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How we drifted into peptide chemistry and where we have arrived at

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Abstract—The history of peptide chemistry in our group is described. It all started with the cyclic undecapeptide cyclosporin, the immunosuppressive compound, which is commercialised as Sandimmune®/Neoral® by Sandoz/Novartis, and which has revolutionized transplant medicine. The discovery that cyclosporin can be deprotonated to a hexalithio derivative, and thus *C*-alkylated on a sarcosine moiety, led us into a research project on *peptide modifications*. We defined structural prerequisites for the use of peptide enolates and for electrolytic decarboxylation of peptides. Parallel to these activities, the group was engaged in developing synthetic methodologies aimed at stereoselective preparations of α-, β-, and γ-amino acid derivatives (cf. diastereoselective alkylations, self regeneration of stereogenic centers, axially chiral enolates). A third avenue into peptide chemistry originated from our investigations on the biopolymer PHB (poly-3-hydroxybutanoic acid); the question arose 'what happens upon replacement of chain-bound O by NH in the polyester?' A brief summary is given of the results obtained in our ensuing discovery tour of β-peptides built of homologated proteinogenic amino acids. They form secondary structures with short chain lengths and they have unexpected physiological properties, rendering them candidates for peptidic drugs. The synthesis of β^3-peptides is straightforward, and in the meantime most of the Fmoc-protected building blocks are commercial. The β^2-homoamino acids are less readily available. Their preparation and the assembly of a β^2-eicosapeptide with the twenty proteinogenic side chains are discussed herein. The reasons for the chosen sequence and the strategy of what turned out to be a 159-step synthesis are described. Full experimental details are given for the preparation of the dimeric Fmoc-β^2hXaa(PG)-β^2hXaa(PG)-OH building blocks used, for their solid-phase coupling to two β^2-decapeptide segments, for the thioligation, and for the purification, isolation and spectroscopic characterization of the resulting 20mer. An outlook to future projects in the exciting field of β- and γ-peptide chemistry and biology is given.
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1. Introduction

At the beginning of the senior author's (D. S.) journey through organic chemistry[1] he would never have expected to become a peptide chemist towards the end of his career. The lectures of his mentor in Karlsruhe, Rudolf Criegee, did not cover this subject at all. If asked, he would probably have answered, like most organic chemists at the time, that peptide chemistry is a highly specialized field, and that it is chemically boring to do nothing but create amide bounds. Thus, D. S. became a physical organic chemist studying the mechanism of peroxide decomposition and of cyclobutene ring-opening reactions. In the postdoctoral work with E. J. Corey in Cambridge and in the first steps into independent research back in Karlsruhe and later in Giessen with a growing group he was engaged in sulfur-, lithium-, nitroso-, and nitro-organic chemistry as a synthetic methodologist (umpolung of reactivity, pool of chiral building blocks). Later, in Zürich, the group moved into the areas of stereoselective transformations, self-regeneration of stereocenters, total synthesis of natural products (such as elaiophylidin and myxovirescin), structure and mechanisms of organolithium compounds, use of organotitanium reagents, TADDOL as a chiral auxiliary system of broad applicability, all the way to novel crosslinkers for polymerization and catalysts immobilized on controlled-pore glass.

The first encounter with peptide chemistry[2,3] occurred in one of the senior author's regular consulting visits at Sandoz in Basel. The issue was to find a more sensitive method of detection of their immunosuppressive drug cyclosporin A in plasma. With the experience of our group in organosulfur and -selenium chemistry[4] we treated cyclosporin with naphtylselenylchloride to induce a selenocyclization of the side chain in the unique C_9-amino acid of the peptide; the product has a much higher extinction coefficient than

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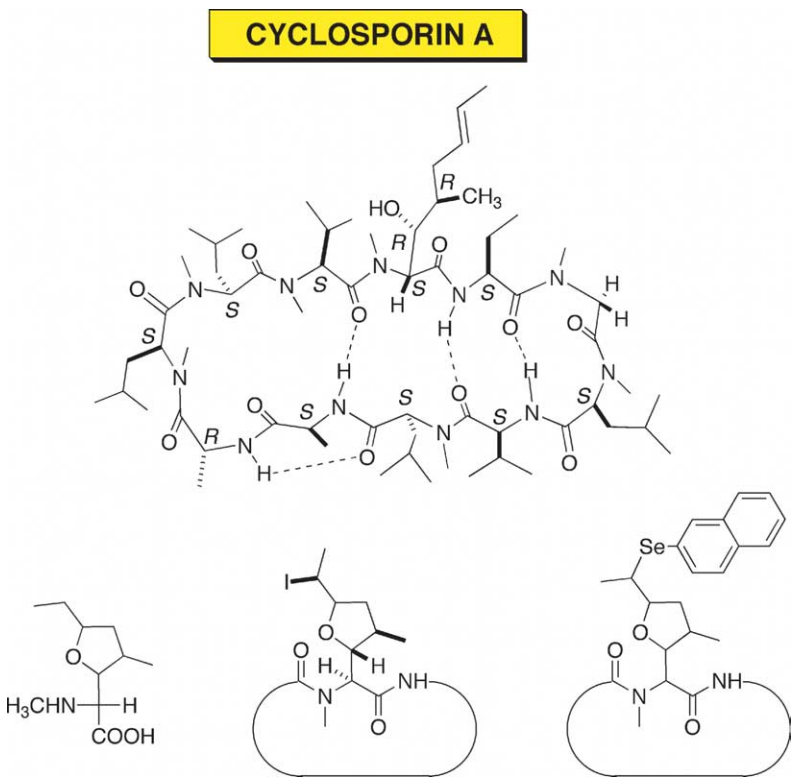

