, 2 H); 5.12 (*d*, *J* = 7.3, 1 H); 5.31 (*m*, 1 H); 6.75 (*d*, *J* = 7.5, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 13.14 (Me); 21.82 (2 Me); 22.76 (Me); 23.33 (Me); 24.84 (2 CH_2); 28.36 (3 Me); 30.43 (Me); 40.79 (CH_2); 41.40 (CH_2); 49.42 (CH); 50.91 (CH); 52.00 (CH); 52.13 (Me); 79.86 (C); 156.09 (C); 170.90 (C); 173.31 (C); 174.12 (C). FAB-MS: (23, $[M + 23]^+$), 444.3 (29, $[M + 1]^+$), 344.2 (19), 299.2 (24), 243.1 (100), 231.2 (36), 199.2 (16), 130.1 (21), 86.0 (34), 56.9 (85). GC: 7.85 (Me-D-Ala), 10.68 (Leu).

73b: ^{1}H-NMR (300 MHz, $CDCl_3$; 2 conformations): 0.88–1.02 (*m*, 12 H); 1.24–1.80 (*m*, 6 H); 1.35 (*d*, *J* = 7.1, 3 H); 1.42, 1.44 (2*s*, 9 H); 2.77, 2.98 (2*s*, 3 H); 3.717, *3.724* (2*s*, 3 H); 4.50–4.68 (*m*, 2 H); 4.80 (*m*, 0.5 H); 5.09–5.28 (*m*, 1.5 H); 6.46 (*d*, *J* = 8.2, 0.5 H); 7.97 (*d*, *J* = 7.9, 0.5 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 13.11 (Me); 21.61 (Me); 21.98 (Me); 22.88 (Me); 23.47 (Me); 24.63 (CH); 24.76 (CH); 28.29 (3 Me); 30.10 (Me); 41.28 (CH_2); 42.41 (CH_2); 50.59 (CH); 51.83 (CH); 52.28 (Me); 55.33 (CH); 80.51 (C); 156.70 (C); 170.50 (C); 173.18 (C); 173.86 (C). FAB-MS: 466.3 (10, $[M + 23]^+$), 444.3 (14, $[M + 1]^+$), 299.2 (42), 243.1 (100), 231.2 (16), 199.2 (10), 130.1 (13), 86.0 (18), 57.9 (63), 56.9 (37). GC: 9.17 (MeAla), 12.26 (Leu).

2-OMe. $[\alpha]_D^{r.t.} -41.0$ (*c* = 1.35, EtOH). ^{1}H-NMR (300 MHz, $CDCl_3$): 0.91–1.01 (*m*, 12 H); 1.36–1.80 (*m*, 6 H); 1.42, *1.43* (2*s*, 3 H); 2.97, *3.19* (2*s*, 2 H); 3.70, 3.72 (2*s*, 3 H); 3.83–3.92 (*m*, 1 H); 4.22–4.29 (*m*, 1 H); 4.42, *4.60* (2*m*, 2 H); 5.02, *5.13* (*d*, *J* = 7.1, 7.5, 1 H); 6.66, 7.83 (2*d*, *J* = 8.3, 7.4, 1 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.69 (Me); 21.88 (Me); 22.73 (Me); 23.37 (Me); 24.70 (CH); 24.83 (CH); 28.36 (3 Me); 36.32 (Me); 41.10 (CH_2); 41.60 (CH_2); 48.98 (CH); 50.75 (CH); 52.28 (Me); 53.57 (CH_2); 78.95 (C); 155.96 (C); 168.46 (C); 173.16 (C); 173.91 (C). FAB-MS: 452.3 (30, $[M + 23]^+$), 430.3 (66, $[M + 1]^+$), 330.2 (90), 229.1 (72), 217.2 (100), 146.1 (28), 130.1 (28), 86.0 (55), 56.9 (72).

Boc-Leu-(2-^{2}H)Gly-MeLeu-OMe (**74**). According to *G.P. 5*, with **3** (274 mg, 0.66 mmol), LiBr (289 mg, 2.98 mmol), THF (10 ml), LDA-soln. (2.90 mmol; 1 h), BuLi (1.9 ml, 2.64 mmol; 30 min), and MeOD (0.28 ml, 6.6 mmol; 1 h at −75°). LC (pentane/Et_2O 1:3) gave 266 mg (94%) of **74**, ^{2}H-incorporation 54% by ^{1}H-NMR.

According to *G.P. 5*, with **3** (290 mg, 0.70 mmol), LiBr (325 mg, 3.74 mmol), THF (9 ml), *t*-BuLi (2.8 ml, 3.08 mmol; 1 h), and MeOD (0.29 ml, 7.0 mmol; 30 min at −75°). Workup gave 301 mg of **74**. ^{1}H-NMR and FAB-MS: 87% of ^{2}H-incorporation.

74: ^{1}H-NMR (400 MHz, $CDCl_3$): 0.90–0.98 (*m*, 12 H); 1.42–1.51 (*m*, 2 H); 1.44, *1.45* (2*s*, 9 H); 2.88, *2.90* (2*s*, 3 H); *3.71*, 3.74 (2*s*, 3 H); 4.08 (*m*, *ca.* 1.1 H); 4.20 (1 H); 4.92 (*d*, *J* = 7.6, 1 H); 5.29 (*dd*, *J* = 5.5, 10.3, 1 H); 7.03 (*m*,

1 H). FAB-MS: 453.2 (28, $[M + 23]^+$), 431.3 (40, $[M + 1]^+$), 375.2 (28), 331.2 (14), 218.1 (51), 160.1 (100), 130.1 (21), 100.0 (88), 86.0 (45), 56.9 (68).

*Boc-Leu-*D*-Ala-MeLeu-OMe* (**75a**), *Boc-Leu-Ala-MeLeu-OMe* (**75b**), *and Boc-Leu-Gly-MeLeu-OMe* (**3**-OMe). According to *G.P.5*, with **3** (287 mg, 0.69 mmol), LiBr (305 mg, 3.51 mmol), THF (9 ml), LDA soln. (10.5 ml, 3.03 mmol; pale yellow, 90 min), BuLi (2.0 ml, 2.78 mmol), and MeI (0.4 ml, 6.43 mmol; 18 h at −75°). LC (hexane/AcOEt 2:1) gave 161 mg (53%) of **75a**, 30 mg (10%) of **75b** and 84 mg (28%) of **3**-OMe.

According to *G.P.5*, with **3** (258 mg, 0.62 mmol), LiBr (301 mg, 3.57 mmol), THF (9 ml), BuLi (2.0 ml, 2.78 mmol; 1 h), and MeI (0.39 ml, 6.26 mmol; 3 h at −75°). LC (hexane/AcOEt 2:1) gave 186 mg (68%) of **75a**, 40 mg (14%) of **75b**, and 32 mg (12%) of **3**-OMe.

According to *G.P.5*, with **3** (292 mg, 0.70 mmol), LiBr (316 mg, 3.64 mmol), THF (10 ml), *t*-BuLi (2.3 ml, 3.01 mmol; yellow soln., 90 min), and MeI (0.4 ml, 6.43 mmol; 20 h at −75°). LC (hexane/AcOEt 2:1) gave 222 mg (71%) of **75a**, 60 mg (19%) of **75b**, and 5 mg (2%) of **3**-OMe.

According to *G.P.5*, with **3** (265 mg, 0.64 mmol), LiBr (313 mg, 3.60 mmol), and THF (10 ml). The soln. was cooled with a rate of *ca.* 5°/h to −50° and then fastly to −75° followed by the addition of *t*-BuLi (2.55 ml, 2.81 mmol; 1 h) and MeI (0.4 ml, 6.43 mmol; 6 h at −75°). LC (hexane/AcOEt 2:1) gave 199 mg (70%) of **75a**, 22 mg (8%) of **75b**, and 41 mg (15%) of **3**-OMe.

75a: $[\alpha]_D^{r.t.} = -35.9$ ($c = 0.99$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; 2 conformations): 0.89–0.97 (*m*, 12 H); 1.29 (*m*, 1 H); 1.33 (*d*, $J = 6.8$, 3 H); 1.44 (*s*, 9 H); 1.46 (*m*, 1 H); 1.62–1.89 (*m*, 4 H); 2.87, *2.98* (2*s*, 3 H); *3.71*, 3.76 (2*s*, 3 H); 4.18 (*m*, 1 H); 4.87–4.96 (*m*, 2 H); 5.23 (*m*, 1 H); 7.06 (*d*, $J = 7.0$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 18.63 (Me); 21.23 (Me); 21.81 (Me); 23.10 (Me); 23.26 (Me); 24.85 (CH); 25.03 (CH); 28.31 (3 Me); 31.28 (Me); 37.30 (CH_2); 42.07 (CH_2); 45.79 (CH); 52.29 (Me); 54.84 (CH); 79.96 (C); 155.46 (C); 171.65 (C); 171.79 (C); 173.31 (C). FAB-MS: 466.2 (24, $[M + 23]^+$), 444.3 (76, $[M + 1]^+$), 338.2 (21), 231.1 (10), 229.1 (9), 160.1 (100), 100.0 (46), 86.0 (27), 56.9 (45). GC: 3.60 (D-Ala), 7.79 (MeLeu), 8.67 (Leu).

75b: $[\alpha]_D^{r.t.} = -59.1$ ($c = 0.88$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.89–1.00 (*m*, 12 H); 1.36 (*d*, $J = 6.8$, 3 H); 1.44 (*s*, 9 H); 1.47 (*m*, 2 H); 1.61–1.75 (*m*, 4 H); 2.86, *2.97* (2*s*, 3 H); *3.70*, 3.71 (2*s*, 3 H); 4.11 (*m*, 1 H); 4.85–4.94 (*m*, 2 H); 5.29 (*dd*, $J = 5.7$, 10.2, 1 H); 6.97 (*d*, $J = 7.3$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 18.17 (Me); 21.28 (Me); 21.97 (Me); 22.96 (Me); 23.22 (Me); 24.77 (CH); 24.86 (CH); 28.31 (3 Me); 30.97 (Me); 36.93 (CH_2); 41.66 (CH_2); 45.54 (CH); 52.21 (Me); 53.23 (CH); 54.63 (CH); 79.94 (C); 155.44 (C); 171.76 (C); 172.03 (C); 173.13 (C). FAB-MS: 466.3 (7, $[M + 23]^+$), 444.3 (85, $[M + 1]^+$), 388.2 (25), 356.2 (11), 229.1 (11), 160.1 (100), 130.1 (16), 100.0 (57), 86.0 (27), 56.9 (42).

3-OMe: $[\alpha]_D^{r.t.} = -52.7$ ($c = 1.38$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; 2 conformations): 0.91–0.98 (*m*, 12 H); *1.44*, 1.45 (2*s*, 9 H); 1.49 (*m*, 2 H); 1.67–1.77 (*m*, 4 H); 2.89, *2.90*, (2*s*, 3 H); *3.71*, 3.74 (2*s*, 3 H); 4.10 (*m*, 2 H); 4.20 (*m*, 1 H); 4.90 (*d*, $J = 6.9$, 1 H); 5.29 (*dd*, $J = 5.5$, 10.4, 1 H); 7.04 (*m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 21.36 (Me); 21.75 (Me); 23.07 (Me); 23.15 (Me); 24.81 (CH); 24.96 (CH); 28.30 (3 Me); 30.13 (Me); 37.17 (CH_2); 41.60 (CH_2); 41.80 (CH_2); 52.28 (Me); 54.73 (CH); 56.73 (CH); 80.01 (C); 155.5 (C); 168.90 (C); 171.86 (C); 172.63 (C). FAB-MS: 452.2 (37, $[M + 23]^+$), 430.2 (100, $[M + 1]^+$), 374.1 (58), 330.2 (22), 217.1 (58), 160.1 (89), 130.0 (26), 100.0 (80), 86.0 (48), 56.9 (57).

*Boc-Leu-*ambo*-Abu-MeLeu-OMe* (**76a**/**76b**). According to *G.P.5*, with **3** (272 mg, 0.655 mmol), LiBr (313 mg, 3.60 mmol) THF (9 ml), *t*-BuLi (2.2 ml, 2.88 mmol; 45 min), and EtI (0.5 ml, 6.22 mmol; 7 h at −75°). LC (pentane/Et_2O 1:1) gave 191 mg (64%) of **76a**/**76b** and 56 mg (20%) of **3**-OMe. GC of the crude product: 4.51 (D-Abu), 4.83 (Abu), 5.71 (Gly), 7.56 (MeLeu), 8.45 (Leu); D-Abu/Abu 2.8:1.

76a/**76b**: ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87–0.97 (*m*, 15 H); 1.39–1.49 (*m*, 2 H); 1.44 (*s*, 9 H); 1.55–1.76 (*m*, 5 H); 1.87 (*m*, 1 H); 2.88, 2.99, *3.00* (3*s*, 3 H); 3.70, *3.71*, 3.76 (3*s*, 3 H); 4.07–4.22 (*m*, 1 H); 4.89 (*m*, 1 H); 4.95 (*m*, 1 H); 5.22 (*m*, 1 H); 6.83, 6.96 (2*d*, $J = 7.7$, 7.4, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 8.95 (Me); 21.19 (Me); 21.78 (Me); 23.07 (Me); 23.31 (Me); 24.89 (CH); 24.98 (CH); 25.67 (CH_2); 28.30 (3 Me); 31.44 (Me); 37.30 (CH_2); 42.00 (CH_2); 50.28 (CH); 52.26 (Me); 54.56 (CH); 54.85 (CH); 79.97 (C); 155.37 (C); 171.83 (C); 172.01 (C); 172.48 (C). FAB-MS: 480.2 (64, $[M + 23]^+$), 458.3 (63, $[M + 1]^+$), 402.2 (24), 243.1 (13), 160.1 (100), 130.1 (16), 100.1 (55), 86.0 (28), 57.9 (86), 56.9 (47).

*Boc-Leu-*D*-Val-MeLeu-OMe* (**77a**) *and Boc-Leu-Val-MeLeu-OMe* (**77b**). According to *G.P.5*, with **3** (228 mg, 0.55 mmol), LiBr (283 mg, 3.26 mmol), THF (7.5 ml), *t*-BuLi (1.8 ml, 2.36 mmol; 1 h), and i-PrI (0.55 ml, 5.50 mmol; 8 h at −75°). LC (pentane/Et_2O 1:1) gave 15 mg (6%) of **77b**, 39 mg (15%) of **77a**, and 171 mg (73%) of **3**-OMe. GC of the crude product: 4.95 (D-Val), 5.17 (Val), 5.97 (Gly), 7.85 (MeLeu), 8.72 (Leu); D-Val/Val 2.7:1.

77a: $[\alpha]_D^{r.t.} = -37.3$ ($c = 1.05$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; 2 conformations): 0.86 (*d*, $J = 6.8$, 3 H); 0.91 (*d*, $J = 6.5$, 3 H); 0.93–0.99 (*m*, 12 H); 1.39–1.49 (*m*, 2 H); 1.44 (*s*, 9 H); 1.69–1.76 (*m*, 4 H); 2.01 (*m*, 1 H); 2.88, 3.02 (2*s*, 3 H); *3.69*, 3.75 (2*s*, 3 H); 4.18 (*m*, 1 H); 4.85 (*m*, 1 H); 4.90 (*dd*, $J = 5.1$, 9.0, 1 H); 5.19 (*m*, 1 H); 6.82 (*d*, $J = 8.8$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.73 (Me); 19.79 (Me); 21.15 (Me); 21.73 (Me); 23.05 (Me); 23.34

(Me); 24.92 (2 CH_2); 28.28 (3 Me); 31.58 (CH); 31.72 (Me); 37.29 (CH_2); 41.74 (CH_2); 52.22 (Me); 53.70 (CH); 54.86 (CH); 57.98 (CH); 80.01 (C); 155.32 (C); 171.83 (C); 172.38 (C); 172.47 (C). FAB-MS: 494.4 (21, $[M + 23]^+$), 472.4 (44), 416.3 (8), 257.2 (6), 160.2 (100), 130.1 (10), 100.1 (32), 86.0 (17), 72.0 (69), 56.9 (31).

77b: ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*d*, J = 6.5, 3 H); 0.91–0.96 (*m*, 12 H); 1.00 (*d*, J = 6.8, 3 H); 1.40–1.48 (*m*, 2 H); 1.43 (*s*, 9 H); 1.58–1.74 (*m*, 4 H); 2.09 (*m*, 1 H); 3.01 (*s*, 3 H); 3.69 (*s*, 3 H); 4.11 (*m*, 1 H); 4.79 (*dd*, J = 6.9, 8.9, 1 H); 4.90 (*d*, J = 8.4, 1 H); 5.34 (*dd*, J = 5.5, 10.3, 1 H); 6.64 (*d*, J = 9.0, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 17.53 (Me); 19.35 (Me); 21.31 (Me); 22.83 (Me); 23.27 (Me); 24.75 (CH); 24.79 (CH); 26.37 (Me); 28.30 (3 Me); 31.28 (CH); 31.39 (Me); 36.90 (CH_2); 41.38 (CH_2); 52.14 (Me); 53.23 (CH); 53.84 (CH); 54.44 (CH); 79.92 (C); 155.43 (C); 172.06 (C); 172.38 (C); 172.56 (C). FAB-MS: 494.3 (28, $[M + 23]^+$), 472.3 (75, $[M + 1]^+$), 416.3 (13), 384.2 (15), 257.2 (13), 229.2 (11), 160.1 (100), 130.1 (16), 100.0 (45), 86.0 (26), 71.9 (80), 56.9 (56).

