Formation of 1,3-Thiazol-5(4*H*)-imines and 1,3-Oxazol-5(4*H*)-imines in Aib-Containing Thiopeptides

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When tripeptides of type Axx[1]-Aib-Axx-OH were coupled with amino acid methyl esters by means of commonly used coupling reagents, the formation of 1,3-thiazol-5(4*H*)-imines and 1,3-oxazol-5(4*H*)-imines was observed. With the aim of understanding which structure elements are required for this reaction, several model peptides have been prepared according to our recently described methodology, a modification of the 'azirine/oxazolone method', followed by selective isomerization of the peptide thioamides. In addition, attempts to prepare peptides that contain more than one C=S group by the same methodology also led to the formation of 1,3-thiazol-5(4*H*)-imine-containing derivatives. An additional C=S group can be introduced into the peptide, when the 1,3-thiazol-5(4*H*)-imines were treated with H_2S, although mixtures of epimers were obtained. The structures of an endothiohexapeptide, two 1,3-thiazol-5(4*H*)-ones, and two peptides containing a 1,3-thiazol-5(4*H*)-imine moiety have been established by X-ray crystal-structure analysis.

Introduction. – Recently, it has been shown that the reaction of 2*H*-azirin-3-amines with α-amino thioic *S*-acids followed by selective isomerization of the thioamide function offers a convenient synthetic access to peptides containing a combination of two backbone modifications, *i.e.*, thioamide groups and α,α-disubstituted α-amino acids [1–5]. A mechanism *via* spirocyclic intermediates is conceivable for the isomerization in which the C=S group is shifted from the last to the penultimate amino acid [5]. With the aim of demonstrating the efficiency of our method, we started a program for the synthesis of Aib-containing endothiopeptides[2]).

The coupling of the peptide acid Boc-Trp-Ile-Ala-Ψ(CS)-Aib-Ile-OH (**1**) with H-Val-Aib-Leu-Aib-Pro-OMe (**2**) with the coupling reagent [(1*H*)-benzotriazol-1-yl)oxy]tris[pyrrolidin-1-yl]phosphonium hexafluorophosphate (PyBOP) in the presence of EtN(i-Pr)$_2$ led unexpectedly to a mixture (ratio 62:38) of the epimeric 1,3-thiazol-5(4*H*)-imine-containing endothiodecapeptide **3** [4] (*Scheme 1*).

Similar to the known epimerization of 1,3-thiazol-5(4*H*)-ones [6], the epimerization of Ala(3) is assumed to be catalyzed by acid during the workup, which includes washing the organic solution of **3** with a 5% $KHSO_4$ solution. The proposed mechanism for the formation of the 1,3-thiazol-5(4*H*)-imines is depicted in *Scheme 2*. Nucleophilic attack of the S-atom of the thioamide group in **A** at the C-atom of the neighboring amide group leads to the zwitterionic heterocycle **B**, which yields the 1,3-thiazol-5(4*H*)-imine **D** after elimination of H_2O.

In the present work, we describe further investigation of the formation of the 1,3-thiazol-5(4*H*)-imines with the intention of clarifying which conditions and structural

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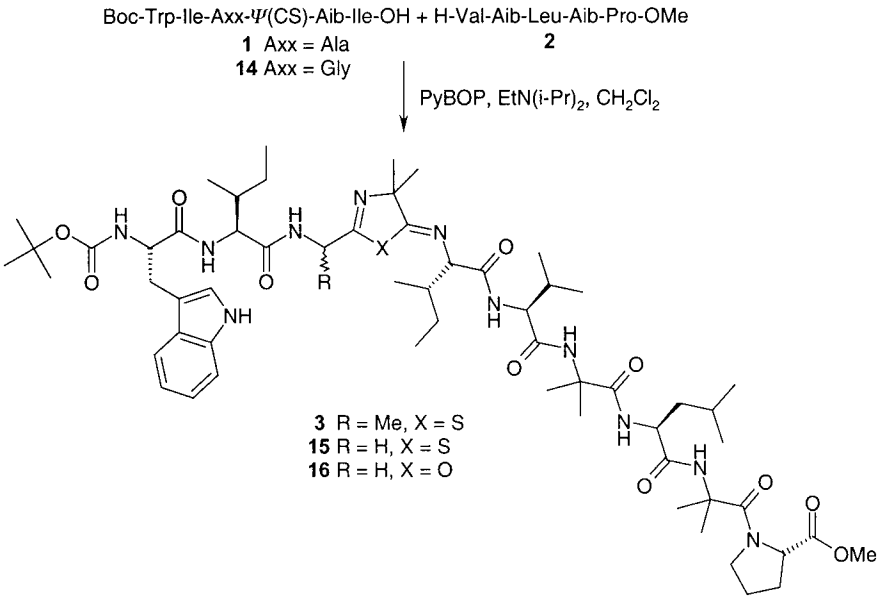
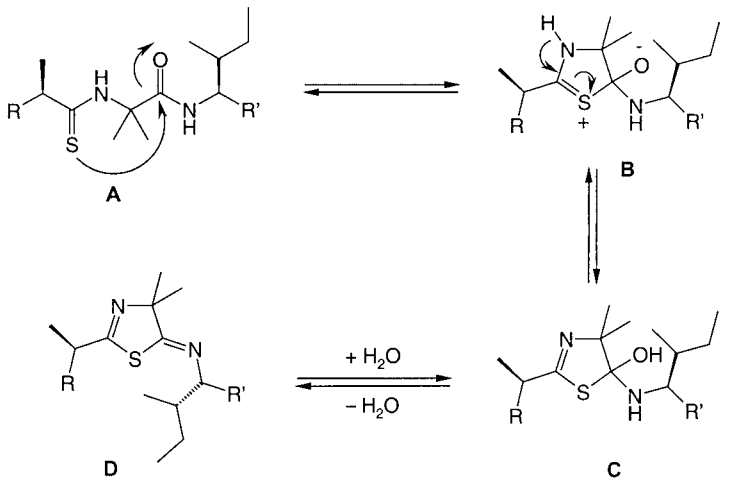
[1]) Part of the Ph.D. thesis of *R. A. B.*, Universität Zürich, 2001.

[2]) Aib = α-aminoisobutyric acid (= 2,2-dimethylglycine).

Scheme 1



Scheme 2

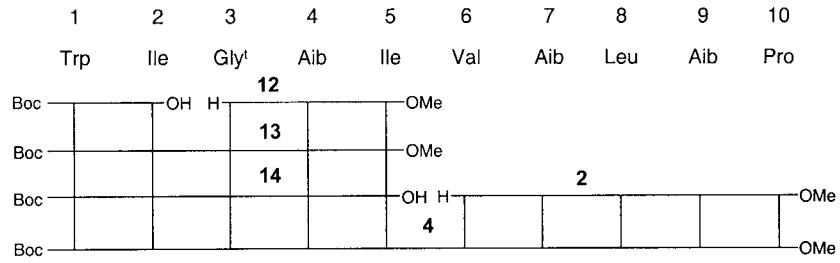


elements are required for this cyclization. The second goal was to avoid this cyclization and to prepare endothiopeptides that have more than one amide group replaced by a thioamide function. Crystal structures were determined with the aim of understanding the influence of the thioamide group and the 1,3-thiazol-5(4*H*)-imine ring with respect to the conformation of the peptide.

Results and Discussion. – *Synthesis of Endothiooligopeptides.* With the aim of improving the epimeric ratio of the endothiodecapeptide **3**, it was resynthesized according to the procedure of *Lehmann* [7], but with washing of the organic solution with a 5% $KHSO_4$ solution during the workup omitted. Analytical HPLC of **3** obtained showed two peaks in a ratio of 83:17, this being a substantial improvement of diastereoisomeric purity (formerly 62:38).

With the intention of studying the influence of different amino acids on the formation of the 1,3-thiazol-5(4*H*)-imine, we substituted alanine in position 3 in the endothiodecapeptide **3** by glycine. The projected synthesis for the endothiodecapeptide **4** is shown in *Scheme 3*.

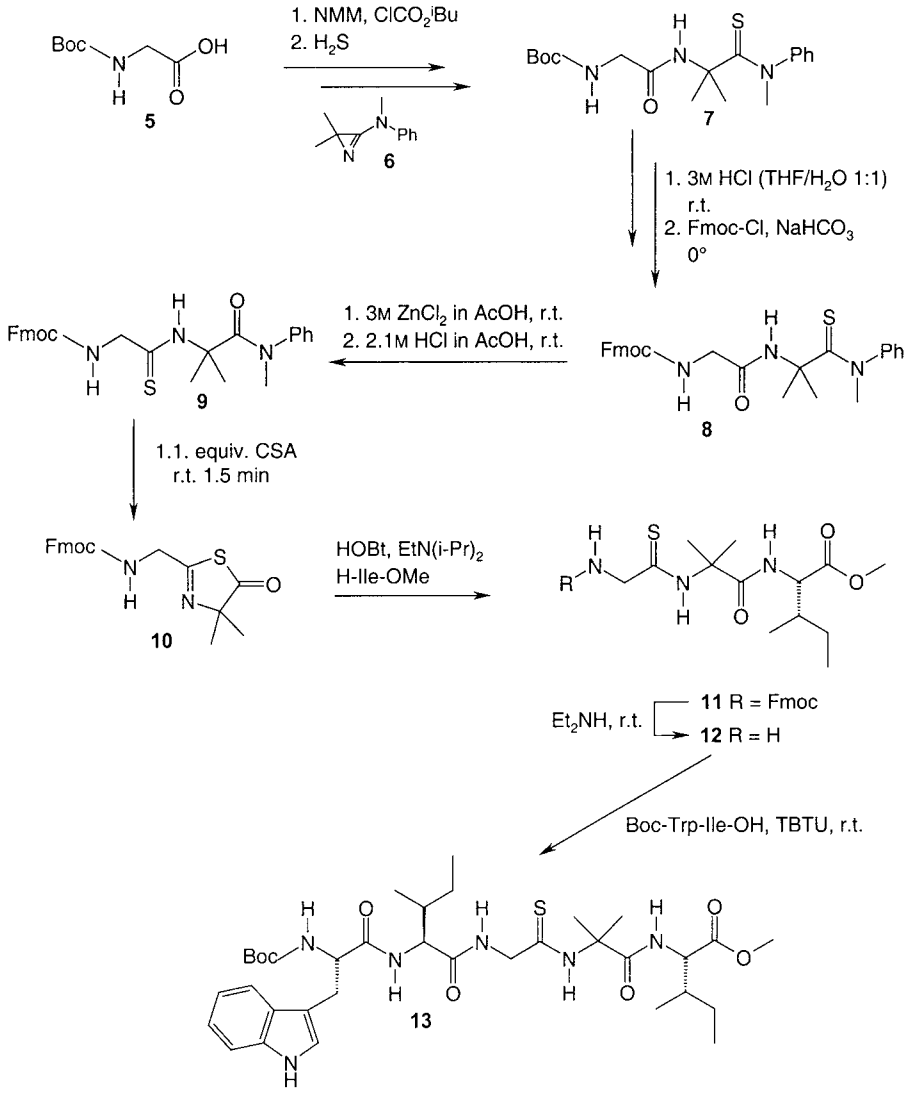
Scheme 3



The segment 3–5, Fmoc-Gly-Ψ(CS)-Aib-Ile-OMe (**11**) was synthesized according to a variation of the 'azirine/oxazolone-method' (*vide supra*). First, Boc-Gly-OH (**5**) was transformed into the thioic *S*-acid *via* reaction of the mixed anhydride with H_2S (*Scheme 4*). The crude thioic *S*-acid was then treated with 2,2,*N*-trimethyl-*N*-phenyl-2*H*-azirin-3-amine (**6**) to afford the dipeptide thioanilide **7** in 76% yield with respect to **5**. Exchange of the *N*-protecting group (Boc → Fmoc) occurred in 90% yield. Then, the dipeptide thioanilide **8** was treated with 3M $ZnCl_2$ in AcOH for 20 min (t_1), 2.1M HCl in AcOH was added, and the mixture was stirred for 10 min (t_2) at room temperature to give the isomeric endothiodipeptide **9** in 98% yield. Under acidic conditions (camphor-9-sulfonic acid; CSA), **9** was converted to the corresponding 1,3-thiazol-5(4*H*)-one **10** in 95% yield, which was coupled with H-Ile-OMe in the presence of 1-hydroxy-1*H*-benzotriazole (HOBt) and EtN(i-Pr)$_2$ to give the endothiotripeptide **11** in 74% yield (calculated for the consumed material). According to the protocol of *Lehmann* [7], Boc-Trp-Ile-OH was coupled with H-Gly-Ψ(CS)-Aib-Ile-OMe (**12**, *O*-(benzotriazole-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium tetrafluoroborate (TBTU), HOBt, EtN(i-Pr)$_2$) to give the endothiopentapeptide Boc-Trp-Ile-Gly-Ψ(CS)-Aib-Ile-OMe (**13**) in 53% yield[3]), which was then hydrolyzed with LiOH to the acid **14** (*Scheme 3*). The latter was coupled with H-Val-Aib-Leu-Aib-Pro-OMe (**2**, segment 6–10; prepared according to [7]) with PyBOP, HOBt, and EtN(i-Pr)$_2$. After 18 h and chromatographic workup, a diastereoisomeric mixture of the 1,3-thiazol-5(4*H*)-imine-containing endothiodecapeptide **15**, as well as the 1,3-oxazol-5(4*H*)-imine derivative **16**, was obtained in a total

[3]) According to ^{1}H-NMR spectra at 300 K, two conformers were present. The doubling of signals disappeared at 353 K.

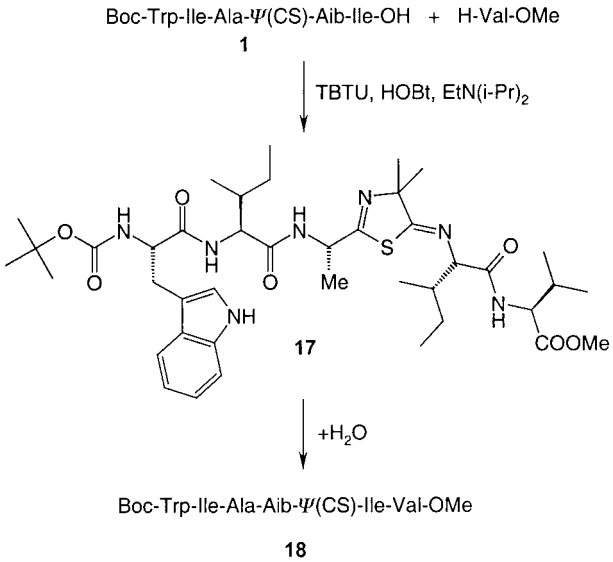
Scheme 4



yield of *ca.* 55% (*Scheme 1*). Separation by HPLC led to the pure products in 12 and 13% yields, respectively. We assume that, due to the less significant steric hindrance of Gly-Ψ(CS) compared with Ala-Ψ(CS), the attack of the neighboring amide O-atom of Aib at the C=S C-atom of Gly-Ψ(CS) is more likely to occur.

With the intention of finding the simplest structural requirements for the formation of 1,3-thiazol-5(4*H*)-imines, the hexapeptide Boc-Trp-Ile-Ala-Ψ(CS)-Aib-Ile-Val-OMe was prepared starting from Boc-Trp-Ile-Ala-Ψ(CS)-Aib-Ile-OH (**1** [7]), which was coupled with H-Val-OMe (TBTU, HOBt, EtN(i-Pr)$_2$; *Scheme 5*). In this case, we

Scheme 5



isolated only the 1,3-thiazol-5(4*H*)-imine-containing endothiohexapeptide **17** in 63% yield. The latter was crystallized from AcOEt/hexane and, after several months, suitable crystals for an X-ray crystallographic analysis were obtained. However, the product was established as the linear endothiohexapeptide **18** with the thioamide group between Aib and Ile(5), *i.e.*, the S-atom has been shifted from Ala to Aib (*Fig. 1*). This result can be explained by the hydrolysis of the 1,3-thiazol-5(4*H*)-imine *via* addition of H_2O to C(2) of the 1,3-thiazole ring, followed by ring opening.

The crystals are enantiomerically pure, and the absolute configuration of the molecule has been established independently by the diffraction experiment. Each stereogenic center in the molecule has the expected (*S*)-configuration. The asymmetric unit contains one peptide molecule plus one molecule of hexane. The peptide molecule forms a helix that is held in place in the usual way for Aib-containing peptides by four intramolecular H-bonds (O(21)$\cdots$HN(7), O(3)$\cdots$HN(10), O(6)$\cdots$HN(13), and O(9)$\cdots$HN(16)[4]), each forming a β-turn.

Synthesis of Model Peptides and Their Cyclization. Next, we shortened the peptide chain of **1** to the endothiotripeptides Z-Axx-Ψ(CS)-Aib-Ile-OH (**19**, Axx=Gly, Ala, Val, Aib), which were used for the coupling with H-Val-OMe. The syntheses are depicted in *Scheme 6*, and the yields are listed in *Table 1*. The *N*-protected α-amino acids **20** were transformed into the thioic *S*-acids, which were then treated with **6** to afford the dipeptide thioanilides **21**. Acid-catalyzed isomerization led to the corresponding endothiodipeptides **22** in good yields and without epimerization. Conversion

[4]) Arbitrary numbering of the atoms used in *Fig. 1*.

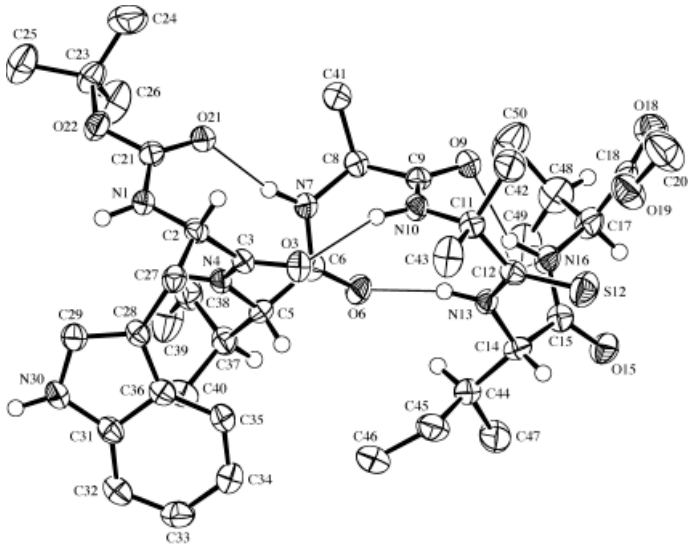


Fig. 1. *ORTEP Plot* [8] *of the molecular structure of* **18** *showing the intramolecular H-bonds* (with 50% probability ellipsoids, arbitrary numbering of the atoms, most H-atoms are omitted for clarity)

Table 1. *Synthesis of Compounds* **21**–**27**: *Overview of Yields* [%]

Amino acid **20**	R	R′	**21**	**22**	**23**	**24**	**25**	**26**	**27**
a	Me	H	73 [7]	89[a])	92	88[a])	60	–	quant.[b])
b	H	H	90 [7]	96 [7]	82	99[a])	39	17	–
c	Me_2CH	H	68	78[a])	88	78[a])	41	–	9
d	Me	Me	77 [7]	96	95	81[a])	–	–	–

[a]) Yields calculated with respect to consumed material. [b]) Formed from **25a** by hydrolysis of the 1,3-thiazol-5(4*H*)-imine on storage of a solution in AcOEt/hexane for several months.

to the 1,3-thiazol-5(4*H*)-ones **23**, and direct coupling with the H-Ile-OMe in the presence of HOBt gave the endothiotripeptides **24**, in good-to-excellent yields[5])[6]).

The structures of two representatives of the 1,3-thiazol-5(4*H*)-ones, **23a**′ (R=H, R′=Me)[7]) and **23d** (R=R′=Me), were established by X-ray crystallography (*Fig. 2*). In both cases, the five-membered ring is planar.

The yields of the endothiotripeptides **24** generally decreased with increasing bulkiness of the substituents of **23**. Therefore, the highest yield was obtained in the case of glycine derivative **24b**, the lowest one for **24c** (Val; *Table 1*).

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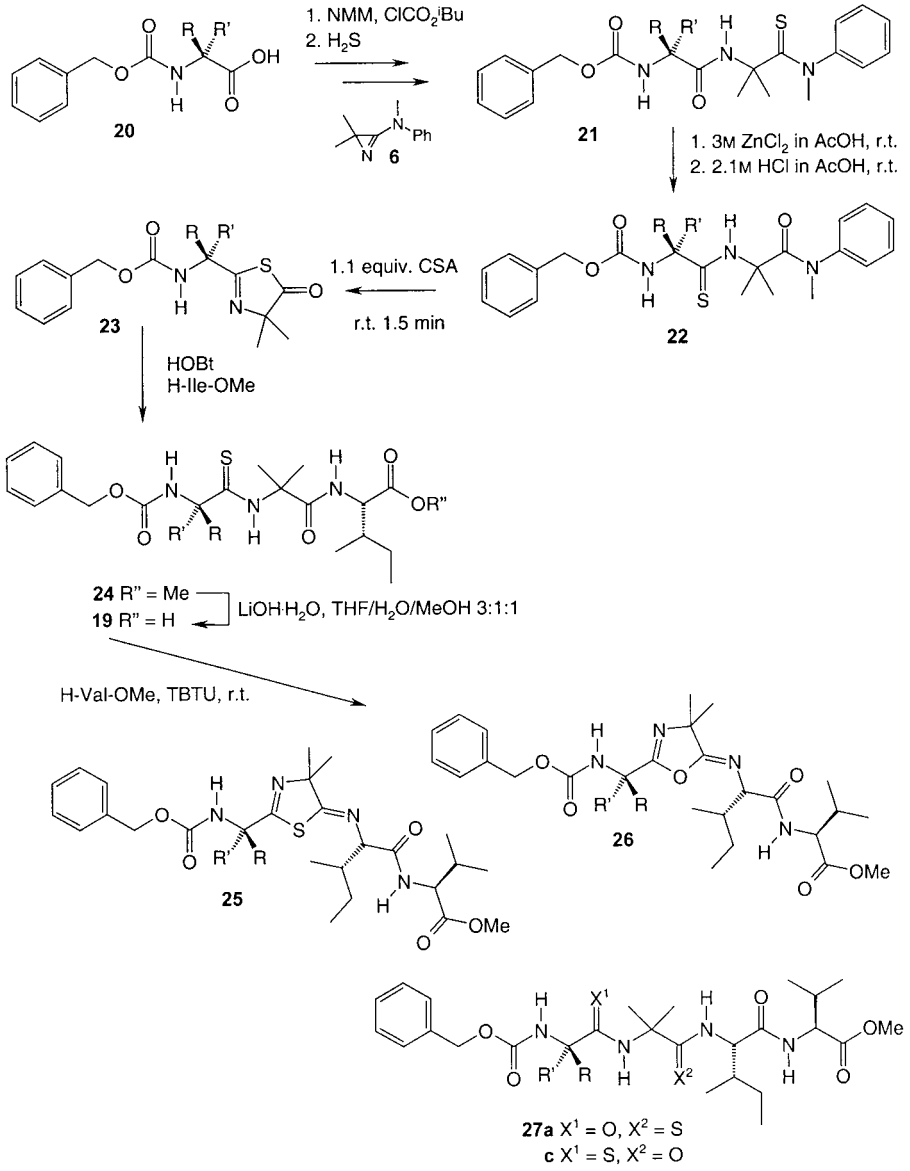
[5]) A control experiment established the enhancing effect of HOBt on the yield of the coupling of **23b** with H–Ile–OMe. Without HOBt, only 17% of **24b** were obtained compared with 74% in the presence of HOBt; 72% of **23b** were recovered, compared with 26% when HOBt had been added.

[6]) Another control experiment showed that the yields of the couplings of **23b** with amino acids increased with their decreasing bulkiness. Coupling of **23b** with H–Gly–OMe led to Z–Gly–Ψ(CS)–Aib–Gly–OMe in 99% yield, compared with 74% of **24b** when H–Ile–OMe was coupled with **23b**.

[7]) This thiazolone has been synthesized from (*R*)-alanine; otherwise (*S*)-alanine was always used.