Figure 1. Formula of cyclosporin A and the THF derivatives formed with strong acid, iodine or $C_{10}H_7SeCl$.

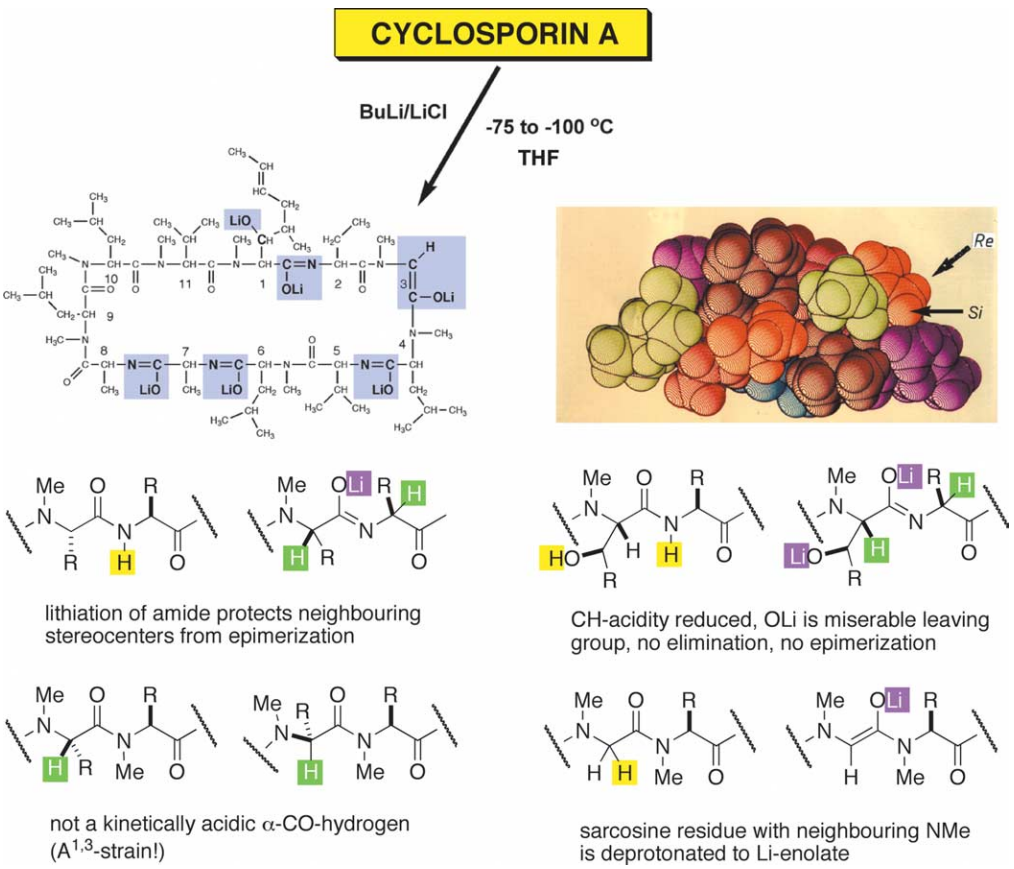

Figure 2. Hexalithiated cyclosporin A with a sarcosine enolate moiety that reacts selectively with electrophiles. Different types of amino-acid building blocks in cyclosporine and rationalization for lack of epimerization and elimination. The sarcosine CH_2-protons are the least acidic ones!