*Boc-Leu-*D*-Nva(4,5-didehydro)-MeLeu-OMe* (**78a**) *and Boc-Leu-Nva(4,5-didehydro)-MeLeu-OMe* (**78b**). According to *G.P. 5*, with **3** (273 mg, 0.66 mmol), LiBr (301 mg, 3.43 mmol), THF (9 ml), *t*-BuLi (2.9 ml, 3.19 mmol; 1 h), allyl bromide (0.56 ml, 6.62 mmol; 17 h at −75°). LC (pentane/Et_2O 1:1) gave 17 mg of **78b**, 124 mg of **78a**/**78b** 1.7:1 (by GC), 111 mg of **78a**, and 36 mg (13%) of **3**-OMe. Yield 82%; diastereoselectivity 3.4:1 (D/L).

According to *G.P. 5*, with **3** (280 mg, 0.67 mmol), LiBr (292 mg, 3.36 mmol) and THF (11 ml). The soln. was cooled with a rate of *ca.* 5°/h to −50° and then fastly to −75°, followed by the addition of *t*-BuLi (2.3 ml, 3.5 mmol; 1 h) and allyl bromide (0.57 ml, 6.74 mmol; 6 h at −75°). LC (pentane/Et_2O 1:1) gave 25 mg of **78b**, 11 mg of **78a**/**78b** 2:1 (by GC), 125 mg (15%) of **78a**, and 112 mg (39%) of **3**-OMe. Yield 51%, **78a**/**78b** 4.6:1.

78a: $[\alpha]_D^{r.t.}$ = −41.7 (*c* = 1.07, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; 2 conformations): 0.89–0.96 (*m*, 12 H); 1.40–1.47 (*m*, 2 H); 1.44 (*s*, 9 H); 1.60–1.75 (*m*, 4 H); 2.34 (*m*, 1 H); 2.57 (*m*, 1 H); 2.88, *3.01* (2*s*, 3 H); *3.71*, 3.76 (2*s*, 3 H); 4.17 (*m*, 1 H); 4.86 (*m*, 1 H); 5.02–5.11 (*m*, 3 H); 5.21 (*m*, 1 H); 5.69 (*m*, 1 H); 6.92 (*d*, J = 7.4, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 21.22 (Me); 21.78 (Me); 23.05 (Me); 23.31 (Me); 24.83 (CH); 24.88 (CH); 28.29 (3 Me); 31.43 (Me); 37.02 (CH_2); 37.28 (CH_2); 42.07 (CH_2); 48.97 (CH); 52.29 (Me); 53.24 (CH); 54.84 (CH); 79.94 (C); 119.08 (CH_2); 131.95 (CH); 155.37 (C); 171.80 (C); 171.87 (C). FAB-MS: 492.2 (21, $[M + 23]^+$), 470.3 (50, $[M + 1]^+$), 414.2 (15), 257.1 (8), 255.1 (8), 160.1 (100), 130.1 (12), 100.0 (54), 86.0 (26), 69.9 (71), 56.9 (32). GC (peptide was first hydrogenated): 6.77 (D-Nva), 7.86 (MeLeu), 8.80 (Leu).

78b: $[\alpha]_D^{r.t.}$ = −65.3 (*c* = 1.25, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; 2 conformations): 0.88–1.00 (*m*, 12 H); 1.41–1.48 (*m*, 2 H); 1.44 (*s*, 9 H); 1.60–1.76 (*m*, 4 H); 2.35–2.42 (*m*, 1 H); 2.54–2.61 (*m*, 1 H); 2.84, *2.99* (2*s*, 3 H); *3.70*, 3.71 (2*s*, 3 H); 4.10 (*m*, 1 H); 4.85 (*d*, J = 7.6, 1 H); 4.97 (*m*, 1 H); 5.09–5.14 (*m*, 2 H); 5.30 (*dd*, J = 5.4, 10.4, 1 H); 5.69–5.80 (*m*, 1 H); 6.80 (*d*, J = 8.2, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 21.28 (Me); 21.97 (Me); 22.92 (Me); 23.23 (Me); 24.75 (CH); 24.81 (CH); 28.29 (3 Me); 31.13 (Me); 36.70 (CH_2); 36.91 (CH_2); 41.54 (CH_2); 48.76 (CH); 52.20 (Me); 53.21 (CH); 54.61 (CH); 80.00 (C); 118.92 (CH_2); 132.25 (CH); 155.38 (C); 171.79 (C); 171.97 (C). FAB-MS: 492.3 (16, $[M + 23]^+$), 470.3 (71, $[M + 1]^+$), 414.2 (19), 382.2 (12), 255.1 (12), 160.1 (100), 130.1 (19), 100.0 (61), 86.0 (35), 69.9 (81), 56.9 (58).

*Boc-Leu-*D*-Phe-MeLeu-OMe* (**79a**) *and Boc-Leu-Phe-MeLeu-OMe* (**79b**). According to *G.P. 5*, with **3** (285 mg, 0.69 mmol), LiBr (317 mg, 3.65 mmol), THF (8 ml), *t*-BuLi (2.3 ml, 3.01 mmol; 1 h), and BzlBr (0.8 ml, 6.75 mmol; 16 h at −75°). LC (toluene/AcOEt 6:1) gave 51 mg (14%) of **79b**, 211 mg (59%) of **79a**, and 54 mg (18%) of **3**-OMe. GC of the crude product: 8.66 (Leu), 18.57 (D-Phe), 18.83 (Phe).

79a: $[\alpha]_D^{r.t.}$ = −43.8 (*c* = 1.04, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; 2 conformations): 0.86–0.88 (*m*, 6 H); 0.91–0.95 (*m*, 6 H); 1.16 (*m*, 1 H); 1.38–1.44 (*m*, 1 H); 1.43, *1.44* (2*s*, 9 H); 1.47–1.67 (*m*, 4 H); *2.73*, 2.88 (2*s*, 3 H); 2.96–3.05 (*m*, 2 H); 3.67 (*s*, 3 H); 4.15 (*m*, 1 H); 4.81 (*m*, 1 H); 5.16 (*dd*, J = 5.1, 10.6, 1 H); 5.23 (*m*, 1 H); 6.81 (*d*, J = 7.1, 1 H); 7.13–7.28 (*m*, 5 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 21.48 (Me); 21.81 (Me); 23.03 (Me); 23.11 (Me); 24.61 (CH); 24.80 (CH); 28.32 (3 Me); 31.22 (Me); 37.30 (CH_2); 39.55 (CH_2); 41.98 (CH_2); 50.43 (CH); 52.21 (Me); 54.72 (CH); 57.87 (CH); 79.99 (C); 127.02 (CH); 128.48 (2 CH); 129.49 (2 CH); 136.00 (C); 155.40 (C); 171.82 (C); 171.84 (C); 172.22 (C). FAB-MS: 542.3 (45, $[M + 23]^+$), 520.3 (46, $[M + 1]^+$), 464.2 (9), 307.2 (5), 305.1 (6), 160.1 (100), 120.0 (82), 100.0 (42), 86.0 (22), 56.9 (37).

79b: $[\alpha]_D^{r.t.}$ = −58.2 (*c* = 0.5, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; 2 conformations): 0.82–0.96 (*m*, 12 H); 1.35–1.48 (*m*, 2 H); *1.44*, 1.45 (2*s*, 9 H); 1.55–1.72 (*m*, 4 H); 2.73, 2.79 (2*s*, 3 H); 2.94, 3.13 (*ABX*, J_{AB} = 13.5, J_{AX} = 5.7, $J = J_{BX}$ = 7.5, 2 H); 3.68 (*s*, 3 H); 4.08 (*m*, 1 H); 4.78 (*m*, 1 H); 5.14 (*m*, 1 H); 5.27 (*dd*, J = 5.3, 10.5, 1 H); 6.73 (*d*, J = 8.3, 1 H); 7.18–7.29 (*m*, 5 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 21.42 (Me); 22.89 (Me); 23.18 (Me); 24.75 (2 CH); 26.37 (Me); 28.31 (3 Me); 31.05 (Me); 37.13 (CH_2); 38.67 (CH_2); 41.64 (CH_2); 50.24 (CH); 52.12 (Me); 53.18 (CH); 54.63 (CH); 80 (C); 126.94 (CH); 128.39 (2 CH); 129.64 (2 CH); 135.89 (CH); 171.78 (C); 171.84 (2 C). FAB-MS: 542.2 (31, $[M + 23]^+$), 520.3 (57, $[M + 1]^+$), 464.2 (12), 432.2 (11), 305.1 (9), 160.1 (100), 130.0 (15), 120.0 (89), 100.0 (50), 86.0 (32), 56.9 (47).

*Boc-Leu-*D*-Asp(OEt)-MeLeu-OMe* (**80a**) *and Boc-Leu-Asp(OEt)-MeLeu-OMe* (**80b**). According to *G.P. 5*, with **3** (240 mg, 0.58 mmol), LiBr (259 mg, 2.98 mmol), THF (11 ml), *t*-BuLi (1.62 ml, 2.54 mmol; 90 min), and

ethyl bromoacetate (0.64 ml, 5.78 mmol; 16 h at −75°). LC (hexane/AcOEt 2:1) gave 150 mg (50%) of **80a**, 73 mg (25%) of **80b**, and 42 mg (10%) of **3**-OMe.

80a: $[\alpha]_D^{r.t.} = +5.0$ ($c = 1.04$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; 2 conformations): 0.87–0.95 (*m*, 12 H); 1.24 (*t*, $J = 7.1$, 3 H); 1.44 (*s*, 9 H); 1.47 (*m*, 2 H); 1.59–1.75 (*m*, 4 H); 2.60, 2.84 (*ABX*, $J_{AB} = 16.0$, $J_{AX} = 5.0$, $J_{BX} = 7.6$, 2 H); 2.87, 3.03 (2*s*, 3 H); 3.70, 3.75 (2*s*, 3 H); 4.08–4.15 (*m*, 3 H); 4.85 (*d*, $J = 7.2$, 1 H); 5.22 (*dd*, $J = 7.5$, 8.5, 1 H); 5.32 (*m*, 1 H); 6.89 (*d*, $J = 8.8$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 14.11 (Me); 21.25 (Me); 21.80 (Me); 23.03 (Me); 23.31 (Me); 24.74 (CH); 24.81 (CH); 28.27 (3 Me); 31.32 (Me); 37.12 (CH_2); 37.33 (CH_2); 41.71 (CH_2); 46.09 (CH); 52.24 (Me); 53.34 (CH); 54.92 (CH); 60.86 (CH_2); 80.08 (C); 155.39 (C); 170.26 (C); 171.23 (C); 171.87 (C); 172.00 (C). FAB-MS: 538.3 (33, $[M + 23]^+$), 516.3 (41, $[M + 1]^+$), 460.3 (19), 428.2 (6), 416.3 (9), 414.2 (7), 357.2 (6), 303.2 (17), 301.1 (19), 257.2 (11), 240.1 (13), 229.2 (11), 160.2 (100), 130.1 (22), 116.0 (74), 100.1 (58), 86.0 (41), 56.9 (50). GC: 7.32 (MeLeu), 8.17 (Leu), 13.77 (D-Asp).

80b: $[\alpha]_D^{r.t.} = -97.6$ ($c = 0.84$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88–1.05 (*m*, 12 H); 1.26 (*t*, $J = 7.1$, 3 H); 1.42–1.48 (*m*, 2 H); 1.44 (*s*, 9 H); 1.58–1.74 (*m*, 4 H); 2.60, 2.81 (*ABX*, $J_{AB} = 15.8$, $J_{AX} = 6.0$, $J_{BX} = 6.4$, 2 H); 2.84, *3.05* (2*s*, 3 H); *3.69*, 3.71 (2*s*, 3 H); 4.10 (*m*, 1 H); 4.14 (*q*, $J = 7.1$, 2 H); 4.84 (*d*, $J = 7.9$, 1 H); 5.22 (*dd*, $J = 6.2$, 9.7, 1 H); 5.31 (*m*, 1 H); 6.90 (*d*, $J = 9.0$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 14.10 (Me); 21.36 (Me); 21.88 (Me); 22.94 (Me); 23.23 (Me); 24.76 (CH); 24.84 (CH); 28.28 (3 Me); 31.43 (Me); 37.09 (CH_2); 37.21 (CH_2); 41.49 (CH_2); 46.24 (CH); 52.21 (Me); 53.10 (CH); 54.96 (CH); 60.97 (CH_2); 80.12 (C); 155.49 (C); 170.39 (C); 171.27 (C); 171.85 (C); 171.95 (C). FAB-MS: 538.3 (38, $[M + 23]^+$), 516.3 (62, $[M + 1]^+$), 470.3 (8), 460.3 (23), 428.2 (17), 414.2 (8), 357.2 (5), 303.2 (12), 301.1 (19), 257.1 (8), 240.1 (14), 229.2 (10), 160.2 (100), 130.1 (25), 116.0 (74), 100.1 (63), 86.0 (42), 56.9 (55). GC: 7.30 (MeLeu), 8.11 (Leu), 13.68 (Asp).

Boc-Leu-ambo-*Gly(2-CO$_2$Me)-MeLeu-OMe* (**81a**/**81b**). According to *G.P. 5*, with **3** (263 mg, 0.63 mmol), LiBr (280 mg, 3.22 mmol), THF (11 ml), *t*-BuLi (1.8 ml, 2.83 mmol; 1 h), and a stream of CO_2 gas which was passed over the mixture during 30 min (2 h at −75°). Workup, esterification with diazomethane, and chromatographic purification (hexane/AcOEt 2:1) gave 204 mg (66%) of **81a**/**81b** and 63 mg (23%) of **3**-OMe.

81a/**81b**: ^{1}H-NMR (400 MHz, $CDCl_3$): 0.86–1.01 (*m*, 12 H); 1.45 (*s*, 9 H); 1.48 (*m*, 2 H); 1.67–1.78 (*m*, 4 H); 2.90, 2.95, 3.05, *3.14* (4*s*, 3 H); 3.70, *3.72*, *3.75*, 3.79 (4*s*, 6 H); 4.24 (*m*, 1 H); 4.90 (*m*, 1 H); 5.20–5.28 (*m*, 1 H); 5.57–5.63 (*m*, 1 H); 7.19 (*d*, $J = 7.4$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 21.07 (Me); 21.29 (Me); 21.81 (Me); 22.97 (Me); 23.04 (Me); 23.23 (Me); 23.28 (Me); 24.71 (CH); 24.75 (CH); 28.27 (3 Me); 31.95 (Me); 37.00 (CH_2); 37.31 (CH_2); 41.30 (CH_2); 41.75 (CH_2); 52.26 (Me); 52.38 (Me); 53.02 (CH); 53.15 (CH); 53.24 (CH); 53.36 (CH); 55.19 (CH); 55.35 (CH); 80.03 (C); 80.15 (C); 155.42 (C); 166.51 (C); 166.54 (C); 166.95 (C); 166.98 (C); 171.46 (C); 171.53 (C); 172.47 (C). FAB-MS: 510.1 (33, $[M + 23]^+$), 488.1 (51, $[M + 1]^+$), 432.1 (42), 400.1 (17), 388.1 (20), 275.1 (55), 215.1 (14), 160.1 (44), 130.0 (17), 100.0 (45), 56.9 (100).

Boc-Leu-ambo-*Gly(2-SMe)-MeLeu-OMe* (**82b**/**82b**). According to *G.P. 5*, with **3** (343 mg, 0.83 mmol), LiBr (338 mg, 3.89 mmol), THF (12 ml), *t*-BuLi (2.3 ml, 6.67 mmol; 1 h) and Me_2S_2 (0.62 ml, 6.99 mmol; 40 min at −75°, then 4.5 h at −18°). LC (pentane/Et_2O 1:1) gave 329 mg (84%) of **82a**/**82b** and 40 mg (12%) of **3**-OMe.

82a/**82b**: ^{1}H-NMR (400 MHz, $CDCl_3$): 0.89–0.97 (*m*, 12 H); 1.44, *1.45* (2*s*, 9 H); 1.49 (*m*, 2 H); 1.64–1.82 (*m*, 4 H); 2.05, *2.09*, 2.10 (3*s*, 3 H); 2.98, *3.04*, 3.05 (3*s*, 3 H); 3.71, *3.72*, 3.73 (3*s*, 3 H); 4.22 (*m*, 1 H); 4.84–4.95 (*m*, 1 H); 5.28 (*dd*, $J = 6.0$, 10.3, 1 H); 5.74 (*d*, $J = 7.8$, 1 H); 7.46 (*d*, $J = 7.5$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.22 (Me); 21.26 (Me); 21.72 (Me); 23.09 (Me); 23.42 (Me); 24.68 (CH); 24.83 (CH); 24.86 (CH); 28.28 (3 Me); 31.14 (Me); 37.45 (CH_2); 41.70 (CH_2); 51.25 (CH); 52.35 (Me); 54.78 (CH); 55.19 (CH); 80.13 (C); 155.44 (C); 167.97 (C); 171.58 (C); 171.75 (C). FAB-MS: 498.1 (15, $[M + 23]^+$), 476.1 (26, $[M + 1]^+$), 420.1 (15), 328.1 (36), 261.0 (11), 215.1 (100), 160.1 (30), 158.1 (29), 130.0 (22), 100.0 (61), 86.0 (47), 75.9 (39), 56.9 (68).