Scheme 6



Base-catalyzed hydrolysis of **24a**–**c** with LiOH (*Scheme 6*) and coupling with H-Val-OMe (TBTU, EtN(i-Pr)$_2$) gave the 1,3-thiazol-5(4*H*)-imine-containing endothiotetrapeptides **25a**–**c**. In the case of **24b**, the 1,3-oxazol-5(4*H*)-imine **26b** was isolated as a side-product, and with **24c**, small amounts of **27c** were obtained. Again, the formation of the 1,3-oxazole-5(4*H*)-imine is observed only in the case of the glycine derivative

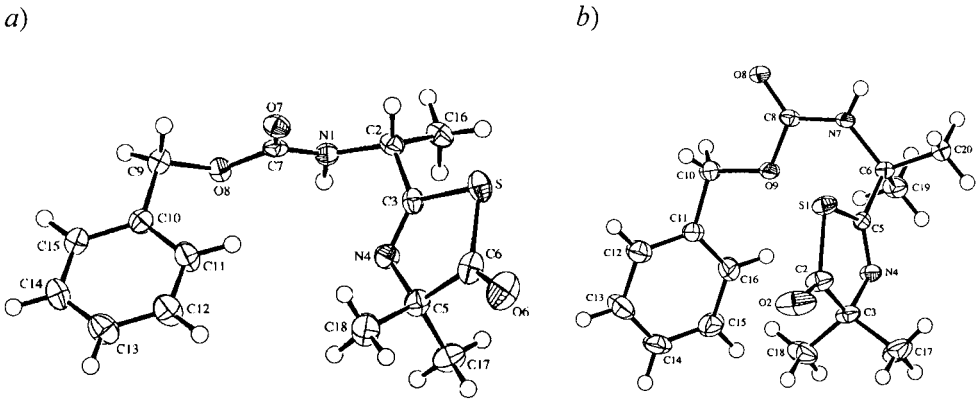


Fig. 2. *ORTEP Plots* [8] *of the molecular structure of* a) **23a′** *and* b) **23d** (50% probability ellipsoids; H-atoms given arbitrary displacement parameters for clarity)

with the lowest steric hindrance of the attack of the amide O-atom of Aib at the C=S C-atom of Gly-Ψ(CS) (*vide supra*).

Surprisingly, the base-catalyzed hydrolysis of Z-Aib-Ψ(CS)-Aib-Ile-OMe (**24d**) with LiOH, followed by the coupling with H-Val-OMe (TBTU, EtN(i-Pr)$_2$), gave the 1,3-oxazolidin-2-one derivative **28**. A feasible mechanistic explanation is depicted in *Scheme 7:* under the chosen conditions, both the methyl ester and the carbamate group are hydrolyzed to give the carbamic acid **29**, which, on treatment with TBTU, EtN(i-Pr)$_2$, undergoes a shift of the S-atom *via* intermediate **30**, cyclization of the carbamic acid function to give **31**, and coupling with H-Val-OMe to yield the final product **28**. Indeed, careful workup after the saponification gave **29** in 59% yield[8]).

So far, only the C-terminal amino acids have been varied to study their influence on the formation of the 1,3-thiazol-5(4*H*)-imines. What remained to be done was the substitution of isoleucine in the peptide Axx-Aib-Ile by other amino acids. Coupling of Z-Val-[1,3-thiazol-5(4*H*)-one]Aib (**23c**) with H-Gly-OMe and H-Ala-OMe in the presence of HOBt gave the endothiotripeptides **33a** and **33b** in 85 and 91% yield, respectively (*Scheme 8*).

Saponification and coupling with H-Val-OMe (TBTU, EtN(i-Pr)$_2$) gave in the case of **33a** the 1,3-thiazol-5(4*H*)-imine-containing endothiotetrapeptide **34a** in 20% yield, as well as the 1,3-oxazol-5(4*H*)-imine **35a** in 35% yield. For **33b**, with Ala in position 3,

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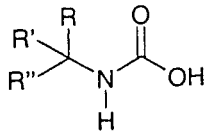
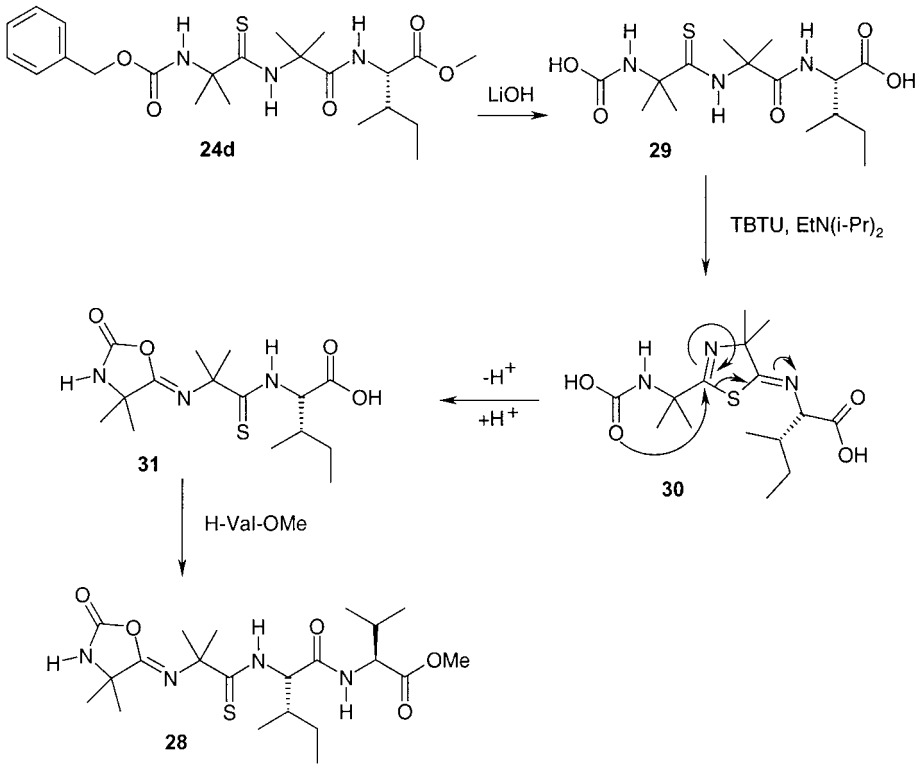
[8]) Normally, carbamic acids are not stable at room temperature and decarboxylate easily. However, several sterically crowded examples of type **32** are known to be stable. These carbamic acids were prepared *via* reaction of the corresponding amine with CO_2. Their structures are quite similar to that of **29** (R=R′=Me, R″=H [9], R=R′=R″=Me [10], R=R′=Me, R″=CN [11]).



32

Scheme 7



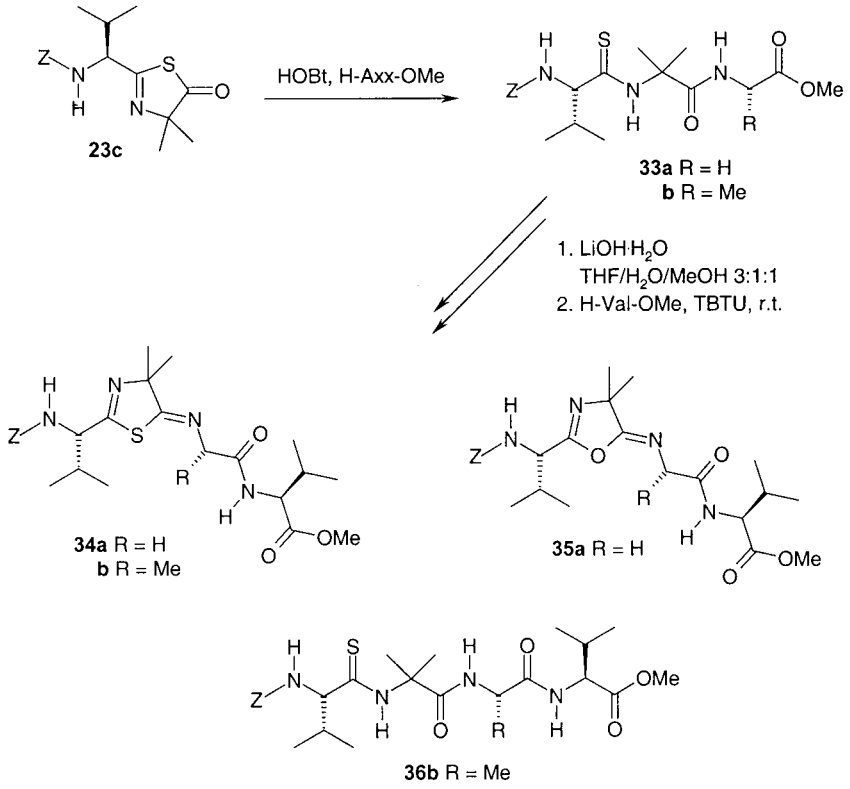
34b was obtained in 32% yield and the Z-Val-Ψ(CS)-Aib-Ala-Val-OMe (**36b**) in 55% yield.

Crystallization of **34a** from CH_2Cl_2/hexane gave crystals suitable for X-ray crystal-structure analysis. The crystals were enantiomerically pure, and the absolute configuration of the molecule (2*S*,11*S*)[9]) has been established independently by the diffraction experiment. There are two symmetry-independent molecules in the asymmetric unit. Both are of the same stereoisomer and have similar conformations (*cf. Fig. 4*). The most significant difference between the molecules is the orientation of the benzoyl group, which, in molecule B, is pivoted about the O–C axis by *ca.* 56° compared with its orientation in molecule A.

Attempts to Prepare Endothiopeptides with Two Thioamide Groups. In a first experiment, Z-Ala-Ψ(CS)-Aib-Ile-OH (**19a**) was treated with isobutyl carbonochloridate and H_2S to transform it into the thioic *S*-acid. The crude material was then treated with **6** leading to the 1,3-thiazol-5(4*H*)-imine-containing endothiotetrapeptide **37** without a second thioamide group. This indicates that no thioc *S*-acid has been formed,

[9]) Arbitrary numbering of the atoms used in *Fig. 3*.

Scheme 8



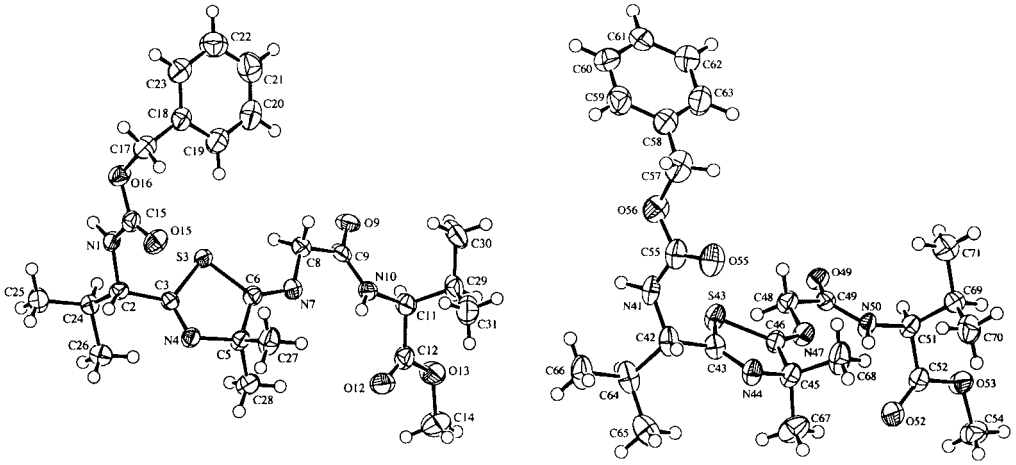
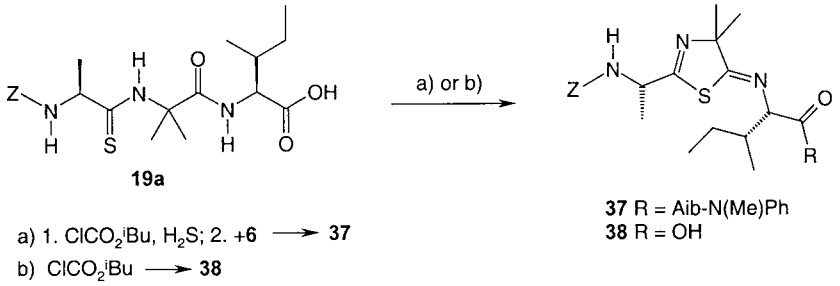


Fig. 3. *ORTEP Plots* [8] *of the structure of the two symmetry-independent molecules of* **34a** (50% probability ellipsoids; H-atoms given arbitrary displacement parameters for clarity)

as the formation of the 1,3-thiazol-5(4*H*)-imine took place during the activation with isobutyl carbonochloridate (*Scheme 9*).

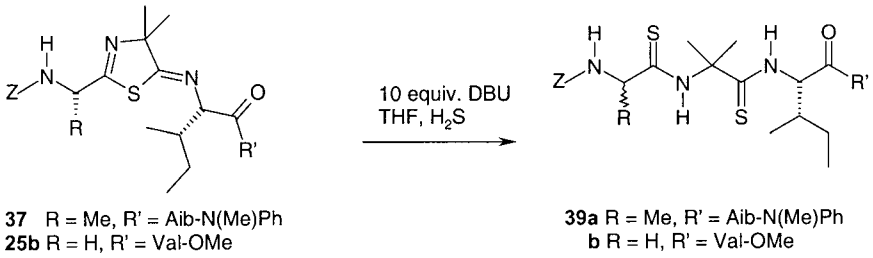
Scheme 9



With the aim of proving this conjecture, a solution of **19a** in THF was treated with isobutyl carbonochloridate only and worked up immediately. As expected, the Z-Ala-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-OH (**38**) was obtained as the only product (*Scheme 9*).

As the addition of H_2O to the 1,3-thiazol-5(4*H*)-imine-containing endothiotetrapeptides led to the epimerized linear endothiotetrapeptides, we tried to make use of this reaction by replacing H_2O by H_2S. When **37** and **25b** were treated with H_2S (*Scheme 10*) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-en (DBU), the epimerized endothiotetrapeptides **39a** and **39b** with two thioamide bond replacements were obtained in 88 and 76% yield, respectively. In the absence of DBU, no reaction occurred, which showed that only HS^- is nucleophilic enough to attack the 1,3-thiazol-5(4*H*)-imine. However, the Ala derivative **39a** was extensively epimerized (ratio 56:44), although it was possible to separate the two epimers by HPLC.

Scheme 10

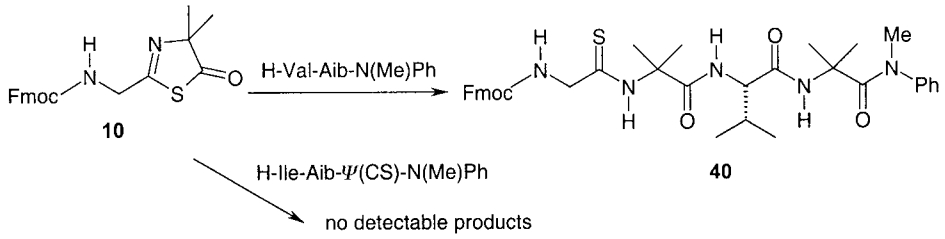


With the intention of preparing longer peptides containing more than one thioamide group, we tried to couple 1,3-thiazol-5(4*H*)-one intermediates with endothiodipeptides. First of all, we reacted Fmoc-Gly-[1,3-thiazol-5(4*H*)-one]Aib (**10**) with H-Ile-Aib-Ψ(CS)-N(Me)Ph (HOBt, EtN(i-Pr)$_2$), but the expected product was not formed at all[10]). Therefore, we carried out a control experiment using H-Val-

[10]) It is known that the coupling reaction with thiazolones is slow and the limiting step in the synthesis.

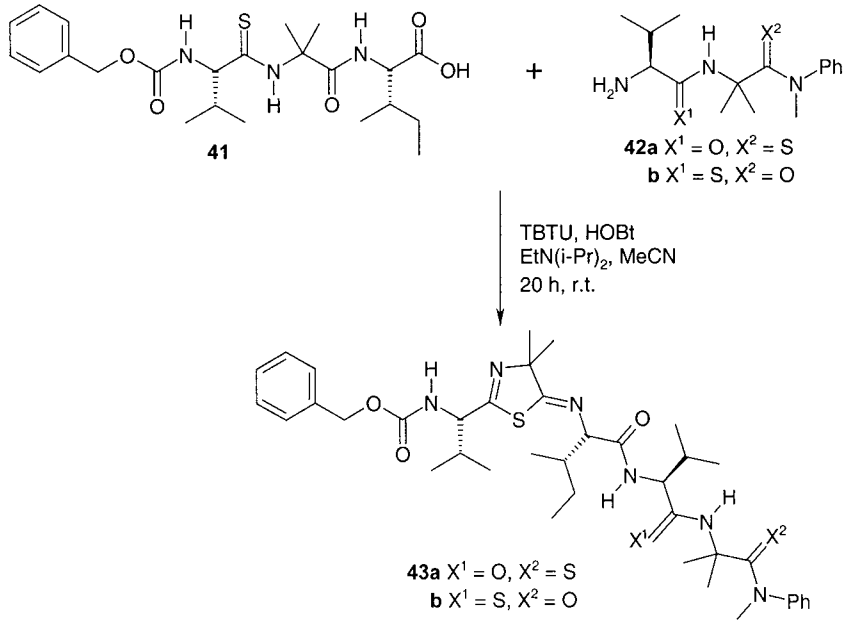
Aib-N(Me)Ph as an analogue of H-Ile-Aib-Ψ(CS)-N(Me)Ph, which does not contain S (*Scheme 11*). In this case, the endothiopentapeptide Fmoc-Gly-Ψ(CS)-Aib-Ile-Val-Aib-N(Me)Ph (**40**) in 15% yield, as well as 27% of **10**, were obtained. The failure to regain starting material in the first reaction is an indication of occurring side-reactions.

Scheme 11



With the aim of omitting the coupling step *via* a thiazolone, the tripeptide acid Z-Val-Ψ(CS)-Aib-Ile-OH (**41**) in MeCN was reacted with H-Val-Aib-Ψ(CS)-N(Me)Ph (**42a**) and H-Val-Ψ(CS)-Aib-N(Me)Ph (**42b**), respectively (TBTU, HOBt, EtN(i-Pr)$_2$) to give **43a** in 45% and **43b** in 43% yield (*Scheme 12*). Again, we did not obtain the expected linear endothiopentapeptides but the 1,3-thiazol-5(4*H*)-imine-containing analogues of type **43**.

Scheme 12



Product **43b** was recrystallized from hexane/CH_2Cl_2, yielding crystals suitable for an X-ray crystal-structure analysis (*Fig. 4*). The crystal was enantiomerically pure, and the compound has the expected (2*S*,8*S*,11*S*,38*S*)-configuration[11]). The Ph ring of the benzyl group is disordered about its pivotal axis with two approximately equally occupied orientations differing by a rotation of *ca.* 28°. The Et group of the i-Bu substituent is also disordered over two orientations, of which the major conformation occurs in *ca.* 70% of the molecules.

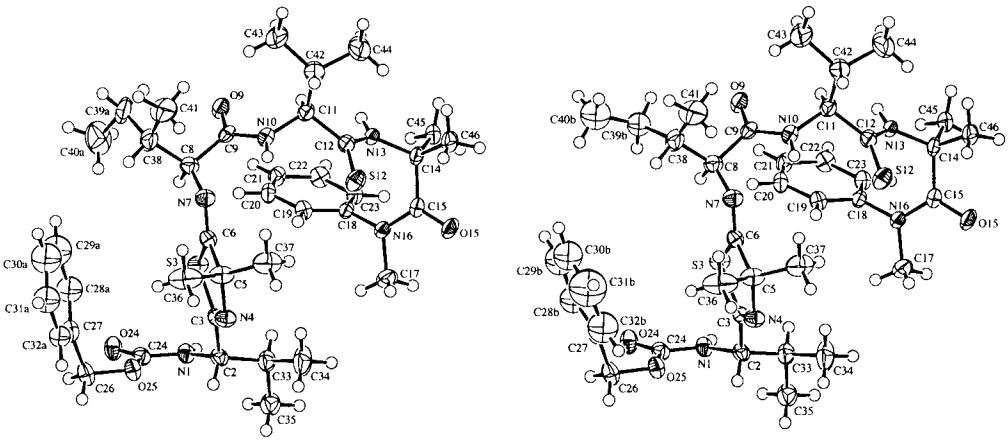


Fig. 4. *ORTEP Plot* [8] *of the structure of* **43b** (two disordered conformations; 50% probability ellipsoids; H-atoms given arbitrary displacement parameters for clarity)

Conclusions. – In summary we have shown that the 1,3-thiazol-5(4*H*)-imines and the 1,3-oxazol-5(4*H*)-imines of Aib-containing endothiopeptides are formed during the activation of the peptide acid with coupling reagents such as TBTU or isobutyl carbonochloridate. The extent of the formation of the 1,3-thiazol-5(4*H*)-imine, the 1,3-oxazol-5(4*H*)-imine, or the open-chain derivative depends upon steric influences in the peptides. Thiopeptides containing these structures are of considerable interest [6]. Furthermore, we showed that an additional C=S group can be introduced into the peptide chain, when the 1,3-thiazol-5(4*H*)-imines are treated with H_2S, although this reaction leads to epimerized products.

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Experimental Part

1. *General*. See [2].

General Procedure A (*GP A*). To a soln. of 1 equiv. of an *N*-protected amino acid in THF, 2 equiv. of *N*-methylmorpholine (NMM) and 1 equiv. of isobutyl carbonochloridate ($ClCO_2{}^iBu$) were added at $-10°$;

[11]) Arbitrary numbering of the atoms used in *Fig. 4*.

immediately a white solid precipitated. The mixture was stirred for *ca.* 5 min, then a slow stream of *in situ* generated H_2S (a 50% H_2SO_4 soln. was dropped slowly to 10–20 equiv. $Na_2S \cdot H_2O$) was bubbled through the soln. After stirring for 1 h at $-10°$, the suspension was transferred into a separatory funnel, diluted with Et_2O, and extracted with 0.1M H_3PO_4 soln. (3×). The combined org. phase was dried ($MgSO_4$) and evaporated, and the residue was dried under high vacuum (h.v.). The crude amino thioic *S*-acid formed was dissolved in CH_2Cl_2 and cooled to 0°, and 1 equiv. of 2,2,*N*-trimethyl-*N*-phenyl-2*H*-azirin-3-amine (**6**) was added slowly. The mixture was allowed to reach r.t. and stirred until the starting material was completely consumed (TLC). Then, the solvent was evaporated, and the residue was dried (h.v.). The crude product was purified by chromatography (SiO_2).

General Procedure B (*GP B*). The intense yellow soln. of a thiodipeptide in AcOH was treated with $ZnCl_2$, and the mixture was stirred at r.t.; the $ZnCl_2$ dissolved only slowly. After t_1, AcOH saturated with HCl (2.1M) was added to the mixture. After t_2, the pale yellow mixture was carefully added to a 5% $NaHCO_3$ soln., and the resulting mixture was extracted with CH_2Cl_2. The combined org. phase was dried ($MgSO_4$) and evaporated, and the residue was chromatographed (SiO_2) if necessary.

General Procedure C (*GP C*). The soln. of a thiodipeptide in CH_2Cl_2 was treated with 1.1 equiv. of (±)-camphor-10-sulfonic acid (CSA). After stirring for 1.5 min at r.t., the reaction was quenched with $NaHCO_3$ soln. and the mixture was extracted with CH_2Cl_2. The org. layers were dried ($MgSO_4$), filtered, the solvent was evaporated, and the residue was chromatographed (SiO_2).

General Procedure D (*GP D*). To a soln. of a thiazolone in MeCN, EtN(i-Pr)$_2$ (2 equiv.), 1-hydroxy-1*H*-benzotriazole (HOBt, 2 equiv.), and the amino acid hydrochloride (1.1 equiv.) were added. The mixture was stirred at r.t. for several days, while the solution turned yellow. The mixture was diluted with CH_2Cl_2 and washed with dil. aq. $NaHCO_3$ and $KHSO_4$ soln. The combined org. phase was dried ($MgSO_4$), filtered, and concentrated. The residue was chromatographed (SiO_2).

General Procedure E (*GP E*). To a soln. of 1 equiv. of an *N*-protected peptide methyl ester in THF/MeOH/H_2O 3:1:1 was added $LiOH \cdot H_2O$ (3 equiv.), and the mixture was stirred at r.t. until the starting material was consumed (TLC). The mixture was diluted with CH_2Cl_2, and washed with 5% $KHSO_4$, soln., the aq. phase was re-extracted with CH_2Cl_2, the combined org. phase was dried ($MgSO_4$), filtered, and evaporated. The crude product was dried (h.v.), and used in the next reaction without further purification.

General Procedure F (*GP F*). To a soln. of 1 equiv. of an *N*-protected peptide acid in MeCN or CH_2Cl_2 were added the amino component (1.1 equiv.), TBTU (1.05 equiv.), HOBt (1.05 equiv.), if indicated, and EtN(i-Pr)$_2$ (3 equiv.). The mixture was stirred at r.t. until the starting material was consumed (TLC). Then, the soln. was concentrated *in vacuo*, and the crude product was purified by chromatography (SiO_2).

General Procedure G (*GP G*). A slow stream of H_2S was bubbled through a soln. of a thiazolimine in THF in the presence of DBU (10 equiv.). After 20 min, a stream of N_2 was bubbled through the soln. for 10 min. Then, the soln. was evaporated, and the residue was purified by chromatography (SiO_2).