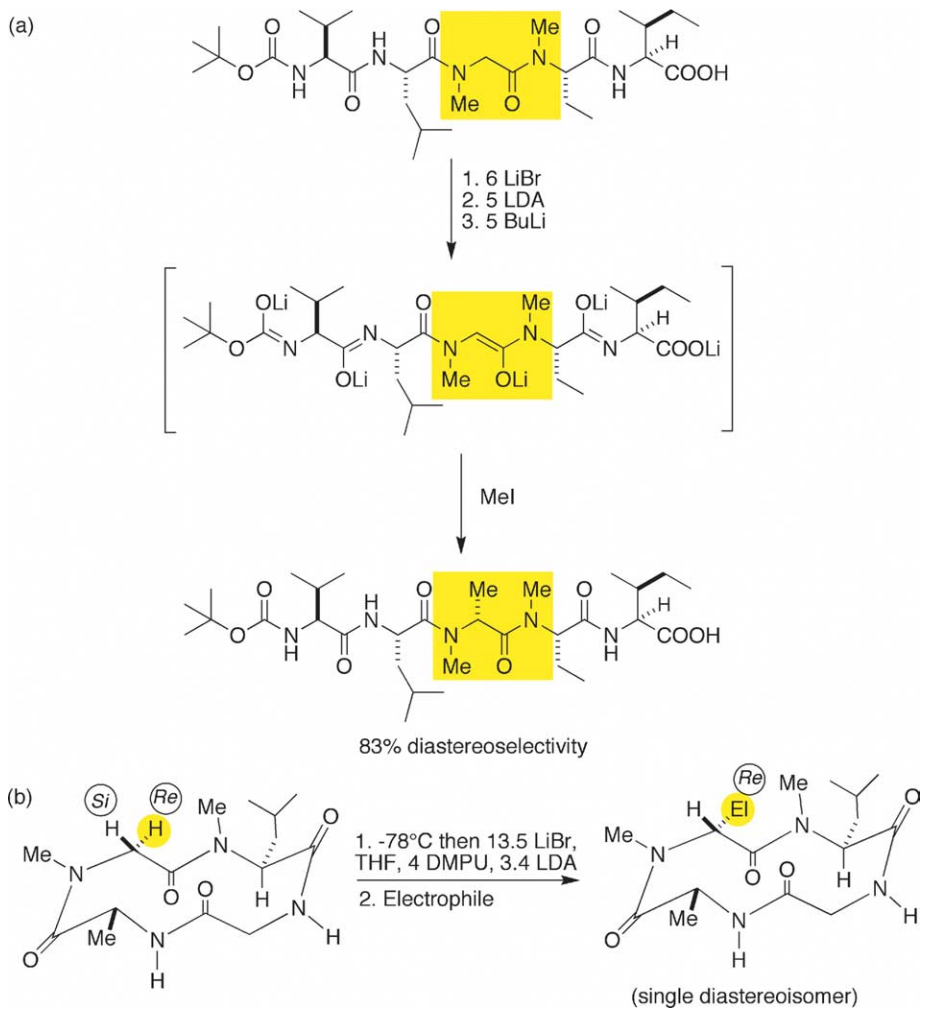

Figure 3. Li-Enolates of peptides and solubilization of peptides in THF; alkylation of open-chain (a) and of cyclic (b) peptides.

cyclosporin itself, which allowed for HPLC analysis with a detection limit of 5 ng (Fig. 1).[5]

The cyclic undecapeptide cyclosporin A containing one (*R*)-amino-acid and seven *N*-methyl-amino-acids has actually been seminal to our group's entry into the field of peptide chemistry. Returning from another visit to Sandoz in 1983, where there was a brain-storming session about possible chemical transformations of cyclosporin, D. S. carried a bottle of the peptide for an experiment he had proposed, causing shaking of heads among experts: why not generate a Li-enolate at the sarcosine residue and introduce side-chains by reactions with electrophiles? Indeed, treatment of cyclosporine with as strong bases/nucleophiles as butyl-lithium (in excess of six equivalents) and addition of typical electrophiles led to highly selective replacement of either the *Re*- or the *Si*-hydrogen in the sarcosine moiety, depending on the particular base and conditions employed;[6–10] an analysis of how this was possible is given in Figure 2.

Thus, we have excised a single proton from a peptide of molecular mass 1200 and replaced it by a side-chain substituent. The derivatives, in which the diastereotopic *Re*-hydrogen had been replaced are immunosuppressive like cyclosporin and have non-altered backbone structures. Those with H^{Si}-replacement have a different structure and exhibit different physiological activities.

The work on cyclosporin alkylations has triggered a series of investigations about peptide enolates,[6,11,12] about solubilization of peptides in THF by addition of Li salts[10,13,14] (Fig. 3), about direct thionations (C═O → C═S) of cyclosporin with Lawesson's reagent,[15] and about cyclosporin as a Li- and Ca-specific ionophor.[16]

We started a program entitled 'chemical modifications of peptides' which led to a number of dissertations in the group. One line of work was dedicated to the use of peptides containing amino-malonic-acid derivatives, which require only weak bases for alkylations[17] (Fig. 4). In a quite different investigation we used electrochemical oxidative decarboxylations of peptides containing up to ten amino-acid residues, a process leading to modifications of the *C*-termini[18] (Fig. 5). Yet another project was the in situ generation of ketenes for certain peptide couplings which enabled us to incorporate a single β-homoamino-acid unit into a larger peptide: activation of the *C*-terminal CO_2H-group, reaction with diazomethane, and decomposition of the resulting diazoketone in the