Boc-Leu-D-*Thr-MeLeu-OMe* (**83a**) *and Boc-Leu-Thr-MeLeu-OMe*/*Boc-Leu*-ambo-*aThr-MeLeu-OMe* (**83b–d**). According to *G.P. 5*, with **3** (277 mg, 0.67 mmol), LiBr (326 mg, 3.75 mmol), THF (11 ml), *t*-BuLi (2.85 ml, 4.51 mmol; 1 h), and acetaldehyde (0.38 ml, 6.61 mmol; 2 h at −75°). LC (pentane/Et_2O 1:3) gave 25 mg of **83a**, 57 mg of **83a–d**, and 217 mg of **83b–d** (containing 8% of **3**-OMe). Yield: 89% of **83a–d**. GC: D-Thr/Thr/D-aThr/aThr 1.0:2.0:1.8:1.3.

83a: ^{1}H-NMR (500 MHz, $CDCl_3$; 2 conformations): 0.90–0.96 (*m*, 12 H); 1.16 (*d*, $J = 6.4$, 3 H); 1.45 (*s*, 9 H); 1.50 (*m*, 2 H); 1.65–1.89 (*m*, 5 H); 2.87, *3.05* (2*s*, 3 H); *3.71*, 3.75 (2*s*, 3 H); 4.08 (*m*, 1 H); 4.17 (*m*, 1 H); 4.85–4.92 (*m*, 2 H); 5.10 (*dd*, $J = 6.1$, 9.7, 1 H); 6.93 (*d*, $J = 9.0$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 18.77 (Me); 21.33 (Me); 21.70 (Me); 23.07 (Me); 23.23 (Me); 24.88 (CH); 24.97 (CH); 28.29 (3 Me); 32.19 (Me); 37.15 (CH_2); 41.54 (CH_2); 52.32 (Me); 52.63 (CH); 55.35 (CH); 58.07 (CH); 68.00 (CH); 80.34 (C); 155.53 (C); 171.61 (C); 172.45 (C); 172.87 (C). FAB-MS: 496.2 (35, $[M + 23]^+$), 474.2 (66, $[M + 1]^+$), 429.2 (11), 418.2 (19), 374.2 (5), 261.2 (11), 259.1 (14), 215.1 (15), 186.1 (10), 160.1 (100), 130.1 (25), 100.1 (71), 86.0 (45), 74.0 (83), 56.9 (88). GC: 4.95 (D-Thr), 7.72 (MeLeu), 8.59 (Leu).

83b–d: ^{1}H-NMR (200 MHz, $CDCl_3$): 0.85–1.02 (*m*, 12 H); 1.16 (*m*, 3 H); 1.45 (*s*, 9 H); 1.47 (*m*, 2 H); 1.65–1.84 (*m*, 5 H); 3.02, 3.07, 3.08 (3*s*, 3 H); 3.70 (*s*, 3 H); 3.80–4.25 (*m*, 2 H); 4.83–5.13 (*m*, 2 H); 5.30 (*m*, 1 H); 6.91 (*d*, *J* = 9.0, 0.5 H); 7.19 (*m*, 0.5 H). FAB-MS: 496.4 (19, $[M + 23]^+$), 474.4 (34), 430.4 (6), 418.3 (16), 374.3 (7), 261.2 (6), 259.2 (9), 217.2 (6), 215.2 (9), 187.2 (8), 160.2 (100), 130.1 (15), 100.1 (62), 86.0 (32), 74.0 (59), 56.9 (66). GC: 5.07 (Thr), 5.86 (Gly), 7.53 (D-aThr), 7.74 (MeLeu), 7.81 (aThr), 8.53 (Leu).

Boc-Leu-Ser(3-Ph)-MeLeu-OMe (**84**). According to *G.P.5*, with **3** (284 mg, 0.68 mmol), LiBr (335 mg, 3.86 mmol), THF (10 ml), *t*-BuLi (2.73 ml, 3.0 mmol; 70 min), and benzaldehyde (0.69 ml, 6.84 mmol; 3.5 h at −75°). LC (pentane/Et_2O 1:2) gave 339 mg (93%) of **84** (4-diastereoisomers). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.80–0.94 (*m*, 12 H); 1.13 (*m*, 1 H); 1.28–1.71 (*m*, 6 H); 1.35, 1.41, 1.43, *1.44* (4*s*, 9 H); 2.85–3.17 (5*s*, 3 H); 3.63, *3.66*, 3.67 (3*s*, 3 H); 3.97–4.40 (*m*, 1.5 H); 4.77–5.50 (*m*, 4.5 H); 7.00, 7.71, 8.00 (3*m*, 1 H); 7.24–7.41 (*m*, 5 H). FAB-MS: 558.3 (12, $[M + 23]^+$), 536.3 (100, $[M + 1]^+$), 480.2 (10), 462.2 (12), 429.2 (17), 373.2 (5), 215.2 (11), 160.2 (44), 136.1 (40), 100.1 (36), 86.0 (20), 56.9 (51).

*Boc-Leu-*ambo-*Thr(3-Me)-MeLeu-OMe* (**85a**/**85b**). According to *G.P.5*, with **3** (293 mg, 0.71 mmol), LiBr (301 mg, 3.47 mmol), THF (11 ml), *t*-BuLi (2.0 ml, 3.14 mmol; 1 h), and acetone (0.52 ml, 7.07 mmol; 2 h at −75°). LC (pentane/Et_2O 1:3) gave 278 mg (81%) of **85a**/**85b** and 49 mg (16%) of **3**-OMe.

85a/**85b**: ^{1}H-NMR (400 MHz, $CDCl_3$): 0.86–0.97 (*m*, 12 H); 1.18–1.30 (*m*, 6 H); 1.40–1.50 (*m*, 2 H); *1.43*, 1.44 (2*s*, 9 H); 1.56–1.78 (*m*, 4 H); 2.81, 2.91, *3.13*, 3.15 (4*s*, 3 H); 3.69, *3.71* (2*s*, H); 4.16 (*m*, 1 H); 4.44, 4.50 (2*s*, 1 H); 4.75–4.79 (*m*, 1 H); 4.85–4.92 (*m*, 1 H); 5.07, 5.37 (2*m*, 1 H); 6.93, 6.99 (2*d*, *J* = 8.3, 9.5, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 21.22 (Me); 22.04 (Me); 22.85 (Me); 23.06 (Me); 23.33 (Me); 24.68 (CH); 24.74 (CH); 24.88 (CH); 25.71 (Me); 26.90 (Me); 27.04 (Me); 28.28 (3 Me); 29.28 (Me); 31.77 (Me); 36.90 (CH_2); 37.01 (CH_2); 41.49 (CH_2); 52.31 (Me); 53.54 (CH); 53.63 (CH); 54.22 (CH); 69.51 (C); 80.03 (C); 80.30 (C); 155.34 (C); 171.74 (C); 172.65 (C); 173.48 (C). FAB-MS: 510.1 (6, $[M + 23]^+$), 488.1 (52), 432.0 (14), 429.1 (7), 414.1 (8), 273.0 (10), 215.0 (10), 160.0 (100), 130.0 (15), 100.0 (58), 87.9 (47), 85.9 (31), 69.9 (27), 56.8 (50).

*Boc-Val-Leu-*D*-Ala-MeAbu-Ile-OMe* (**86a**), *Boc-Val-Leu-Ala-MeAbu-Ile-OMe* (**86b**), *and Boc-Val-Leu-Gyl-MeAbu-Ile-OMe* (**6**-OMe). According to *G.P.5*, with **6** (247 mg, 0.41 mmol), LiBr (268 mg, 3.09 mmol), THF (6 ml), LDA soln. (9 ml, 2.72 mmol; 50 min), BuLi (1.73 ml, 2.72 mmol), and MeI (0.25 ml, 4.02 mmol; 17 h at −75°). LC (hexane/AcOEt 3:1) gave 46 mg (17%) of **86a**, 39 mg (15%) of **86b**, and 146 mg (58%) of **6**-OMe.

According to *G.P.5*, with **6** (295 mg, 0.49 mmol), LiBr (300 mg, 3.45 mmol), THF (11 ml), *t*-BuLi (2.1 ml, 3.30 mmol; 1 h), and MeI (0.31 ml, 4.98 mmol; 24 h at −75°). LC (hexane/AcOEt 3:1) gave 67 mg (22%) of **86a**, 83 mg (27%) of **86b**, and 123 mg (41%) of **6**-OMe.

According to *G.P.5*, with **6** (328 mg, 0.55 mmol), LiBr (346 mg, 3.98 mmol), THF (11 ml), *t*-BuLi (2.3 ml, 3.61 mmol; 30 min at −75°, then 30 min at −18°, and again −75°), and MeI (0.34 ml, 5.47 mmol; 30 min at −75°, 5.5 h −18°). LC (hexane/AcOEt 3:1) gave 38 mg (11%) of Boc-MeVal-Leu-Ala-MeAbu-Ile-OMe, 165 mg (48%) of **86a**, 79 mg (23%) of **86b**, and 29 mg (9%) of **6**-OMe.

86a: $[\alpha]_D^{r.t.} = -83.1$ (*c* = 1.15, EtOH). ^{1}H-NMR (500 MHz, $CDCl_3$): 0.83–0.98 (*m*, 21 H); 1.14–1.21 (*m*, 1 H); 1.35 (*d*, *J* = 6.9, 3 H); 1.37–1.44 (*m*, 1 H); 1.44 (*s*, 9 H); 1.47–1.57 (*m*, 1 H); 1.59–1.72 (*m*, 3 H); 1.92 (br. *m*, 1 H); 2.01–2.10 (*m*, 1 H); 2.13 (*m*, 1 H); 3.02 (*s*, 3 H); 3.73 (*s*, 3 H); 3.94 (*m*, 1 H); 4.50–4.56 (*m*, 2 H); 4.77 (*m*, 1 H); 5.01 (*dd*, *J* = 10.0, 5.7, 1 H); 5.06 (*d*, *J* = 7.8, 1 H); 6.69 (*d*, *J* = 7.2, 1 H); 6.84 (*d*, *J* = 8.3, 1 H); 7.02 (*d*, *J* = 6.2, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.3 (Me); 11.4 (Me); 15.6 (Me); 17.6 (Me); 17.8 (Me); 19.4 (Me); 20.7 (CH_2); 21.9 (Me); 23.0 (Me); 24.7 (CH); 25.3 (CH_2); 28.3 (3 Me); 30.7 (Me); 30.7 (CH); 37.5 (CH); 41.2 (CH_2); 46.0 (CH); 51.3 (CH); 52.1 (Me); 56.5 (CH); 58.4 (CH); 60.2 (CH); 80.1 (C); 156.1 (C); 170.2 (C); 171.7 (C); 172.5 (C); 174.0 (C). FAB-MS: 650.2 (54, $[M + 23]^+$), 628.2 (22, $[M + 1]^+$), 528.2 (7), 483.2 (49), 427.2 (57), 384.2 (16), 328.1 (11), 257.1 (26), 245.2 (48), 154.0 (21), 136.0 (16), 86.0 (79), 72.0 (100), 56.9 (62). GC: 3.56 (D-Ala), 5.14 (Val), 5.46 (MeAbu), 7.03 (Ile), 8.56 (Leu).

86b: $[\alpha]_D^{r.t.} = -103.7$ (*c* = 1.17, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; 2 conformations): 0.82–0.98 (*m*, 21 H); 1.06–1.16 (*m*, 1 H); 1.28 (*d*, *J* = 6.8, 3 H); 1.30–1.39 (*m*, 1 H); 1.44 (*m*, 9 H); 1.55 (*t*, *J* = 7.1, 2 H); 1.66 (*m*, 2 H); 1.84–1.98 (*m*, 2 H); 2.00–2.14 (*m*, 1 H); 2.79, 3.05, *3.09* (3*s*, 3 H); 3.73 (*s*, 3 H); 3.95 (br. *m*, 1 H); 4.55 (*dd*, *J* = 8.9, 5.2, 1 H); 4.71 (*m*, 1 H); 4.82 (*m*, 0.3 H); 4.99 (*m*, 0.7 H); 5.14 (*t*, *J* = 7.8, 1 H); 5.43 (*d*, *J* = 8.8, 1 H); 6.51, *6.64* (2*d*, *J* = 8.3, 1 H); 7.30 (br. *m*, 1 H); 7.77, *8.00* (2*d*, *J* = 8.3, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.3 (Me); 11.4 (Me); 15.4 (Me); 18.0 (Me); 18.5 (Me); 19.2 (Me); 21.4 (CH_2); 21.9 (Me); 23.0 (Me); 24.6 (CH); 24.9 (CH_2); 28.3 (3 Me); 30.5 (Me); 31.0 (CH); 37.4 (CH); 41.5 (CH_2); 45.4 (CH); 51.4 (CH); 52.1 (Me); 56.2 (CH); 57.5 (CH); 59.9 (CH); 79.6 (C); 155.9 (C); 170.6 (C); 171.3 (C); 171.8 (C); 172.3 (C); 173.2 (C). FAB-MS: 650.4 (23, $[M + 23]^+$), 628.4 (15, $[M + 1]^+$), 483.3 (93), 427.3 (50), 384.2 (20), 328.2 (12), 257.2 (29), 245.2 (34), 154.1 (34), 136.1 (28), 86.1 (76), 72.0 (100), 56.9 (52). GC: 3.81 (Ala), 5.15 (Val), 5.47 (MeAbu), 7.05 (Ile), 8.59 (Leu).

6-OMe: $[\alpha]_D^{r.t.} = -90.8$ (*c* = 1.01, EtOH). ^{1}H-NMR (500 MHz, $CDCl_3$): 0.84–0.95 (*m*, 21 H); 1.14 (*m*, 1 H); 1.37 (*m*, 1 H); 1.44 (*s*, 9 H); 1.55–1.72 (*m*, 4 H); 1.85 (*m*, 1 H); 1.94 (*m*, 1 H); 2.09 (*m*, 1 H); 2.98, *3.01* (2*s*, 3 H); 3.73,

3.74 (2*s*, 3 H); 3.95, 4.29 (*ABX*, J_{AB} = 17.7, J_{AX} = 2.8, J_{BX} = 5.5, 2 H); 3.99 (*m*, 1 H); 4.52 (*dd*, *J* = 5.2, 8.6, 1 H); 4.74 (*m*, 1 H); 5.12 (*dd*, *J* = 6.8, 8.9, 1 H); 5.30 (*d*, *J* = 3.2, 1 H); 6.79 (*d*, *J* = 7.4, 1 H); 7.12 (*d*, *J* = 8.1, 1 H); 7.52 (*m*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 10.53 (Me); 11.53 (Me); 15.53 (Me); 17.89 (Me); 19.37 (Me); 21.89 (CH_2); 21.89 (Me); 23.04 (Me); 24.68 (CH); 25.25 (CH_2); 28.33 (3 Me); 29.87 (Me); 30.99 (CH); 37.60 (CH); 41.69 (CH_2); 41.90 (CH_2); 51.42 (CH); 52.10 (Me); 56.30 (CH); 57.82 (CH); 59.92 (CH); 79.73 (C); 155.95 (C); 169.20 (C); 170.70 (C); 171.85 (C); 172.30 (C). FAB-MS: 636.2 (49, $[M + 23]^+$), 614.2 (11, $[M + 1]^+$), 514.2 (5), 497.1 (9), 469.1 (83), 413.1 (91), 370.1 (10), 369.1 (10), 314.0 (14), 270.0 (8), 257.0 (17), 245.1 (26), 157.0 (24), 116.0 (15), 86.0 (69), 71.9 (100), 56.9 (60).

*Boc-Val-Leu-*D*-Abu-MeAbu-Ile-OMe* (**87a**) *and Boc-Val-Leu-Abu-MeAbu-Ile-OMe* (**87b**). According to *G.P.5*, with **6** (262 mg, 0.44 mmol), LiBr (278 mg, 3.20 mmol), THF (8 ml), *t*-BuLi (1.75 ml, 2.75 mmol; 1 h), and EtI (0.35 ml, 4.33 mmol; 13 h at −75°). LC (pentane/Et_2O 1:9) gave 18 mg (6%) of **87a**, 69 mg (25%) of **87b**, and 93 mg (35%) of **6**-OMe.

According *G.P.5*, with **6** (302 mg, 0.50 mmol), LiBr (355 mg, 4.09 mmol), THF (9 ml), *t*-BuLi (2.1 ml, 3.3 mmol; 1 h), and EtI (0.41 ml, 5.07 mmol; 30 min at −75°, 7.5 h at −18°). LC (hexane/AcOEt 1:1) gave 50 mg (15.5%) of **87a**, 101 mg (31%) of **87b**, and 128 mg (41%) of **6**-OMe.

87a: $[\alpha]_D^{r.t.}$ = −85.8 (*c* = 1.03, EtOH). ^{1}H-NMR (500 MHz, $CDCl_3$): 0.85–0.97 (*m*, 24 H); 1.13–1.25 (*m*, 1 H), 1.44 (*s*, 9 H); 1.51 (*m*, 1 H); 1.60–1.72 (*m*, 4 H); 1.81–1.86 (*m*, 1 H); 1.95 (*m*, 2 H); 2.10 (*m*, 2 H); 2.89, *3.05* (2*s*, 3 H); 3.74 (*s*, 3 H); 3.95 (*m*, 1 H); 4.53 (*m*, 2 H); 4.68 (*dd*, *J* = 6.7, 13.5, 1 H); 5.04 (*m*, 2 H); 6.73 (*d*, *J* = 7.9, 1 H); 6.85 (*d*, *J* = 6.6, 1 H); 6.91 (*d*, *J* = 8.6, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 9.51 (Me); 9.78 (Me); 10.47 (Me); 11.38 (Me); 15.54 (Me); 19.45 (Me); 20.62 (CH_2); 21.91 (Me); 22.98 (Me); 24.74 (CH); 25.05 (CH_2); 25.36 (CH_2); 28.31 (3 Me); 30.71 (Me); 30.83 (CH); 37.47 (CH); 41.02 (CH_2); 51.19 (CH); 51.33 (CH); 52.15 (Me); 56.50 (CH); 58.56 (CH); 60.18 (CH); 79.98 (C); 156.03 (C); 170.16 (C); 171.84 (C); 172.13 (C); 172.68 (C); 173.46 (C). FAB-MS: 664.2 (52, $[M + 23]^+$), 642.2 (30, $[M + 1]^+$), 542.2 (8), 497.1 (69), 441.1 (70), 398.1 (27), 342.1 (13), 313.1 (9), 257.1 (32), 245.1 (58), 154.0 (28), 136.0 (21), 116.0 (19), 86.0 (82), 72.0 (100), 56.9 (77). GC: 4.71 (D-Abu), 5.18 (Val), 5.48 (MeAbu), 7.11 (Ile), 8.67 (Leu).