2. *Synthesis of Methyl (2*S*)-1-(2-[(2*S*)-2-[2-((2*S*)-2-[(2*S*,3*S*)-2-[(2-[1-[(2*S*,3*S*)-2-((2*S*)-[[(*tert*-Butoxy)carbonyl]amino]-3-(indol-3-yl)propanamido)-3-methylpentanamido]methyl]-4,5-dihydro-4,4-dimethyl-1,3-thiazol-5-yliden)amino]-3-methylpentanamido]-3-methylbutanamido)-2-methylpropanamido]-4-methylpentanamido]-2-methylpropanoyl)pyrrolidine-2-carboxylate* (Boc-Trp-Ile-Gly-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-Val-Aib-Leu-Aib-Pro-OMe; **15**). 2.1. tert-*Butyl* N-*[(2-[1,1-Dimethyl-2-[methyl(phenyl)amino]-2-thioxoethyl]amino)-2-oxoethyl]carbamate* (Boc-Gly-Aib-Ψ(CS)-N(Me)Ph; **7**). According to the *GP A*, with Boc-Gly-OH (**5**; 1435 mg, 8.19 mmol), THF (30 ml), NMM (1.80 ml, 16.4 mmol), $ClCO_2{}^iBu$ (1.07 ml, 8.2 mmol), $Na_2S \cdot H_2O$ (10.7 g, 82.0 mmol), CH_2Cl_2 (60 ml), and **6** (1430 mg, 8.20 mmol); reaction time: 4 h. Chromatography (SiO_2; AcOEt/hexane 1:2) gave 2259 mg (76%) of **7**. Yellow, thick oil, which solidified under h.v. IR (KBr): 3401*m*, 3051*s*, 2979*m*, 2956*m*, 1711*s*, 1668*s*, 1595*m*, 1500*s*, 1392*s*, 1368*s*, 1288*s*, 1253*m*, 1227*m*, 1174*s*, 1129*m*, 1106*s*, 1064*m*, 1024*w*, 1007*w*, 997*w*, 976*w*, 942*w*, 932*w*, 862*w*, 790*w*, 762*w*, 700*m*. ^{1}H-NMR: 7.43–7.19 (*m*, 10 arom. H); 6.88 (br. *s*, NH); 5.03 (br. *s*, NH); 3.71 (*s*, MeN); 3.46 (*s*, CH_2(Gly)); 1.66 (*s*, 2 Me(Aib)); 1.44 (*s*, *t*-Bu). ^{13}C-NMR: 208.3 (*s*, CS(Aib^t)); 167.6 (*s*, CO(Gly)); 156.7 (*s*, CONH); 147.7 (*s*, 1 arom. C); 129.6, 128.3, 126.0 (3*d*, 5 arom. C); 80.0 (*s*, Me_3C); 62.8 (*s*, C(α)(Aib^t)); 51.2 (*q*, MeN); 44.7 (*t*, CH_2(Gly)); 30.1 (*q*, 2 Me(Aib^t)); 28.3 (*q*, Me_3C). CI-MS: 366 (100, $[M+H]^+$), 310 (80). Anal. calc. for $C_{18}H_{27}N_3O_3S \cdot 0.2\ H_2O$ (369.10): C 58.58, H 7.48, N 11.38, S 8.69; found: C 58.51, H 7.35, N 11.28, S 8.55.

2.2. *(9*H*-Fluoren-9-yl)methyl* N-*[(2-[1,1-Dimethyl-2-[methyl(phenyl)amino]-2-thioxoethyl]amino)-2-oxoethyl]carbamate* (Fmoc-Gly-Aib-Ψ(CS)-N(Me)Ph; **8**). A soln. of **7** (1382 mg, 3.78 mmol) in 3M HCl (THF/H_2O, 40 ml) was stirred for 20 h at r.t. The soln. was cooled to 0°, alkalinized with $NaHCO_3$, and diluted with dioxane (50 ml) and H_2O (10 ml). The yellow suspension was treated with Fmoc-Cl (1172 mg, 4.53 mmol) dissolved in dioxane (20 ml). After 1 h, the mixture was warmed to r.t. and stirred for another 20 h. The

suspension was diluted with H_2O and extracted with Et_2O. The combined org. phase was dried ($MgSO_4$), filtered, evaporated, and the yellow residue was chromatographed (SiO_2; AcOEt/hexane 1:1) to give 1651 mg (90%) of **8**. Yellow viscous oil, which solidified under h.v. IR (KBr): 3331*s*, 3262*m*, 3062*w*, 2937*w*, 1718*s*, 1681*s*, 1592*w*, 1507*s*, 1466*m*, 1447*s*, 1372*m*, 1357*s*, 1216*s*, 1169*m*, 1002*s*, 1078*m*, 1042*m*, 1004*m*, 994*w*, 770*m*, 757*m*, 740*m*, 708*w*. ^{1}H-NMR: 7.70–7.09 (*m*, 13 arom. H); 6.76, 5.18 (2br. *s*, 2 NH); 4.31 (*d*, $J = 6.9$, CH_2(Fmoc)); 4.14 (*t*, $J = 6.9$, CH(Fmoc)); 3.71 (*s*, MeN); 3.47 (*d*, $J = 5.3$, CH_2(Gly)); 1.57 (*s*, 2 Me(Aib^t)). ^{13}C-NMR: 208.1 (*s*, CS(Aib^t)); 166.8 (*s*, CO(Gly)); 156.1 (*s*, CONH); 147.5, 143.7, 141.2 (3*s*, 5 arom. C); 129.5, 128.3, 127.7, 127.0, 125.9, 125.0, 119.9 (7*d*, 13 arom. C); 67.1 (*t*, CH_2(Fmoc)); 62.8 (*s*, C(α)(Aib^t)); 51.3 (*q*, MeN); 47.0 (*d*, CH(Fmoc)); 44.8 (*t*, CH_2(Gly)); 29.9 (*q*, 2 Me(Aib^t)). CI-MS: 488 (100, $[M+H]^+$), 266 (90). Anal. calc. for $C_{28}H_{29}N_3O_3S$ (487.63): C 68.97, H 5.99, N 8.62, S 6.58; found: C 68.76, H 5.86, N 8.60, S 6.14.

2.3. *(9*H*-Fluoren-9-yl)methyl* N*-[(2-[1,1-Dimethyl-2-[methyl(phenyl)amino]-2-oxoethyl]amino)-2-thioxoethyl]carbamate* (Fmoc-Gly-Ψ(CS)-Aib-N(Me)Ph; **9**). According to the *GP B*, with **8** (1663 mg, 3.39 mmol), AcOH (35 ml), $ZnCl_2$ (16.93 g, 102.6 mmol), and 2.1M HCl in AcOH (3.5 ml); reaction time: $t_1 = 20$ min, $t_2 = 10$ min: 1615 mg (98%) of crude **9**. Thick oil, which solidified under h.v. IR (KBr): 3250*m*, 3057*m*, 2941*m*, 1723*s*, 1632*s*, 1592*s*, 1494*s*, 1450*s*, 1423*s*, 1387*s*, 1361*s*, 1227*s*, 1171*m*, 1116*m*, 1090*m*, 1043*m*, 987*w*, 910*w*, 760*s*, 741*s*, 706*s*. ^{1}H-NMR: 7.79–7.26 (*m*, 13 arom. H, NH); 5.05 (br. *s*, NH); 4.39 (*d*, $J = 6.8$, CH_2(Fmoc)); 4.21 (*t*, $J = 6.8$, CH(Fmoc)); 3.78 (*d*, $J = 5.9$, CH_2(Gly^t)); 3.24 (*s*, MeN); 1.68 (*s*, 2 Me(Aib)). ^{13}C-NMR: 197.0 (*s*, CS(Gly^t)); 171.1 (*s*, CO(Aib)); 156.1 (*s*, CONH); 144.4, 143.6, 141.4 (3*s*, 5 arom. C); 129.2, 127.9, 127.8, 127.3, 127.0, 124.9, 120.0 (7*d*, 13 arom. C); 67.2 (*t*, CH_2(Fmoc)); 61.3 (*s*, C(α)(Aib)); 52.7 (*t*, CH_2(Gly^t)); 46.7 (*d*, CH(Fmoc)); 41.0 (*q*, MeN); 25.9 (*q*, 2 Me(Aib)). ESI-MS: 526 ($[M+K]^+$), 510 ($[M+Na]^+$), 381 ($[M-(Me(Ph)N)]^+$). Anal. calc. for $C_{28}H_{29}N_3O_3S \cdot 0.25\ H_2O$ (492.13): C 68.34, H 6.04, N 8.54, S 6.52; found: C 68.33, H 5.80, N 8.54, S 6.40.

2.4. *(9*H*-Fluoren-9-yl)methyl* N*-[1-(4,5-Dihydro-4,4-dimethyl-5-oxo-1,3-thiazol-2-yl)methyl]carbamate* (Fmoc-Gly-[1,3-thiazol-5(4*H*)-one]Aib; **10**). According to the *GP C*, with **9** (117 mg, 0.24 mmol) in CH_2Cl_2 (10 ml), and CSA (61 mg, 0.26 mmol). Chromatography (SiO_2; AcOEt/hexane 1:3) yielded 86 mg (95%) of **10**. Thick oil, which solidified under h.v. IR (KBr): 3214*m*, 3039*w*, 2976*w*, 2961*w*, 2828*w*, 1731*s*, 1707*s*, 1630*m*, 1540*s*, 1479*w*, 1452*m*, 1418*w*, 1376*w*, 1355*w*, 1274*s*, 1262*s*, 1204*w*, 1180*w*, 1162*m*, 1106*w*, 1086*m*, 1047*m*, 989*w*, 964*m*, 937*m*, 914*w*, 856*w*, 796*w*, 750*m*, 735*m*, 706*w*. ^{1}H-NMR: 7.77–7.25 (*m*, 8 arom. H, NH); 5.53 (br. *s*, NH); 4.46 (*d*, $J = 6.7$, CH_2(Fmoc)); 4.32 (*d*, $J = 5.6$, CH_2(Gly^t)); 4.23 (*t*, $J = 6.7$, CH(Fmoc)); 1.40 (*s*, 2 Me(Aib)). ^{13}C-NMR: 210.2 (*s*, C(5)(thiazolone)); 162.5 (*s*, C(2)(thiazolone)); 156.0 (*s*, CONH); 143.6, 141.3 (2*s*, 4 arom. C); 127.7, 127.0, 124.9, 120.0 (4*d*, 8 arom. C); 82.9 (*s*, C(4)(thiazolone)); 67.1 (*t*, CH_2(Fmoc)); 47.1 (*d*, CH(Fmoc)); 45.1 (*t*, CH_2(Gly^t)); 24.3 (*q*, 2 Me(Aib)). ESI-MS: 526 ($[M+K]^+$), 510 ($[M+Na]^+$), 381 ($[M-(Me(Ph)N]^+$). Anal. calc. for $C_{21}H_{20}N_2O_3S$ (380.47): C 66.30, H 5.30, N 7.36; found: C 66.04, H 5.29, N 7.39.

2.5. *Methyl (2*S*,3*S*)-2-[2-[([(9*H*-Fluoren-9-yl)methoxy]carbonyl]amino)ethanethioamido]-2-methylpropanamido]-3-methylpentanoate* (Fmoc-Gly-Ψ(CS)-Aib-Ile-OMe; **11**). According to the *GP D*, with **10** (803 mg, 2.11 mmol) in MeCN (40 ml), EtN(i-Pr)$_2$ (0.73 ml, 4.22 mmol), HOBt (639 mg, 4.22 mmol), and H-Ile-OMe·HCl (422 mg, 2.32 mmol); reaction time: 10 d. Chromatography (SiO_2; AcOEt/hexane 1:1) yielded 567 mg (51%) of **11** and 245 mg (31%) of **10**. Yield of **11** calc. for the consumed material: 74%. Thick oil, which solidified under h.v. IR (KBr): 3335*m*, 3041*w*, 2967*m*, 2877*w*, 1734*s*, 1664*m*, 1522*s*, 1450*m*, 1414*m*, 1383*m*, 1362*m*, 1334*m*, 1249*s*, 1104*w*, 1084*w*, 1045*w*, 990*w*, 940*w*, 760*m*, 742*m*. ^{1}H-NMR: 8.61 (br. *s*, NH); 7.77–7.26 (*m*, 8 arom. H); 6.42 (br. *d*, $J = 8.2$, NH); 5.74, 5.52 (2 br. *s*, 2 NH); 4.55 (*dd*, $J = 8.2$, 4.9, CH(α)(Ile)); 4.43 (*d*, $J = 6.7$, CH_2(Fmoc)); 4.21 (*t*, $J = 6.8$, CH(Fmoc)); 4.15–4.11 (*m*, CH_2(Gly^t)); 3.70 (*s*, MeO); 1.93–1.88 (*m*, CH(β)(Ile)); 1.76, 1.75 (2*s*, 2 Me(Aib)); 1.45–1.15 (*m*, CH_2(Ile)); 0.94–0.87 (*m*, 2 Me(Ile)). ^{13}C-NMR: 199.1 (*s*, CS(Gly^t)); 172.6, 172.2 (2*s*, 2 CO); 157.0 (*s*, CONH); 143.6, 141.2 (2*s*, 4 arom. C); 127.7, 127.0, 125.0, 119.9 (4*d*, 8 arom. C); 67.5 (*t*, CH_2(Fmoc)); 60.5 (*s*, C(α)(Aib)); 56.8 (*t*, CH_2(Gly^t)); 53.4 (*d*, CH(α)(Ile)); 52.0 (*q*, MeO); 47.0 (*d*, CH(Fmoc)); 37.8 (*t*, CH(β)(Ile)); 25.2 (*t*, CH_2(Ile)); 24.3, 23.6 (2*q*, 2 Me(Aib)); 15.4 (*q*, Me(γ)(Ile)); 11.4 (*q*, Me(δ)(Ile)). ESI-MS: 526 ($[M+K]^+$), 510 ($[M+Na]^+$), 381 ($[M-(Me(Ph)N]^+$). Anal. calc. for $C_{28}H_{35}N_3O_5S \cdot 0.2\ H_2O$ (529.27): C 63.54, H 6.74, N 7.94, S 6.06; found: C 63.51, H 6.65, N 7.35, S 6.05.

2.6. *Methyl (2*S*,3*S*)-2-(2-[2-[(2*S*,3*S*)-2-((2*S*)-[[(*tert*-Butoxy)carbonyl]amino]-3-(indol-3-yl)propanamido)-3-methylpentanamido]ethanethioamido]-2-methylpropanamido)-3-methylpentanoate* (Boc-Trp-Ile-Gly-Ψ(CS)-Aib-Ile-OMe; **13**). To **11** (271 mg, 0.515 mmol), Et_2NH (1.2 ml) was added, and the resulting soln. stirred for 1 h at r.t., while the color became an intense yellow. According to the *GP F*, with crude **12**, Boc-Trp-Ile-OH ([7], 238 mg, 0.57 mmol), PyBOP (268 mg, 0.52 mmol), MeCN (10 ml), and EtN(i-Pr)$_2$ (0.18 ml, 1.03 mmol); reaction time: 17 h. Chromatography (SiO_2; AcOEt/hexane 1:1 → AcOEt) gave 191 mg (53%) of **13**. Thick oil, which solidified under h.v. IR (KBr): 3324*m*, 2968*m*, 2935*w*, 2878*w*, 1663*s*, 1522*s*, 1458*m*, 1437*m*, 1386*m*, 1366*m*,

1251*m*, 1170*s*, 1100*w*, 1050*w*, 1012*w*, 852*m*, 743*m*. ^{1}H-NMR ((D$_6$)DMSO)[12]: 10.77 (br. *d*, *J* = 6.7, NH); 9.40, 9.34 (2 br. *d*, NH); 8.39, 8.33 (2 br. *d*, NH); 7.87 – 6.89 (*m*, 5 arom. H, 3 NH); 4.34 – 3.96 (*m*, CH(α)(Gly^t), CH(α)(Ile^1), CH(α)(Ile^2), CH(α)(Trp)); 3.60, 3.58 (2*s*, MeO); 3.14 – 2.91 (*m*, CH$_2$(Trp)); 1.99 – 1.79 (*m*, CH(β)(Ile^1), CH(β)(Ile^2)); 1.59, 1.55 (2*s*, 2 Me(Aib)); 1.54 – 1.15 (*m*, CH$_2$(Ile^1), CH$_2$(Ile^2)); 1.32, 1.30 (2*s*, *t*-Bu); 0.87 – 0.74 (*m*, 2 Me(Ile^1), 2 Me(Ile^2)). ^{13}C-NMR ((D$_6$)DMSO): 198.0 (*s*, CS(Gly^t)); 171.7, 171.5, 171.1, 170.8 (4*s*, 4 CO); 154.5 (*s*, CO(carbamate)); 135.8 (*s*, C(δ^2)(Trp)); 127.0 (*s*, C(ε^2)(Trp)); 122.8, 120.1, 117.6, 111.1, 110.5, 109.8 (6*d*, 6 arom. C); 77.9 (*s*, Me$_3$*C*); 59.7 (*s*, C(α)(Aib)); 57.0, 56.3, 55.2, 55.0 (4*d*, CH(α)(Trp), CH(α)(Ile^1), CH(α)(Ile^2)); 51.3 (*q*, MeO); 51.0, 50.6 (2*t*, CH$_2$(Gly^t)); 36.1, 35.8 (2*d*, CH(β)(Ile^1), CH(β)(Ile^2)); 27,5 (*q*, *Me*$_3$C); 27.0 (*t*, CH$_2$(Trp)); 24.8, 24.6, 22.7, 22.4 (4*q*, 2 Me(Aib)); 23.9, 22.7 (2*t*, CH$_2$(Ile^1), CH$_2$(Ile^2)); 15.3, 14.2, 13.9, 11.3, 10.9, 10.6 (6*q*, 2 Me(Ile^1), 2 Me(Ile^2)). ESI-MS: 725 ([*M* + Na]$^+$).

2.7. *Boc-Trp-Ile-Gly-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-Val-Aib-Leu-Aib-Pro-OMe* (**15**). According to the *GP E*, with **13** (75 mg, 0.14 mmol), THF/MeOH/H$_2$O 3 : 1 : 1 (2 ml), and LiOH · H$_2$O (12 mg, 0.28 mmol); reaction time: 3 h. According to the *GP F*, with H-Val-Aib-Ile-Aib-Pro-OMe (**2**; preparation according to the procedure in [7] from Z-Val-Aib-Ile-Aib-Pro-OMe (108 mg, 0.17 mmol) and Pd/C (10 mg) in MeOH (4 ml)), crude Boc-Trp-Ile-Gly-Ψ(CS)-Aib-Ile-OH (**14**), PyBOP (87 mg, 0.17 mmol), CH_2Cl_2 (2 ml), and EtN(i-Pr)$_2$ (0.05 ml, 0.28 mmol); reaction time: 18 h. Chromatography (SiO_2; AcOEt/MeOH 30 : 1) gave 91 mg of a mixture of **15** and the corresponding 1,3-oxazole derivative **16** in a combined yield of *ca*. 55%. Thick oil. HPLC (*Macherey-Nagel*, *Nucleosil 100-7 C$_8$*, MeCN/H$_2$O 70 : 30, 10.5 ml/min, 254 nm) gave 20 mg (12%) of **15** and 21 mg (13%) of **16**.

Data of **15**: IR (KBr): 3324*s*, 3058*w*, 2965*s*, 2934*m*, 2876*m*, 1662*s*, 1515*s*, 1459*s*, 1416*m*, 1383*m*, 1365*m*, 1280*m*, 1250*m*, 1170*s*, 1094*w*, 1050*w*, 1012*w*, 928*w*, 857*w*, 742*w*. ^{1}H-NMR (600 MHz; ^{13}C,^{1}H-HMBC, conformers): 8.97, 8.87 (2*s*, NH(ε^1)(Trp)); 7.64, 7.61 (2*d*, *J* = 7.9, CH(ε^3)(Trp)); 7.41, 7.39 (2*d*, *J* = 8.1, CH(ξ^1)(Trp)); 7.27 (*s*, NH(Aib^3)); 7.20 – 7.07 (*m*, CH(η)(Trp), CH(ξ^2)(Trp), CH(δ^1)(Trp), NH(Val), NH(Leu)); 6.88 (*s*, NH(Gly)); 6.30, 6.15 (*s*, NH(Aib^2)); 6.25 (*d*, *J* = 8.3, NH(Ile^1)); 5.26, 5.22 (2*s*, NH(Trp)); 4.56 – 4.52 (*m*, CH(α)(Pro)); 4.44 – 4.39 (*m*, CH$_2$(Gly)); 4.33 – 4.30 (*m*, CH(α)(Trp)); 4.26 – 4.23 (*m*, CH(α)(Ile^1)); 4.21 – 4.11 (*m*, CH(α)(Val), CH(α)(Leu)); 3.80 – 3.69 (*m*, H$_a$ of CH$_2$(δ)(Pro)); 3.68, 3.60 (2*s*, MeO); 3.65 – 3.55 (*m*, H$_b$ of CH$_2$(δ)(Pro)); 3.31 (*d*, *J* = 3.7, CH(α)(Ile^2)); 3.30 – 3.16 (*m*, CH$_2$(Trp)); 2.19 – 2.15 (*m*, CH(β)(Val)); 2.08 – 2.05 (*m*, CH(β)(Ile^1), CH(β)(Ile^2)); 1.96 – 1.66 (*m*, CH$_2$(γ)(Pro), CH$_2$(Leu), CH$_2$(β)(Pro)); 1.55 – 1.42 (*m*, CH(γ)(Leu)); 1.55, 1.54, 1.52, 1.50, 1.49, 1.45, 1.44, 1.43 (8*s*, 2 Me(Aib^1), 2 Me(Aib^2), 2 Me(Aib^3)); 1.42 (*s*, *t*-Bu); 1.31 – 1.23 (*m*, CH$_2$(Ile^1), CH$_2$(Ile^2)); 1.04, 1.02 (2*d*, *J* = 6.8, 2 Me(Val)); 0.94 – 0.74 (*m*, 2 Me(Ile^1), 2 Me(Ile^2), 2 Me(Leu)). ^{13}C-NMR (75 and 150 MHz, conformers): 179.2, 179.1 (2*s*, C(5)(thiazolimine)); 173.7, 173.6, 173.5, 173.4, 173.2, 172.5, 172.4, 172.1, 171.4, 171.2, 170.9, 170.7 (12*s*, 8 CO); 161.6, 160.7 (2*s*, C(2)(thiazolimine)); 156.1 (*s*, CO(carbamate)); 136.5 (*s*, C(δ^2)(Trp)); 127.2 (*s*, C(ε^2)(Trp)); 123.7 (*d*, CH(δ^1)(Trp)); 122.3 (*d*, CH(η)(Trp)); 119.8, 119.7 (2*d*, CH(ξ^2)(Trp)); 118.6, 118.5 (2*d*, CH(ε^3)(Trp)); 111.7 (*d*, CH(ξ^1)(Trp)); 109.7, 109.5 (2*s*, C(γ)(Trp)); 83.1, 82.8 (2*s*, C(4)(thiazolimine)); 80.6 (*s*, Me$_3$*C*); 78.3, 78.0 (2*d*, CH(α)(Ile^2)); 61.2, 60.9 (2*s*, CH(α)(Val)); 60.6 (*d*, CH(α)(Pro)); 57.9 (*d*, CH(α)(Ile^1)); 57.4 (*s*, C(α)(Aib^2)); 56.6 (*s*, C(α)(Aib^3)); 55.8 (*d*, CH(α)(Trp)); 52.9 (*d*, CH(α)(Leu)); 52.0 (*q*, MeO); 48.0 (*t*, CH$_2$(δ)(Pro)); 42.9, 42.8 (*t*, CH$_2$(Gly^t)); 40.0 (*d*, CH(β)(Ile^2)); 39.4 (*t*, CH$_2$(Leu)); 36.3 (*d*, CH(β)(Ile^1)); 29.7, 29.6 (*d*, CH(β)(Val)); 28.2 (*q*, *Me*$_3$C); 27.9 (*t*, CH$_2$(β)(Pro)); 27.6 (*q*, Me(β^1)(Aib^1)); 26.5 (*q*, Me(β^1)(Aib^2)); 26.4 (*t*, CH$_2$(Trp)); 26.3 (*q*, Me(β^2)(Aib^1)); 25.9 (*q*, Me(β^1)(Aib^3)); 25.8 (*t*, CH$_2$(γ)(Pro)); 25.5 (*q*, Me(β^2)(Aib^3)); 25.3 (*t*, CH$_2$(Ile^1)); 25.2 (*d*, CH$_2$(Leu)); 24.2 (*t*, CH$_2$(Ile^2)); 24.4 (*q*, Me(β^2)(Aib^2)); 23.4 (*q*, Me(δ^2)(Leu)); 21.1, 21.0 (2*q*, Me(δ^1)(Leu)); 19.4, 19.3 (2*q*, 2 Me(Val)); 15.8 (*q*, Me(γ^2)(Ile^2)); 15.6 (*q*, Me(γ^2)(Ile^1)); 11.8 (*q*, Me(δ)(Ile^2)); 11.6 (*q*, Me(δ)(Ile^1)). ESI-MS: 1186 ([*M* + Na]$^+$), 605 ([*M* + Na]$^{2+}$).