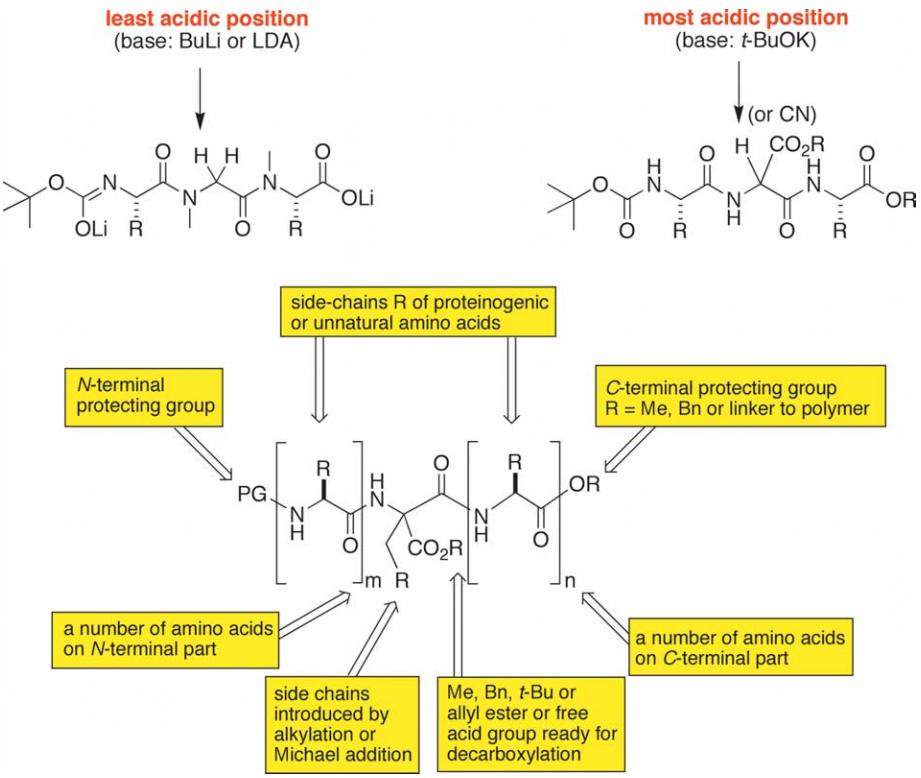

Figure 4. Peptide alkylation by going from the least to the most acidic CH group and application for peptide modification. The process is highly stereoselective in some cases and is amenable to combinatorial applications.

presence of a second peptide with unprotected *N*-terminus provides a homologative fragment coupling (Arndt–Eistert sequence of reactions, see Figure 6).[19] The intermediate activate β-homoamino-acid derivative can also be trapped with carbohydrates or nucleosides to give chimeric products.[20,21]

β-Homoamino acids had been part of our projects on synthetic methods for a long time. Following the work on dilithiated β-hydroxyesters, for instance malates,[22,23] we had generated aspartate-enolates[24,25] as early as 1981. A general method for the diastereoselective preparation of enantiopure $\beta^{2,3}$-homoamino acids involves formation of the Li_2-derivative and alkylation of the corresponding β^3-homoamino acids[26,27] (for nomenclature see an extensive review article on β-peptides[28]). A route to α-branched aspartates employs the principle of self-regeneration of stereocenters (SRS),[25,29,30] and chiral enolates of the achiral 3-amino-propanoic acid can be generated from suitable hydropyrimidines.[31] Formulae of some of these nucleophilic reagents are shown in Figure 7.

We actually conceived the idea of studying β-peptides in the course of our work on the biopolymer PHB (= poly(3-

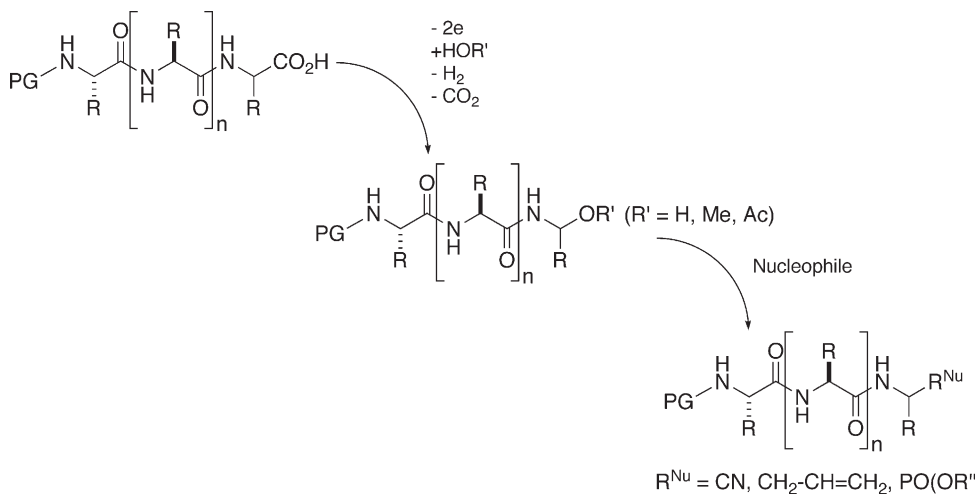

Figure 5. Hofer-Moest Electrolysis of peptides in a protic solvent (H_2O, MeOH, AcOH) and subsequent Lewis-acid-mediated nucleophilic substitution to *N*-terminally modified peptides.