87b: $[\alpha]_D^{r.t.}$ = −104.9 (*c* = 1.03, EtOH). ^{1}H-NMR (500 MHz, $CDCl_3$; 2 conformations): 0.83–0.96 (*m*, 24 H); 1.06 (*m*, 1 H); 1.35 (*m*, 1 H); *1.43*, 1.44 (*s*, 9 H); 1.52–1.70 (*m*, 5 H); 1.74 (*m*, 1 H); 1.86 (*m*, 1 H); 1.93 (*m*, 1 H); 2.07 (*m*, 1 H); 2.80, 3.08, *3.14* (3*s*, 3 H); 3.73 (*s*, 3 H); 3.94 (*m*, 1 H); 4.56 (*dd*, *J* = 5.5, 8.9, 1 H); 4.82 (*dd*, *J* = 7.7, 15.0, 1 H); 5.01 (*m*, 1 H); 5.15 (*t*, *J* = 7.8, 1 H); 5.58 (br. *d*, *J* = 8.2, 1 H); 6.60 (*d*, *J* = 7.8, 1 H); 7.56 (br. *m*, 1 H); 7.98 (br. *m*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 9.68 (Me); 10.34 (Me); 10.46 (Me); 11.31 (Me); 15.42 (Me); 18.14 (Me); 19.22 (Me); 21.84 (CH_2); 22.14 (Me); 22.97 (Me); 24.99 (CH); 26.12 (CH_2); 28.33 (3 Me); 30.81 (Me); 31.12 (CH); 37.44 (CH); 41.74 (CH_2); 50.11 (CH); 51.42 (CH); 52.02 (Me); 56.18 (CH); 57.07 (CH); 59.99 (CH); 61.36 (CH); 79.35 (C); 155.96 (C); 171.25 (C); 171.80 (C); 171.96 (C); 172.56 (C); 172.69 (C). FAB-MS: 664.2 (7, $[M + 23]^+$), 640.2 (5, $[M + 1]^+$), 497.1 (100), 441.1 (46), 398.1 (18), 342.1 (7), 313.1 (6), 257.1 (26), 245.1 (29), 154.0 (9), 116.0 (15), 86.0 (66), 72.0 (78), 56.9 (61). GC: 5.18 (Abu), 5.35 (Val), 5.62 (MeAbu), 7.23 (Ile), 8.69 (Leu).

*Boc-Val-Leu-*D*-Val-MeAbu-Ile-OMe* (**88a**) *and Boc-Val-Leu-Val-MeAbu-Ile-OMe* (**88b**). According to *G.P.5*, with **6** (340 mg, 0.57 mmol), LiBr (355 mg 4.09 mmol), THF (13 ml), *t*-BuLi (2.4 ml, 3.77 mmol; 45 min), and i-PrI (0.57, 5.70 mmol; 45 min at 75°, 7 h at −18°). LC (hexane/AcOEt 3:1) gave 22 mg (6%) of **88a**, 19 mg (5%) of **88b**, and 277 mg (81%) of **6**-OMe.

88a: $[\alpha]_D^{r.t.}$ = −81.0 (*c* = 1.0, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.85–1.01 (*m*, 27 H); 1.24 (*m*, 1 H); *1.43*, 1.44 (2*s*, 9 H); 1.51 (*m*, 1 H); 1.60–1.71 (*m*, 3 H); 1.95–2.19 (*m*, 5 H); 3.07 (*s*, 3 H); 3.74 (*s*, 3 H); 3.97 (*dd*, *J* = 6.3, 8.6, 1 H); 4.46 (*m*, 1 H); 4.52–4.60 (*m*, 2 H); 5.05–5.10 (*m*, 2 H); 6.90 (*d*, *J* = 6.7, 1 H); 6.95 (*d*, *J* = 8.1, 1 H); 7.01 (*d*, *J* = 8.6, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.64 (Me); 11.30 (Me); 15.51 (Me); 17.76 (Me); 18.68 (Me); 19.34 (Me); 19.48 (Me); 20.68 (CH_2); 21.93 (Me); 22.95 (Me); 24.70 (CH); 25.43 (CH_2); 28.30 (3 Me); 30.49 (CH); 30.79 (CH); 31.08 (Me); 37.41 (CH); 40.73 (CH_2); 51.03 (CH); 52.22 (Me); 55.84 (CH); 56.50 (CH); 58.62 (CH); 60.04 (CH); 79.82 (C); 155.95 (C); 170.18 (C); 172.08 (C); 172.68 (C); 173.03 (C); 173.64 (C). FAB-MS: 678.2 (18, $[M + 23]^+$), 656.3 (4, $[M + 1]^+$), 511.2 (24), 455.2 (31), 412.2 (10), 356.1 (5), 257.1 (16), 245.1 (48), 116.0 (8), 86.0 (57), 71.9 (100), 56.9 (33). GC: 5.14 (D-Val), 5.39 (Val), 5.67 (MeAbu), 7.30 (Ile), 8.83 (Leu).

88b: $[\alpha]_D^{r.t.}$ = −93.8 (*c* = 0.95, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; several conformations): 0.82–0.97 (*m*, 27 H); 1.14 (*m*, 1 H); 1.36 (*m*, 1 H); *1.43*, 1.44 (2*s*, 9 H); 1.51–1.65 (*m*, 4 H); 1.83–1.96 (*m*, 3 H); 2.05 (*m*, 1 H); 2.81, *3.15* (2*s*, 3 H); *3.73*, 3.75 (2*s*, 3 H); 3.87 (*m*, 1 H); 4.57 (*dd*, *J* = 5.4, 8.8, 1 H); 4.75 (*m*, 1 H); 4.87 (*m*, 1 H); 5.22 (*m*, 1 H); 5.54 (*m*, 1 H); 6.42 (*m*, 1 H); 7.37 (*m*, 1 H); 7.73 (*m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.24 (Me); 11.43 (Me); 15.44 (Me); 17.74 (Me); 18.12 (Me); 19.24 (Me); 19.39 (Me); 21.89 (CH_2); 22.13 (Me); 22.95 (Me); 24.64 (CH); 25.00 (CH_2); 28.32 (3 Me); 30.88 (CH); 31.01 (Me); 31.52 (CH); 37.55 (CH); 41.53 (CH_2); 51.53 (CH); 52.09 (Me); 53.94 (CH); 56.24 (CH); 57.27 (CH); 60.21 (CH); 79.58 (C); 155.97 (C); 171.00 (C); 171.67 (C); 171.97 (C); 172.47

(C); 172.75 (C). FAB-MS: 678.2 (1, $[M + 23]^+$), 656.3 (1, $[M + 1]^+$), 654.3 (1), 511.3 (83), 455.2 (23), 412.2 (8), 257.1 (19), 245.1 (18), 116.0 (8), 86.0 (56), 71.9 (100), 56.9 (33). GC: 5.36 (Val), 6.04 (MeAbu), 7.27 (Ile), 8.80 (Leu).

Boc-Val-Leu-D-Nva(4,5-didehydro)-MeAbu-Ile-OMe (**89a**) *and Boc-Val-Leu-Nva(4,5-didehydro)-MeAbu-Ile-OMe* (**89b**). According to *G.P. 5*, with **6** (238 mg, 0.40 mmol), LiBr (402 mg, 4.63 mmol), THF (8.5 ml), *t*-BuLi (1.88 ml, 2.48 mmol; 1 h), and allyl bromide (0.34 ml, 3.97 mmol; 19 h at −75°). LC (hexane/AcOEt 4:1) gave 57 mg (22%) of **89a**, 65 mg (25%) of **89b**, and 96 mg (39%) of **6**-OMe.

89a: $[\alpha]_D^{rt} = -28.3$ ($c = 1.37$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.83–0.97 (*m*, 21 H); 1.15–1.28 (*m*, 1 H); 1.44 (*s*, 9 H); 1.45–1.55 (*m*, 1 H); 1.57–1.71 (*m*, 4 H); 1.89–2.00 (*m*, 1 H); 2.05–2.16 (*m*, 2 H); 2.43 (*m*, 1 H); 2.55 (*m*, 1 H); 3.04 (*s*, 3 H); 3.74 (*s*, 3 H); 3.96 (*m*, 1 H); 4.50–4.59 (*m*, 2 H); 4.78 (*q*, $J = 6.7$, 1 H); 5.04 (*dd*, $J = 5.4$, 10.4, 1 H); 5.10–5.20 (*m*, 3 H); 5.72 (*m*, 1 H); 6.86 (*d*, $J = 8.2$, 1 H); 6.99 (*d*, $J = 8.1$, 2 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.5 (Me); 11.4 (Me); 15.5 (Me); 17.8 (Me); 19.4 (Me); 20.7 (CH_2); 21.9 (Me); 23.0 (Me); 24.7 (CH); 25.4 (CH_2); 28.3 (3 Me); 30.7 (Me); 30.8 (CH); 36.1 (CH_2); 37.4 (CH); 41.1 (CH_2); 49.8 (CH); 51.1 (CH); 52.2 (Me); 56.5 (CH); 58.5 (CH); 60.1 (CH); 79.9 (C); 119.5 (CH_2); 132.0 (CH); 156.0 (C); 170.2 (C); 171.8 (C); 172.1 (C); 172.7 (C); 172.9 (C). FAB-MS: 676.2 (80, $[M + 23]^+$), 654.2 (29, $[M + 1]^+$), 554.2 (10), 509.2 (64), 453.1 (80), 410.1 (22), 354.0 (10), 313.1 (12), 300.1 (7), 283.0 (7), 257.0 (38), 245.1 (68), 154.0 (23), 136.0 (16), 116.0 (19), 86.0 (93), 71.9 (100), 56.9 (61). GC: 5.15 (Val), 5.48 (MeAbu), 6.55 (D-Nva), 7.05 (Ile), 8.56 (Leu).

89b: $[\alpha]_D^{rt} = -41.1$ ($c = 1.34$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; 2 conformations): 0.83–0.97 (*m*, 21 H); 1.09–1.18 (*m*, 1 H); 1.34–1.41 (*m*, 1 H); 1.44 (*s*, 9 H); 1.51–1.59 (*m*, 2 H); 1.59–1.70 (*m*, 2 H); 1.82–1.89 (*m*, 1 H); 1.89–1.98 (*m*, 1 H); 2.03–2.14 (*m*, 1 H); 2.29–2.37 (*m*, 1 H); 2.43 (*m*, 1 H); 2.79, *3.13* (2*s*, 3 H); 3.74 (*s*, 3 H); 3.91 (*m*, H); 4.56 (*dd*, $J = 5.4$, 8.8, 1 H); 4.75 (*m*, 1 H); 5.00–5.15 (*m*, 3 H); 5.21 (*t*-$J = 7.9$, 1 H); 5.49 (*d*, $J = 8.0$, 1 H); 5.00–5.15 (*m*, 3 H); 5.21 (*t*, $J = 7.9$, 1 H); 5.49 (*d*, $J = 8.0$, 1 H); 5.71 (*m*, 1 H); 6.48, *6.54* (2*d*, $J = 8.0$, 1 H); 7.39 (br. *s*, 1 H); 7.83 (br. *s*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.3 (Me); 11.4 (Me); 15.5 (Me); 18.1 (Me); 19.3 (Me); 21.9 (CH_2); 22.1 (Me); 23.0 (Me); 24.6 (CH); 25.1 (CH_2); 28.3 (3 Me); 30.9 (Me); 30.9 (CH); 37.3 (CH_2); 37.6 (CH); 41.7 (CH_2); 48.8 (CH); 51.4 (CH); 52.1 (Me); 56.2 (CH); 57.4 (CH); 60.2 (CH); 79.6 (C); 118.8 (CH_2); 132.4 (CH); 156.0 (C); 170.9 (C); 171.6 (C); 172.1 (C); 172.5 (C). FAB-MS: 676.2 (5, $[M + 23]^+$), 654.2 (5, $[M + 1]^+$), 652.2 (4), 509.2 (100), 453.1 (45), 410.1 (13), 354.0 (6), 313.1 (5), 257.0 (26), 245.1 (26), 154.0 (8), 136.0 (5), 116.0 (13), 86.0 (60), 71.9 (66), 56.9 (39). GC: 5.31 (Val), 5.63 (MeAbu), 7.19 (Nva), 7.23 (Ile), 8.70 (Leu).

Boc-Val-Leu-D-Phe-MeAbu-Ile-OMe (**90a**) *and Boc-Val-Leu-Phe-MeAbu-Ile-OMe* (**90b**). According to *G.P. 5*, with **6** (240 mg, 0.40 mmol), LiBr (436 mg, 5.02 mmol), THF (9 ml), *t*-BuLi (1.9 ml, 2.51 mmol; 1 h), and benzyl bromide (0.47 ml, 4.00 mmol; 20 h at −75°). LC (hexane/AcOEt 3:1) gave 49 mg (17%) of **90a**, 74 mg (27%) of **90b**, and 111 mg (45%) of **6**-OMe.

According to *G.P. 5*, with **6** (342 mg, 0.57 mmol), LiBr (387 mg, 4.46 mmol), THF (12 ml), *t*-BuLi (2.4 ml, 3.77 mmol; 1 h), and benzyl bromide (0.67 ml, 5.66 mmol; 30 min at −75°, 7 h at −18°). LC (hexane/AcOEt 4:1) gave 127 mg (32%) of **90a**, 99 mg (25%) of **90b**, and 126 mg (36%) of **6**-OMe.

90a: $[\alpha]_D^{rt} = -48.6$ ($c = 0.85$, EtOH). ^{1}H-NMR (500 MHz, $CDCl_3$): 0.57 (*t*, $J = 7.4$, 3 H); 0.82–0.98 (*m*, 18 H); 1.14–1.24 (*m*, 1 H); 1.29–1.37 (*m*, 1 H); 1.45 (*s*, 9 H); 1.40–1.50 (*m*, 2 H); 1.55–1.61 (*m*, 1 H); 1.61–1.69 (*m*, 1 H); 1.90–2.04 (2*m*, 2 H); 2.11 (*m*, 1 H); 2.70 (*s*, 3 H); 3.00–3.08 (*m*, 2 H); 3.73 (*s*, 3 H); 3.96 (*dd*, $J = 6.2$, 8.1, 1 H); 4.49 (*dd*, $J = 6.3$, 8.6, 1 H); 4.53 (*m*, 1 H); 4.90–4.96 (*m*, 2 H); 5.06 (*d*, $J = 7.8$, 1 H); 6.81 (*d*, $J = 7.9$, 1 H); 6.96–6.98 (*m*, 2 H); 7.20–7.29 (*m*, 5 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 10.4 (Me); 11.3 (Me); 15.5 (Me); 17.8 (Me); 19.5 (Me); 20.6 (CH_2); 21.9 (Me); 22.9 (Me); 24.7 (CH); 25.4 (CH_2); 28.3 (3 Me); 30.6 (Me); 30.7 (CH); 37.3 (CH); 38.1 (CH_2); 40.7 (CH_2); 51.0 (CH); 51.6 (CH); 52.1 (Me); 56.5 (CH); 58.6 (CH); 60.2 (CH); 80.0 (C); 127.3 (CH); 128.7 (CH); 129.4 (CH); 135.7 (C); 156.1 (C); 170.1 (C); 171.9 (C); 172.2 (C); 172.8 (C); 172.9 (C). FAB-MS: 726.2 (94, $[M + 23]^+$), 704.2 (21, $[M + 1]^+$), 626.2 (5), 604.2 (6), 559.2 (75), 503.1 (79), 460.1 (18), 404.1 (5), 257.1 (13), 245.2 (48), 154.1 (22), 120.1 (88), 86.0 (88), 72.0 (96), 56.9 (100). GC: 5.07 (Val), 5.39 (MeAbu), 6.97 (Ile), 8.49 (Leu), 18.39 (D-Phe).