*Methyl (2*S*)-1-(2-{(2*S*)-2-[2-((2*S*)-2-{(2*S*,3*S*)-2-[(2-{1-[(2*S*,3*S*)-2-((2*S*)-{[(*tert*-Butoxy)carbonyl]amino}-3-(indol-3-yl)propanamido)-3-methylpentanamido]methyl}-4,5-dihydro-4,4-dimethyl-1,3-oxazol-5-yliden)amino]-3-methylpentanamido}-3-methylbutanamido)-2-methylpropanamido]-4-methylpentanamido}-2-methylpropanoyl)pyrrolidine-2-carboxylate* (Boc-Trp-Ile-Gly-[1,3-oxazol-5(4*H*)-imine]Aib-Ile-Val-Aib-Leu-Aib-Pro-OMe; **16**). IR (KBr): 3327*s*, 2967*s*, 2935*m*, 2876*m*, 1663*s*, 1521*s*, 1458*s*, 1413*m*, 1384*m*, 1366*m*, 1253*m*, 1210*m*, 1170*s*, 1094*w*, 1050*w*, 1012*w*, 927*w*, 856*w*, 743*m*. ^{1}H-NMR (600 MHz; ^{13}C,^{1}H-HMBC, conformers): 9.28 (br. *s*, NH(ε^1)(Trp)); 8.70, 7.92 (2 br. *s*, 2 NH); 7.61 – 6.91 (*m*, NH(Aib^3), CH(η)(Trp), CH(ξ^2)(Trp), CH(δ^1)(Trp), NH(Val), NH(Leu), NH(Gly)); 6.60 (br. *s*, NH(Aib^2)); 6.26 (br. *s*, NH(Ile^1)); 5.44, 5.38 (2 br. *s*, NH(Trp)); 4.65 – 4.48 (*m*, CH(α)(Pro)); 4.45 – 4.38 (*m*, CH$_2$(Gly)); 4.34 – 4.28 (*m*, CH(α)(Trp)); 4.17 – 4.15

[12] ^{1}H-NMR ((D$_6$)DMSO, 388 K) evidenced the presence of conformers and not epimers as the double signals (^{1}H-NMR ((D$_6$)DMSO, 300 K)) merged into single signals at 388 K.

(*m*, CH(α)(Ile^1)); 4.11–3.89 (*m*, CH(α)(Val), CH(α)(Leu)); 3.80–3.71 (*m*, H_a of CH_2(δ)(Pro)); 3.69, 3.68 (2*s*, MeO); 3.66–3.55 (*m*, H_b of CH_2(δ)(Pro)); 3.28 (br. *s*, CH(α)(Ile^2)); 3.26–3.21 (*m*, CH_2(Trp)); 2.48 (br. *s*, CH(β)(Ile^2)); 2.36 (br. *s*, CH(β)(Val)); 2.14–2.03 (*m*, CH(β)(Ile^1)); 2.02–1.72 (*m*, CH_2(γ)(Pro), CH_2(Leu), CH_2(β)(Pro)); 1.66–1.35 (*m*, CH(γ)(Leu)); 1.60, 1.58, 1.56, 1.54, 1.49, 1.45, 1.42, 1.38 (8*s*, 2 Me(Aib^1), 2 Me(Aib^2), 2 Me(Aib^3)); 1.43 (*s*, *t*-Bu); 1.32–1.23 (*m*, CH_2(Ile^1), CH_2(Ile^2)); 1.18–0.65 (*m*, 2 Me(Val), 2 Me(Ile^1), 2 Me(Ile^2), 2 Me(Leu)). ^{13}C-NMR (75 and 150 MHz, conformers): 186.7, 186.5 (2*s*, C(5)(oxazolimine)); 174.2, 174.2, 174.0, 173.8, 173.7, 173.6, 172.9, 172.7, 172.6, 172.1, 171.8, 171.6, 171.5, 171.4, 170.7, 170.7 (16*s*, 8 CO); 159.0, 158.6 (2*s*, C(2)(oxazolimine)); 156.6, 156.4 (2*s*, CO(carbamate)); 136.9, 136.7 (2*s*, C(δ^2)(Trp)); 127.5, 127.2 (2*s*, C(ε^2)(Trp)); 124.3, 123.7 (2*d*, CH(δ^1)(Trp)); 122.4, 122.3 (2*d*, CH(η)(Trp)); 119.9, 119.8 (2*d*, CH(ξ^2)(Trp)); 118.7, 118.5 (2*d*, CH(ε^3)(Trp)); 112.1, 111.8 (2*d*, CH(ξ^1)(Trp)); 110.3, 109.2 (2*s*, C(γ)(Trp)); 81.2, 80.7 (2*s*, Me_3C); 67.3, 67.1 (2*s*, C(4)(oxazolimine)); 62.7, 62.5 (2*d*, CH(Ile^2)); 61.7, 61.3 (2*d*, CH(α)(Pro)); 61.0, 60.9 (2*d*, CH(α)(Ile^1)); 58.7 (*d*, CH(α)(Val)); 57.3 (*s*, C(α)(Aib^2)); 56.9, 56.6 (2*s*, C(α)(Aib^3)); 56.4, 56.2 (2*d*, CH(α)(Trp)); 52.6 (*d*, CH(α)(Leu)); 52.2 (*q*, MeO); 48.6, 48.4 (2*t*, CH_2(δ)(Pro)); 40.7, 40.2 (2*t*, CH_2(Gly)); 38.6, 38.2 (*t*, CH_2(Leu)); 36.6, 36.5 (2*d*, CH(β)(Ile^1)); 35.0, 33.6 (2*d*, CH(β)(Ile^2)); 29.9, 29.7 (2*d*, CH(β)(Val)); 28.5 (*q*, Me_3C); 28.2 (*t*, CH_2(β)(Pro)); 27.5, 27.3, 26.7, 25.2, 24.9, 24.9, 24.8, 24.7, 24.4, 24.3, 23.9, 23.5 (12*q*, 6 Me(Aib)); 26.1 (*t*, CH(γ)(Pro)); 26.0 (*t*, CH_2(Trp)); 25.6 (*t*, CH_2(Ile^1)); 25.4 (*d*, CH(γ)(Leu)); 24.5 (*t*, CH_2(Ile^2)); 21.7, 21.5 (2*q*, Me(δ^2)(Leu)); 21.4, 21.2 (2*q*, Me(δ^1)(Leu)); 19.7, 19.6 (2*q*, 2 Me(Val)); 18.3, 16.8 (2*q*, Me(γ)(Ile^2)); 15.7, 14.5 (2*q*, Me(γ)(Ile^1)); 11.9, 11.8 (2*q*, Me(δ)(Ile^2)); 11.5, 11.1 (2*q*, Me(δ)(Ile^1)). ESI-MS: 1170 ([M + Na]$^+$), 661, 597 ([M + Na]$^{2+}$).

3. *Synthesis of Methyl (2*S*)-2-[(2*S*,3*S*)-2-(2-[(2*S*)-2-[(2*S*,3*S*)-2-((2*S*)-[[(*tert*-Butoxy)carbonyl]amino]-3-(indol-3-yl)propanamido)-3-methylpentanamido]propanamido]-2-methylpropanethioamido)-3-methylpentanamido]-3-methylbutanoate* (Boc-Trp-Ile-Ala-Aib-Ψ(CS)-Ile-Val-OMe; **18**). 3.1. *(2*S*,3*S*)-2-(2-[2-[(2*S*,3*S*)-2-((2*S*)-[[(*tert*-Butoxy)carbonyl]amino]-3-(indol-3-yl)propanamido)-3-methylpentanamido]ethanethioamido]-2-methylpropanamido)-3-methylpentanoate* (Boc-Trp-Ile-Ala-Ψ(CS)-Aib-Ile-OH; **1**). According to the *GP E*, with Boc-Trp-Ile-Ala-Ψ(CS)-Aib-Ile-OMe [7] (92 mg, 0.128 mmol), THF/MeOH/H_2O 3:1:1 (2.5 ml), LiOH · H_2O (16 mg, 0.38 mmol); reaction time: 3 h; yield of crude **1**: 91%.

3.2. *Methyl (2*S*)-2-[(2*S*,3*S*)-2-[2-[(2*S*)-1-[(2*S*,3*S*)-2-((2*S*)-[[(*tert*-Butoxy)carbonyl]amino]-3-(indol-3-yl)-propanamido)-3-methylpentanamido]ethyl]-4,5-dihydro-4,4-dimethyl-1,3-thiazol-5-yliden)amino]-3-methylpentanamido]-3-methylbutanoate* (Boc-Trp-Ile-Ala-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-Val-OMe; **17**). According to the *GP F*, with **1** (48 mg, 0.07 mmol), H-Val-OMe · HCl (13 mg, 0.08 mmol), TBTU (23 mg, 0.07 mmol), MeCN (2 ml) and EtN(i-Pr)$_2$ (0.03 ml, 0.2 mmol); reaction time: 17 h. Chromatography (SiO_2; AcOEt/hexane 2:1 → AcOEt) gave 34 mg (63%) of **17**. Thick oil, which solidified under h.v. IR (KBr): 3320*s*, 2967*s*, 2876*m*, 1666*s*, 1514*s*, 1458*s*, 1368*s*, 1250*s*, 1167*s*, 1010*m*, 927*w*, 856*w*, 741*m*. ^{1}H-NMR: 8.46 (br. *s*, NH(ε^1)(Trp)); 7.67 (*d*, J = 7.7, CH(ε^3)(Trp)); 7.37–7.33 (*m*, CH(ξ^1)(Trp)); 7.21–7.06 (*m*, CH(η)(Trp), CH(ξ^2)(Trp), CH(δ^1)(Trp), NH); 6.72 (*d*, J = 7.3, NH); 6.46 (*d*, J = 8.4, NH); 5.14 (*d*, J = 4.2, NH); 4.81–4.76 (*m*, CH(α)(Ala^t)); 4.56 (*dd*, J = 8.8, 4.4, CH(α)(Val)); 4.48–4.43, 4.28–4.24 (2*m*, CH(α)(Ile^1), CH(α)(Trp)); 3.68 (*s*, MeO); 3.31 (*d*, J = 4.3, CH(α)(Ile^2)); 3.29–3.24 (*m*, CH_2(Trp)); 2.23–2.17 (*m*, CH(β)(Val)); 1.96–1.91 (*m*, CH(β)(Ile^1), CH(β)(Ile^2)); 1.58–1.23 (*m*, CH_2(Ile^1), CH_2(Ile^2)); 1.49, 1.46 (2*s*, 2 Me(Aib)); 1.42 (*s*, *t*-Bu); 1.00–0.77 (*m*, 2 Me(Val), 2 Me(Ile^1), 2 Me(Ile^2), Me(Ala^t)). ^{13}C-NMR: 177.4 (*s*, C(5)(thiazolimine)); 172.1, 171.7, 171.0, 170.3 (4*s*, 4 CO); 164.8, (*s*, C(2)(thiazolimine)); 156.1 (*s*, CO(carbamate)); 136.4 (*s*, C(δ^2)(Trp)); 127.4 (*s*, C(ε^2)(Trp)); 123.3 (*d*, CH(δ^1)(Trp)); 122.3 (*d*, CH(η)(Trp)); 119.7 (*d*, CH(ξ^2)(Trp)); 118.8 (*d*, CH(ε^3)(Trp)); 111.3 (*d*, CH(ξ^1)(Trp)); 110.3 (*s*, C(γ)(Trp)); 82.8 (*s*, C(4)(thiazolimine)); 80.6, 80.5 (*s*, Me_3C); 80.0 (*d*, CH(α)(Ile^2)); 58.0 (*d*, CH(α)(Val)); 57.8 (*d*, CH(α)(Ile^1)); 56.7 (*d*, CH(α)(Trp)); 52.0 (*q*, MeO); 48.9 (*d*, CH(α)(Ala^t)); 39.8, 36.9 (2*d*, CH(β)(Ile^1), CH(β)(Ile^2)); 31.5 (*d*, CH(β)(Val)); 28.3 (*q*, Me_3C); 27.8 (*t*, CH_2(Trp)); 27.5, 26.7 (2*q*, 2 Me(Aib)); 25.2, 24.6 (2*t*, CH_2(Ile^1), CH_2(Ile^2)); 19.2, 19.1, 17.8 (3*q*, 2 Me(Val), Me(Ala^t)); 15.9, 15.4, 11.8, 11.4 (4*q*, 2 Me(Ile^1), 2 Me(Ile^2)). ESI-MS: 820 ([M + Na]$^+$), 798 ([M + H]$^+$).

3.3. *Boc-Trp-Ile-Ala-Aib-Ψ(CS)-Ile-Val-OMe* (**18**). A soln. of **17** in AcOEt/hexane was kept at r.t. for several months. Colorless tablets, suitable for an X-ray crystal-structure determination were obtained from AcOEt/hexane. M.p. 109–110° (dec.). IR (KBr): 3430*m*, 3311*s*, 2969*s*, 2932*m*, 2877*m*, 1718*s*, 1693*s*, 1667*s*, 1530*s*, 1458*m*, 1434*m*, 1366*s*, 1285*s*, 1258*m*, 1161*s*, 1124*w*, 1107*w*, 1069*w*, 1056*w*, 1021*m*, 860*w*, 762*w*, 741*m*. ^{1}H-NMR (conformers): 8.89–8.32 (*m*, 2 NH); 7.65–7.57 (*m*, CH(ε^3)(Trp)); 7.40–7.37 (*m*, CH(ξ^1)(Trp)); 7.26–6.96 (*m*, CH(η)(Trp), CH(ξ^2)(Trp), CH(δ^1)(Trp), NH); 6.89 (br. *s*, NH); 6.75 (*d*, J = 8.3, NH); 6.54–6.44, 5.18–5.07 (2*m*, 2 NH); 4.94–4.88 (*m*, CH(α)(Ala)); 4.51–3.99 (*m*, CH(α)(Ile^1), CH(α)(Ile^2), CH(α)(Trp), CH(α)(Val)); 3.69, 3.68 (2*s*, MeO); 3.30–3.21 (*m*, CH_2(Trp)); 2.25–2.13 (*m*, CH(β)(Val), CH(β)(Ile^1)); 1.98–1.82 (*m*, CH(β)(Ile^2)); 1.82–0.60 (*m*, CH_2(Ile^1), CH_2(Ile^2)); 1.74, 1.73, 1.72, 1.65 (4*s*, 2 Me(Aib^t)); 1.43, 1.42, 1.41, 1.40 (4*s*, *t*-Bu); 1.03–0.60 (*m*, 2 Me(Val), 2 Me(Ile^1), 2 Me(Ile^2), Me(Ala)). ^{13}C-NMR: 207.5, 207.2

(2*s*, CS(Aib^t)); 173.4, 172.8, 172.4, 172.1, 171.9, 171.5, 171.2, 170.3, 170.0, 169.9 (10*s*, 5 CO); 156.1 (*s*, CO(carbamate)); 136.6, 136.4 (2*s*, C(δ^2)(Trp)); 127.2, 127.1 (2*s*, C(ε^2)(Trp)); 123.6, 123.4 (2*d*, CH(δ^1)(Trp)); 122.7, 122.4 (2*d*, CH(η)(Trp)); 119.9 (*d*, CH(ξ^2)(Trp)); 118.7, 118.5 (2*d*, CH(ε^3)(Trp)); 111.6, 111.5 (2*d*, CH(ξ^1)(Trp)); 110.0, 109.9 (2*s*, C(γ)(Trp)); 81.6 (*s*, Me_3C); 64.3 (*d*, CH(α)(Val)); 63.2, 62.8 (2*s*, C(α)(Aib^t)); 58.8, 58.1, 56.4, 56.4, 55.4 (5*d*, CH(α)(Trp), CH(α)(Ile^1), CH(α)(Ile^2)); 52.0 (*q*, MeO); 50.1 (*d*, CH(α)(Ala)); 35.9, 35.8 (2*d*, CH(β)(Ile^1), CH(β)(Ile^2)); 30.9, 30.7 (2*d*, CH(β)(Val)); 28.9 (*q*, Me_3C); 27.8 (*t*, CH_2(Trp)); 28.3, 27.8 (2*q*, 2 Me(Aib^t)); 25.5, 25.2, 24.9, 24.7 (4*t*, CH_2(Ile^1), CH_2(Ile^2)); 19.0, 18.1 (2*q*, 2 Me(Val)); 16.3, 15.7, 15.5, 15.4, 11.6, 11.4, 11.2, 11.0 (8*q*, 2 Me(Ile^1), 2 Me(Ile^2), Me(Ala)). ESI-MS: 838 ([M + Na]$^+$), 816 ([M + H]$^+$), 685.

4. *Synthesis of Methyl (2*S*,3*S*)-2-((2*S*)-2-[[2-((2*S*)-[[(Benzyloxy)carbonyl]amino}ethyl)-4,5-dihydro-4,4-dimethyl-1,3-thiazol-5-yliden]amino}-3-methylpentanamido)-3-methylbutanoate* (Z-Ala-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-Val-OMe; **25a**). 4.1. *Benzyl N-[(*S*)-1-Methyl-(2-[1,1-dimethyl-2-[methyl(phenyl)amino]-2-oxoethyl}amino)-2-thioxoethyl]carbamate* (Z-Ala-Ψ(CS)-Aib-N(Me)Ph; **22a**). According to the *GP B*, with Z-Ala-Aib-Ψ(CS)-N(Me)Ph (**21a**; prepared according to the procedure in [7], 611 mg, 1.48 mmol), AcOH (15 ml), $ZnCl_2$ (6150 mg, 46.5 mmol), and 2.1M HCl in AcOH (1.5 ml); reaction time: t_1 = 1.5 min, t_2 = 2 min. Chromatography (SiO_2; AcOEt/hexane 1:1) led to 499 mg (82%) of **22a** and 48 mg (8%) of **21a**.

Data of **22a**: Thick oil, which solidified under h.v. IR (KBr): 3233*s*, 3053*m*, 1720*s*, 1632*s*, 1592*s*, 1493*s*, 1423*s*, 1362*s*, 1231*s*, 1092*s*, 1049*m*, 771*m*, 743*w*, 706*s*. ^{1}H-NMR: 8.18 (br. *s*, NH); 7.36–7.23 (*m*, 10 arom. H); 5.74 (*d*, J = 7.6, NH); 5.09 (*s*, PhCH_2); 4.12 (*q*, J = 6.8, CH(α)(Ala^t)); 3.23 (*s*, MeN); 1.64, 1.60 (2*s*, 2 Me(Aib)); 1.35 (*d*, J = 6.7, Me(Ala^t)). ^{13}C-NMR: 202.4 (*s*, CS(Ala^t)); 171.4 (*s*, CO(Aib)); 155.6 (*s*, CONH); 144.2, 136.3 (2*s*, 2 arom. C); 129.2, 128.6, 128.2, 128.0, 127.6 (5*d*, 10 arom. C); 67.0 (*t*, PhCH_2); 61.5 (*s*, C(α)(Aib)); 56.4 (*d*, CH(α)(Ala^t)); 40.9 (*q*, MeN); 25.6, 25.0 (2*q*, 2 Me(Aib)); 21.9 (*q*, Me(Ala^t)). CI-MS: 307 (100, [M – (Me(Ph)N)]$^+$), 108 (65, [Me(Ph)NH_2]$^+$). Anal. calc. for $C_{22}H_{27}N_3O_3S \cdot 0.1\ H_2O$ (415.34): C 63.62, H 6.60, N 10.12, S 7.72; found: C 63.36, H 6.60, N 9.86, S 7.63.

4.2. *Benzyl N-[(1*S*)-1-(4,5-Dihydro-4,4-dimethyl-5-oxo-1,3-thiazol-2-yl)ethyl]carbamate* (Z-Ala-[1,3-thiazol-5(4*H*)-one]Aib; **23a**). According to the *GP C*, with **22a** (432 mg, 1.04 mmol) in CH_2Cl_2 (10 ml), and CSA (267 mg, 1.15 mmol). Chromatography (SiO_2; AcOEt/hexane 1:3) yielded 293 mg (92%) of **23a**. Thick oil, which solidified under h.v. Crystals suitable for X-ray crystal-structure determination were obtained from hexane/CH_2Cl_2[7]. M.p. 100–102°. IR (KBr): 3297*s*, 3029*w*, 2984*m*, 2952*w*, 1722*s*, 1698*s*, 1632*s*, 1538*s*, 1496*m*, 1452*m*, 1381*m*, 1359*m*, 1300*s*, 1260*s*, 1200*m*, 1124*m*, 1085*w*, 1052*s*, 1039*m*, 1007*s*, 925*m*, 912*m*, 843*m*, 778*m*, 744*m*, 729*m*. ^{1}H-NMR: 7.36–7.30 (*m*, 5 arom. H); 5.60 (br. *s*, NH); 5.13 (*s*, PhCH_2); 4.72–4.68 (*m*, CH(α)(Ala^t)); 1.48 (*d*, J = 7.0, Me(Ala^t)); 1.37 (*s*, 2 Me(Aib)). ^{13}C-NMR: 210.5 (*s*, C(5)(thiazolone)); 166.6 (*s*, C(2)(thiazolone)); 155.5 (*s*, CONH); 136.2 (*s*, 1 arom. C); 128.6, 128.3, 128.2 (3*d*, 5 arom. C); 83.2 (*s*, C(4)(thiazolone)); 67.1 (*t*, PhCH_2); 51.1 (*d*, CH(α)(Ala^t)); 24.3 (*q*, 2 Me(Aib)); 19.6 (*q*, Me(Ala^t)). CI-MS: 308 (100), 307 (15, [M + H]$^+$). Anal. calc. for $C_{15}H_{18}N_2O_3S$ (306.39): C 58.80, H 5.92, N 9.14, S 10.47; found: C 58.62, H 5.92, N 9.05, S 10.47.

4.3. *Methyl (2*S*-3*S*)-2-[2-((2*S*)-[[(Benzyloxy)carbonyl]amino}propanethioamido)-2-methylpropanamido]-3-methylpentanoate* (Z-Ala-Ψ(CS)-Aib-Ile-OMe; **24a**). According to the *GP D*, with **23a** (208 mg, 0.68 mmol) in MeCN (5 ml), EtN(i-Pr)$_2$ (0.23 ml, 1.36 mmol), HOBt (199 mg, 1.36 mmol), and H-Ile-OMe · HCl (136 mg, 0.75 mmol); reaction time: 4 d. Chromatography (SiO_2; AcOEt/hexane 1:2) yielded 162 mg (53%) of **24a** and 83 mg (40%) of **23a**.

Data of **24a**: Thick oil, which solidified under h.v. IR (KBr): 3426*m*, 3375*s*, 3259*s*, 3037*m*, 2963*m*, 1718*s*, 1651*s*, 1530*s*, 1450*m*, 1430*m*, 1372*m*, 1331*m*, 1274*s*, 1251*s*, 1200*m*, 1175*m*, 1153*m*, 1112*w*, 1049*m*, 995*m*, 828*w*, 778*w*, 777*w*, 740*w*, 697*m*. ^{1}H-NMR: 8.39 (br. *s*, NH); 7.36–7.30 (*m*, 5 arom. H); 6.46 (*d*, J = 8.0, NH); 5.58 (*d*, J = 7.3, NH); 5.17–5.06 (*m*, PhCH_2); 4.54 (*dd*, J = 8.2, 4.9, CH(α)(Ile)); 4.48–4.43 (*m*, CH(α)(Ala^t)); 3.72 (*s*, MeO); 1.92–1.87 (*m*, CH(β)(Ile)); 1.96, 1.72 (2*s*, 2 Me(Aib)); 1.45 (*d*, J = 6.8, Me(Ala^t)); 1.42–1.13 (*m*, CH_2(Ile)); 0.93–0.87 (*m*, 2 Me(Ile)). ^{13}C-NMR: 203.6 (*s*, CS(Ala^t)); 172.3, 172.1 (2*s*, CO(Aib), CO(Ile)); 155.9 (*s*, CO(carbamate)); 136.0 (*s*, 1 arom. C); 128.4, 128.1, 127.9 (3*d*, 5 arom. C); 67.0 (*t*, PhCH_2); 60.5 (*s*, C(α)(Aib)); 57.1 (*d*, CH(α)(Ile)); 56.7 (*d*, CH(α)(Ala^t)); 51.9 (*q*, MeO); 37.7 (*d*, CH(β)(Ile)); 25.2 (*t*, CH_2(Ile)); 24.6, 23.5 (2*q*, 2 Me(Aib)); 21.5 (*q*, Me(Ala^t)); 15.4, 11.4 (2*q*, 2 Me(Ile)). ESI-MS: 490 ([M + K]$^+$), 474 ([M + Na]$^+$), 307 ([Z-Ala-[1,3-thiazol-5(4*H*)-one]Aib + H]$^+$). Anal. calc. for $C_{22}H_{33}N_3O_5S \cdot 0.25\ H_2O$ (456.09): C 57.94, H 7.40, N 9.21, S 7.03; found: C 57.98, H 7.63, N 9.09, S 6.59.

4.4. *(2*S*,3*S*)-2-[2-((2*S*)-[[(Benzyloxy)carbonyl]amino}propanethioamido)-2-methylpropanamido]-3-methylpentanoate* (Z-Ala-Ψ(CS)-Aib-Ile-OH; **19a**). According to the *GP E*, with **24a** (119 mg, 0.26 mmol), THF/MeOH/H_2O 3:1:1 (5 ml) and LiOH · H_2O (32 mg, 0.79 mmol); reaction time: 3 h; yield of crude **19a**: 96%.