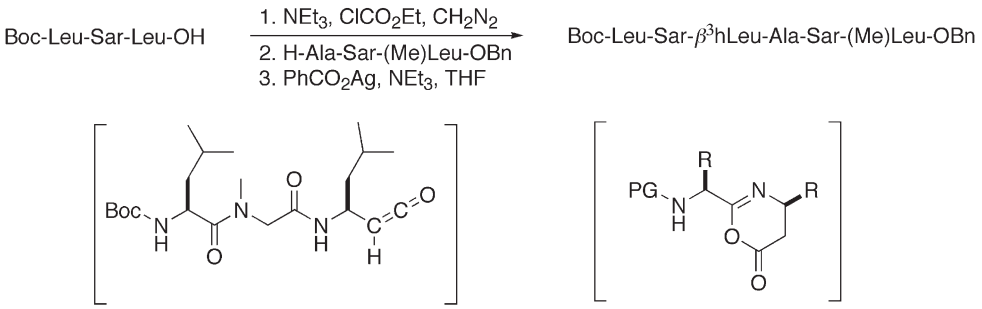

Figure 6. Homologative peptide-fragment coupling through a peptidic ketene intermediate. In the absence of an *N*-methyl-group the actual acylating reagent may be a di-dehydro-oxazinone. H-β^{3}hLeu-OH: (*S*)-3-amino-5-methyl-hexanoic acid.

hydroxybutyrate)): the backbones of cyclic oligo-((*R*)-3-hydroxybutanoates) were found to have a propensity to form (*P*)-helical conformations from which a helix could be modelled, containing chain-bound and carbonyl oxygens at such a distance and relative position that replacement of the former by an NH was expected to lead to hydrogen bonding, and thus stabilization of the helix[28,32] (Fig. 8, top). Exchange of O by NH in the backbone of a poly(3-hydroxyalkanoate) renders the same backbone structure as insertion of a CH_2-group in each and every amino-acid residue of a peptide (Fig. 8, bottom). The experimental test of these ideas led to many chemical, structural, and biological surprises, a full account of which is given in a review article[28] and in ca. 100 papers of our group since 1996 (see the attached complete list of publications of D. S.).

As expected, the additional tetrahedral carbon atom in each amino-acid residue of β-peptides leads to greater structural variety. There are not just two enantiomeric forms but also positional isomers (β^2- and β^3-homoamino acids), diastereoisomers (*l*- and *u*-β^{2,3}-homoamino acids with two side chains), and there can be heteroatoms on the backbone (cf. 2-halo- or 2-hydroxy-3-amino acids). As a consequence, five β-peptidic helices have been identified: an 8-,[28,33] 10-,[34] 10/12-,[35] 12-,[36] and 14-helix[37,38] (the numbers refer to the size of the hydrogen-bonded rings within the helix structures). Also, the β-peptidic backbone can be forced to adopt a pleated-sheet structure or to form a hairpin turn.[39] With two exceptions,[34,39] these structures are seen in solution with as few as six residues, they can be designed and found by molecular-modelling programs.[40] Thus, there are more secondary structures than in the 'α-world', but they can be predicted and constructed from a small number of β-homoamino acid residues. Some of the structures are shown in Figure 9.

Due to the different dimensions, geometries, and polarities of the β-peptidic structures the biological properties of β-peptides differ from those of α-peptides in those cases where exact fitting is mandatory: they do not bind to the active sites of peptidases and are proteolytically stable.[41] More surprisingly, they are even metabolically most stable in mammals, such as rats,[42,43] in insects, and in plant-cell cultures,[44] and very slow biodegradation by environmental microorganisms has been demonstrated in one case.[45] On the other hand, β-peptides can be used to mimic α-peptidic hairpin turns, motifs which are often decisive for so-called ligand–receptor recognitions. This was demonstrated by the design of *N*-acyl-β-tetrapeptide amides with specific nanomolar binding as agonists at one of the human receptors for the peptidic hormone somatostatin (Fig. 10).[46,47]

One of these peptides was recently shown to be orally bioavailable, to pass the blood-brain barrier and to regulate numerous genes in brain tissues.[43] Many other biological tests have been performed with β-peptides (for instance inhibition of an intestinal transport protein, antibiotic and hemolytic activities, binding to DNA and RNA; see references in a review article[28]). In recent investigations of β-oligoarginine derivatives,[48] it was shown that these polyelectrolytes enter mammalian cells in vitro and in vivo to end up in the nucleoli of cell nuclei (Fig. 11), where they remain located for longer periods of time (in contrast to corresponding α-oligoarginines, which are proteolytically degraded once having entered cells). There seem to be no toxic effects; the cell

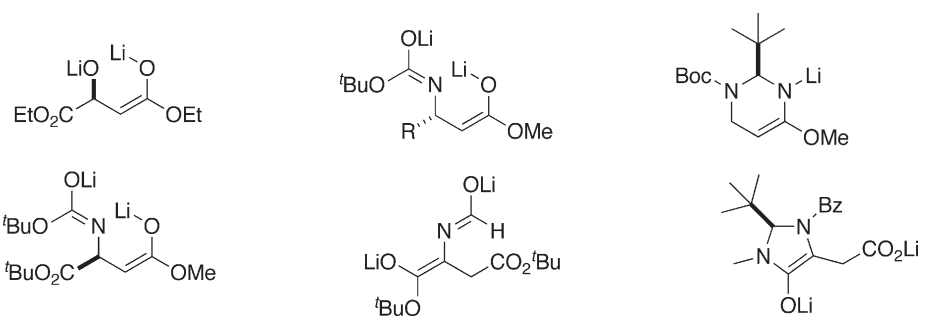

Figure 7. Chiral Li-enolates of β-heterosubstituted carboxylic acid esters. Malic acid, β-amino acids, aspartic acid.