90b: $[\alpha]_D^{rt} = -32.3$ ($c = 1.76$, EtOH). ^{1}H-NMR (500 MHz, $CDCl_3$; 2 conformations): 0.65 (*t*, $J = 7.4$, 1 H); 0.81–0.97 (*m*, 20 H); 1.12–1.25 (*m*, 1 H); 1.45 (*s*, 9 H); 1.36–1.50 (*m*, 2 H); 1.50–1.58 (*m*, 2 H); 1.58–1.68 (*m*, 1 H); 1.75–1.82 (*m*, 0.3 H); 1.83–1.94 (*m*, 1.7 H); 2.08–2.18 (*m*, 1 H); *2.88*, 2.70 (2*s*, 3 H); 2.84–2.88 (*m*, 0.7 H); 2.92–2.97 (*m*, 0.3 H); 3.06 (*dd*, $J = 7.2$, 13.6, 0.7 H); 3.18 (*dd*, $J = 8.8$, 13.1, 0.3 H); 3.72, *3.74* (2*s*, 3 H); 3.87 (*m*, 1 H); 4.43–4.48 (*m*, 0.5 H); 4.53 (*m*, 0.5 H); 4.53, 4.62 (2*m*, 1 H); 4.96 (*m*, 0.3 H); 5.06 (*t*, $J = 7.9$, 0.7 H); 5.12 (*m*, 0.3 H); 5.18 (*m*, 0.7 H); 5.23 (*m*, 11 H); 6.40 (*m*, 1 H); 6.98 (*d*, $J = 8.3$, 1 H); 7.14–7.31 (*m*, 5 H); 7.43, 7.91 (2*d*, $J = 7.7$, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 10.3 (Me); 11.5 (Me); 15.5 (Me); 18.0 (Me); 19.4 (Me); 21.7 (CH_2); 22.1 (Me); 22.9 (Me); 24.6 (CH); 25.3 (CH_2); 28.3 (3 Me); 30.7 (Me); 30.7 (CH); 37.6 (CH); 39.1 (CH_2); 41.7 (CH_2); 50.5 (CH); 51.5 (CH); 52.1 (Me); 56.4 (CH); 58.0 (CH); 61.6 (CH); 79.9 (C); 127.0 (CH); 128.6 (CH); 129.2 (CH); 136.1 (C); 156.0 (C); 168.8 (C); 170.4 (C); 171.3 (C); 172.3 (C); 172.4 (C). FAB-MS: 726.2 (26, $[M + 23]^+$), 559.1 (100), 503.1

(37), 460.1 (8), 257.1 (6), 245.1 (13), 154.0 (10), 120.0 (38), 86.0 (36), 72.0 (39), 56.9 (56). GC: 5.08 (Val), 5.40 (MeAbu), 6.96 (Ile), 8.46 (Leu), 18.65 (Phe).

Boc-Val-Leu-D-Asp(OEt)-MeAbu-Ile-OMe (**91a**) *and Boc-Val-Leu-Asp(OEt)-MeAbu-Ile-OMe* (**91b**). According to *G.P. 5*, with **6** (296 mg, 0.49 mmol), LiBr (351 mg, 4.04 mmol), THF (10 ml), *t*-BuLi (2.05 ml, 3.22 mmol; 1 h) and ethyl bromoacetate (0.54 ml, 4.89 mmol; 16 h at −75°). LC (hexane/AcOEt 3.5:1) gave 51 mg (15%) of **91a**, 114 mg (33%) of **91b**, and 133 mg (44%) of **6**-OMe.

91a: $[\alpha]_D^{r.t.} = -67.3$ ($c = 1.02$, EtOH). ^{1}H-NMR (500 MHz, $CDCl_3$; 3 conformations): 0.77–0.97 (*m*, 21 H); 1.13 (*s*, 1 H); 1.24 (*t*, $J = 7.1$, 3 H); 1.27 (*m*, 1 H); 1.42, *1.43*, 1.44, 145 (4*s*, 9 H); 1.50 (*m*, 1 H); 1.59–1.72 (*m*, 3 H); 1.94 (*m*, 1 H); 2.06–2.18 (*m*, 2 H); 2.65–2.70 (*m*, 1 H); 2.80, 3.03, 3.08, *3.16* (4*s*, 3 H); *2.96*, 3.31 (2*m*, 1 H); 3.68, 3.69, 3.71, *3.75* (4*s*, 3 H); 3.84–3.89 (*m*, 0.5 H); 3.93 (*m*, 0.5 H); 4.12 (*q*, $J = 7.1$, 2 H); 4.17 (*m*, 0.3 H); 4.44–4.62 (*m*, 2 H); 5.02–5.10 (*m*, 2 H); 5.26, 5.37 (2*m*, 0.7 H); 6.33, 6.34 (2*d*, $J = 7.9$, 6.8, 0.4 H); 6.75 (*m*, 0.3 H); 6.86–6.92 (*m*, 1 H); 6.97–7.08 (*m*, 1 H); 7.68 (*d*, $J = 8.4$, 0.3 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 10.21 (Me); 11.38 (Me); 14.11 (Me); 15.49 (Me); 17.80 (Me); 19.46 (Me); 20.76 (CH_2); 21.86 (Me); 22.95 (Me); 24.70 (CH); 25.47 (CH_2); 26.40 (Me); 28.31 (3 Me); 30.91 (CH); 31.06 (Me); 36.55 (CH_2); 37.66 (CH); 40.36 (CH_2); 46.40 (CH); 51.02 (CH); 52.26 (Me); 56.51 (CH); 58.93 (CH); 60.27 (CH); 61.05 (CH_2); 80.06 (C); 156.08 (C); 170.22 (C); 171.16 (C); 172.06 (C); 172.30 (C); 172.36 (C); 173.13 (C). FAB-MS: 722.2 (16, $[M + 23]^+$), 700.2 (17, $[M + 1]^+$), 641.1 (52), 585.1 (10), 567.2 (86), 555.1 (68), 511.1 (19), 499.1 (74), 456.1 (16), 400.1 (9), 257.0 (24), 245.1 (47), 136.0 (20), 116.0 (48), 86.0 (93), 71.9 (100), 56.9 (79). GC: 5.23 (Val), 5.55 (MeAbu), 7.17 (Ile), 8.65 (Leu), 14.31 (D-Asp).

91b: $[\alpha]_D^{r.t.} = -112.4$ ($c = 1.0$, EtOH). ^{1}H-NMR (500 MHz, $CDCl_3$; 2 conformations): 0.82 (*t*, $J = 7.4$, 3 H); 0.87–0.97 (*m*, 18 H); 1.21 (*m*, 1 H); 1.24 (*t*, $J = 7.2$, 3 H); 1.41–1.52 (*m*, 1 H); 1.44 (*s*, 9 H); 1.57–1.69 (*m*, 3 H); 1.88–1.95 (*m*, 2 H); 2.04–2.14 (*m*, 2 H); 2.59, 3.02 (*ABX*, $J_{AB} = 16.6$, $J_{AX} = 4.4$, $J_{BX} = 9.9$, 2 H); 2.80, *3.07* (2*s*, 3 H); *3.69*, 3.76 (2*s*, 3 H); 3.88 (*m*, 1 H); 4.11 (*m*, 2 H); 4.50 (*m*, 2 H); 5.08 (*dd*, $J = 5.7$, 10.0, 1 H); 5.31 (*m*, 2 H); 6.46 (br. *m*, 1 H); 6.83 (*d*, $J = 8.4$, 1 H); 7.28 (br. *m*, 1 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 10.05 (Me); 11.42 (Me); 14.09 (Me); 15.52 (Me); 18.05 (Me); 19.34 (Me); 20.68 (CH_2); 22.08 (Me); 22.72 (Me); 24.77 (CH); 25.15 (CH_2); 28.32 (3 Me); 30.63 (CH); 30.94 (Me); 37.01 (CH_2); 37.18 (CH); 41.24 (CH_2); 45.38 (CH); 51.59 (CH); 51.88 (Me); 56.80 (CH); 58.35 (CH); 60.36 (CH); 61.07 (CH_2); 80.13 (C); 156.12 (C); 170.36 (C), 171.14 (C); 171.36 (C); 171.76 (C); 172.08 (C); 172.18 (C). FAB-MS: 722.2 (15, $[M + 23]^+$), 555.2 (100), 499.1 (46), 456.1 (9), 400.1 (7), 257.0 (22), 245.1 (21), 116.0 (44), 86.0 (67), 71.9 (71.0), 56.9 (49). GC: 5.18 (Val), 5.51 (MeAbu), 7.08 (Ile), 14.19 (Asp).

*Boc-Val-Leu-*ambo*-Gly(2-CO$_2$Me)-MeAbu-Ile-OMe* (**92a**/**92b**). According to *G.P. 5*, with **6** (291 mg, 0.485 mmol), LiBr (310 mg, 3.57 mmol), THF (10 ml), *t*-BuLi (2.1 ml, 3.23 mmol; 1.5 h) and a stream of CO_2 gas which was passed over the mixture for 30 min (30 min at −75°). Workup, esterification with diazomethane, and chromatographic purification (hexane/AcOEt 3:2) gave 97 mg (30%) of **92a**/**92b** and 85.5 mg (29%) of **6**-OMe.

92a/**92b**. $[\alpha]_D^{r.t.} = -57.7$ ($c = 0.74$, EtOH). ^{1}H-NMR (500 MHz, $CDCl_3$): 0.84–0.98 (*m*, 21 H); 1.23 (*m*, 1 H); *1.42*, 1.438, 1.443 (3*s*, 9 H); 1.45 (*m*, 1 H); 1.55 (*m*, 1 H); 1.63–1.73 (*m*, 3 H); 1.94 (*m*, 1 H); 2.05–2.16 (*m*, 2 H); 2.86, 3.12, *3.17* (3*s*, 3 H); 3.72, 3.74, *3.75* (3*s*, 3 H); 3.76, *3.79*, 380 (3*s*, 3 H); 3.88, *3.98* (2*m*, 1 H); 4.56 (*m*, 1 H); 4.59–4.66 (*m*, 1 H); 5.03 (*dd*, $J = 5.1$, 10.7, 1 H); 5.10 (*d*, $J = 8.5$, 1 H); *5.41*, 5.59, 5.75 (3*d*, $J = 6.0$, 7.6, 7.7, 1 H); 6.35, *6.75* (2*d*, $J = 7.6$, 1 H); 6.58, *6.88* (2*d*, $J = 8.8$, 8.6, 1 H); 7.34 (*m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 9.98 (Me); 11.44 (Me); 15.58 (Me); 17.84 (Me); 19.39 (Me); 20.81 (CH_2); 22.06 (Me); 22.89 (Me); 24.61 (CH); 25.32 (CH_2); 28.29 (3 Me); 30.97 (Me); 31.44 (CH); 37.59 (CH); 41.01 (CH_2); 50.99 (CH); 52.26 (Me); 53.34 (Me); 53.67 (CH); 56.54 (CH); 58.99 (CH); 59.85 (CH); 79.68 (C); 155.83 (C); 166.46 (C); 167.42 (C); 169.78 (C); 171.75 (C); 172.04 (C); 172.35 (C); 172.64 (C). FAB-MS: 694.2 (58, $[M + 23]^+$), 672.2 (13, $[M + 1]^+$), 572.2 (38), 527.1 (42), 471 (100), 427.1 (6), 372.0 (6), 372.0 (6), 328.1 (8), 257.0 (7), 245.1 (14), 215.0 (20), 187.0 (10), 136.0 (9), 116.0 (16), 86.0 (68), 71.9 (89), 56.9 (84).

Boc-Val-Leu-D-Gly(2-SMe)-MeAbu-Ile-OMe (**93a**) *and Boc-Val-Leu-Gly(2-SMe)-MeAbu-Ile-OMe* (**93b**). According to *G.P. 5*, with **6** (269 mg, 0.45 mmol), LiBr (279 mg, 3.21 mmol), THF (8 ml) *t*-BuLi (1.8 ml, 2.86 mmol; 1 h), and Me_2S_2 (0.4 ml, 4.51 mmol; 30 min at −75°, 7.5 h at −18°). LC (pentane/Et_2O 1:4) gave 59 mg (20%) of **93a**, 84 mg (28%) of **93b**, and 106 mg (39%) of **6**-OMe.

93a: $[\alpha]_D^{r.t.} = -133.1$ ($c = 1.0$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; 2 conformations): 0.84–0.98 (*m*, 21 H); 1.15 (*m*, 1 H); 1.37 (*m*, 1 H); 1.44 (*s*, 9 H); 1.59 (*m*, 1 H); 1.68–1.79 (*m*, 3 H); 1.86 (*m*, 1 H); 1.97–2.17 (*m*, 2 H); *2.08*, 2.17 (2*s*, 3 H); 2.85, *3.08* (2*s*, 3 H); 3.73, *3.74* (2*s*, 3 H); 3.78–4.01 (*m*, 1 H); 4.39 (*m*, 0.4 H); 4.54–4.65 (*m*, 2 H); 5.07–5.15 (*m*, 1.6 H); 5.69, 5.86 (2*d*, $J = 7.5$, 1 H); 6.67 (*d*, $J = 8.0$, 0.3 H); 6.84 (*m*, 1.3 H); 7.30 (*d*, $J = 8.5$, 0.3 H); 7.46 (*d*, $J = 7.3$, 0.7 H); 7.61 (*d*, $J = 7.3$, 0.3 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.00 (Me); 11.45 (Me); 11.71 (Me); 15.89 (Me); 17.71 (Me); 19.49 (Me); 21.49 (CH_2); 21.77 (Me); 23.15 (Me); 24.76 (CH); 25.37 (CH_2); 28.31 (3 Me); 30.84 (CH); 30.93 (Me); 37.68 (CH); 41.77 (CH_2); 51.71 (CH); 51.83 (CH); 52.19 (Me); 56.31 (CH); 58.50 (CH); 59.89 (CH); 61.31 (CH); 79.80 (C); 168.32 (C); 170.41 (C); 171.26 (C); 171.93 (C); 172.59 (C). FAB-MS: 682.3 (13, $[M + 23]^+$), 660.3 (12, $[M + 1]^+$), 612.3 (8), 560.2 (10), 515.2 (25), 468.2 (9), 459.1 (30), 412.2 (9), 313.2 (19), 300.1

(26), 283.1 (26), 257.1 (29), 255.1 (18), 245.2 (18), 243.1 (11), 155.1 (42), 127.1 (23), 116.0 (22), 86.0 (100), 72.0 (97), 56.9 (61).

93b: $[\alpha]_D^{r.t.} = -34.1$ ($c = 0.86$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.84–0.94 (*m*, 21 H); 1.10–1.21 (*m*, 1 H); 1.37 (*m*, 1 H); 1.43 (*s*, 9 H); 1.56–1.69 (*m*, 4 H); 1.83–1.90 (*m*, 1 H); 1.96–2.07 (*m*, 2 H); 2.10 (*m*, 3 H); 2.86, 2.95, 3.12, *3.17* (4*s*, 3 H); 3.73 (*s*, 3 H); 3.92 (*m*, 1 H); 4.59 (*dd*, $J = 5.3, 8.9$, 1 H); 4.77 (*dd*, $J = 7.4, 14.7$, 1 H); 5.19 (*t*, $J = 7.7, 15.6$, 1 H); 5.53 (br. *d*, $J \approx 5$, 1 H); 5.79 (*d*, $J = 8.7$, 1 H); 6.54 (br. *d*, $J \approx 5$, 1 H); 7.30 (br. *m*, 1 H); 8.25 (br. *m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.46 (Me); 11.46 (Me); 12.03 (Me); 15.56 (Me), 18.11 (Me); 19.29 (Me); 21.84 (CH_2); 22.04 (Me); 22.99 (Me); 24.64 (CH); 24.99 (CH_2), 28.33 (3 Me); 30.79 (CH); 30.87 (Me); 37.69 (CH); 41.34 (CH_2); 51.49 (CH); 51.65 (CH); 52.08 (Me); 56.27 (CH); 57.72 (CH); 60.03 (CH); 79.60 (C); 155.96 (C); 167.82 (C); 170.44 (C); 171.55 (C); 172.15 (C); 172.44 (C). FAB-MS: 682.2 (6, $[M + 23]^+$), 660.2 (5), 515.2 (43), 459.1 (25), 412.1 (8), 360.1 (4), 313.2 (17), 300.1 (19), 283.1 (29), 257.1 (28), 255.1 (17), 245.2 (13), 127.1 (22), 116.0 (23), 98.0 (16), 86.0 (100), 72.0 (96), 56.9 (57).

*Boc-Val-Leu-*D*-Ala-BzlAbu-Ile-OMe* (**94a**), *Boc-Val-Leu-Ala-BzlAbu-Ile-OMe* (**94b**), *Boc-Val-Leu-Gly-BzlAbu-Ile-OMe* (**8**-OMe), *and Boc-Val-Leu-*D*-Ala-(PhCHMe)Abu-Ile-OMe* (**101**). According to *G.P.5*, with **8** (303 mg, 0.45 mmol), LiBr (284 mg, 3.27 mmol), THF (10 ml), *t*-BuLi (2.5 ml, 2.75 mmol; 20 min), MeI (0.28 ml, 4.50 mmol; 21 h at −75°). LC (hexane/AcOEt 3:2) gave 11 mg (3%) of **101**, 87 mg (28%) of **94a**, 92 mg (29%) of **94b**, and 61 mg (20%) of **8**-OMe.

According to *G.P.5*, with **8** (304 mg, 0.45 mmol), LiBr (324 mg, 3.73 mmol), THF (8 ml), DMPU (0.4 ml, 3.32 mmol), *t*-BuLi (1.8 ml, 2.83 mmol; 45 min), and MeI (0.28 ml, 4.50 mmol; 8 h at −75°). LC (hexane/AcOEt 3:2) gave 58 mg (18%) of **94a**, 106 mg (33%) of **94b**, and 106 mg (34%) of **8**-OMe.