4.5. *Z-Ala-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-Val-OMe* (**25a**). According to the *GP F*, with **19a** (49 mg, 0.11 mmol), H-Val-OMe · HCl (22 mg, 0.12 mmol), TBTU (38 mg, 0.12 mmol), MeCN (2 ml), and EtN(i-Pr)$_2$ (0.06 ml, 0.34 mmol); reaction time: 19 h. Chromatography (SiO_2; AcOEt) gave 37 mg (60%) of **25a**. Thick oil. IR (neat): 3378*s*, 3298*s*, 3064*m*, 3035*m*, 2966*s*, 2934*s*, 2876*s*, 1732*s*, 1668*s*, 1588*m*, 1512*s*, 1455*s*, 1374*s*, 1311*s*, 1245*s*, 1151*s*, 1113*m*, 1057*s*, 1005*s*, 927*s*, 846*w*, 823*w*, 802*w*, 778*m*, 742*m*, 698*s*. ^{1}H-NMR: 7.37 – 7.28 (*m*, 5 arom. H); 7.07 (*d*, *J* = 8.8, NH); 5.55 (br. *s*, NH); 5.13 (*s*, PhCH_2); 4.67 – 4.64 (*m*, CH(α)(Ala^t)); 4.56 (*dd*, *J* = 8.9, 4.4, CH(α)(Val)); 3.70 (*s*, MeO); 3.31 (*d*, *J* = 4.3, CH(α)(Ile)); 2.23 – 2.17 (*m*, CH(β)(Val)); 2.00 – 1.95 (*m*, CH(β)(Ile)); 1.64 – 1.22 (*m*, CH_2(Ile)); 1.47 – 1.39 (*m*, Me(Ala^t)); 1.43, 1.39 (2*s*, 2 Me(Aib)); 0.99 – 0.86 (*m*, 2 Me(Ile), 2 Me(Val)). ^{13}C-NMR: 177.1 (*s*, C(5)(thiazolimine)); 171.9, 170.6 (2*s*, CO(Val), CO(Ile)); 169.8 (*s*, C(2)(thiazolimine)); 155.3 (*s*, CO(carbamate)); 136.1 (*s*, 1 arom. C); 128.4, 128.1, 128.0 (3*d*, 5 arom. C); 82.6 (*s*, C(4)(thiazolimine)); 79.9 (*d*, CH(α)(Ile)); 66.9 (*t*, PhCH_2); 56.6 (*d*, CH(α)(Val)); 51.9 (*q*, MeO); 50.4 (*d*, CH(α)(Ala^t)); 39.6 (*d*, CH(β)(Ile)); 31.4 (*d*, CH(β)(Val)); 27.3, 26.5 (2*q*, 2 Me(Aib)); 25.1 (*t*, CH_2(Ile)); 19.7, 18.9, 17.6 (3*q*, Me(Ala^t), 2 Me(Val)); 15.4, 11.4 (2*q*, 2 Me(Ile)). ESI-MS: 555 ([*M* + Na]$^+$). Anal. calc. for $C_{27}H_{40}N_4O_5S$ (532.71): C 60.88, H 7.57, N 10.52, S 6.02; found: C 60.98, H 7.74, N 10.37, S 5.89.

4.6. *Methyl (2*S*)-2-{(2*S*,3*S*)-2-[2-((2*S*)-{[(Benzyloxy)carbonyl]amino}propanethioamido)-2-methylpropanamido]-3-methylpentanamido}-3-methylbutanoate* (Z-Ala-Aib-Ψ(CS)-Ile-Val-OMe; **27a**). Storage of a soln. of **25a** in AcOEt/hexane for several months led to **27a** in quant. yield. Yellow thick oil. IR (neat): 3305*s*, 3035*m*, 2936*s*, 2937*s*, 2877*s*, 1740*s*, 1668*s*, 1530*s*, 1455*s*, 1372*s*, 1313*m*, 1248*s*, 1155*m*, 1115*m*, 1073*m*, 1021*m*, 913*w*, 868*w*, 823*w*, 781*w*, 739*w*. ^{1}H-NMR (conformers): 8.64 (*d*, *J* = 7.3, NH); 7.36 – 7.30 (*m*, 5 arom. H); 6.98, 6.91 (2*s*, NH); 6.59 (br. *s*, NH); 5.47 – 5.35 (*m*, NH); 5.13 (*s*, PhCH_2); 4.67 – 4.64 (*td*, *J* = 6.6, 1.5, CH(α)(Ala)); 4.52 – 4.47 (*m*, CH(α)(Val)); 4.20 – 4.11 (*m*, CH(α)(Ile)); 3.72, 3.70 (2*s*, MeO); 2.23 – 2.14 (*m*, CH(β)(Val), CH(β)(Ile)); 1.68, 1.66, 1.65, 1.64 (4*s*, 2 Me(Aib^t)); 1.38 – 1.33 (*m*, Me(Ala)); 1.33 – 1.12 (*m*, CH_2(Ile)); 0.98 – 0.84 (*m*, 2 Me(Ile), 2 Me(Val)). ^{13}C-NMR (conformers): 206.8, 206.6 (2*s*, CS(Aib^t)); 172.0, 171.8, 169.4 (3*s*, 3 CO); 156.2 (*s*, CO(carbamate)); 136.0 (*s*, 1 arom. C); 128.5, 128.2, 128.1, 128.0 (4*d*, 5 arom. C); 67.1 (*t*, PhCH_2); 63.9, 63.7 (2*d*, CH(α)(Ile)); 62.3 (*s*, C(α)(Aib^t)); 57.4 (*d*, CH(α)(Val)); 51.9 (*q*, MeO); 51.8, 51.2 (2*d*, CH(α)(Ala)); 35.9 (*d*, CH(β)(Ile)); 30.7, 30.1 (2*d*, CH(β)(Val)); 28.5, 28.0, 27.2, 26.5 (4*q*, 2 Me(Aib^t)); 25.4, 25.1 (2*t*, CH_2(Ile)); 19.7, 18.9, 18.7, 17.8, 17.7 (5*q*, Me(Ala), 2 Me(Val)); 15.2, 11.1 (2*q*, 2 Me(Ile)). ESI-MS: 573 ([*M* + Na]$^+$), 235.

5. *Synthesis of Methyl (2*S*)-2-((2*S*,3*S*)-2-{[2-({[(Benzyloxy)carbonyl]amino}methyl)-4,5-dihydro-4,4-dimethyl-1,3-thiazol-5-yliden]amino}-3-methylpentanamido)-3-methylbutanoate* (Z-Gly-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-Val-OMe; **25b**). 5.1. *Benzyl* N*-[1-(4,5-Dihydro-4,4-dimethyl-5-oxo-1,3-thiazol-2-yl)methyl]-carbamate* (Z-Gly-[1,3-thiazol-5(4*H*)-one]Aib; **23b**). According to the *GP C*, with Z-Gly-Ψ(CS)-Aib-N(Me)Ph (**22b**; prepared according to the procedure in [7], 1836 mg, 4.56 mmol) in CH_2Cl_2 (60 ml), and CSA (1176 mg, 5.06 mmol). Chromatography (SiO_2; AcOEt/hexane 3 : 1) yielded 1104 mg (82%) of **23b**. Thick oil. IR (neat): 3330*s*, 3065*m*, 3035*m*, 2980*m*, 2933*m*, 2868*w*, 1956*w*, 1724*s*, 1629*s*, 1587*w*, 1530*s*, 1455*s*, 1377*m*, 1358*m*, 1250*s*, 1161*s*, 1124*s*, 1044*m*, 976*m*, 920*m*, 841*m*, 777*m*, 737*m*, 698*m*. ^{1}H-NMR: 7.36 – 7.30 (*m*, 5 arom. H); 5.65 (br. *s*, NH); 5.14 (*s*, PhCH_2); 4.32 (*d*, *J* = 5.5, CH_2(Gly^t)); 1.38 (*s*, 2 Me(Aib)). ^{13}C-NMR: 210.2 (*s*, C(5)(thiazolone)); 162.3 (*s*, C(2)(thiazolone)); 156.0 (*s*, CONH); 136.0 (*s*, 1 arom. C); 128.5, 128.2, 128.1 (3*d*, 5 arom. C); 82.8 (*s*, C(4)(thiazolone)); 67.2 (*t*, PhCH_2); 45.1 (*t*, CH_2(Gly^t)); 24.2 (*q*, 2 Me(Aib)). CI-MS: 294 (20), 293 (100, [*M* + H]$^+$). Anal. calc. for $C_{14}H_{16}N_2O_2S \cdot 0.2\ H_2O$ (295.96): C 56.82, H 5.59, N 9.46, S 10.83; found: C 56.93, H 5.53, N 9.47, S 10.30.

5.2, *Methyl (2*S*,3*S*)-2-[2-({[(Benzyloxy)carbonyl]amino}ethanethioamido)-2-methylpropanamido]-3-methylpentanoate* (Z-Gly-Ψ(CS)-Aib-Ile-OMe; **24b**). According to the *GP D*, with **23b** (147 mg, 0.50 mmol) in MeCN (5 ml), EtN(i-Pr)$_2$ (0.17 ml, 1.00 mmol), HOBt (151 mg, 1.00 mmol), and H-Ile-OMe · HCl (100 mg, 0.55 mmol); reaction time: 5 d. Chromatography (SiO_2; AcOEt/hexane 1 : 1) yielded 162 mg (74%) of **24b** and 39 mg (26%) of **23b**.

Data of **24b**: Thick oil, which solidified under h.v.[13]). IR (KBr): 3421*s*, 3389*s*, 3249*s*, 3050*m*, 2974*m*, 1717*s*, 1651*s*, 1531*s*, 1453*s*, 1429*s*, 1385*m*, 1327*s*, 1282*s*, 1237*s*, 1199*s*, 1176*s*, 1044*m*, 1009*m*, 988*m*, 909*w*, 829*w*, 779*m*, 767*m*, 749*m*, 734*m*, 698*s*. ^{1}H-NMR: 8.63 (br. *s*, NH); 7.42 – 7.30 (*m*, 5 arom. H); 6.50 (br. *d*, *J* = 8.0, NH); 6.00 (br. *s*, NH); 5.15 (*s*, PhCH_2); 4.52 (*dd*, *J* = 8.1, CH(α)(Ile)); 4.13 (*d*, *J* = 5.3, CH_2(Gly^t)); 3.71 (*s*, MeO); 1.92 – 1.87 (*m*, CH(β)(Ile)); 1.71, 1.69 (2*s*, 2 Me(Aib)); 1.48 – 1.15 (*m*, CH_2(Ile)); 0.94 – 0.88 (*m*, 2 Me(Ile)). ^{13}C-NMR: 198.1 (*s*, CS(Gly^t)); 172.5, 172.2 (2*s*, CO(Aib), CO(Ile)); 156.9 (*s*, CO(carbamate)); 136.0

[13]) The same experiment (reaction time: 4 d) was carried out in the absence of HOBt, leading to 17% of **24b** and 72% of **23b**.

(*s*, 1 arom. C); 128.4, 128.2, 128.0 (3*d*, 5 arom. C); 67.2 (*t*, Ph*C*H$_2$); 60.5 (*s*, C(α)(Aib)); 56.8 (*d*, CH(α)(Ile)); 53.5 (*t*, CH$_2$(Gly^t)); 51.9 (*q*, MeO); 37.6 (*d*, CH(β)(Ile)); 25.2 (*t*, CH$_2$(Ile)); 24.4, 23.7 (2*q*, 2 Me(Aib)); 15.6, 11.5 (2*q*, 2 Me(Ile)). ESI-MS: 460 ([*M* + Na]$^+$), 293 ([Z-Gly-[1,3-thiazol-5(4*H*)-one]Aib]$^+$). Anal. calc. for $C_{21}H_{31}N_3O_5S$ (437.56): C 57.65, H 7.14, N 9.60, S 7.33; found: C 57.96, H 7.48, N 9.58, S 7.22.

5.3. *Methyl (2S,3S)-2-[2-([[(Benzyloxy)carbonyl]amino}ethanethioamido)-2-methylpropanamido]ethanoate* (Z-Gly-Ψ(CS)-Aib-Gly-OMe). According to the *GP D*, with **23b** (147 mg, 0.50 mmol) in MeCN (5 ml), EtN(i-Pr)$_2$ (0.17 ml, 1.00 mmol), HOBt (151 mg, 1.00 mmol), and H-Gly-OMe · HCl (69 mg, 0.55 mmol); reaction time: 5 d. Chromatography (SiO$_2$; AcOEt/hexane 2:1) yielded 191 mg (99%) of Z-Gly-Ψ(CS)-Aib-Gly-OMe. Thick oil. IR (neat): 3692*w*, 3442*w*, 3033*m*, 2998*m*, 2957*w*, 1744*s*, 1682*s*, 1513*s*, 1439*s*, 1412*m*, 1367*m*, 1266*m*, 1232*s*, 1223*m*, 1219*w*, 1212*w*, 1183*w*, 984*w*, 919*w*. ^{1}H-NMR: 8.66 (br. *s*, NH); 7.43–7.28 (*m*, 5 arom. H); 6.81 (br. *d*, *J* = 8.0, NH); 6.12 (br. *s*, NH); 5.12 (*s*, PhC*H*$_2$); 4.12 (*d*, *J* = 5.8, CH$_2$(Gly^t)); 4.12 (*d*, *J* = 5.2, CH$_2$(Gly)); 3.70 (*s*, MeO); 1.68 (*s*, 2 Me(Aib)). ^{13}C-NMR: 198.5 (*s*, CS(Gly^t)); 173.3, 170.1 (2*s*, CO(Aib), CO(Gly)); 157.0 (*s*, CO(carbamate)); 135.9 (*s*, 1 arom. C); 128.5, 128.2, 127.9 (3*d*, 5 arom. C); 67.3 (*t*, Ph*C*H$_2$); 60.4 (*s*, C(α)(Aib)); 53.0 (*t*, CH$_2$(Gly^t)); 52.2 (*q*, MeO); 41.5 (*t*, CH$_2$(Gly)); 24.1 (*q*, 2 Me(Aib)). ESI-MS: 404 ([*M* + Na]$^+$), 348, 293 ([Z-Gly-[1,3-thiazol-5(4*H*)-one]Aib]$^+$). Anal. calc. for $C_{17}H_{23}N_3O_5S \cdot 0.66$ H_2O (384.45): C 53.11, H 6.12, N 10.93; found: C 53.27, H 6.41, N 10.62.

5.4. *(2S,3S)-2-[2-([[(Benzyloxy)carbonyl]amino}ethanethioamido)-2-methylpropanamido]-3-methylpentanoic Acid* (Z-Gly-Ψ(CS)-Aib-Ile-OH, **19b**). According to the *GP E*, with **24b** (270 mg, 0.62 mmol), THF/MeOH/H_2O 3:1:1 (10 ml) and LiOH · H_2O (78 mg, 1.85 mmol); reaction time 4 h; yield of crude **19b**: quant.

5.5. *Z-Gly-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-Val-OMe* (**25b**). According to the *GP F*, with **19b** (261 mg, 0.62 mmol) in MeCN (15 ml), H-Val-OMe · HCl (114 mg, 0.68 mmol), TBTU (209 mg, 0.65 mmol), and EtN(i-Pr)$_2$ (0.32 ml, 1.86 mmol); reaction time: 18 h. Chromatography (SiO$_2$; AcOEt/hexane 1:1) gave 124 mg (39%) of **25b** and 58 mg (17%) of **26b**.

Data for **25b**: Thick oil. IR (CHCl$_3$): 3678*w*, 3422*w*, 3020*m*, 2969*m*, 1731*s*, 1677*s*, 1509*s*, 1456*m*, 1375*m*, 1313*w*, 1225*s*, 1207*s*, 1154*w*, 1051*w*, 1004*w*, 781*m*. ^{1}H-NMR: 7.35–7.29 (*m*, 5 arom. H); 7.05 (br. *d*, *J* = 8.9, NH); 5.81 (br. *s*, NH), 5.14 (*s*, PhC*H*$_2$); 4.55 (*dd*, *J* = 8.9, 4.4, CH(α)(Val)); 4.10 (br. *d*, *J* = 7.1, CH$_2$(Gly^t)); 3.68 (*s*, MeO); 3.30 (*d*, *J* = 4.2, CH(α)(Ile)); 2.22–2.16 (*m*, CH(β)(Val)); 2.00–1.95 (*m*, CH(β)(Ile)); 1.63–1.21 (*m*, CH$_2$(Ile)); 1.51, 1.46 (2*s*, 2 Me(Aib)); 0.98–0.86 (*m*, 2 Me(Ile), 2 Me(Val)). ^{13}C-NMR: 177.0 (*s*, C(5)(thiazolimine)); 171.8, 170.6 (2*s*, CO(Val), CO(Ile)); 160.7 (*s*, C(2)(thiazolimine)); 156.1 (*s*, CO(carbamate)); 136.1 (*s*, 1 arom. C); 128.4, 128.1, 128.0 (3*d*, 5 arom. C); 82.4 (*s*, C(4)(thiazolimine)); 79.9 (*d*, CH(α)(Ile)); 67.0 (*t*, Ph*C*H$_2$); 60.2 (*d*, CH(α)(Val)); 51.8 (*q*, MeO); 44.4 (*t*, CH$_2$(Gly^t)); 39.5 (*d*, CH(β)(Ile)); 31.3 (*d*, CH(β)(Val)); 27.2, 26.5 (2*q*, 2 Me(Aib)); 25.0 (*t*, CH$_2$(Ile)); 18.9, 17.6 (2*q*, 2 Me(Val)); 15.8, 11.6 (2*q*, 2 Me(Ile)). ESI-MS: 564 ([*M* + 2Na]$^+$), 559, 519 ([*M* + H]$^+$), 406.

Methyl (2S)-2-((2S,3S)-2-{[2-([[(Benzyloxy)carbonyl]amino}methyl)-4,5-dihydro-4,4-dimethyl-1,3-oxazol-5-yliden]amino}-3-methylpentanamido)-3-methylbutanoate (Z-Gly-[1,3-oxazol-5(4*H*)-imine]Aib-Ile-Val-OMe; **26b**). Thick oil. IR (CHCl$_3$): 3692*w*, 3420*w*, 3034*w*, 2971*m*, 2935*w*, 2879*w*, 1721*s*, 1680*m*, 1645*m*, 1512*m*, 1457*m*, 1439*w*, 1412*w*, 1366*w*, 1323*w*, 1232*w*, 1223*w*, 1211*w*, 1203*m*, 1155*w*, 1055*w*, 1003*w*, 938*w*, 909*w*. ^{1}H-NMR (epimers): 7.39–7.29 (*m*, 5 arom. H, NH); 7.05 (br. *s*, NH) 5.73 (br. *s*, NH); 5.14 (*s*, PhC*H*$_2$); 4.55 (*m*, CH(α)(Val), CH(α)(Ile)); 4.10 (*td*, *J* = 13.1, 4.5, CH$_2$(Gly^t)); 3.71 (br. *d*, *J* = 6.6, NH); 3.70, 3.68 (2*s*, MeO); 2.61 (br. *s*, CH(β)(Val)); 2.23–2.16 (*m*, CH(β)(Ile)); 1.53–0.81 (*m*, CH$_2$(Ile)); 1.32, 1.29 (2*s*, 2 Me(Aib)); 0.99–0.81 (*m*, 2 Me(Ile), 2 Me(Val)). ^{13}C-NMR (epimers): 187.6 (*s*, C(5)(oxazolimine)); 171.7, 169.5 (2*s*, CO(Val), CO(Ile)); 158.4 (*s*, C(2)(oxazolimine)); 156.0 (*s*, CO(carbamate)); 136.4 (*s*, 1 arom. C); 128.5, 128.2 (2*d*, 5 arom. C); 67.3 (*t*, Ph*C*H$_2$); 67.1 (*s*, C(4)(oxazolimine)); 64.3 (*d*, CH(α)(Ile)); 57.5, 57.3 (*d*, CH(α)(Val)); 52.1 (*q*, MeO); 39.8 (*t*, CH$_2$(Gly^t)); 32.8, 32.4 (2*d*, CH(β)(Ile)); 30.5, 30.4 (2*d*, CH(β)(Val)); 26.0 (*t*, CH$_2$(Ile)); 23.8, 23.7 (2*q*, 2 Me(Aib)); 19.2, 17.5 (2*q*, 2 Me(Val)); 15.7, 15.1, 10.8, 10.2 (4*q*, 2 Me(Ile)). ^{1}H-NMR (500 MHz): EXCY experiment[14]): no exchange peaks could be detected, and therefore, the presence of epimers was established. ESI-MS: 503 ([*M* + H]$^+$). Anal. calc. for $C_{26}H_{38}N_4O_6$ (502.62): S 0.00; found: S 0.03.

6. *Synthesis of Methyl (2S)-2-((2S,3S)-2-{[2-((2S)-{[(Benzyloxy)carbonyl]amino}-2-methylpropyl)-4,5-dihydro-4,4-dimethyl-1,3-thiazol-5-yliden]amino}-3-methylpentanamido)-3-methylbutanoate* (Z-Val-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-Val-OMe; **25c**). 6.1. *Benzyl* N-*[(S)-1-(1-Methylethyl)-2-([1,1-dimethyl-2-[methyl(phen-*

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[14]) The 2D-EXCY-NMR experiment is similar to a NOESY-NMR experiment with shorter mixing times to avoid NOE signals (*ca.* 40 ms). Exchange peaks have the same phase as the diagonal and are usually of higher intensity than NOE peaks, which have the opposite phase of the diagonal for smaller molecules (*ca.* 500–800 u). For slow exchanges, longer mixing times are necessary, in the above-described case 1 s.

yl)amino]-2-thioxoethyl]amino)-2-oxoethyl]carbamate (Z-Val-Aib-Ψ(CS)-(Me)Ph; **21c**). According to the *GP A*, with Z-Val-OH (**20c**; 3000 mg, 12.0 mmol), THF (50 ml), NMM (2.40 ml, 24.0 mmol), $ClCO_2{}^i$Bu (1.70 ml, 12.0 mmol), CH_2Cl_2 (50 ml), and **6** (2082 mg, 13 mmol); reaction time: 19 h. Chromatography (SiO_2; AcOEt/hexane 1:3) gave 3600 mg (68%) of **21c**. Yellow, thick oil, which solidified under h.v. IR (KBr): 3318*w*, 3062*w*, 3032*w*, 2962*w*, 2932*w*, 2873*w*, 1715*m*, 1664*s*, 1594*w*, 1492*s*, 1462*m*, 1368*m*, 1283*w*, 1232*m*, 1167*w*, 1101*m*, 1025*w*, 1004*w*, 837*w*, 772*w*, 738*w*, 697*m*. ^{1}H-NMR: 7.40–7.14 (*m*, 10 arom. H, NH); 5.43 (*d*, J = 8.3, NH); 5.17–5.07 (*m*, PhCH_2); 3.79–3.75 (*m*, CH(α)(Val)); 3.69 (*s*, MeN); 2.09–2.03 (*m*, CH(β)(Val)); 1.63, 1.55 (2*s*, 2 Me(Aib^t)); 0.92, 0.85 (2*d*, J = 6.9, 2 Me(Val)). ^{13}C-NMR: 208.3 (*s*, CS(Aib^t); 168.7 (*s*, CO(Val)); 156.1 (*s*, CO(carbamate)); 147.1, 136.4 (2*s*, 2 arom. C); 129.5, 128.4, 128.3, 128.0, 127.9, 126.3 (6*d*, 10 arom. C); 66.7 (*t*, PhCH$_2$); 62.7 (*s*, CH(α)(Aib^t)); 60.1 (*d*, CH(α)(Val)); 51.2 (*q*, MeN); 31.5 (*d*, CH(β)(Val)); 28.7, 28.5 (2*q*, 2 Me(Aib^t)); 19.0, 17.4 (2*q*, 2 Me(Val)). CI-MS: 442 ([M + H]$^+$), 334 ([M – (Me(Ph)NH)]$^+$). Anal. calc. for $C_{24}H_{31}N_3O_3S \cdot 0.2\ H_2O$ (445.20): C 64.75, H 7.11, N 9.44, S 7.20; found: C 64.89, H 6.94, N 9.23, S 6.61.

6.2. *Benzyl* N-*[(*S*)-1-(1-Methylethyl)-2-([1,1-dimethyl-2-[methyl(phenyl)amino]-2-oxoethyl]amino)-2-thioxoethyl]carbamate* (Z-Val-Ψ(CS)-Aib-N(Me)Ph; **22c**). According to the *GP B*, with **21c** (1000 mg, 2.26 mmol), AcOH (37 ml), $ZnCl_2$ (15.312 g, 110 mmol), and 2.1M HCl in AcOH (3.7 ml); reaction time: t_1 = 15 min, t_2 = 20 min: 724 mg (72%) of **22c** and 80 mg (8%) of **21c**.