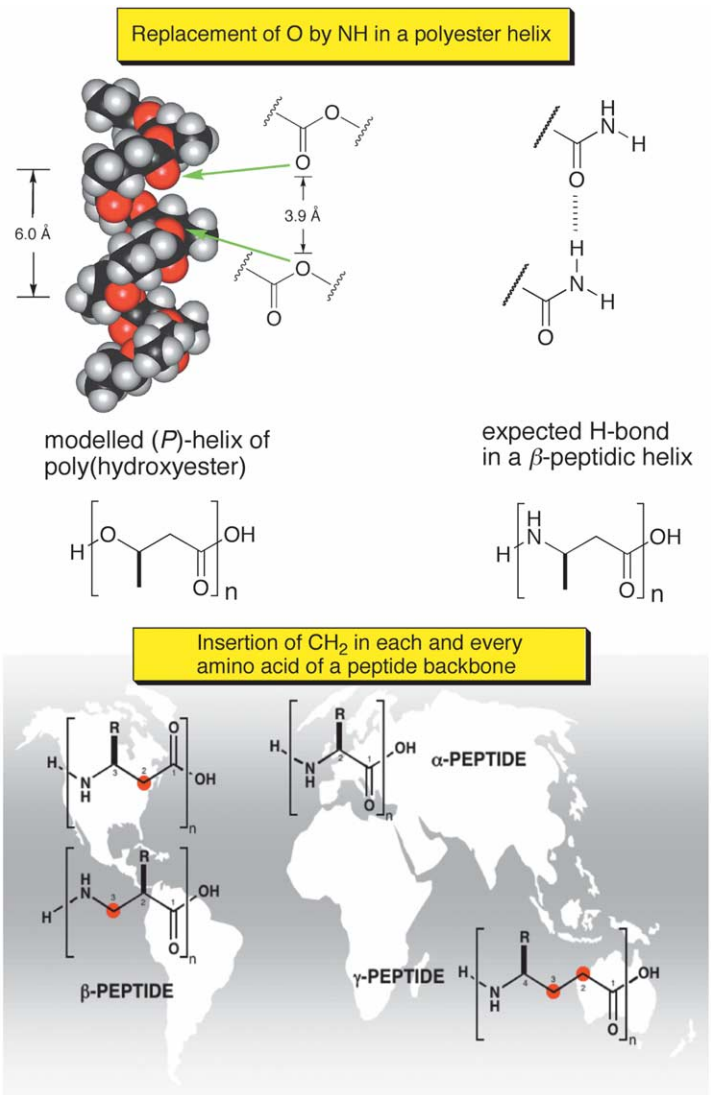

Figure 8. The question 'what happens upon replacement of O by NH in the modeled helix of PHB?' (top) is structurally equivalent to the question 'what happens upon CH_2-insertion in the amino acids of a peptide backbone?' (bottom).

culture of human keratinocytes keeps growing in the presence of the β-oligoarginines.

Thus we have gone a long way from the first experiments with cyclosporin A in 1980 to animal experiments with ^{14}C-labelled β-peptides in 2003.

So far, there was no mention made about synthesis of the β-peptides, which was actually the main occupation of everybody in the group! At the beginning, we prepared the β^3-homoamino acids from the corresponding α-amino acids by Arndt–Eistert homologation ourselves. In the meantime, 18 of the 20 β^3-homoamino acids with the side chains of the proteinogenic α-amino acid analogs are commercial (*N*-Fmoc- and acid labile side-chain protection); the exceptions are β^3hCys and β^3hHis.[49] The β^2-homoamino acids, on the other hand, have to be prepared enantioselectively. Since our research on β-peptides was focused on oligomers of homologs of the natural α-amino acids, we prepared the whole set of the 19 β^2-homoamino acids (β^2hGly = β^3hGly!). We use the chiral-auxiliary approach applying the modified Evans oxazolidinone DIOZ,[50,51] as outlined in Figure 12; for details see the original publications.[46,48,52–57]

Notably, it takes up to 13 steps to prepare some of the acids Fmoc-β^2hXaa(PG)-OH! Having the β-homoamino acids available for solid-phase synthesis by the Fmoc strategy (manual or in a synthesizer), we could make use of all the methods common in α-peptide synthesis, purification, analysis, structure determination, and modelling (Fig. 13), with certain adjustments (see discussion in a review article[28]).