94a: $[\alpha]_D^{r.t.} = -59.4$ ($c = 1.02$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88–0.99 (*m*, 21 H); 1.16 (*d*, $J = 6.7$, 3 H); 1.23 (*m*, 1 H); 1.45 (*s*, 9 H); 1.48 (*m*, 2 H); 1.55–1.76 (*m*, 3 H); 1.91 (*m*, 1 H); 2.10–2.17 (*m*, 2 H); 3.72 (*s*, 3 H); 3.92 (*dd*, $J = 6.1, 7.9$, 1 H); 4.44–4.58 (*m*, 3 H); 4.60 (*m*, 1 H); 4.72 (*m*, 1 H); 4.94 (*d*, $J = 17.3$, 1 H); 5.03 (*d*, $J = 7.9$, 1 H); 6.63 (*d*, $J = 7.6$, 1 H); 6.87 (*d*, $J = 5.5$, 1 H); 7.23–7.36 (*m*, 6 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.40 (Me); 11.50 (Me); 15.60 (Me); 17.76 (2 Me); 19.43 (Me); 21.83 (Me); 22.19 (CH_2); 23.01 (Me); 24.70 (CH); 25.50 (CH_2); 28.31 (3 Me); 30.62 (CH); 37.26 (CH); 40.87 (CH_2); 46.63 (CH); 50.17 (CH_2); 51.18 (CH); 52.04 (Me); 56.67 (CH); 60.27 (CH); 61.81 (CH); 80.14 (C); 126.75 (CH); 127.74 (CH); 128.84 (CH); 137.04 (C); 156.07 (C); 170.34 (C); 171.70 (C); 171.76 (C); 172.61 (C); 175.18 (C). FAB-MS: 726.1 (10, $[M + 23]^+$), 704.1 (3, $[M + 1]^+$), 559.0 (32), 503.0 (23), 328.0 (7), 321.0 (23), 319.0 (8), 257.0 (20), 148.0 (23), 116.0 (11), 104.9 (11), 90.9 (38), 85.9 (34), 56.8 (100). GC: 3.45 (D-Ala), 4.88 (Abu), 5.03 (Val), 6.92 (Ile), 8.46 (Leu).

94b: $[\alpha]_D^{r.t.} = -80.2$ ($c = 0.97$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; 3 conformations): 0.78–0.98 (*m*, 21 H); 1.21 (*d*, $J = 6.7$, 3 H); 1.32–1.50 (*m*, 2 H); *1.41*, 1.440, 1.445 (3*s*, 9 H); 1.55–1.72 (*m*, 4.5 H); 1.82–2.20 (*m*, 2.5 H); 3.70, 3.71, *3.73* (3*s*, 3 H); 3.91 (*m*, 1 H); 4.09–5.37 (several *m*, 7 H); 6.43 (*d*, $J = 8.1$, 0.6 H); 6.65–7.95 (2.4 H); 7.14–7.38 (*m*, 5 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.67 (Me); 11.43 (Me); 15.57 (Me); 17.89 (Me); 19.10 (Me); 19.24 (Me); 22.04 (Me); 22.83 (CH_2); 23.07 (Me); 24.65 (CH); 24.92 (CH_2); 28.29 (3 Me); 31.00 (CH); 37.29 (CH); 41.56 (CH_2); 46.09 (CH); 48.24 (CH_2); 51.38 (CH); 52.07 (Me); 56.38 (CH); 59.95 (CH); 61.76 (CH); 63.68 (CH); 79.65 (C); 126.06 (CH); 127.48 (CH); 128.73 (CH); 137.53 (C); 155.91 (C); 170.97 (C); 171.17 (C); 171.72 (C); 172.33 (C); 174.47 (C). FAB-MS: 726.2 (18, $[M + 23]^+$), 702.5 (5, $[M + 1]^+$), 559.2 (100), 503.0 (38), 328.0 (10), 321.0 (20), 319.0 (15), 257.1 (34), 229.1 (7), 148.1 (50), 116.0 (19), 105.0 (22), 90.9 (69), 85.9 (76), 71.9 (29), 56.8 (86). GC: 3.83 (Ala), 5.28 (Abu), 5.47 (Val), 7.87 (Ile), 9.78 (Leu).

8-OMe: $[\alpha]_D^{r.t.} = -81.5$ ($c = 1.02$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.79–0.93 (*m*, 21 H); 1.16 (*m*, 1 H); 1.38 (*m*, 1 H); 1.42 (*s*, 9 H); 1.55–1.64 (*m*, 4 H); 1.85 (*m*, 1 H); 1.94 (*m*, 2 H); 2.09 (*m*, 1 H); 3.72 (*s*, 3 H); 3.91 (*m*, 2 H); 4.12 (*dd*, $J = 5.2, 17.6$, 1 H); 4.46 (*dd*, $J = 5.1, 8.4$, 1 H); 4.67 (*m*, 1 H); 4.71 (br. *s*, 2 H); 4.93 (*m*, 1 H); 5.18 (*d*, $J = 8.0$, 1 H); 6.59 (*d*, $J = 8.2$, 1 H); 7.14–7.33 (*m*, 7 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.75 (Me); 11.57 (Me); 15.57 (Me); 17.84 (Me); 19.34 (Me); 21.84 (Me); 22.44 (CH_2); 23.04 (Me); 24.65 (CH); 25.27 (CH_2); 28.30 (3 Me); 30.76 (CH); 37.32 (CH); 41.58 (CH_2); 41.92 (CH_2); 48.03 (CH_2); 51.34 (CH); 52.05 (Me); 56.54 (CH); 59.96 (CH); 60.07 (CH); 79.90 (C); 125.90 (CH); 127.57 (CH); 128.93 (CH); 136.72 (C); 155.98 (C); 170.29 (C); 170.37 (C); 171.76 (C); 172.02 (C); 172.19 (C). FAB-MS: 712.3 ($[M + 23]^+$), 690.3 ($[M + 1]^+$), 545.2 (79), 489.2 (50), 321.1 (21), 319.1 (16), 314.1 (10), 257.1 (13), 233.1 (15), 148.1 (100), 146.1 (13), 116.0 (14), 91.0 (82), 86.0 (96), 71.9 (32), 56.9 (49).

101: ^{1}H-NMR (400 MHz, $CDCl_3$): 0.39 (*t*, $J = 7.4$, 2 H); 0.87–0.99 (*m*, 18 H); 1.15–1.29 (*m*, 2 H); 1.34–1.50 (*m*, 2 H); 1.44, 1.447, *1.452* (3*s*, 9 H); 1.58–1.75 (*m*, 3 H); 1.68 (*d*, $J = 7.0$, 3 H); 1.93 (*m*, 1 H); 2.05–2.17 (*m*, 2 H); 3.38 (*m*, 1 H); 3.71, 3.72 (2*s*, 3 H); 3.90 (*m*, 1 H); 4.50 (*dd*, $J = 4.5, 8.5$, 1 H); 4.55 (*m*, 1 H); 5.03 (*d*, $J = 8.4$, 1 H); 5.21 (*m*, 2 H); 6.35 (*d*, $J = 7.8$, 1 H); 6.96 (*d*, $J = 6.7$, 1 H); 7.30–7.44 (*m*, 5 H); 8.11 (*d*, $J = 8.4$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.07 (Me); 11.69 (Me); 15.86 (Me); 16.94 (Me); 17.91 (Me); 18.78 (Me); 19.30 (Me); 21.83 (Me); 23.06 (Me); 23.83 (CH_2); 24.73 (CH); 24.99 (CH_2); 28.31 (3 Me); 30.62 (CH); 37.24 (CH); 41.31 (CH_2); 46.80 (CH); 51.62 (CH); 51.86 (Me); 56.08 (CH); 56.50 (CH); 60.23 (CH); 64.09 (CH); 80.12 (C); 127.78 (CH); 128.35

(CH); 128.67 (CH); 138.16 (C); 156.00 (C); 171.11 (C); 171.55 (C); 172.22 (C); 172.95 (C); 173.72 (C). FAB-MS: 740.5 (41, $[M + 23]^+$), 718.5 (33, $[M + 1]^+$), 573.4 (31), 413.3 (13), 384.3 (15), 335.3 (29), 328.2 (34), 319.2 (18), 257.2 (42), 162.2 (26), 146.2 (23), 116.1 (19), 105.1 (85), 86.1 (100), 72.0 (33), 56.9 (62). GC: 3.59 (D-Ala), 5.30 (Abu), 5.49 (Val), 7.91 (Ile), 9.82 (Leu).

*Boc-Val-Leu-*D*-Abu-BzlAbu-Ile-OMe* (**95a**), *Boc-Val-Leu-Abu-BzlAbu-Ile-OMe* (**95b**), *and Boc-Val-Leu-Gly-(PhCHEt)Abu-Ile-OMe* (**102**). According to *G.P. 5*, with **8** (234 mg, 0.35 mmol), LiBr (233 mg, 2.68 mmol), THF (6 ml), *t*-BuLi (1.37 ml, 2.17 mmol; 30 min), EtI (0.28 ml, 3.46 mmol; 30 min at −75°, 8.5 h at −18°). LC (hexane/AcOEt 2:1) gave 31 mg (12%) of **95a**, 86 mg (35%) of **95b**, 13 mg (5%) of **102**, and 81 mg (26%) of **8**-OMe.

95a: ^{1}H-NMR (400 MHz, $CDCl_3$): 0.70–0.99 (*m*, 24 H); 1.23 (*m*, 1 H); 1.45 (*s*, 3 H); 1.50–1.91 (*m*, 8 H); 2.12 (*m*, 2 H); 3.72 (*s*, 3 H); 3.92 (*dd*, *J* = 6.2, 8.1, 1 H); 4.45 (*dd*, *J* = 5.4, 8.3, 1 H); 4.51, 4.88 (*AB*, *J* = 17.1, 2 H); 4.45–4.59 (*m*, 2 H); 4.64 (*m*, 1 H); 5.02 (*d*, *J* = 7.8, 1 H); 6.54 (*d*, *J* = 7.9, 1 H); 6.74 (*d*, *J* = 7.4, 1 H); 7.21–7.35 (*m*, 6 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.01 (Me); 11.26 (Me); 11.53 (Me); 15.60 (Me); 17.81 (Me); 19.42 (Me); 21.80 (Me); 22.16 (CH_2); 23.02 (Me); 24.72 (CH); 25.45 (CH_2); 25.65 (CH_2); 28.31 (3 Me); 30.62 (CH); 37.32 (CH); 41.13 (CH_2); 50.34 (CH_2); 51.41 (CH); 52.05 (CH, Me); 56.59 (CH); 60.24 (CH); 62.06 (CH); 80.13 (C); 127.01 (CH); 127.79 (CH); 128.83 (CH); 137.07 (C); 156.03 (C); 170.34 (C); 171.71 (C); 172.01 (C); 172.55 (C); 174.66 (C). FAB-MS: 740.2 (16, $[M + 23]^+$), 718.2 (18, $[M + 1]^+$), 601.2 (9), 573.2 (70), 517.1 (35), 398.1 (13), 347.1 (10), 342.1 (13), 321.1 (69), 257.1 (34), 148.1 (64), 136.0 (22), 116.0 (22), 91.0 (81), 86.0 (100), 71.9 (38), 57.9 (92), 56.9 (73). GC: 4.51 (D-Abu), 4.83 (Abu), 4.98 (Val), 6.85 (Ile), 8.35 (Leu).

95b: ^{1}H-NMR (200 MHz, $CDCl_3$): 0.72–1.02 (*m*, 24 H); 1.05–1.30 (*m*, 2 H); 1.35 (*m*, 1 H); *1.42*, 1.44 (2*s*, 9 H); 1.48–1.70 (*m*, 5 H); 1.73–1.98 (*m*, 2 H); 2.07 (*m*, 1 H); 3.70 3.72 (2*s*, 3 H); 3.88 (*m*, 1 H); 4.45–5.10 (*m*, 6.5 H); 5.37 (*d*, *J* = 7.5, 0.5 H); 6.30, 6.40 (2*d*, *J* = 8.5, 1 H); 6.88 (*d*, *J* = 7.0, 0.3 H); 7.12–7.37 (*m*, 5.5 H); 7.52 (*m*, 1 H); 7.83 (*d*, *J* = 8.0, 0.2 H). FAB-MS: 740.3 (3, $[M + 23]^+$), 716.2 (2), 573.2 (100), 517.2 (18), 342.1 (4), 321.1 (14), 319.1 (12), 257.1 (22), 148.1 (36), 116.0 (13), 90.9 (58), 86.0 (55), 56.9 (68). GC: 5.04 (Abu), 5.19 (Val), 7.07 (Ile), 8.57 (Leu).

102: ^{1}H-NMR (200 MHz, $CDCl_3$): 0.73–1.09 (*m*, 24 H); 1.22 (*m*, 1 H); 1.43 (*s*, 9 H); 1.50–1.79 (*m*, 5 H); 1.80–2.02 (*m*, 2 H); 2.04–2.08 (*m*, 2 H); 2.40 (*m*, 1 H); 3.48 (*m*, 1 H); *3.63*, 3.68 (2*s*, 3 H); 3.93 (*m*, 1 H); 4.10–4.28 (*m*, 2 H); 3.38–4.65 (*m*, 2 H); 4.75 (*m*, 1 H); 5.07 (*d*, *J* = 9.6, 1 H); 6.52 (*d*, *J* = 9.1, 1 H); 6.73 (*d*, *J* = 9.2, 1 H); 7.03 (*m*, 1 H); 7.33 (*m*, 5 H). FAB-MS: 740.4 (25, $[M + 1]^+$), 573.3 (44), 517.2 (5), 455.2 (9), 399.1 (13), 370.1 (6), 349.2 (9), 347.1 (9), 319.1 (8), 314.1 (52), 270.1 (12), 257.1 (25), 231.1 (13), 176.1 (18), 146.1 (36), 119.0 (47), 116.0 (17), 91.0 (65), 86.0 (100), 71.9 (31), 56.9 (63). GC: 5.08 (Abu), 5.23 (Val), 5.97 (Gly), 7.13 (Ile), 8.66 (Leu).

*Boc-Val-Leu-*D*-Nva(4,5-didehydro)-BzlAbu-Ile-OMe* (**96a**), *Boc-Val-Leu-Nva(4,5-didehydro)-BzlAbu-Ile-OMe* (**96b**), *Boc-Val-Leu-*D*-Nva(4,5-didehydro)-(PhCHCH$_2$=CH$_2$)Abu-Ile-OMe* (**103**), *and Boc-Val-Leu-Gly-(PhCHCH$_2$CH=CH$_2$)Abu-Ile-OMe* (**104**). According to *G.P. 5*, with **8** (230 mg, 0.34 mmol), LiBr (216 mg, 2.49 mmol), THF (8 ml), *t*-BuLi (2.0 ml, 2.2 mmol), and allyl bromide (0.29 ml, 3.43 mmol; 18 h at −75°). LC (hexane/AcOEt 2:1 gave 6 mg (2%) of **103** (D/L 1:3), 48 mg (20%) of **96a**, 67 mg (27%) of **96b**, 20 mg (8%) of **104**, and 49 mg (21%) of **8**-OMe.

96a: $[\alpha]_D^{r.t.} = -46.2$ (*c* = 1.4, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.79–0.97 (*m*, 21 H); 1.24 (*m*, 1 H); 1.44 (*s*, 9 H); 1.48 (*m*, 2 H); 1.63 (*m*, 2 H); 1.75 (*m*, 1 H); 1.89 (*m*, 1 H); 2.09–2.22 (*m*, 3 H); 2.25–2.33 (*m*, 1 H); 3.70, *3.73* (2*s*, 3 H); 3.94 (*m*, 1 H); 4.45–4.54 (*m*, 3 H); 4.63 (*m*, 1 H); 4.72 (*m*, 1 H); 4.90–5.20 (*m*, 4 H); 5.47 (*m*, 1 H); 6.68 (*d*, *J* = 6.5, 1 H); 6.82 (*d*, *J* = 6.3, 1 H); 7.23–7.36 (*m*, 6 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 11.31 (Me); 11.50 (Me); 15.59 (Me); 17.82 (Me); 19.43 (Me); 21.91 (Me); 22.18 (CH_2); 22.95 (Me); 24.65 (CH); 25.47 (CH_2); 28.31 (3 Me); 30.71 (CH); 36.37 (CH_2); 37.31 (CH); 41.20 (CH_2); 50.25 (CH_2); 50.34 (CH); 51.26 (CH); 52.07 (Me); 56.62 (CH); 60.09 (CH); 61.78 (CH); 79.99 (C); 118.94 (CH_2); 126.94 (CH); 127.81 (CH); 128.86 (CH); 132.56 (CH); 137.13 (C); 155.97 (C); 170.24 (C); 171.73 (C); 171.94 (C); 172.61 (C); 174.08 (C). FAB-MS: 752.1 (15, $[M + 23]^+$), 730.1 (7, $[M + 1]^+$), 625.1 (6), 585.5 (34), 529.0 (28), 409.9 (5), 359.0 (7), 354.0 (9), 321.0 (41), 319.0 (25), 257.1 (31), 229.1 (7), 148.0 (51), 116.0 (21), 90.9 (77), 85.9 (100), 71.9 (31), 69.9 (51), 56.8 (87). GC: 4.75 (Abu), 4.89 (Val), 6.29 (D-Nva), 6.79 (Ile), 8.31 (Leu).