Data of **22c**: Thick oil, which solidified under h.v. IR (KBr): 3418*w*, 3228*s*, 3056*m*, 2964*w*, 2934*w*, 2873*w*, 1877*w*, 1728*s*, 1635*s*, 1594*m*, 1555*w*, 1503*s*, 1453*w*, 1427*m*, 1395*m*, 1364*m*, 1310*w*, 1255*m*, 1221*m*, 1172*w*, 1128*w*, 1094*m*, 1072*w*, 1042*w*, 1025*w*, 903*w*, 852*w*, 765*w*, 746*m*, 712*m*, 704*m*. ^{1}H-NMR: 8.09 (br. *s*, NH); 7.39–7.21 (*m*, 10 arom. H); 5.74 (br. *d*, J = 6.9, NH); 5.12 (*s*, PhCH_2); 3.86 (*t*-like, J = 8.0, CH(α)(Val^t)); 3.23 (*s*, MeN); 2.18–2.03 (*m*, CH(β)(Val^t)); 1.69, 1.61 (2*s*, 2 Me(Aib)); 0.91, 0.90 (2*d*, J = 6.7, 2 Me(Val^t)). ^{13}C-NMR: 201.1 (*s*, CS(Val^t)); 171.5 (*s*, CO(Aib)); 155.7 (*s*, CONH); 143.7, 136.3 (2*s*, 2 arom. C); 129.2, 128.4, 128.0, 127.8, 127.7 (5*d*, 10 arom. C); 67.1 (*d*, CH(α)(Val^t)); 66.8 (*t*, PhCH$_2$); 61.7 (*s*, CH(α)(Aib)); 40.8 (*q*, MeN); 34.1 (*d*, CH(β)(Val^t)); 25.3, 23.8 (2*q*, 2 Me(Aib)); 19.4, 17.9 (2*q*, 2 Me(Val^t)). CI-MS: 442 ([M + H]$^+$), 335 ([M – (Me(Ph)N)]$^+$). Anal. calc. for $C_{24}H_{31}N_3O_3S$ (441.60): C 65.28, H 7.08, N 9.52; found: C 65.21, H 6.77, N 9.33.

6.3. *Benzyl* N-*[(1*S*)-2-Methyl-1-(4,5-dihydro-4,4-dimethyl-5-oxo-1,3-thiazol-2-yl)propyl]carbamate* (Z-Val-[1,3-thiazol-5(4*H*)-one]Aib; **23c**). According to the *GP C*, with **22c** (1660 mg, 3.76 mmol) in CH_2Cl_2 (42 ml), and CSA (2100 mg, 6.84 mmol). Chromatography (SiO_2; AcOEt/hexane 1:4) yielded 1116 mg (88%) of **23c**. Thick oil, which solidified under h.v. IR (KBr): 3322*w*, 3065*w*, 3034*w*, 2968*m*, 2933*m*, 2875*w*, 1722*s*, 1624*m*, 1587*w*, 1523*s*, 1455*m*, 1391*w*, 1375*w*, 1307*w*, 1263*m*, 1231*s*, 1100*w*, 1026*w*, 991*m*, 919*m*, 864*w*, 846*w*, 776*w*, 753*w*, 698*m*. ^{1}H-NMR: 7.36–7.30 (*m*, 5 arom. H); 5.45 (*d*, J = 7.5, NH); 5.13 (*s*, PhCH_2); 4.63–4.59 (*m*, CH(α)(Val^t)); 2.20 (*sept.*, J = 5.9, CH(β)(Val^t)); 1.38 (*s*, 2 Me(Aib)); 1.04, 0.93 (2*d*, J = 6.8, 2 Me(Val^t)). ^{13}C-NMR: 210.5 (*s*, C(5)(thiazolone)); 165.1 (*s*, C(2)(thiazolone)); 156.0 (*s*, CONH); 136.1 (*s*, arom. C); 128.4, 128.1, 127.9 (3*d*, 5 arom. C); 83.0 (*s*, C(4)(thiazolone)); 67.1 (*t*, PhCH$_2$); 59.9 (*d*, CH(α)(Val^t)); 31.4 (*d*, CH(β)(Val^t)); 24.4, 24.1 (2*q*, 2 Me(Aib)); 19.2, 16.6 (2*q*, 2 Me(Val^t)). CI-MS: 335 ([M + H]$^+$). Anal. calc. for $C_{17}H_{22}N_2O_3S$ (334.44): C 61.05, H 6.63, N 8.38; found: C 61.09, H 6.62, N 8.33.

6.4. *Methyl (2*S*,3*S*)-2-[2-((2*S*)-{[(Benzyloxy)carbonyl]amino}-3-methylbutanethioamido)-2-methylpropanamido]-3-methylpentanoate* (Z-Val-Ψ(CS)-Aib-Ile-OMe; **24c**). According to the *GP D*, with **23c** (981 mg, 2.93 mmol) in MeCN (40 ml), EtN(i-Pr)$_2$ (1.04 ml, 5.87 mmol), HOBt (888 mg, 6.57 mmol), and H-Ile-OMe·HCl (586 mg, 3.23 mmol); reaction time: 7 d. Chromatography (SiO_2; AcOEt/hexane 2:1) yielded 521 mg (37%) of **24c** and 518 mg (52%) of **23c**.

Data of **24c**: Thick oil, which solidified under h.v. IR (KBr): 3357*m*, 3234*m*, 3042*m*, 2964*m*, 2876*w*, 1721*s*, 1656*s*, 1521*s*, 1454*m*, 1426*m*, 1384*m*, 1313*m*, 1265*s*, 1228*s*, 1170*m*, 1130*w*, 1103*w*, 1024*m*, 969*w*, 911*w*, 848*w*, 781*m*, 737*m*, 696*m*. ^{1}H-NMR: 8.33 (br. *s*, NH); 7.35–7.29 (*m*, 5 arom. H); 6.48 (*d*, J = 8.0, NH); 5.59 (*d*, J = 8.4, NH); 5.17–5.04 (*m*, PhCH_2); 4.56–4.52 (*dd*, J = 8.2, 5.0, CH(α)(Ile)); 4.03 (*t*-like, J = 8.2, CH(α)(Val^t)); 3.71 (*s*, MeO); 2.22–2.18 (*m*, CH(β)(Val^t)); 1.92–1.87 (*m*, CH(β)(Ile)); 1.75, 1.70 (2*s*, 2 Me(Aib)); 1.47–1.39, 1.23–1.13 (2*m*, CH$_2$(Ile)); 0.98–0.87 (*m*, 2 Me(Val^t), 2 Me(Ile)). ^{13}C-NMR: 202.7 (*s*, CS(Val^t)); 172.3, 172.1 (2*s*, 2 CO); 156.3 (*s*, CONH); 136.0 (*s*, arom. C); 128.4, 128.0, 127.7 (3*d*, 5 arom. C); 68.2 (*d*, CH(α)(Val^t)); 66.9 (*t*, PhCH$_2$); 60.6 (*s*, C(α)(Aib)); 56.7 (*d*, CH(α)(Ile)); 51.8 (*q*, MeO); 37.6 (*d*, CH(β)(Ile)); 33.1 (*d*, CH(β)(Val^t)); 25.2 (*t*, CH$_2$(Ile)); 25.1, 22.7 (2*q*, 2 Me(Aib)); 19.4, 18.2 (2*q*, 2 Me(Val^t)); 15.4, 11.3 (2*q*, 2 Me(Ile)). ESI-MS: 502 ([M + K]$^+$). Anal. calc. for $C_{24}H_{37}N_3O_5S$ (479.64): C 60.10, H 7.78, N 8.76; found: C 60.03, H 7.29, N 8.59.

6.5. *(2*S*,3*S*)-2-[2-((2*S*)-{[(Benzyloxy)carbonyl]amino}butanethioamido)-2-methylpropanamido]-3-methylpentanoate* (Z-Val-Ψ(CS)-Aib-Ile-OH; **19c**). According to the *GP E*, with **24c** (200 mg, 0.42 mmol), THF/MeOH/H_2O 3:1:1 (10 ml) and LiOH·H_2O (54 mg, 1.29 mmol); reaction time: 4.5 h; yield of crude **19c**: quant.

6.6. *Z-Val-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-Val-OMe* (**25c**). According to the *GP F*, with **19c** (194 mg, 0.42 mmol), H-Val-OMe · HCl (77 mg, 0.46 mmol), TBTU (140 mg, 0.44 mmol), MeCN (8 ml), and EtN(i-Pr)$_2$ (0.20 ml, 1.25 mmol); reaction time: 18 h. Chromatography (SiO_2; AcOEt/hexane 1:1) gave 95 mg (41%) of **25c** and 22 mg (9%) of **27c**.

Data for **25c**: Thick oil. IR (neat): 3299*m*, 3033*w*, 2965*s*, 2933*m*, 2876*m*, 1737*s*, 1699*s*, 1513*s*, 1455*m*, 1390*w*, 1373*m*, 1354*w*, 1311*m*, 1263*m*, 1233*m*, 1207*s*, 1151*w*, 1111*w*, 1024*m*, 927*m*, 776*w*, 736*w*, 698*m*. ^{1}H-NMR: 7.27–7.21 (*m*, 5 arom. H); 7.07–7.03 (*m*, NH); 5.48 (br. *d*, *J* = 6.4, NH); 5.05 (*s*, PhC*H*$_2$); 4.50–4.46 (*m*, CH(α)(Val), CH(α)(Val^t)); 3.60 (*s*, MeO); 3.23 (*d*, *J* = 4.3, CH(α)(Ile)); 2.17–2.08 (*m*, CH(β)(Val), CH(β)(Val^t)); 1.56–1.35 (*m*, CH(β)(Ile)); 1.45, 1.35 (2*s*, 2 Me(Aib)); 1.08–0.83 (*m*, 2 Me(Val), 2 Me(Val^t), 2 Me(Ile)). ^{13}C-NMR: 177.5 (*s*, C(5)(thiazolimine)); 171.8, 170.5 (2*s*, 2 CO); 163.5 (*s*, C(2)(thiazolimine)); 156.0 (*s*, CO(carbamate)); 136.2 (*s*, arom. C); 128.4, 128.0, 127.9, 127.2, 126.7 (5*d*, 5 arom. C); 82.8 (*s*, C(4)(thiazolimine)); 79.8 (*d*, CH(α)(Ile)); 66.9 (*t*, PhCH$_2$); 59.4, 56.6 (2*d*, 2 CH(α)(Val)); 51.8 (*q*, MeO); 39.5 (*d*, CH(β)(Ile)); 31.5, 31.3 (2*d*, CH(β)(Val), CH(β)(Val^t)); 27.3, 27.2, 26.7, 26.5 (4*q*, 2 Me(Aib)); 25.1 (*t*, CH$_2$(Ile)); 19.2, 18.9, 17.6, 16.7 (4*q*, 2 Me(Val), 2 Me(Val^t)); 15.8, 11.0 (2*q*, 2 Me(Ile)). ESI-MS: 561 ([*M* + H]$^+$).

*Methyl (2*S*)-2-{(2*S*,3*S*)-2-[2-((2*S*)-{[(Benzyloxy)carbonyl]amino}-3-methylbutanethioamido)-2-methylpropanamido]-3-methylpentanamido}-3-methylbutanoate* Z-Val-Ψ(CS)-Aib-Ile-Val-OMe; **27c**). Yellow thick oil. IR (neat): 3270*w*, 3034*w*, 2963*m*, 2933*w*, 2875*w*, 2082*w*, 1695*m*, 1646*s*, 1506*s*, 1453*m*, 1432*m*, 1384*w*, 1307*w*, 1261*m*, 1213*m*, 1152*w*, 1024*w*, 774*w*, 734*w*. ^{1}H-NMR (conformers): 8.61, 8.43 (2*s*, NH); 7.38–7.26 (*m*, 5 arom. H); 6.66, 6.60 (2*d*, *J* = 8.8, 2 NH); 5.57, 5.43 (2*d*, *J* = 7.1, NH); 5.16–5.03 (*m*, PhC*H*$_2$); 4.48 (*dd*, *J* = 8.6, 5.4, CH(α)(Ile)); 4.33 (*t*-like, *J* = 6.8, CH(α)(Val)); 4.18 (*t*-like, *J* = 6.5, CH(α)(Val^t)); 3.71 (*s*, MeO); 2.24–2.11 (*m*, CH(β)(Val), CH(β)(Val^t)); 1.98–1.92 (*m*, CH(β)(Ile)); 1.73, 1.71 (2*s*, 2 Me(Aib)); 1.58–1.11 (*m*, CH$_2$(Ile)); 0.98–0.84 (*m*, 2 Me(Val), 2 Me(Val^t), 2 Me(Ile)). ^{13}C-NMR (conformers): 202.9 (*s*, CS(Val^t)); 172.7, 171.9, 171.2 (3*s*, 3 CO); 136.1 (*s*, 1 arom. C); 128.6, 128.3, 127.9 (3*d*, 5 arom. C); 67.9 (*d*, CH(α)(Val^t)); 67.2 (*t*, PhCH$_2$); 61.0 (*s*, C(α)(Aib)); 58.3, 57.5 (2*d*, CH(α)(Ile), CH(α)(Val)); 52.0 (*q*, MeO); 36.8 (*d*, CH(β)(Ile)); 33.2 (*d*, CH(β)(Val^t)); 31.0 (*d*, CH(β)(Val)); 25.4 (*t*, CH$_2$(Ile)); 25.0, 23.6 (2*q*, 2 Me(Aib)); 19.5, 18.9, 18.1, 15.5 (4*q*, 2 Me(Val), 2 Me(Val^t)); 14.2, 11.1 (2*q*, 2 Me(Ile)). ESI-MS: 601 ([*M* + Na]$^+$).

7. *Attempt to Prepare Z-Aib-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-Val-OMe.* 7.1. *Benzyl* N-*[1,1-Dimethyl-(2-{1,1-dimethyl-2-[methyl(phenyl)amino]-2-oxoethyl}amino)-2-thioxoethyl]carbamate* (Z-Aib-Ψ(CS)-Aib-N(Me)Ph; **22d**). According to the *GP B*, with Z-Aib-Aib-Ψ(CS)-N(Me)Ph (**21d** [7]; 2598 mg, 6.08 mmol), AcOH (72 ml), $ZnCl_2$ (2826 mg, 208 mmol), and 2.1M HCl in AcOH (7.2 ml); reaction time: t_1 = 30 min, t_2 = 15 min: 2499 mg (96%) of **22d**. Thick oil, which solidified under h.v. The spectroscopic data are identical with the data described in [7].

7.2. *Benzyl* N-*[1-Methyl-1-(4,5-dihydro-4,4-dimethyl-5-oxo-1,3-thiazol-2-yl)ethyl]carbamate* (Z-Aib-[1,3-thiazol-5(4*H*)-one]Aib; **23d**). According to the *GP C*, with **22d** (2368 mg, 5.54 mmol) in CH_2Cl_2 (60 ml), and CSA (1415 mg, 6.09 mmol). Chromatography (SiO_2; AcOEt/hexane 3:1) yielded 1695 mg (95%) of **23d**. Colorless prisms. Suitable crystals for an X-ray crystal-structure determination were obtained from hexane/CH_2Cl_2. M.p. 109–110°. IR (KBr): 3382*w*, 3264*s*, 3149*s*, 3031*m*, 2972*w*, 1708*s*, 1629*s*, 1499*m*, 1471*m*, 1455*m*, 1407*s*, 1382*m*, 1339*s*, 1250*s*, 1225*m*, 1167*m*, 1036*s*, 995*s*, 917*s*, 887*s*, 835*m*, 824*w*, 778*s*, 745*s*, 697*s*. ^{1}H-NMR: 7.36–7.31 (*m*, 5 arom. H); 5.63 (br. *s*, NH); 5.09 (*s*, PhC*H*$_2$); 1.67 (*s*, 2 Me(Aib^t)); 1.38 (*s*, 2 Me(Aib)). ^{13}C-NMR: 211.2 (*s*, C(5)(thiazolone)); 170.0 (*s*, C(2)(thiazolone)); 154.4 (*s*, CONH); 136.2 (*s*, 1 arom. C); 128.4, 128.1, 128.0 (3*d*, 5 arom. C); 83.7 (*s*, C(4)(thiazolone)); 66.6 (*t*, PhCH$_2$); 56.9 (*s*, C(α)(Aib)); 26.0, 24.3 (2*q*, 2 Me(Aib), 2 Me(Aib^t)). CI-MS: 322 (20), 321 (100, [*M* + H]$^+$). Anal. calc. for $C_{16}H_{20}N_2O_3S$ (320.41): C 59.98, H 6.29, N 8.74, S 10.01; found: C 60.02, H 6.12, N 8.68, S 10.02.

7.3. *Methyl (2*S*,3*S*)-2-[2-({[(Benzyloxy)carbonyl]amino}-2-methylpropanethioamido)-2-methylpropanamido]-3-methylpentanoate* (Z-Aib-Ψ(CS)-Aib-Ile-OMe; **24d**). According to the *GP D*, with **23d** (615 mg, 1.92 mmol) in MeCN (30 ml), EtN(i-Pr)$_2$ (0.66 ml, 3.84 mmol), HOBt (3.84 mg, 589 mmol), and H-Ile-OMe · HCl (383 mg, 2.11 mmol); reaction time: 10 d. Chromatography (SiO_2; AcOEt/hexane 1:1) yielded 189 mg (21%) of **24d** and 454 mg (74%) of **23d**.

Data of **24d**: Thick oil, which solidified under h.v. IR (KBr): 3312*s*, 3261*s*, 3034*s*, 2963*s*, 2878*m*, 1726*s*, 1700*s*, 1664*s*, 1539*s*, 1456*m*, 1433*s*, 1383*s*, 1362*s*, 1264*s*, 1211*s*, 1074*s*, 1048*s*, 1015*m*, 978*m*, 953*m*, 913*w*, 851*w*, 822*w*, 758*w*, 725*m*, 699*s*. ^{1}H-NMR: 8.28 (br. *s*, NH); 7.39–7.30 (*m*, 5 arom. H); 6.94 (br. *d*, *J* = 7.1, NH); 5.50 (br. *s*, NH); 5.20–5.06 (*m*, PhC*H*$_2$); 4.45 (*dd*, *J* = 7.7, 5.9, CH(α)(Ile)); 3.69 (*s*, MeO); 1.94–1.88 (*m*, CH(β)(Ile)); 1.69, 1.63, 1.60, 1.52 (4*s*, 2 Me(Aib), 2 Me(Aib^t)); 1.56–1.20 (*m*, CH$_2$(Ile)); 0.94–0.87 (*m*, 2 Me(Ile)). ^{13}C-NMR: 204.3 (*s*, CS(Aib^t)); 172.5, 172.3 (2*s*, CO(Aib), CO(Ile)); 155.2 (*s*, CO(carbamate)); 135.9 (*s*, 1 arom. C); 128.6, 128.4, 128.3, 128.1, 128.0 (5*d*, 5 arom. C); 67.1 (*t*, PhCH$_2$); 63.2, 60.2 (2*s*, C(α)(Aib), C(α)(Aib^t)); 57.2 (*d*, CH(α)(Ile)); 51.6 (*q*, MeO); 37.1 (*d*, CH(β)(Ile)); 29.2, 27.8, 25.3, 23.0 (4*q*, 2 Me(Aib), 2 Me(Aib^t)); 26.0 (*t*, CH$_2$(Ile)); 15.5,

11.3 (2*q*, 2 Me(Ile)). ESI-MS: 493, 488 ([*M* + Na]$^+$), 321 ([Z-Aib[1,3-thiazol-5(4*H*)-one]Aib + H]$^+$). CI-MS: 321 (100). Anal. calc. for $C_{23}H_{35}N_3O_5S$ (465.62): C 59.33, H 7.58, N 9.02, S 6.89; found: C 59.36, H 7.65, N 8.90, S 6.83.

7.4. *(2S,3S)-2-[2-(2-Carbamido-2-methylpropanethioamido)-2-methylpropanamido]-3-methylpentanoic Acid* (HOOC-NH-Aib-Ψ(CS)-Aib-Ile-OH; **29**). According to the *GP E*, with **24d** (407 mg, 0.89 mmol), THF/MeOH/H_2O 3:1:1 (25 ml) and LiOH · H_2O (111 mg, 2.67 mmol); reaction time: 18 h. Chromatography (SiO_2; AcOEt → AcOEt/MeOH 10:1) yielded 103 mg (59%) of **29**. IR (KBr): 3291*s*, 2790*s*, 2936*s*, 2878*m*, 1745*s*, 1663*s*, 1524*s*, 1464*m*, 1381*s*, 1300*s*, 1206*s*, 1226*m*, 1036*w*, 1011*w*, 988*w*, 922*w*, 759*w*, 712*w*. ^{1}H-NMR: 8.20, 7.12 (2 br. *s*, 2 NH); 6.34 (br. *d*, *J* = 7.8, NH); 4.51 (*dd*, *J* = 7.9, 5.0, CH(α)(Ile)); 1.98–1.89 (*m*, CH(β)(Ile)); 1.92, 1.86, 1.48, 1.47 (4*s*, 2 Me(Aib), 2 Me(Aib^t)); 1.55–1.17 (*m*, CH_2(Ile)); 0.96–0.90 (*m*, 2 Me(Ile)). ^{13}C-NMR: 211.0 (*s*, CS(Aib^t)); 175.2, 172.3 (2*s*, CO(Aib), CO(Ile)); 157.4 (*s*, COOH); 66.0, 65.0 (2*s*, C(α)(Aib), C(α)(Aib^t)); 56.7 (*d*, CH(α)(Ile)); 37.6 (*d*, CH(β)(Ile)); 29.0, 24.4, 23.7 (3*q*, 2 Me(Aib), 2 Me(Aib^t)); 25.2 (*t*, CH_2(Ile)); 15.3, 11.4 (2*q*, 2 Me(Ile)). ESI-MS: 493, 488 ([*M* + Na]$^+$), 321 ([Z-Aib-[1,3-thiazol-5(4*H*)-one]Aib + H]$^+$). CI-MS: 361 (15, $M^{+\cdot}$), 213 (100). Anal. calc. for $C_{15}H_{27}N_3O_5S$ (361.46): C 49.84, H 7.53, N 11.62, S 8.87; found: C 50.05, H 7.44, N 11.23, S 8.68.

7.5. *Methyl (2S)-2-((2S,3S)-2-[2-[(4,4-Dimethyl-2-oxo-1,3-oxazolidin-5-yliden)amino]-2-methylpropanethioamido]-3-methylpentanamido)-3-methylbutanoate* (**28**). According to the *GP F*, with **29** (175 mg, 0.39 mmol), H-Val-OMe · HCl (71 mg, 0.43 mmol), TBTU (130 mg, 0.41 mmol), MeCN (3 ml), and EtN(i-Pr)$_2$ (0.2 ml, 1.2 mmol); reaction time: 16 h. Chromatography (SiO_2; AcOEt/hexane 1:1) gave 104 mg (59%) of **28**. Thick oil. IR (KBr): 3305*s*, 3137*m*, 2967*s*, 2878*m*, 1746*s*, 1650*s*, 1535*s*, 1466*m*, 1437*m*, 1380*s*, 1296*s*, 1208*s*, 1155*m*, 1126*m*, 1033*m*, 990*w*, 930*w*, 815*w*, 760*w*, 699*w*. ^{1}H-NMR: 7.28 (br. *s*, NH); 6.75 (br. *d*, *J* = 8.1, NH); 6.64 (br. *d*, *J* = 8.3, NH); 4.38 (*dd*, *J* = 8.3, 5.0, CH(α)(Ile)); 4.14 (*t*-like, *J* = 8.0, CH(α)(Val)); 3.66 (*s*, MeO); 2.15–2.08 (*m*, CH(β)(Ile)); 1.83, 1.78 (2*s*, 2 Me(Aib)); 1.56–1.44 (*m*, CH(β)(Val)); 1.39, 1.37 (2*s*, 2 Me(Aib^t)); 1.34–1.05 (*m*, CH_2(Ile)); 0.91–0.80 (*m*, 2 Me(Ile), 2 Me(Val)). ^{13}C-NMR: 211.2 (*s*, CS(Aib^t)); 172.2, 171.8, 171.6 (3*s*, 2 CO, C(5)(oxazolidine)); 156.7 (*s*, C(2)(oxazolidine)); 65.3, 64.8 (2*s*, C(4)(oxazolidine), C(α)(Aib^t)); 58.4, 57.4 (2*d*, CH(α)(Ile), CH(α)(Val)); 51.9 (*s*, MeO); 36.9 (*d*, CH(β)(Ile)); 30.8 (*d*, CH(β)(Val)); 29.0, 24.3, 23.7 (3*q*, 2 Me(Aib), 2 Me(Aib^t)); 25.1 (*t*, CH_2(Ile)); 18.9, 17.8 (2*q*, 2 Me(Val)); 15.2, 10.9 (2*q*, 2 Me(Ile)). ESI-MS: 479 ([*M* + Na]$^+$), 457 ([*M* + H]$^+$), 245. Anal. calc. for $C_{21}H_{36}N_4O_5S \cdot 0.33\ H_2O$ (462.62): C 54.52, H 7.99, N 12.11; found: C 54.45, H 7.92, N 12.00.