For longer-chain β-peptides the thioligation method,[58] which works equally well for α-, β^2-, and β^3-peptide couplings,[59] turned out advantageous. We have recently addressed the issue, to which chain lengths a β-peptide might form the 3_{14}-helix: α-peptidic helices in proteins are typically only 15–20 residues long, one reason being a destabilization by the resulting macrodipole which increases with chain-length.[60] Thus, we have prepared a

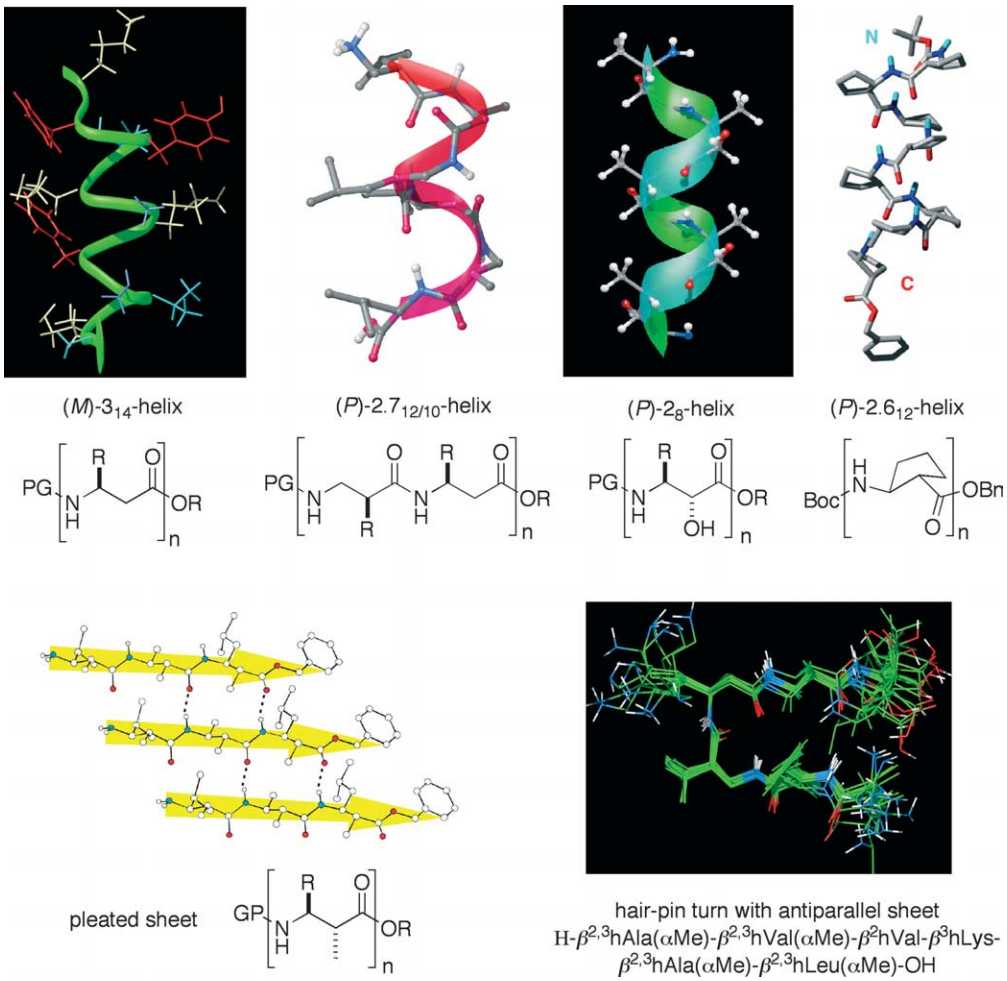

Figure 9. Helix, sheet, and turn structures of β-peptides. Except for the parallel pleated-sheet structure all secondary structures shown can be observed by NMR spectroscopy of solutions. This Figure has, in part, been reproduced by permission of the Verlag Helvetica Chimica Acta. [Rossi, F.; Lelais, G.; Seebach, D. *Helv. Chim. Acta*, **2003**, *86*, 2653. Etezady-Esfarjani, T.; Hilty, C.; Wüthrich, K.; Rueping, M.; Schreiber, J.; Seebach, D. *Helv. Chim. Acta*, **2002**, *85*, 1197.]

β^3-eicosapeptide consisting of the 20 different β^3-homoamino acids;[61] the sequence was chosen such that an amphiphatic helix would result, and stabilization by salt bridges between (*i*) and (*i*+3)-positions was part of its design, see the helical-wheel-type presentation in Figure 14. The CD spectra in methanol and water exhibit an intensive negative Cotton effect between 210 and 220 nm which we may consider typical of a 3$_{14}$-helical secondary structure, however without the usually more intensive short-wavelength maximum seen with short β^3-peptides. The NMR-solution structure determination of this 20mer is underway, and it looks like there is a helix in methanol over the full length of the 20 residues.[62]

As the last major project of our group before retirement of D. S. (with the concomitant necessary reduction of the research-group size) we joined forces and made essentially everybody (from advanced lab-course students, through master-thesis candidates, the last PhD students all the way to the post-doctoral co-workers) part of a team to synthesize the *all*-β^2-eicosapeptide **1** with the 20 proteinogenic amino-acid side chains (see below, Fig. 16).