96b: $[\alpha]_D^{r.t.} = -62.6$ (*c* = 0.84, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; 3 conformations): 0.35 (*t*, *J* = 7.5, 1 H); 0.78–0.98 (*m*, 20 H); 1.19 (*m*, 1 H); 1.40, 1.44, *1.45* (3*s*, 9 H); 1.54–1.72 (*m*, 4 H); 1.78–2.17 (*m*, 5 H); 2.30 (*m*, 1 H); 2.55, 2.75–2.90 (2*m*, 1 H); 3.47 (*m*, 0.5 H); 3.70, *3.72*, 3.78 (3*s*, 3 H); 3.86–4.33 (4*m*, 1.5 H); 4.42–4.67 (*m*, 2 H); 4.80–5.18 (3*m*, 5.6 H); 5.45 (*m*, 0.4 H); 5.57, 5.76 (2*m*, 1 H); 6.42, 6.66 (2*m*, 1 H); 7.07–7.40 (*m*, 6 H); 7.72, 7.86 (2*m*, 0.8 H); 8.26 (*d*, *J* = 8.5, 0.2 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.60 (Me); 11.43 (Me); 15.57 (Me); 17.98 (Me); 19.37 (Me); 22.14 (Me); 23.07 (Me); 23.61 (CH_2); 24.71 (CH); 25.15 (CH_2); 28.30 (3 Me); 30.94 (CH); 34.83 (CH_2); 37.29 (CH); 41.78 (CH_2); 48.36 (CH_2); 49.63 (CH); 51.51 (Me); 52.05 (CH); 56.45 (CH); 60.96 (CH); 64.14 (CH); 79.55 (C); 118.79 (CH_2); 126.20 (CH); 127.44 (CH); 128.67 (CH); 132.30 (CH); 137.74 (C); 155.92 (C); 169.11 (C); 171.48 (C); 171.87 (C); 172.48 (C); 173.44 (C). FAB-MS: 752.1 (6, $[M + 23]^+$), 730.1 (2, $[M + 1]^+$), 585.1 (100),

529.0 (20), 321.0 (14), 319.0 (17), 257.0 (21), 229.1 (6), 148.0 (38), 146.0 (13), 131.0 (12), 116.0 (17), 90.9 (61), 85.9 (70), 70.0 (32), 56.8 (70). GC: 4.81 (Abu), 4.97 (Val), 6.85 (Nva), 6.88 (Ile), 8.39 (Leu).

103: FAB-MS: 792.5 (5, $[M + 23]^+$), 641.5 (25), 625,4 (23), 585.4 (14), 410.3 (13), 375.3 (24), 359.2 (22), 354.2 (21), 319.2 (64), 257.2 (44), 146.1 (43), 131.1 (40), 116.0 (28), 91.0 (39), 86.0 (100), 72.0 (42), 69.9 (69), 56.9 (74). GC: 4.78 (Abu), 4.93 (Val), 6.28 (D-Nva), 6.79 (Nva), 6.81 (Ile), 8.33 (Leu); D-Nva/Nva 1:3.

104: FAB-MS: 752.4 (21, $[M + 23]^+$), 730.0 (4, $[M + 1]^+$), 585.2 (51), 529.1 (17), 455.0 (6), 399.0 (11), 359.0 (39), 319.1 (65), 314.0 (44), 257.1 (28), 188.1 (22), 146.1 (58), 131.0 (61), 116.0 (29), 90.9 (33), 85.9 (100), 71.9 (43), 56.8 (70). GC: 4.80 (Abu), 4.95 (Val), 5.67 (Gly), 6.83 (Ile), 8.36 (Leu).

Procedure for Debenzylation. To a soln. of Na (57 mg, 2.48 mmol) in liq. NH_3 (*ca.* 8 ml) educt (**96a** after saponification and hydrogenolysis; 44 mg, 0.06 mmol), THF (3 ml) was added. After 20 min, the reaction was stopped by the addition of NH_4Cl and CH_2Cl_2, the mixture warmed to r.t. and evaporated, the residue taken up in CH_2Cl_2 and 1N H_2SO_4; and the aq. layer additionally extracted twice with CH_2Cl_2. All org. layers were washed 3 times with sat. aq. NaCl soln., dried ($MgSO_4$) and evaporated. Esterification according to *G.P. 5* gave 35 mg (89%) of Boc-Val-Leu-D-Nva-Abu-Ile-OMe. $[\alpha]_D^{r.t.} = -15.9$ ($c = 0.74$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.86–0.96 (*m*, 24 H); 1.14–1.40 (*m*, 4 H); *1.42*, 1.45 (2*s*, 9 H); 1.52–1.74 (*m*, 5 H); 1.81–1.92 (*m*, 3 H); 2.05 (*m*, 1 H); 3.72 *3.75* (2*s*, 3 H); 4.01 (*m*, 1 H); 4.48–4.60 (*m*, 4 H); 5.18 (*m*, 1 H); 7.18–7.53 (*m*, 4 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 9.97 (Me); 11.53 (Me); 13.78 (Me); 15.42 (Me); 17.90 (Me); 18.81 (CH_2); 19.37 (Me); 22.08 (Me); 22.96 (Me); 24.77 (CH); 25.21 (CH_2); 25.64 (CH_2); 28.32 (3 Me); 29.71 (CH_2); 31.05 (CH); 34.12 (CH_2); 37.87 (CH); 41.06 (CH_2); 51.96 (CH); 52.17 (Me); 52.98 (CH); 54.69 (CH); 56.38 (CH); 60.00 (CH); 80.02 (C); 156.05 (C); 171.39 (C); 171.53 (C); 171.99 (C); 172.30 (C); 172.91 (C). FAB-MS: 664.3 (8, $[M + 23]^+$), 642.3 (36, $[M + 1]^+$), 542.3 (14), 497.2 (19), 441.2 (32), 412.2 (11), 397.2 (6), 356.1 (37), 330.1 (11), 312.1 (12), 257.1 (35), 231.1 (27), 213.1 (24), 185.1 (20), 146.1 (28), 136.0 (17), 116.0 (16), 86.0 (94), 71.9 (100), 57.9 (58), 54.9 (32). GC: 5.06 (Abu), 5.21 (Val), 6.63 (D-Nva), 7.12 (Ile), 8.62 (Leu).

*Boc-Val-Leu-*ambo*-Phe-BzlAbu-Ile-OMe* (**97a**/**97b**) *and Boc-Val-Leu-Gly-(PhCHCH$_2$Ph)Abu-Ile-OMe* (**105**). According to *G.P. 5*, with **8** (310 mg, 0.46 mmol), LiBr (304 mg, 3.50 mmol), THF (10.5 ml), *t*-BuLi (2.6 ml, 2.86 mmol; 30 min), and benzyl bromide (0.54 ml, 4.56 mmol; 90 min at −75°, 6.5 h at −18°). LC (hexane/AcOEt 2:1) gave 168 mg (47%) of **97a**/**97b**, 66 mg (18%) of **105**, and 55 mg (21%) of **8**-OMe.

97a/**97b**: ^{1}H-NMR (400 MHz, $CDCl_3$): 0.77–0.97 (*m*, 21 H); 1.23 (*m*, 1 H); 1.31–1.51 (*m*, 2 H); 1.43, 1.44, 145 (3*s*, 9 H); 1.51–1.68 (*m*, 3 H); 1.91 (*m*, 1 H); 2.09 (*m*, 2 H); 2.80–3.00 (*m*, 1.4 H); 3.21–3.40 (*m*, 0.4 H); 3.68, 3.70, 3.73, 3.74 (4*s*, 3 H); 3.81–4.07 (*m*, 1.5 H); 4.35–5.18 (*m*, 6.5 H); 6.33, 6.40, 6.65 (3*d*, $J = 8.4$, 8.2, 8.0, 1 H); 6.78 (*m*, 1 H); 6.95, 7.02 (2*m*, 1 H); 7.12–7.40 (*m*, 10 H). ^{13}C-NMR (100 MHz, $CDCl_3$; only main signals): 10.65 (Me); 11.49 (Me); 15.59 (Me); 17.85 (Me); 19.45 (Me); 22.14 (Me); 22.79 (Me); 23.33 (Me); 24.45 (CH); 25.47 (CH_2); 28.30 (3 Me); 30.82 (CH); 37.39 (CH); 38.30 (CH_2); 41.18 (CH_2); 49.81 (CH); 51.13 (CH); 52.07 (Me); 56.56 (CH); 59.95 (CH); 61.82 (CH); 79.87 (C); 126.32 (CH); 126.62 (CH); 127.91 (CH); 128.56 (CH); 128.75 (CH); 129.17 (CH); 136.09 (C); 137.52 (C); 155.59 (C); 168.35 (C); 170.17 (C); 171.68 (C); 171.87 (C); 174.28 (C). FAB-MS: 802.2 (8, $[M + 23]^+$), 780.2 (5, $[M + 1]^+$), 635.2 (100), 579.1 (24), 460.0 (5), 404.0 (3), 321.0 (27), 319.0 (22), 257.1 (15), 181.1 (13), 148.1 (43), 136.0 (21), 120.0 (70), 116.0 (18), 90.9 (73), 85.9 (84), 71.9 (27), 56.8 (70). GC: 4.81 (Abu), 4.96 (Val), 6.82 (Ile), 8.35 (Leu), 18.16 (D-Phe), 18.45 (Phe); D-Phe/L-Phe 1:1.2.

105: FAB-MS: 802.2 (5, $[M + 23]^+$), 645.1 (22), 579.1 (10), 409.0 (26), 319.0 (56), 314.0 (26), 257.1 (21), 196.0 (23), 181.1 (49), 146.0 (38), 116.0 (23), 90.9 (35), 85.9 (100), 71.9 (40), 56.8 (88). GC: 4.83 (Abu), 4.98 (Val), 5.70 (Gly), 6.87 (Ile), 8.41 (Leu).

*Boc-Val-Leu-*ambo*-Asp(OEt)-BzlAbu-Ile-OMe* (**98a**/**98b**). According to *G.P. 5*, with **8** (298 mg, 0.44 mmol), LiBr (298 mg, 3.43 mmol), THF (7 ml), *t*-BuLi (1.75 ml, 2.78 mmol; 30 min), ethyl bromoacetate (0.24 ml, 2.17 mmol; 13 h at −75°). LC (hexane/AcOEt 3:2) gave 106 mg (31%) of **98a**/**98b** and 124 mg (41%) of **8**-OMe.

98a/**98b**: ^{1}H-NMR (400 MHz, $CDCl_3$): 0.76–0.98 (*m*, 24 H); 1.14–1.28 (*m*, 4 H); 1.43, 1.44, 1.45 (3*s*, 9 H); 1.48–1.78 (3*m*, 3.5 H); 1.86–2.17 (3*m*, 3.5 H); 2.53–3.20 (serveral *m*, 2 H); 3.70, 3.71, 3.73, 3.74 (4*s*, 3 H); 3.87 (*m*, 1 H); 4.06–4.18 (*m*, 2 H); 4.41–4.76 (3*m*, 4.6 H); 4.90–5.51 (6*m*, 2.4 H); 6.34, 6.41, 6.48, 6.57 (4*d*, $J = 8.2$, 7.8, 8.0, 7.5, 1 H); 7.02, 7.50, 7.72 (2*m*, *d*, $J = 6.9$, 1 H); 7.15–7.37 (*m*, 6 H). ^{13}C-NMR (100 MHz, $CDCl_3$; only main signals): 10.90 (Me); 11.91 (Me); 14.12 (Me); 15.67 (Me); 17.86 (Me); 19.33 (Me); 21.88 (Me); 22.49 (CH_2); 23.00 (Me); 24.64 (CH); 25.2 (CH_2); 28.29 (3 Me); 30.61 (CH); 39.91 (CH_2); 37.14 (CH); 41.21 (CH_2); 47.27 (CH); 51.49 (CH); 52.20 (Me); 56.64 (CH); 60.17 (CH); 60.89 (CH_2); 61.82 (CH); 80.05 (C); 127.04 (CH); 127.63 (CH); 128.73 (CH); 136.65 (C); 155.92 (C); 168.66 (C); 170.63 (C); 171.31 (C); 171.78 (C); 172.53 (C). FAB-MS: 798.4 (24, $[M + 23]^+$), 776.4 (3, $[M + 1]^+$), 631.3 (100), 575.2 (29), 456.2 (4), 400.2 (7), 321.2 (20), 319.2 (21), 257.1 (20), 229.2 (6), 148.1 (45), 116.1 (37), 91.0 (45), 86.0 (63), 72.0 (20), 56.9 (39). GC: 4.74 (Abu), 4.91 (Val), 6.80 (Val), 8.32 (Leu), 13.86 (D-Asp), 14.00 (Asp); D-Asp/L-Asp 1:1.7.

*Boc-Val-Leu-*ambo-*Gly(2-CO_2Me)-BzlAbu-Ile-OMe* (**99a**/**99b**) *and Boc-Val-Leu-Gly(CO_2Me)-Bzl-Abu-Ile-OMe* (**106**). According to *G.P. 5*, with **8** (259 mg, 0.38 mmol), LiBr (356 mg, 4.10 mmol), THF (7.5 ml), *t*-BuLi (1.50 ml, 2.38 mmol; 30 min), and a stream of CO_2 gas which was passed over the mixture for 30 min. Workup, esterification with diazomethane, and chromatographic purification (hexane/AcOEt 3:2) gave 118 mg (41%) of **99a**/**99b**, 33 mg (12%) of **106**, and 109 mg (41%) of **8**-OMe.

99a/**99b**: ^{1}H-NMR (400 MHz, $CDCl_3$): 0.76–0.98 (*m*, 21 H); 1.16 (*m*, 1 H); 1.36 (*m*, 1 H); 1.43, 1.44 (2*s*, 9 H); 1.52–1.80 (*m*, 5 H); 1.93 (*m*, 1 H); 2.10 (*m*, 1 H); 3.68, 3.71, 3.72, 3.73, 3.74, 3.80, 3.81 (7*s*, 6 H); 3.91 (*m*, 1 H); 4.15–4.22 (*m*, 0.4 H); 4.44 (*dd*, *J* = 5.1, 8.3, 0.3 H); 4.51–5.17 (*m*, 5.3 H); 5.47 (*t*, *J* = 7.4, 0.6 H); 5.53, 5.83 (2*d*, *J* = 6.1, 7.5, 0.4 H); 6.39, 6.46, 6.53 (3*d*, *J* = 8.2, 8.0, 6.0, 1 H); 7.00, 7.08 (2*d*, *J* = 8.3, 7.6, 0.6 H); 7.17–7.40 (*m*, 5.7 H); 7.54, 7.60, 7.79 (3*d*, *J* = 7.1, 6.0, 6.6, 0.7 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.76 (Me); 11.62 (Me); 15.49 (Me); 17.90 (Me); 19.29 (Me); 21.88 (Me); 21.93 (CH_2); 22.99 (Me); 24.61 (CH); 25.35 (CH_2); 28.28 (3 Me); 30.71 (CH); 37.27 (CH); 41.29 (CH_2); 46.80 (CH_2); 51.27 (CH); 52.18 (Me); 53.08 (Me); 54.01 (CH); 56.53 (CH); 59.98 (CH); 61.97 (CH); 79.93 (C); 126.18 (CH); 127.73 (CH); 128.79 (CH); 136.13 (C); 155.92 (C); 166.99 (C); 168.51 (C); 169.88 (C); 171.84 (C); 172.32 (C); further signals of the second diastereoisomer. FAB-MS: 770.5 (14, $[M + 23]^+$), 748.6 (8, $[M + 1]^+$), 603.4 (85), 547.3 (62), 372.2 (7), 321.3 (16), 319.2 (15), 291.2 (12), 263.2 (10), 257.2 (8), 229.2 (7), 148.1 (85), 116.1 (17), 91.0 (97), 86.0 (100), 72.0 (41), 56.9 (76).

106: FAB-MS: 770.5 (45, $[M + 23]^+$), 748.5 (8, $[M + 1]^+$), 603.4 (64), 547.3 (35), 379.2 (48), 319.2 (20), 314.2 (11), 257.2 (17), 206.2 (100), 149.1 (24), 146.1 (21), 121.1 (32), 91.0 (21), 86.0 (91), 72.0 (33), 56.9 (84).

*Boc-Val-Leu-*D*-Gly(2-SMe)-BzlAbu-Ile-OMe* (**100a**), *Boc-Val-Leu-Gly(2-SMe)-BzlAbu-Ile-OMe* (**100b**), *and Boc-Val-Leu-Gly-(PhCHSMe)Abu-Ile-OMe* (**107**). According to *G.P. 5*, with **8** (367 mg, 0.54 mmol), LiBr (347 mg, 4.0 mmol), THF (9 ml), *t*-BuLi (2.25 ml, 3.53 mmol; 30 min), and Me_2S_2 (0.48 ml, 5.41 mmol; 1 h at −75°, 7 h at −18°). LC (hexane/AcOEt 2:1) gave 123 mg (31%) of **100a** (slightly contaminated with a doubly alkylated product), 41 mg (10%) of **100b**, 95 mg (24%) of **107**, and 88 mg (24%) of **8**-OMe.

100a: $[\alpha]_D^{r.t.} = -38.2$ (*c* = 1.14, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$; 2 conformations): 0.74–0.97 (*m*, 21 H); 1.20 (*m*, 1 H); *1.38*, 1.43 (2*s*, 9 H); 1.52–1.70 (*m*, 3 H); 1.81 (*m*, 1 H); 1.90 (*m*, 1 H); 1.92 (*m*, 1 H); 2.06, *2.08*, 2.17, 2.18 (4*s*, 3 H); 2.1 (*m*, 1 H); 3.716, *3.724* (2*s*, 3 H); 3.87 (*m*, 1 H); 4.53–4.65 (*m*, 1.7 H); 4.94–5.26 (*m*, 3.3 H); 5.70 (*m*, 1 H); 5.74, 6.39 (2*d*, *J* = 9.1, 8.4, 1 H); 7.10 (*m*, 1.8 H); 7.22–7.39 (*m*, 3.8 H); 7.86 (br. *m*, 0.8 H); 8.57 (br. *m*, 0.6 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.69 (Me); 11.46 (Me); 12.44 (Me); 15.65 (Me); 18.04 (Me); 19.20 (Me); 22.10 (Me); 23.03 (CH_2); 23.11 (Me); 24.67 (CH); 24.96 (CH_2); 28.29 (3 Me); 31.12 (CH); 37.53 (CH); 41.58 (CH_2); 48.28 (CH_2); 51.39 (CH); 52.02 (Me); 52.33 (CH); 56.31 (CH); 58.53 (CH); 59.94 (CH); 79.36 (C); 125.55 (CH); 127.41 (CH); 128.81 (CH); 137.56 (C); 155.92 (C); 168.73 (C); 171.06 (C); 171.49 (C); 172.18 (C); 172.57 (C). FAB-MS: 758.4 (9, $[M + 23]^+$), 591.3 (94), 544.3 (10), 535.2 (22), 376.2 (11), 359.2 (24), 331.2 (21), 319.2 (58), 257.1 (28), 231.1 (29), 203.1 (22), 148.1 (47), 146.1 (21), 137.0 (38), 116.0 (22), 91.0 (64), 86.0 (87), 72.0 (30), 56.9 (100).