8. *Syntheses of* **34**, **35**, *and* **36**. 8.1. *Methyl 2-[2-((2S)-{[(Benzyloxy)carbonyl]amino}-3-methylbutanethioamido)-2-methylpropanamido]ethanoate* (Z-Val-Ψ(CS)-Aib-Gly-OMe; **33a**). According to the *GP D*, with **23c** (381 mg, 1.14 mmol) in MeCN (15 ml), EtN(i-Pr)$_2$ (0.40 ml, 2.27 mmol), HOBt (345 mg, 2.55 mmol), and H-Gly-OMe · HCl (157 mg, 1.25 mmol); reaction time: 7 d. Chromatography (SiO_2; AcOEt/hexane 2:1) yielded 394 mg (82%) of **33a**, as well as 13 mg (3%) of **23c**.

Data of **33a**: Thick oil, which solidified under h.v. IR (KBr): 3273*s*, 3036*m*, 2964*s*, 2874*w*, 1666*s*, 1530*s*, 1427*s*, 1386*m*, 1364*m*, 1270*s*, 1230*s*, 1129*m*, 1100*m*, 1025*m*, 980*m*, 911*w*, 891*w*, 848*w*, 824*w*, 781*w*, 737*m*. ^{1}H-NMR ((D$_6$)DMSO): 9.98 (*s*, NH); 7.72–7.58 (*m*, NH); 7.43–7.33 (*m*, 5 arom. H); 5.15–5.02 (*m*, PhCH_2); 4.11 (*t*-like, *J* = 8.3, CH(α)(Val^t)); 3.84, 3.48 (2*dd*, *J* = 17.1, 6.0, CH_2(Gly)); 3.64 (*s*, MeO); 2.06 (*sept.*, *J* = 7.5, CH(β)(Val^t)); 1.66, 1.58 (2*s*, 2 Me(Aib)); 0.94, 0.92 (2*d*, *J* = 6.7, 2 Me(Val^t)). ^{13}C-NMR ((D$_6$)DMSO): 203.4 (*s*, CS(Val^t)); 172.9, 170.1 (2*s*, 2 CO); 156.8 (*s*, CO(carbamate); 136.0 (*s*, 1 arom. C); 128.4, 128.1, 127.6 (3*d*, 5 arom. C); 68.2 (*d*, CH(α)(Val^t)); 66.9 (*t*, PhCH_2); 60.6 (*s*, C(α)(Aib)); 52.0 (*q*, MeO); 41.4 (*t*, CH_2(Gly)); 33.0 (*d*, CH(β)(Val)); 25.6, 22.9 (2*q*, 2 Me(Aib)); 19.3, 18.3 (2*q*, 2 Me(Val^t)). ESI-MS: 446 ([*M* + Na]$^+$). Anal. calc. for $C_{20}H_{29}N_3O_5S$ (423.64): C 56.70, H 6.89, N 9.92; found: C 56.39, H 6.45, N 9.62.

8.2. *Methyl (2S)-2-[2-((2S)-{[(Benzyloxy)carbonyl]amino}-3-methylbutanethioamido)-2-methylpropanamido]propanoate* (Z-Val-Ψ(CS)-Aib-Ala-OMe; **33b**). According to the *GP D*, with **23c** (518 mg, 1.55 mmol) in MeCN (15 ml), EtN(i-Pr)$_2$ (0.55 ml, 3.10 mmol), HOBt (484 mg, 3.10 mmol), and H-Ala-OMe · HCl (100 mg, 1.70 mmol); reaction time: 6 d. Chromatography (SiO_2; AcOEt/hexane 1:1) yielded 268 mg (40%) of **33b**, as well as 294 mg (57%) of **23c**.

Data of **33b**: Thick oil, which solidified under h.v. IR (KBr): 3264*s*, 3036*m*, 2966*s*, 2874*m*, 1744*s*, 1709*s*, 1661*s*, 1529*s*, 1454*s*, 1428*s*, 1384*m*, 1315*s*, 1271*s*, 1232*s*, 1172*s*, 1021*m*, 1027*m*, 979*m*, 926*w*, 870*w*, 850*w*, 826*w*, 782*w*, 738*m*, 697*m*. ^{1}H-NMR (conformers): 8.20 (br. *s*, NH); 7.37–7.30 (*m*, 5 arom. H); 6.57 (br. *d*, *J* = 6.9, NH); 5.57 (*d*, *J* = 8.0, NH); 5.15–5.04 (*m*, PhCH_2); 4.59–4.49 (*m*, CH(α)(Ala)); 3.92 (*t*-like, *J* = 8.1, CH(α)(Val^t)); 3.72, 3.71 (2*s*, MeO); 2.17–2.06 (*m*, CH(β)(Val^t)); 1.74, 1.68 (2*s*, 2 Me(Aib)); 1.40, 1.33 (2*d*, *J* = 6.7, Me(Ala)); 0.98, 0.92 (2*d*, *J* = 6.8, 2 Me(Val^t)). ^{13}C-NMR (conformers): 203.4 (*s*, CS(Val^t)); 173.2, 171.8 (2*s*, 2 CO); 156.6 (*s*, CO(carbamate)); 136.0 (*s*, 1 arom. C); 128.4, 128.1, 127.7 (3*d*, 5 arom. C); 68.7 (*d*, CH(α)(Val^t)); 67.0 (*t*, PhCH_2); 60.6 (*s*, C(α)(Aib)); 52.2 (*q*, MeO); 48.3 (*d*, CH(Ala)); 32.9 (*d*, CH(β)(Val)); 25.9 (*q*, 2 Me(Aib));

22.4 (*q*, Me(Ala)); 19.3, 17.8 (2*q*, 2 Me(Val^t)). ESI-MS: 460 ([M + Na]$^+$). Anal. calc. for $C_{21}H_{31}N_3O_5S$ (437.56): C 57.65, H 7.14, N 9.60, S 7.33; found: C 57.85, H 7.19, N 9.33, S 7.33.

8.3. *2-[2-((2*S*)-{[(Benzyloxy)carbonyl]amino}butanethioamido)-2-methylpropanamido]ethanoic Acid* (Z-Val-Ψ(CS)-Aib-Gly-OH). According to the *GP E*, with **33a** (146 mg, 0.345 mmol), THF/MeOH/H_2O 3:1:1 (5 ml), and LiOH · H_2O (43 mg, 0.03 mmol); reaction time: 2.5 h; yield: 93%.

8.4. *Methyl (2*S*)-2-(2-{[2-((2*S*)-{[(Benzyloxy)carbonyl]amino}-2-methylpropyl)-4,5-dihydro-4,4-dimethyl-1,3-oxazol-5-yliden]amino}ethanamido)-3-methylbutanoate* (Z-Val-[1,3-oxazol-5(4*H*)-imine]Aib-Gly-Val-OMe; **35a**). According to the *GP F*, with Z-Val^t-Aib-Gly-OH (80 mg, 0.21 mmol) in MeCN (6 ml), H-Val-OMe (39 mg, 0.23 mmol), TBTU (71 mg, 0.22 mmol), and EtN(i-Pr)$_2$ (0.11 ml, 0.62 mmol); reaction time: 8 h. Chromatography (SiO_2; AcOEt/hexane 1:2) gave 42 mg (35%) of **35a**, as well as 21 mg (20%) of **34a**.

Data of **35a**: Thick oil, which solidified under h.v. IR (KBr): 3342*s*, 3035*w*, 2969*s*, 2934*m*, 2876*m*, 1740*s*, 1695*s*, 1632*s*, 1534*s*, 1456*m*, 1436*m*, 1376*m*, 1312*m*, 1238*s*, 1206*s*, 1151*m*, 1114*m*, 1094*m*, 1025*m*, 964*m*, 879*w*, 778*m*, 753*w*, 699*m*. ^{1}H-NMR (conformers): 7.36–7.27 (*m*, 5 arom. H); 6.55–6.51 (*m*, NH); 5.37 (br. *d*, *J* = 8.9, NH); 5.15–5.04 (*m*, PhCH_2); 4.48 (*dd*, *J* = 8.7, 4.8, CH(α)(Val^t)); 4.41–4.29 (*m*, CH(α)(Val)); 4.25 (*d*, *J* = 6.0, CH_2(Gly)); 3.72, 3.71 (2*s*, MeO); 2.23–2.13 (*m*, CH(β)(Val^t), CH(β)(Val)); 1.36, 1.34, 1.32, 1.31 (4*q*, 2 Me(Aib)); 1.03–0.87 (*m*, 2 Me(Val^t), 2 Me(Val)). ^{1}H-NMR ((D$_6$)DMSO)), 380 K)[15]: 7.92 (br. *d*, *J* = 8.3, NH); 7.34–7.27 (*m*, 5 arom. H); 6.88 (br. *d*, *J* = 8.2, NH); 5.05 (*s*, PhCH_2); 4.30–4.12 (*m*, CH(α)(Val^t), CH(α)(Val)); 4.23 (*d*, *J* = 3.6, CH_2(Gly)); 3.64 (*s*, MeO); 2.19 (*sept.*, *J* = 5.3, CH(β)(Val^t)); 2.07 (*sept.*, *J* = 4.9, CH(β)(Val)); 1.18, 1.17 (2*q*, 2 Me(Aib)); 0.93–0.85 (*m*, 2 Me(Val^t), 2 Me(Val)). ^{13}C-NMR (conformers): 186.3 (*s*, C(5)(oxazolimine)); 171.9, 166.5 (2*s*, 2 CO); 160.7 (*s*, C(2)(oxazolimine)); 156.2 (*s*, CO(carbamate)); 136.0 (*s*, 1 arom. C); 128.4, 128.1, 128.0 (3*d*, 5 arom. C); 67.1 (*t*, PhCH_2); 67.1 (*s*, C(4)(oxazolimine)); 57.3 (*s*, C(α)(Aib)); 57.3 (*d*, CH(α)(Val^t)); 53.4 (*d*, CH(α)(Val)); 52.0 (*q*, MeO); 43.7 (*t*, CH_2(Gly)); 30.9, 30.5 (2*d*, CH(β)(Val^t), CH(β)(Val)); 23.7, 23.4 (2*q*, 2 Me(Aib)); 19.6, 18.7, 17.5, 17.2 (4*q*, 2 Me(Val^t), 2 Me(Val)). ESI-MS: 511 ([M + Na]$^+$), 489 ([M + H]$^+$).

*Methyl (2*S*)-2-(2-{[2-((2*S*)-{[(Benzyloxy)carbonyl]amino}-2-methylpropyl)-4,5-dihydro-4,4-dimethyl-1,3-thiazol-5-yliden]amino}ethanamido)-3-methylbutanoate* (Z-Val-[1,3-thiazol-5(4*H*)-imine]Aib-Gly-Val-OMe; **34a**). A crystal suitable for an X-ray crystal-structure determination was obtained from CH_2Cl_2/hexane. M.p. 86–87°. IR (KBr): 3360*s*, 3236*s*, 2966*s*, 2933*s*, 2874*m*, 1746*s*, 1720*s*, 1673*s*, 1639*s*, 1531*s*, 1456*m*, 1393*s*, 1374*s*, 1355*s*, 1308*s*, 1262*s*, 1231*s*, 1180*m*, 1153*s*, 1127*s*, 1061*m*, 1020*s*, 981*m*, 927*m*, 886*w*, 835*w*, 805*w*, 786*w*, 755*m*, 697*m*. ^{1}H-NMR: 7.50 (br. *d*, *J* = 8.8, NH); 7.36–7.26 (*m*, 5 arom. H); 5.39 (br. *d*, *J* = 7.8, NH); 5.14 (*s*, PhCH_2); 4.62 (*m*, CH(α)(Val^t), CH(α)(Val)); 3.83 (*s*, CH_2(Gly)); 3.75 (*s*, MeO); 2.25–2.17 (*m*, CH(β)(Val^t), CH(β)(Val)); 1.47 (*q*, 2 Me(Aib)); 1.04–0.88 (*m*, 2 Me(Val^t), 2 Me(Val)). ^{13}C-NMR: 178.6 (*s*, C(5)(thiazolimine)); 172.3, 169.1 (2*s*, 2 CO); 163.4 (*s*, C(2)(thiazolimine)); 156.2 (*s*, CO(carbamate)); 136.7 (*s*, 1 arom. C); 128.8, 128.5, 128.4 (3*d*, 5 arom. C); 83.0 (*s*, C(4)(thiazolimine)); 67.4 (*t*, PhCH_2); 62.3 (*t*, CH_2(Gly)); 59.7 (*d*, CH(α)(Val^t)); 57.0 (*d*, CH(α)(Val)); 52.3 (*q*, MeO); 31.9, 31.5 (2*d*, CH(β)(Val^t), CH(β)(Val)); 27.2 (*q*, 2 Me(Aib)); 19.5, 19.2, 17.9, 17.0 (4*q*, 2 Me(Val^t), 2 Me(Val)). ESI-MS: 527 ([M + Na]$^+$), 505 ([M + H]$^+$).

8.5. *(2*S*)-2-[2-((2*S*)-{[(Benzyloxy)carbonyl]amino}-3-methylbutanethioamido)-2-methylpropanamido]-propanoic Acid* (Z-Val-Ψ(CS)-Aib-Ala-OH). According to the *GP E*, with **33b** (73 mg, 0.167 mmol), THF/MeOH/H_2O 3:1:1 (5 ml), and LiOH · H_2O (21 mg, 0.50 mmol); reaction time: 3 h; yield: 94%.

8.6. *Methyl (2*S*)-2-((2*S*)-2-{[2-((2*S*)-{[(Benzyloxy)carbonyl]amino}-2-methylpropyl)-4,5-dihydro-4,4-dimethyl-1,3-thiazol-5-yliden]amino}propanamido)-3-methylbutanoate* (Z-Val-[1,3-thiazol-5(4*H*)-imine]Aib-Ala-Val-OMe; **34b**). According to the *GP F*, with Z-Val^t-Aib-Ala-OH (67 mg, 0.158 mmol) in MeCN (5 ml), H-Val-OMe (29 mg, 0.174 mmol), TBTU (53 mg, 0.165 mmol), HOBt (26 mg, 0.165 mmol), and EtN(i-Pr)$_2$ (0.08 ml, 0.474 mmol); reaction time: 18 h. Chromatography (SiO_2; AcOEt/hexane 1:1) gave 26 mg (32%) of **34b**, as well as 38 mg (55%) of **36b**.

Data of **34b**: Thick oil, which solidified under h.v. IR (neat): 3377*s*, 3298*s*, 2967*s*, 2975*s*, 2875*s*, 1742*s*, 1674*s*, 1520*s*, 1467*s*, 1390*m*, 1373*s*, 1311*s*, 1263*s*, 1234*s*, 1153*s*, 1120*m*, 1025*s*, 1094*m*, 1025*m*, 970*m*, 925*m*, 871*w*, 820*w*, 776*m*, 754*m*, 698*m*. ^{1}H-NMR: 7.34–7.19 (*m*, 5 arom. H, NH); 5.33 (br. *d*, *J* = 7.3, NH); 5.05 (*s*, PhCH_2); 4.52–4.46 (*m*, CH(α)(Val^t), CH(α)(Val)); 4.25 (*d*, *J* = 6.0, CH_2(Gly)); 3.64 (*s*, MeO); 3.36 (*q*, *J* = 6.9, CH(α)(Ala)); 2.20–2.08 (*m*, CH(β)(Val^t), CH(β)(Val)); 1.43, 1.36, 1.31, 1.29 (4*q*, 2 Me(Aib)); 0.96 (*d*, *J* = 6.9, Me(Ala)); 0.91–0.75 (*m*, 2 Me(Val^t), 2 Me(Val)). ^{13}C-NMR: 175.9 (*s*, C(5)(thiazolimine)); 171.4, 171.1 (2*s*, 2 CO); 162.3 (*s*, C(2)(thiazolimine)); 155.2 (*s*, CO(carbamate)); 135.3 (*s*, 1 arom. C); 127.5, 127.2, 127.1 (3*d*, 5 arom. C); 81.8

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[15]) This high-temp. experiment (380 K) established the presence of conformers at 300 K, when more signals were doubled and/or further separated.

(*s*, C(4)(thiazolimine)); 68.2 (*d*, CH(*α*)(Ala)); 66.2 (*t*, Ph*C*H$_2$); 58.5 (*d*, CH(*α*)(Val^t)); 55.6 (*d*, CH(*α*)(Val)); 51.0 (*q*, MeO); 30.6, 30.5 (2*d*, CH(*β*)(Val^t), CH(*β*)(Val)); 26.3, 25.7 (2*q*, 2 Me(Aib)); 18.3, 17.9, 17.2, 16.6, 15.8 (5*q*, 2 Me(Val^t), 2 Me(Val), Me(Ala)). ESI-MS: 541 ([*M* + Na]$^+$).

*Methyl (2*S*)-2-{(2*S*)-2-[2-((2*S*)-{[(Benzyloxy)carbonyl]amino}-3-methylbutanethioamido)-2-methylpropanamido]propanamido}-3-methylbutanoate* (Z-Val-*Ψ*(CS)-Aib-Ala-Val-OMe; **36b**). IR (KBr): 3325*s*, 3042*m*, 2966*s*, 2934*m*, 2875*m*, 1742*s*, 1653*s*, 1525*s*, 1469*m*, 1453*m*, 1443*m*, 1384*m*, 1373*m*, 1315*m*, 1269*s*, 1230*s*, 1128*m*, 1101*m*, 1026*m*, 979*w*, 915*w*, 862*w*, 827*w*, 776*w*, 739*m*, 698*m*. ^{1}H-NMR: 8.00 (br. *s*, NH); 7.37 – 7.30 (*m*, 5 arom. H); 6.82 (*d*, *J* = 8.3, NH); 6.64 (*d*, *J* = 6.4, NH); 5.45 (*d*, *J* = 5.3, NH); 5.15 – 5.04 (*m*, PhC*H*$_2$); 4.50 – 4.38 (*m*, CH(*α*)(Val^t), CH(*α*)(Val)); 3.91 (*t*, *J* = 7.2, CH(*α*)(Ala)); 3.72 (*s*, MeO); 2.25 – 2.13 (*m*, CH(*β*)(Val^t), CH(*β*)(Val)); 1.68 (*q*, 2 Me(Aib)); 1.32 (*d*, *J* = 7.2, Me(Ala)); 0.99 – 0.78 (*m*, 2 Me(Val^t), 2 Me(Val)). ^{13}C-NMR: 203.2 (*s*, CS(Val)); 172.2, 171.9, 171.8 (3*s*, 3 CO); 156.7 (*s*, CO(carbamate)); 135.8 (*s*, 1 arom. C); 128.5, 128.2, 127.8 (3*d*, 5 arom. C); 69.2 (*d*, CH(*α*)(Val^t)); 67.2 (*t*, Ph*C*H$_2$); 60.6 (*s*, C(*α*)(Aib)); 57.3 (*d*, CH(*α*)(Val)); 51.9 (*q*, MeO); 49.5 (*d*, CH(*α*)(Ala); 32.6, 31.0 (2*d*, CH(*β*)(Val^t), CH(*β*)(Val)); 25.7, 23.4 (2*q*, 2 Me(Aib)); 19.4, 18.8, 17.9, 17.3 (4*q*, 2 Me(Val^t), 2 Me(Val)); 14.1 (*q*, Me(Ala)). ESI-MS: 559 ([*M* + Na]$^+$).

9. *Control Experiments.* 9.1. *Benzyl {(2*S*)-1-[4,4-Dimethyl-5-((2*S*,3*S*)-2-methyl-1-{1-methyl-1-[methyl(phenyl)carbamoyl]ethylcarbamoyl}butylimino)-4,5-dihydro-1,3-thiazol-2-yl]ethyl}carbamate* (Z-Ala-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-Aib-N(Me)Ph; **37**). According to the *GP A*, with **19a** (58 mg, 0.13 mmol) in THF (5 ml), NMM (0.03 ml, 0.27 mmol), ClCO$_2$^{i}Bu (18 mg, 0.14 mmol), Na$_2$S · H$_2$O (620 mg, 3.99 mmol), **6** (23 mg, 0.13 mmol); reaction time: 22 h. Chromatography (SiO$_2$; AcOEt/hexane 1:2) led to 55 mg (70%) of **37**. Thick oil. IR (neat): 3303*s*, 2967*s*, 2934*s*, 1722*s*, 1666*s*, 1594*s*, 1496*s*, 1455*s*, 1385*s*, 1249*s*, 1116*m*, 1054*m*, 1003*m*, 930*m*, 848*w*, 777*m*, 741*m*, 704*s*. ^{1}H-NMR (conformers): 7.37 – 7.14 (*m*, 10 arom. H); 7.03, 6.92 (2 br. *s*, NH); 5.65 (br. *s*, NH); 5.15 (*s*, PhC*H*$_2$); 4.71 – 4.66 (*m*, CH(*α*)(Ala^t)); 3.22 (*s*, MeN); 3.08 (*t*-like, *J* = 3.7, CH(*α*)(Ile)); 1.99 – 1.90 (*m*, CH(*β*)(Ile)); 1.58 – 1.20 (*m*, CH$_2$(Ile), Me(Ala^t), 2 Me(Aib^1), 2 Me(Aib^2)); 1.00 – 0.81 (*m*, 2 Me(Ile)). ^{13}C-NMR (conformers): 175.8 (*s*, C(5)(thiazolimine)); 172.8, 169.6 (2*s*, CO(Aib), CO(Ile)); 170.4, 169.1 (2*s*, C(2)(thiazolimine)); 155.4 (*s*, CO(carbamate)); 144.4, 136.1 (2*s*, 2 arom. C); 129.2, 128.4, 128.1, 128.0, 127.8 (5*d*, 10 arom. C); 82.5, 82.3 (2*s*, C(4)(thiazolimine)); 79.1 (*d*, CH(*α*)(Ile)); 66.9 (*t*, Ph*C*H$_2$); 57.8 (*s*, C(*α*)(Aib)); 50.5 (*d*, CH(*α*)(Ala^t)); 41.3 (*q*, MeN); 40.3, 40.2 (2*d*, CH(*β*)(Ile)); 27.6, 26.3, 26.1, 25.9 (4*q*, 2 Me(Aib^1), 2 Me(Aib^2)); 24.9 (*t*, CH$_2$(Ile)); 19.7 (*q*, Me(Ala^t); 15.9, 11.9 (2*q*, 2 Me(Ile)). ESI-MS: 616 ([*M* + Na]$^+$), 594 ([*M* + H]$^+$), 487 ([*M* – (Me(Ph)N)]$^+$). Anal. calc. for C$_{32}$H$_{43}$N$_5$O$_4$S · 0.66 H$_2$O (605.80): C 63.45, H 7.38, N 11.56, S 5.29; found: C 63.77, H 7.29, N 11.27, S 4.52.

9.2. *(2*S*,3*S*)-2-{[2-((2*S*)-{[(Benzyloxy)carbonyl]amino}ethyl)-4,5-dihydro-4,4-dimethyl-1,3-thiazol-5-yliden]amino}-3-methylpentanoic Acid* (Z-Ala-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-OH; **38**). To a soln. of **19a** (50 mg, 0.114 mmol) in THF (5 ml) were added ClCO$_2$^{i}Bu (16 mg, 0.114 mmol) and NMM (0.04 ml, 0.342 mmol), and the mixture was stirred for 1 h. The suspension was transferred into a separatory funnel, diluted with CH$_2$Cl$_2$, and extracted with 0.1M H$_3$PO$_4$ soln. (3×). The combined org. phase was dried (MgSO$_4$) and evaporated: 48 mg (quant.) of crude **38**. Thick oil, which solidified under h.v. ^{1}H-NMR (conformers): 7.29 – 7.19 (*m*, 5 arom. H); 5.57 (br. *s*, NH); 5.05 (*s*, PhC*H*$_2$); 4.62 (br. *s*, CH(*α*)(Ala^t)); 3.34 – 3.31 (*m*, CH(*α*)(Ile)); 1.98 – 1.89 (*m*, CH(*β*)(Ile)); 1.42 – 1.13 (*m*, CH$_2$(Ile), Me(Ala^t)); 1.41, 1.38, 1.37, 1.36 (4*s*, 2 Me(Aib)); 0.94 – 0.75 (*m*, 2 Me(Ile)). ^{13}C-NMR: 178.4 (*s*, C(5)(thiazolimine)); 172.4 (*s*, CO(Ile)); 164.6 (*s*, C(2)(thiazolimine)); 155.5 (*s*, CO(carbamate)); 136.2 (*s*, 1 arom. C); 128.4, 128.1, 128.0 (3*d*, 5 arom. C); 82.9 (*s*, C(4)(thiazolimine)); 80.0 (*d*, CH(*α*)(Ile)); 67.0 (*t*, Ph*C*H$_2$); 50.4 (*d*, CH(*α*)(Ala^t)); 38.9 (*d*, CH(*β*)(Ile)); 27.0, 26.5 (2*q*, 2 Me(Aib)); 25.4 (*t*, CH$_2$ (Ile)); 19.6 (*q*, Me(Ala^t)); 15.5, 11.4 (2*q*, 2 Me(Ile)). ESI-MS: 420 ([*M* + Na]$^+$), 307 ([Z-Ala-[1,3-thiazol-5(4*H*)-one]Aib]$^+$).

10. *Reactions of Some 1,3-Thiazol-5(4*H*)-imines with H$_2$S.* 10.1. *Benzyl {1-[(2*R*/2*S*)-1-Methyl-(2*S*,3*S*)-1-(2-methyl-1-{1-methyl-1-[methyl(phenyl)carbamoyl]ethylcarbamoyl}butylthiocarbamoyl)ethylthiocarbamoyl]-ethyl}carbamate* (Z-Ala-*Ψ*(CS)-Aib-*Ψ*(CS)-Ile-Aib-N(Me)Ph; **39a**). According to the *GP G*, with **37** (18 mg, 0.03 mmol) in THF (5 ml), and DBU (0.05 ml, 0.303 mmol)[16]). Chromatography (SiO$_2$; AcOEt/hexane 1:1) yielded 16 mg (88%) of **39a**. Viscous, pale yellow oil. HPLC (*Macherey-Nagel*, *Nucleosil 100-7*; AcOEt/hexane 1:1; 2 ml/min, 254 nm) showed the presence of epimers (ratio 56:44). IR (neat): 3293*s*, 3036*m*, 2967*s*, 2934*s*, 2877*m*, 1704*s*, 1636*s*, 1594*s*, 1520*s*, 1455*s*, 1391*s*, 1362*s*, 1255*s*, 1174*m*, 1117*m*, 1091*m*, 1050*m*, 1027*m*, 911*m*, 867*w*,

[16]) When the same experiment was carried out in the absence of DBU, no reaction took place.

847*w*, 771*w*, 733*m*, 701*m*. ^{1}H-NMR[17]) ((D$_6$)DMSO): 10.33, 10.26 (2*s*, NH); 8.96, 8.84 (2*d*, J = 6.6, NH); 8.42, 8.22 (2*s*, NH); 7.76, 7.69 (2*d*, J = 4.8, NH); 7.51 – 7.27 (*m*, 10 arom. H); 5.19 – 5.14 (*m*, PhCH_2); 5.05 – 4.86 (*m*, CH(α)(Ala^t)); 4.67 – 4.61 (*m*, CH(α)(Ile)); 3.31 (*s*, MeN); 2.21 – 2.05 (*m*, CH(β)(Ile)); 1.93, 1.80 (2*s*, 2 Me(Aib^t)); 1.67 – 1.19 (*m*, CH$_2$(Ile)); 1.52 (*s*, 2 Me(Aib)); 1.42 – 1.37 (*m*, Me(Ala^t)); 1.05 – 0.88 (*m*, 2 Me(Ile)). ^{13}C-NMR: 204.7, 204.6 (2*s*, CO(Aib^t)); 202.9, 202.6 (2*s*, CO(Ala^t)); 172.9, 167.7 (2*s*, CO(Val), CO(Ile)); 156.1, 158.8 (2*s*, CO(carbamate)); 144.1, 136.2 (2*s*, 2 arom. C); 129.7, 128.6, 128.2 (3*d*, 10 arom. C); 67.2 (*t*, Ph*C*H$_2$); 65.2, 65.1 (2*s*, C(α)(Aib^t)); 63.3, 63.1 (2*d*, CH(α)(Ile), CH(α)(Ala^t)); 58.9 (*s*, C(α)(Aib)); 41.5 (*q*, MeN); 36.6, 31.5 (2*d*, CH(β)(Ile)); 26.3 (*t*, CH$_2$(Ile)); 26.0 (*q*, 2 Me(Aib)); 25.6, 25.5 (2*q*, 2 Me(Aib^t)); 21.8, 21.7 (2*q*, Me(Ala)); 15.0, 11.7 (2*q*, 2 Me(Ile)). ESI-MS: 650 ([M + Na]$^+$), 594, 521 ([M – (Me(Ph)N)]$^+$), 484, 436.[17])

10.2. *Methyl (2*S*)-2-{(2*S*,3*S*)-2-[2-(2-{[(Benzyloxy)carbonyl]amino}methanethioamido)-2-methylpropanethioamido]-3-methylpentanamido}-3-methylbutanoate* (Z-Gly-Ψ(CS)-Aib-Ψ(CS)-Ile-Val-OMe; **39b**). According to the *GP G*, with **25b** (62 mg, 0.12 mmol) in THF (6 ml), and DBU (0.18 ml, 1.20 mmol). Chromatography (SiO$_2$; AcOEt/hexane 2 : 3) yielded 40 mg (67%) of **39b**. Viscous, pale yellow oil. IR (neat): 3293*s*, 3036*m*, 2965*s*, 2877*m*, 1744*s*, 1709*s*, 1661*s*, 1521*s*, 1455*s*, 1372*s*, 1312*s*, 1215*s*, 1154*s*, 1084*m*, 1045*m*, 1027*m*, 913*m*, 867*w*, 775*m*, 735*s*, 698*s*. ^{1}H-NMR: 9.17 (br. *s*, NH); 8.32 (br. *d*, J = 7.7, NH); 7.37 – 7.31 (*m*, 5 arom. H); 6.37 (br. *d*, J = 8.4, NH); 5.72 (br. *s*, NH); 5.16 (*s*, PhCH_2); 4.91 (*t*-like, J = 7.2, CH(α)(Ile)); 4.51 (*dd*, J = 8.5, 4.9, CH(α)(Val)); 4.18 (*d*, J = 6.0, CH$_2$(Gly^t)); 3.74 (*s*, MeO); 2.21 – 2.13 (*m*, CH(β)(Val), CH(β)(Ile)); 1.86 (*s*, 2 Me(Aib^t)); 1.62 – 1.23 (*m*, CH$_2$(Ile)); 0.97 – 0.86 (*m*, 2 Me(Ile), 2 Me(Val)). ^{13}C-NMR: 205.6 (*s*, CO(Aib^t)); 197.6 (*s*, CO(Gly^t)); 172.0, 169.7 (2*s*, CO(Val), CO(Ile)); 157.1 (*s*, CO(carbamate)); 136.2 (*s*, 1 arom. C); 128.8, 128.5, 128.4 (3*d*, 5 arom. C); 67.7 (*t*, Ph*C*H$_2$); 65.5 (*s*, C(α)(Aib^t)); 64.3 (*d*, CH(α)(Ile)); 64.1, 57.8 (2*d*, CH(α)(Val), CH(α)(Ile); 54.1 (*t*, CH$_2$(Gly^t)); 52.4 (*q*, MeO); 36.5, 31.2 (2*d*, CH(β)(Ile), CH(β)(Val)); 26.45, 26.40 (2*q*, 2 Me(Aib^t)); 25.8 (*t*, CH$_2$(Ile)); 19.2, 18.1 (2*q*, 2 Me(Val)); 15.3, 11.4 (2*q*, 2 Me(Ile)). ESI-MS: 575 ([M + Na]$^+$), 541 ([M – H$_2$S + Na]$^+$), 519 ([M – H$_2$S + H]$^+$).

11. *Trials to Prepare Endothiopeptides Containing More Than One Thioamide Group*. 11.1. *(9*H*-Fluoren-9-yl)methyl {[1-Methyl-1-(2-methyl-1-{1-methyl-1-[methyl(phenyl)carbamoyl]ethylcarbamoyl}propylcarbamoyl)-ethylthiocarbamoyl]methyl}carbamate* (Fmoc-Gly-Ψ(CS)-Aib-Val-Aib-N(Me)Ph; **40**). According to the *GP D*, with **10** (75 mg, 0.20 mmol) in MeCN (10 ml), EtN(i-Pr)$_2$ (0.07 ml, 0.39 mmol), HOBt (59 mg, 0.39 mmol), and H-Val-Aib-N(Me)Ph ([7]; 68 mg, 0.22 mmol); reaction time: 5 d. Chromatography (SiO$_2$; AcOEt/hexane 1 : 2) yielded 20 mg (15%) of **40** and 20 mg (27%) of **10**.

Data of **40**: Thick oil, which solidified under h.v. IR (KBr): 3311*s*, 2931*s*, 1655*s*, 1593*s*, 1522*s*, 1450*s*, 1248*s*, 1091*m*, 989*w*, 919*w*, 760*m*, 741*s*, 706*m*. ^{1}H-NMR (conformers): 8.52, 8.38 (2 br. *s*, NH); 7.70 – 7.09 (*m*, 13 arom. H, NH); 6.87, 6.70 (2 br. *s*, NH); 5.94, 5.78 (2*t*, J = 5.7, NH); 5.58 (*d*, J = 7.3, NH); 4.37 – 4.33 (*m*, CH$_2$(Fmoc)); 4.26 – 4.01 (*m*, CH(α)(Val), CH$_2$(Gly)); 3.17 (*s*, MeN); 2.18 – 2.11 (*m*, CH(β)(Val)); 1.69, 1.65, 1.37, 1.36 (4*s*, 4 Me(Aib)); 0.82, 0.80 (2*d*, J = 6.9, 2 Me(Val)). ^{13}C-NMR: 198.3 (*s*, CS(Gly^t)); 173.1, 172.5, 169.6 (3*s*, 3 CO); 156.0 (*s*, CO(Fmoc)); 144.2, 143.5, 141.2 (3*s*, 5 arom. C); 129.4, 127.9, 127.7, 127.0, 124.9, 119.9 (6*d*, 13 arom. C); 67.4 (*t*, Ph*C*H$_2$); 60.8, 60.3 (2*s*, 2 C(α)(Aib)); 58.3 (*d*, CH(α)(Ile)); 53.5 (*t*, CH$_2$(Gly^t)); 46.9 (*d*, CH(Fmoc)); 41.1 (*q*, MeN); 30.8 (*d*, CH(β)(Val)); 25.9, 25.6, 24.2, 23.6 (4*q*, 4 Me(Aib)); 19.2, 17.4 (2*q*, 2 Me(Val)). ESI-MS: 694 ([M + Na]$^+$).

11.2. *Benzyl [1-(2*S*)-{4,4-Dimethyl-5-(2*S*,3*S*)-[2-methyl-1-(2-methyl-1-(2*S*)-{1-methyl-1-[methyl(phenyl)-thiocarbamoyl]ethylcarbamoyl}propylcarbamoyl)butylimino]-4,5-dihydro-1,3-thiazol-2-yl}-2-methylpropyl]carbamate* (Z-Val-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-Val-Aib-Ψ(CS)-N(Me)Ph; **43a**). According to the *GP F*, with Z-Val-Ψ(CS)-Aib-Ile-OH (**41**; 61 mg, 0.127 mmol) in MeCN (5 ml), H-Val-Aib^t-N(Me)Ph (**42a** [7]; 45 mg, 0.14 mmol), TBTU (43 mg, 0.133 mmol), HOBt (21 mg, 0.133 mmol), and EtN(i-Pr)$_2$ (0.07 ml, 0.38 mmol); reaction time: 20 h. Chromatography (SiO$_2$; AcOEt/hexane 1 : 1) gave 93 mg (45%) of **43a**. Thick oil, which solidified under h.v. IR (KBr): 3305*s*, 3060*m*, 3034*m*, 2965*s*, 2931*s*, 2875*s*, 1713*s*, 1658*s*, 1594*m*, 1493*s*, 1463*s*, 1369*s*, 1262*s*, 1231*s*, 1203*m*, 1168*m*, 1103*s*, 1073*m*, 1026*m*, 1005*m*, 928*m*, 876*w*, 840*w*, 821*w*, 774*m*, 753*m*, 737*m*, 699*s*. ^{1}H-NMR: 7.36 – 7.09 (*m*, 10 arom. H, 2 NH); 5.54 (br. *d*, J = 8.5, NH); 5.12 (*s*, PhCH_2); 4.56 (*dd*, J = 8.2, 4.1, CH(α)(Val^1)); 4.00 (*dd*, J = 8.4, 4.7, CH(α)(Val^2)); 3.62 (*s*, MeN); 3.37 (*d*, J = 4.2, CH(α)(Ile)); 2.21 – 2.13 (*m*, 2 CH(β)(Val)); 2.05 – 1.98 (*m*, CH(β)(Ile)); 1.65 – 1.17 (*m*, CH$_2$(Ile)); 1.58, 1.53, 1.51, 1.46 (4*q*, 2 Me(Aib), 2 Me(Aib^t)); 1.02 – 0.83 (*m*, 2 Me(Ile), 4 Me(Val)). ^{13}C-NMR: 208.6 (*s*, CS(Aib^t)); 177.3 (*s*, C(5)(thiazolimine)); 170.9, 168.5 (2*s*, CO(Val), CO(Ile)); 163.3 (*s*, C(2)(thiazolimine)); 156.2 (*s*, CO(carbamate)); 147.3,

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[17]) ^{1}H-NMR ((D$_6$)DMSO, 380 K) established the presence of epimers and not rotamers, as the double signals (^{1}H-NMR ((D$_6$)DMSO, 293 K)) did not merge into single signals at higher temp. (380 K).

136.3 (2*s*, 2 arom. C); 129.6, 128.6, 128.2, 128.1, 127.6, 126.4 (6*d*, 10 arom. C); 82.8 (*s*, C(4)(thiazolimine)); 80.4 (*d*, CH(*α*)(Ile)); 67.1 (*t*, PhCH$_2$); 62.7 (*s*, C(*α*)(Aib^t)); 59.4, 58.2 (2*d*, CH(*α*)(Val), CH(*α*)(Ile)); 51.2 (*q*, MeN); 39.7 (*d*, CH(*β*)(Ile)); 31.7, 31.0 (2*d*, CH(*β*)(Val), CH(*β*)(Ile)); 28.6, 28.3, 27.6, 26.8 (4*q*, 2 Me(Aib), 2 Me(Aib^t)); 25.2 (*t*, CH$_2$(Ile)); 19.3 (double intensity), 17.8, 16.7 (3*q*, 4 Me(Val)); 16.0, 11.8 (2*q*, 2 Me(Ile)). ESI-MS: 759 ([*M* + Na]$^+$), 737 ([*M* + H]$^+$).

11.3. *Benzyl (1-(2*S*)-{4,4-Dimethyl-5-(2*S*,3*S*)-[2-methyl-1-(2-methyl-1-(2*S*)-{1-methyl-1-[methyl(phenyl)-carbamoyl]ethylthiocarbamoyl}propylcarbamoyl)butylimino]-4,5-dihydrothiazol-2-yl}-2-methylpropyl)carbamate* (Z-Val-[1,3-thiazol-5(4*H*)-imine]Aib-Ile-Val-*Ψ*(CS)-Aib-N(Me)Ph; **43b**). According to the *GP F*, with **41** (75 mg, 0.156 mmol) in MeCN (5 ml), H-Val^t-Aib-N(Me)Ph (**42b**, 55 mg, 0.172 mmol [7]), TBTU (53 mg, 0.164 mmol), HOBt (26 mg, 0.164 mmol), and EtN(i-Pr)$_2$ (0.09 ml, 0.47 mmol); reaction time: 20 h. Chromatography (SiO$_2$; AcOEt/hexane 1:1) gave 51 mg (46%) of **43b**. Thick oil, which solidified under h.v. A crystal suitable for an X-ray crystal-structure determination was obtained from hexane/CH$_2$Cl$_2$. M.p. 190–191°. IR (KBr): 3259*s*, 3051*m*, 2965*s*, 2931*s*, 2874*m*, 1707*s*, 1656*s*, 1594*m*, 1497*s*, 1454*s*, 1424*s*, 1387*s*, 1358*s*, 1308*m*, 1262*m*, 1230*s*, 1200*m*, 1176*m*, 1112*m*, 1091*m*, 1070*m*, 1026*m*, 927*m*, 867*w*, 775*m*, 738*m*, 704*s*. ^{1}H-NMR: 8.20 (br. *s*, NH); 7.59 (*d*, *J* = 9.0, NH); 7.34–7.12 (*m*, 10 arom. H); 5.37 (br. *d*, *J* = 8.7, NH); 5.10 (*s*, PhC*H*$_2$); 4.52–4.50 (*m*, CH(*α*)(Val^t)); 4.30–4.24 (*t*-like, *J* = 8.2, CH(*α*)(Ile)); 3.24 (*d*, *J* = 6.1, CH(*α*)(Ile)); 3.16 (*s*, MeN); 2.17–2.05 (*m*, 2 CH(*β*)(Val)); 2.03–1.94 (*m*, CH(*β*)(Ile)); 1.69, 1.56, 1.54, 1.47 (4*q*, 4 Me(Aib)); 1.42–1.17 (*m*, CH$_2$(Ile)); 1.02–0.85 (*m*, 2 Me(Ile), 4 Me(Val)). ^{13}C-NMR: 200.8 (*s*, CS(Val^t)); 177.2 (*s*, C(5)(thiazolimine)); 171.1, 170.1 (2*s*, CO(Val), CO(Ile)); 163.5 (*s*, C(2)(thiazolimine)); 156.0 (*s*, CO(carbamate)); 143.8, 136.0 (2*s*, 2 arom. C); 129.2, 128.4, 128.1, 127.9, 127.6 (5*d*, 10 arom. C); 82.8 (*s*, C(4)(thiazolimine)); 80.7 (*d*, CH(*α*)(Ile)); 67.0 (*t*, PhCH$_2$); 64.0, 59.2 (2*d*, CH(*α*)(Val^t), CH(*α*)(Ile)); 61.6 (*s*, C(*α*)(Aib)); 40.3 (*q*, MeN); 39.8 (*d*, CH(*β*)(Ile)); 34.3, 31.6 (2*d*, CH(*β*)(Val), CH(*β*)(Ile)); 27.5, 27.0, 25.9, 24.1, (4*q*, 4 Me(Aib)); 25.1 (*t*, CH$_2$(Ile)); 19.3, 19.1, 18.5, 16.5 (4*q*, 2 Me(Val^t), 2 Me(Val)); 15.9, 11.6 (2*q*, 2 Me(Ile)). ESI-MS: 775 ([*M* + K]$^+$), 759 ([*M* + Na]$^+$), 737 ([*M* + H]$^+$), 630 ([*M* – (N(Me)Ph)]$^+$). Anal. calc. for C$_{39}$H$_{56}$N$_6$O$_4$S$_2$·0.5 H$_2$O (746.06): C 62.79, H 7.70, N 11.26, S 8.60; found: C 62.95, H 7.57, N 11.26, S 8.37.

12. *X-Ray Crystal-Structure Determination for Compounds* **18**, **23a′**, **23d**, **34a**, *and* **43b** (see *Table 2* and *Figs. 1–4*)[18]). All measurements were conducted at low temp. with graphite-monochromated MoK_α radiation (λ = 0.71069 Å). The data collection and refinement parameters are given in *Table 2*, and views of the molecules are shown in *Figs. 1–4*. Except for **23d**, the data collections included the measurement of the *Friedel* opposites of most of the unique reflections. The intensities were corrected for *Lorentz* and polarization effects, and an absorption correction based on the multiscan method [12] was applied for **23a′**, **23d**, and **43b**. Equivalent reflections, other than *Friedel* pairs, were merged (*Friedel* pairs for **23d** were merged). Each structure was solved by direct methods with SHELXS97 [13] or SIR92 [14]. The asymmetric unit of **18** contains one peptide molecule plus one molecule of hexane. Enlarged atomic displacement parameters for the hexane molecule suggest that it is slightly disordered, but attempts to develop a disordered model were unsuccessful. In the case of **34a**, there are two symmetry-independent molecules in the asymmetric unit. Their conformations are sufficiently different that the presence of additional crystallographic symmetry is precluded. For **43b**, the Ph ring of the benzoyl group is disordered about its pivotal axis. Two positions were defined for each of the five free C-atoms of the ring, with the two orientations having relative site occupation factors of 0.544:0.456. The Et group of the i-Bu substituent is also disordered over two orientations, and the best results were obtained when the site-occupation factors of the atoms of the major conformation were set to 0.7, although the geometry of the minor conformation is poorly defined.

The non-H-atoms of each structure were refined anisotropically, except in the case of **43b**, where the atoms of the disordered Ph ring and the minor conformation of the disordered Et group were refined isotropically. For **23a′** and **23d**, the amide H-atom was placed in the position indicated by a difference electron-density map, and its position was allowed to refine together with an isotropic displacement parameter. All other H-atoms in the structures were fixed in geometrically calculated positions (d(C–H) = d(N–H) = 0.95 Å), and each was assigned a fixed isotropic displacement parameter with a value equal to 1.2U_{eq} of its parent atom. Refinement of each structure was carried out on *F* by means of full-matrix least-squares procedures, which minimized the

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[18]) Crystallographic data (excluding structure factors) for structures **18**, **23a′**, **23d**, **34a**, and **43b** reported in this paper have been deposited with the *Cambridge Crystallographic Data Centre* as supplementary publications No. CCDC-172812 to CCDC-172816, respectively. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

Table 2. *Crystallographic Data of Compounds* **18**, **23a′**, **23d**, **34a**, *and* **43b**

	18	**23a′**	**23d**	**34a**	**43b**
Crystallized from	AcOEt/hexane	CH_2Cl_2/hexane	CH_2Cl_2/hexane	CH_2Cl_2/hexane	CH_2Cl_2/hexane
Empirical formula	$C_{41}H_{65}N_7O_8S \cdot C_6H_{14}$	$C_{15}H_{18}N_2O_3S$	$C_{16}H_{20}N_2O_3S$	$C_{25}H_{36}N_4O_5S$	$C_{39}H_{56}N_6O_4S_2$
Formula weight [g mol^{-1}]	902.24	306.38	320.40	504.64	737.03
Crystal color, habit	colorless, tablet	colorless, prism	colorless, prism	colorless, prism	colorless, prism
Crystal dimensions [mm]	$0.20 \times 0.42 \times 0.43$	$0.18 \times 0.20 \times 0.25$	$0.20 \times 0.25 \times 0.35$	$0.15 \times 0.15 \times 0.20$	$0.17 \times 0.20 \times 0.25$
Temp. [K]	173(1)	160(1)	160(1)	160(1)	160(1)
Crystal system	monoclinic	orthorhombic	monoclinic	monoclinic	orthorhombic
Space group	$P2_1$	$P2_12_12_1$	$P2_1/n$	$P2_1$	$P2_12_12_1$
Z	2	4	4	4[a])	4
Reflections for cell determination	25	37841	34012	6408	95956
2θ Range for cell determination [°]	33–38	2–60	2–60	2–55	2–60
Unit-cell parameters a [Å]	8.933(5)	8.4721(1)	6.2160(1)	7.8535(1)	11.7176(1)
b [Å]	28.659(4)	8.7770(1)	16.0454(2)	26.8747(3)	15.0103(1)
c [Å]	10.089(5)	20.7492(2)	16.5924(2)	13.6234(2)	23.9457(2)
β [°]	91.56(4)	90	90.4259(4)	104.5781(5)	90
V [Å^3]	2582(2)	1542.90(3)	1654.85(4)	2782.79(6)	4211.68(6)
D_x [g cm^{-3}]	1.160	1.319	1.286	1.204	1.162
μ(MoK_α) [mm^{-1}]	0.118	0.221	0.209	0.156	0.170
Transmission factors (min; max)	–	0.874; 0.963	0.804; 0.963	–	0.856; 0.984
Diffractometer	*Rigaku AFC5R*	*Nonius KappaCCD*	*Nonius KappaCCD*	*Nonius KappaCCD*	*Nonius KappaCCD*
Scan type	ω	ω	ϕ and ω	ϕ and ω	ϕ and ω
$2\theta_{(max)}$ [°]	55	60	60	55	60
Total reflections measured	11380	47336	42228	52985	105536
Symmetry independent reflections	10479	4498	4838	12595	12337
Reflections used [$I > 2\sigma(I)$]	8628	3983	4042	8368	7100
Parameters refined	567	196	204	632	465
Final R	0.0562	0.0326	0.0394	0.0410	0.0381
wR	0.0516	0.0327	0.0485	0.0374	0.0418
Weights: p in $w = [\sigma^2(F_o) + (pF_o)^2]^{-1}$	0.005	0.007	0.010	0.010	0.002
Goodness-of-fit	2.241	1.973	2.548	1.254	0.968
Secondary extinction coefficient	–	$1.2(2) \times 10^{-6}$	$1.3(5) \times 10^{-6}$	$1.6(1) \times 10^{-6}$	$6.2(6) \times 10^{-7}$
Final Δ_{max}/σ	0.0002	0.002	0.0005	0.0007	0.0002
$\Delta\rho$(max; min) [e Å^{-3}]	0.45; −0.38	0.20; −0.18	0.26; −0.23	0.40; −0.34	0.25; −0.26

[a]) 2 Formula units per asymmetric unit.

function $\Sigma w(|F_o| - |F_c|)^2$. A correction for secondary extinction was applied, except for **18**. Neutral-atom-scattering factors for non-H-atoms were taken from [15a], and the scattering factors for H-atoms were taken from [16]. Anomalous dispersion effects were included in F_c [17]; the values for f' and f'' were those [15b], and the values of the mass-attenuation coefficients those of [15c]. All calculations were performed with the teXsan crystallographic software package [18].

Compounds **18**, **23a′**, **34a**, and **43b** are enantiomerically pure and the absolute configuration of each compound has been determined independently by the diffraction experiment and found to agree with expectations based on the starting materials and synthetic route. The absolute structure parameter [19] refined to 0.08(6), −0.02(3), 0.01(4), and 0.01(6), respectively.

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