100b: $[\alpha]_D^{r.t.} = -93.6$ (*c* = 0.9, EtOH). ^{1}H-NMR (500 MHz, $CDCl_3$): 0.73–0.97 (*m*, 21 H); 1.07, 1.16 (2*m*, 1 H); 1.36 (*m*, 1 H); 1.41, *1.44* (2*s*, 9 H); 1.51–1.74 (*m*, 4.5 H); 1.84, 1.92, 2.03 (3*m*, 1.5 H); *2.09*, 2.16 (2*s*, 3 H); 2.13 (*m*, 1 H); 3.70, 3.72 (2*s*, 3 H); 3.91 (*m*, 1 H); 4.30 (*dd*, *J* = 4.6, 7.8, 0.4 H); 4.35 (*dd*, *J* = 4.8, 8.1, 0.4 H); 4.41 (*m*, 0.4 H); 4.50–4.61 (*m*, 2.4 H); 4.74, 4.81 (*AB*, *J* = 17.2, 1 H); 4.95 5.04 (*m*, 1.4 H); 5.62, 5.88 (2*d*, *J* = 7.9, 7.5, 1 H); 6.33, *6.41*, 6.48 (3*d*, *J* = 7.3, 7.6, 7.2, 1 H); 6.92, 7.14, *7.58* (3*d*, *J* = 8.1, 7.1, 7.4, 1 H); 7.19–7.32 (*m*, 6 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 10.03 (Me); 11.68 (Me); 12.46 (Me); 15.33 (Me); 17.90 (Me); 19.37 (Me); 21.84 (Me); 22.67 (CH_2); 23.04 (Me); 24.73 (CH); 25.61 (CH_2); 28.29 (3 Me); 30.60 (CH); 37.36 (CH); 41.36 (CH_2); 46.60 (CH_2); 51.71 (CH); 52.06 (Me); 53.18 (CH); 56.79 (CH); 60.06 (CH); 61.61 (CH); 80.05 (C); 126.76 (CH); 128.24 (CH); 128.88 (CH); 137.68 (C); 155.93 (C); 167.28 (C); 168.25 (C); 169.61 (C); 171.65 (C); 172.02 (C). FAB-MS: 758.4 (13, $[M + 23]^+$), 736.4 (3, $[M + 1]^+$), 688.4 (5), 591.3 (42), 544.3 (8), 535.2 (16), 488.2 (5), 376.2 (14), 359.2 (25), 331.2 (19), 321.2 (14), 319.2 (25), 313.2 (9), 257.1 (25), 231.1 (36), 203.1 (23), 148.1 (51), 116.0 (21), 91.0 (68), 86.0 (100), 72.0 (31), 56.9 (74).

107: FAB-MS: 758.4 (11, $[M + 23]^+$), 736.4 (4, $[M + 1]^+$), 591.3 (2), 588.4 (3), 376.2 (6), 319.2 (63), 257.1 (10), 146.1 (24), 137.0 (100), 116.0 (11), 106.0 (12), 86.0 (44), 72.0 (18), 56.9 (34).

*Boc-Leu-*D*-Ala-Pro-Leu-OMe* (**108a**) *and Boc-Leu-Ala-Pro-Leu-OMe* (**108b**). According to *G.P. 5*, with **9** (403 mg, 0.81 mmol), LiBr (708 mg, 8.2 mmol), THF (11 ml), *t*-BuLi (2.7 ml, 4.3 mmol; 30 min), and MeI (0.51 ml, 8.2 mmol; 24 h at −75°). LC (hexane/AcOEt 1:4) gave 152 mg of **108a**/**108b**, 185 mg of **108b** (containing 20% of **108a**). Total yield 69%; D/L 6:1.

108b: $[\alpha]_D^{r.t.} = -58.6$ (*c* = 1.04, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.91–0.97 (*m*, 12 H); 1.33 (*d*, *J* = 6.8, 3 H); 1.42–1.49 (*m*, 1 H); 1.44 (*s*, 9 H); 1.64 (*m*, 5 H); 1.99 (*m*, 3 H); 2.21 (*m*, 1 H); 3.51 (*m*, 1 H); 3.72 (*s*, 3 H); 3.86 (*m*, 1 H); 4.15 (*m*, 1 H); 4.54 (*m*, 1 H); 4.61 (*m*, 1 H); 4.68 (*m*, 1 H); 5.25 (*d*, *J* = 7.5, 1 H); 6.97 (*d*, *J* = 8.3, 1 H); 7.10 (*d*, *J* = 6.2, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.83 (Me); 21.92 (Me); 22.08 (Me); 22.85 (2 Me); 24.63 (CH_2); 24.74 (CH); 25.01 (CH); 28.33 (3 Me); 28.92 (CH_2); 40.98 (2 CH_2); 46.96 (CH); 47.08 (CH_2); 50.54 (CH); 52.30 (Me);

52.67 (CH); 60.73 (CH); 79.99 (C); 156.07 (C); 171.13 (C); 171.46 (C); 172.83 (C); 173.91 (C). FAB-MS: 549.2 (39, $[M + 23]^+$), 527.2 (13, $[M + 1]^+$), 427.2 (17), 243.1 (77), 241.1 (17), 86.0 (21), 69.9 (100), 56.9 (33).

Boc-Leu-D-Nva(4,5-didehydro)-Pro-Leu-OMe (**109a**), *Boc-Leu-Nva(4,5-didehydro)-Pro-Leu-OMe* (**109b**), *and Boc-Leu-Gly-Pro-Leu-OMe* (**9**-OMe). According to *G.P.5*, with **9** (405 mg, 0.81 mmol), LiBr (704 mg, 8.1 mmol), THF (11 ml), *t*-BuLi (3.3 ml, 4.4 mmol; 30 min), and allyl bromide (0.69 ml, 8.1 mmol, 22 h at −75°). LC (Et_2O) gave 77 mg (17%) of **109b**, 232 mg (52%) of **109a**, and 78 mg (19%) of **9**-OMe.

109a: $[\alpha]_D^{r.t.} = -64.8$ ($c = 0.92$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.92–0.94 (*m*, 12 H); 1.38–1.47 (*m*, 1 H); 1.44 (*s*, 9 H); 1.58–1.70 (*m*, 5 H); 1.92–2.12 (*m*, 3 H); 2.13–2.25 (*m*, 1 H); 2.41 (*m*, 1 H); 2.53 (*m*, 1 H); 3.51–3.59 (*m*, 1 H); 3.71 (*s*, 3 H); 3.84–3.90 (*m*, 1 H); 4.11–4.18 (*m*, 1 H); 4.54 (*m*, 1 H); 4.61–4.70 (*m*, 2 H); 5.13 (*m*, 1 H); 5.17 (*m*, 1 H); 5.26 (*d*, $J = 7.7$, 1 H); 5.71–5.81 (*m*, 1 H); 6.98 (*d*, $J = 8.6$, 1 H); 7.08 (*d*, $J = 6.1$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 21.88 (Me); 22.04 (Me); 22.86 (2 Me); 24.60 (CH_2); 24.70 (CH); 25.01 (CH); 28.33 (3 Me); 29.08 (CH_2); 35.65 (CH_2); 40.83 (CH_2); 40.96 (CH_2); 47.16 (CH_2); 50.45 (CH); 50.67 (CH); 52.29 (Me); 52.70 (CH); 60.79 (CH); 79.94 (C); 119.08 (CH_2); 132.64 (CH); 156.02 (C); 170.30 (C); 171.14 (C); 173.11 (C); 173.95 (C). FAB-MS: 575.4 (68, $[M + 23]^+$), 553.4 (24, $[M + 1]^+$), 475.3 (11), 453.3 (23), 352.2 (4), 340.2 (6), 311.2 (8), 255.2 (15), 243.2 (76), 86.0 (28), 69.9 (100), 56.9 (36). GC: 6.45 (D-Nva), 8.48 (Leu), 10.30 (Pro).

109b: $[\alpha]_D^{r.t.} = -70.8$ ($c = 0.6$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.91–0.94 (*m*, 12 H); 1.22–1.28 (*m*, 1 H); 1.45 (*s*, 9 H); 1.45–1.72 (*m*, 5 H); 1.82–2.04 (*m*, 2 H); 2.04–2.18 (*m*, 1 H); 2.29–2.43 (*m*, 2 H); 2.47–2.57 (*m*, 1 H); 3.57–3.77 (*m*, 2 H); 3.73 (*m*, 3 H); 4.11–4.20 (*m*, 1 H); 4.49–4.54 (*m*, 1 H); 4.61 (*m*, 1 H); 4.76–4.81 (*m*, 1 H); 4.87 (*d*, $J = 6.8$, 1 H); 5.09–5.13 (*m*, 2 H); 5.68–5.79 (*m*, 1 H); 6.91–6.97 (*m*, 1 H); 7.06 (*d*, $J = 7.5$, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 21.81 (Me); 21.92 (Me); 22.77 (Me); 23.09 (Me); 24.70 (CH); 24.79 (CH); 25.06 (CH_2); 27.28 (CH_2); 28.31 (3 Me); 36.97 (CH_2); 41.33 (CH_2); 41.51 (CH_2); 47.55 (CH_2); 50.08 CH); 50.95 (CH); 52.23 (Me); 53.03 (CH); 59.80 (C); 80.06 (C); 119.07 (CH_2); 132.22 (CH); 155.55 (C); 170.73 (C); 171.05 (C); 172.17 (C); 173.18 (C). FAB-MS: 591.4 (21, $[M + 39]^+$), 575.4 (40, $[M + 23]^+$), 553.4 (37, $[M + 1]^+$), 497.3 (8), 475.3 (6), 453.3 (4), 340.2 (5), 311.2 (10), 281.2 (12), 255.2 (16), 243.2 (80), 86.0 (33), 69.9 (100), 56.9 (43). GC: 6.94 (Nva), 8.56 (Leu), 10.42 (Pro).

9-OMe: $[\alpha]_D^{r.t.} = -90.9$ ($c = 0.89$, EtOH). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.89–0.95 (*m*, 12 H); 1.44 (*s*, 9 H); 1.46–1.69 (*m*, 6 H); 1.99 (*m*, 2 H); 2.17 (*m*, 1 H); 2.26 (*m*, 1 H); 3.45 (*m*, 1 H); 3.60 (*m*, 1 H); 3.72 (*s*, 3 H); 3.95–4.00 (*m*, 1 H); 4.11–4.17 (*m*, 1 H); 4.33 (*m*, 1 H); 4.51 (*m*, 1 H); 4.63 (*m*, 1 H); 5.09 (*d*, $J = 8.4$, 1 H); 7.14 (*d*, $J = 7.8$, 1 H); 7.41 (br. *m*, 1 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 21.79 (Me); 21.92 (Me); 22.76 (Me); 23.12 (Me); 24.73 (CH); 24.78 (CH_2); 24.94 (CH); 28.10 (CH_2); 28.35 (3 Me); 40.96 (CH_2); 42.07 (CH_2); 42.22 (CH_2); 46.51 (CH_2); 50.94 (CH); 52.20 (Me); 52.77 (CH); 60.01 (CH); 79.93 (C); 155.67 (C); 167.67 (C); 170.98 (C); 172.96 (C); 173.35 (C). FAB-MS: 551.2 (17, $[M + 23]^+$), 513.2 (26, $[M + 1]^+$), 413.2 (15), 300.1 (12), 243.1 (41), 241.1 (15), 86.0 (23), 69.9 (100), 56.9 (29).

Boc-Leu-D-Phe-Pro-Leu-OMe (**110a**) *and Boc-Leu-Phe-Pro-Leu-OMe* (**110b**). According to *G.P.5*, with **9** (359 mg, 0.72 mmol), LiBr (684 mg, 7.9 mmol), THF (10 ml), *t*-BuLi (2.9 ml, 3.8 mmol; 30 min), and benzyl bromide (0.85 ml, 7.2 mmol; 21 h at −75°). LC (pentane/Et_2O 1:5) gave 51 mg of **110b**, 15 mg of **110a**/**110b** 1.6:1, 211 mg of **110a**, and 87 mg (24%) of **9**-OMe. Total yield 64%; D/L 4:1.

110a: $[\alpha]_D^{r.t.} = -93.7$ ($c = 1.02$, EtOH). ^{1}H-NMR (500 MHz, $CDCl_3$): 0.90–0.92 (*m*, 12 H); 1.37–1.45 (*m*, 1 H); 1.46 (*s*, 9 H); 1.54–1.67 (*m*, 5 H); 1.70–1.83 (*m*, 2 H); 1.89 (*m*, 1 H); 2.07–2.13 (*m*, 1 H); 2.75 (*m*, 1 H); 2.97 (*m*, 1 H); 3.06 (*m*, 1 H); 3.64 (*m*, 1 H); 3.72 (*s*, 3 H); 4.15 (*m*, 1 H); 4.43 (*m*, 1 H); 4.60 (*m*, 1 H); 4.77 (*m*, 1 H); 5.26 (*d*, $J = 7.8$, 1 H); 6.97 (*d*, $J = 8.5$, 1 H); 7.07 (*d*, $J \approx 5$, 1 H); 7.22–7.29 (*m*, 5 H). ^{13}C-NMR (125 MHz, $CDCl_3$): 21.92 (Me); 22.02 (Me); 22.84 (Me); 22.90 (Me); 24.29 (CH_2); 24.69 (CH); 25.00 (CH); 28.35 (3 Me); 28.71 (CH_2); 38.06 (CH_2); 40.74 (CH_2); 40.97 (CH_2); 46.87 (CH_2); 50.45 (CH); 52.27 (Me); 52.58 (CH); 52.92 (CH); 60.59 (CH); 80.05 (C); 127.16 (CH); 128.57 (CH); 129.41 (CH); 136.08 (C); 156.15 (C); 170.53 (C); 170.99 (C); 173.02 (C); 173.83 (C). FAB-MS: 625.1 (100, $[M + 23]^+$), 603.1 (32, $[M + 1]^+$), 525.1 (12), 503.1 (18), 361.0 (10), 305.0 (10), 243.1 (78), 136.0 (23), 120.0 (92), 91.0 (13), 86.0 (27), 69.9 (94), 56.9 (68). GC: 8.55 (Leu), 10.41 (Pro), 18.42 (D-Phe).

110b: $[\alpha]_D^{r.t.} = -43.5$ ($c = 0.9$, EtOH). ^{1}H-NMR (500 MHz, $CDCl_3$; 3 conformations): 0.94–1.00 (*m*, 12 H); 1.22–1.28 (*m*, 1 H); 1.45 (2*s*, 9 H); 1.50–1.76 (*m*, 5 H); 1.76–1.97 (*m*, 3 H); 2.24–2.33 (*m*, 1 H); 2.96 (*m*, 0.5 H); 3.00–3.08 (*m*, 1.5 H); 3.45–3.57 (*m*, 1.5 H); 3.62, 3.70, *3.74* (3*s*, 3 H); 4.07–4.20 (*m*, 1 H); 4.20–4.32 (br. *m*, 0.5 H); 4.42–4.60 (*m*, 2 H); 4.79 (*m*, 1 H); 4.93 (*m*, 1 H); 6.65, 6.89 (2 br. *m*, 0.8 H); 6.96 (*d*, $J = 7.1$, 0.2 H); 7.09 (*d*, $J = 7.06$, 0.6 H); 7.17–7.34 (*m*, 5 H); 7.55 (*d*, $J = 8.7$, 0.2 H); 8.99 (*d*, $J = 0.2$ H). ^{13}C-NMR (125 MHz, $CDCl_3$): 21.80 (Me); 22.14 (Me); 22.72 (Me); 23.06 (Me); 24.68 (CH); 24.88 (CH); 25.00 (CH_2); 27.40 (CH_2); 28.32 (3 Me); 30.80 (CH_2); 39.15 (CH_2); 41.36 (CH_2); 41.50 (CH_2); 47.45 (CH_2); 51.08 (CH); 51.98 (CH); 52.23 (Me); 53.94 (CH); 59.94 (CH); 80.04 (C); 127.05 (CH); 128.54 (CH); 129.46 (CH); 136.01 (C); 155.53 (C); 170.53 (C); 171.11 (C); 172.05 (C); 173.23 (C). FAB-MS: 625.0 (41, $[M + 23]^+$), 603.0 (45, $[M + 1]^+$), 547.0 (6), 525.0 (5), 361.0 (12), 305.0 (17), 243.1 (70), 120.0 (100), 91.0 (17), 86.0 (38), 69.9 (86), 56.9 (87). GC: 8.50 (Leu), 10.35 (Pro), 18.67 (Phe).

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