The reason for embarking on this adventure, which eventually turned out to be a 159-step synthesis, was manifold. First of all, we wanted to demonstrate that we actually can synthesize all the necessary β^2-homoamino-acid building blocks with the chiral auxiliary DIOZ. Then, we decided to find ways of avoiding racemization/epimerization in β^2-homoamino-acid coupling, a problem we had noticed some time ago.[63] Also, the 3$_{14}$-helix of short-chain β^2-peptides has turned out to be less stable than that of isomeric β^3-peptides,[64,65] so that a comparison of larger β^2- and β^3-peptides was important, to find out, whether the former ones fold to other secondary structures. Finally, there was an atmosphere of sportive ambition in the group about getting it done!

The synthesis of the β^2-eicosapeptide **1** was designed to be as safe as possible. To make sure that there would not be insurmountable problems in the purification of the final product, we used a convergent synthesis for the β^2-peptide (Fig. 15), aware of the fact that there would be more danger of epimerization/racemization than with β^3-homoamino acids, and remembering that the isolation of the pure β ^{3}-eicosapeptide (Fig. 14), assembled in one stroke, had been quite cumbersome.[28,61]

For the choice of the sequence (there are more than 10^{18} possibilities) we applied several different criteria:

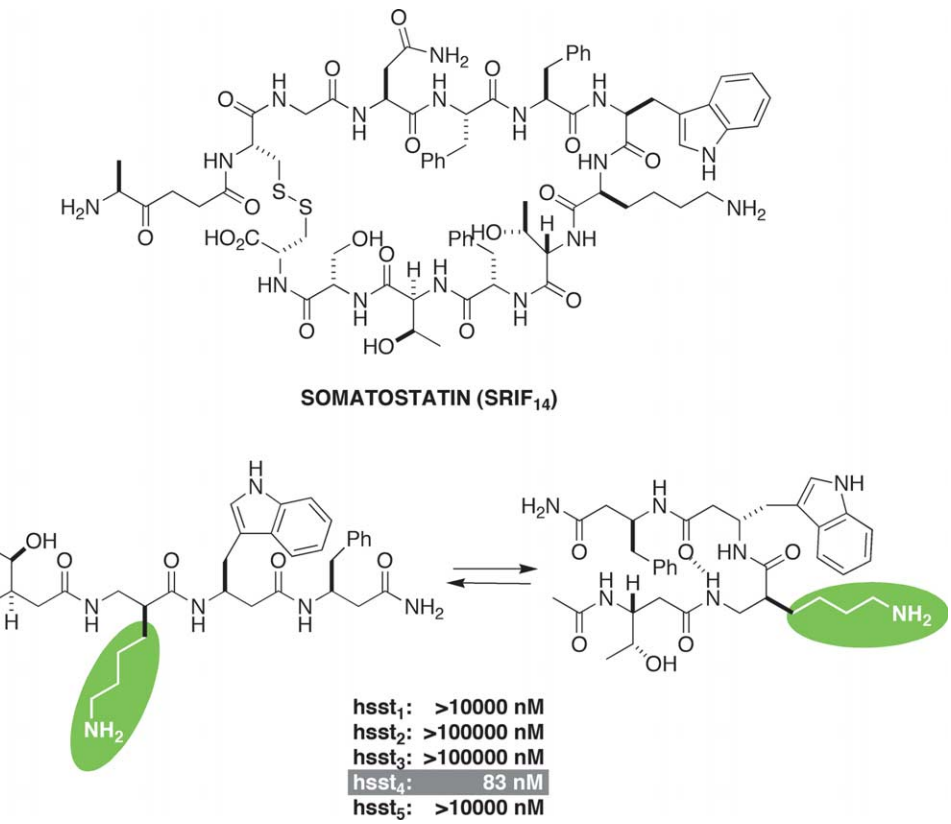

Figure 10. Formula of somatostatin and of a β-tetrapeptide derivative binding to one of the five human somatostatin receptors.

- The 3_{14}-helix of the eicosapeptide, should it be formed, was supposed to be amphipathic, with stripes of polar and non-polar side chains on its surface (Fig. 16).
- Also, the helix should experience salt-bridge stabilization, by putting the two pairs of positively and negatively charged side chains of Arg/Glu and Lys/Asp in (*i*)- and (*i*+3)-positions, that is, in juxtaposition on the helix at a distance of approximately 5 Å (cf. Fig. 9, 3_{14}-helix, top left).
- Next, we considered the well known 'capping effect',[60] according to which negative side chains near the positive and positive side chains near the negative end of a peptidic helix dipol[66] (Fig. 17) have a stabilizing effect, also in β-peptides,[67] thus we placed the β^{2}hArg in position 3 and the β^{2}hAsp in position 17 of the β^2-eicosapeptide **1**.
- The choice of β^{2}hCys in position 11 is dictated by the thioligation, and we put β^{2}hAla next to it (position 10) to reduce steric hindrance in the course of this coupling process.
- Also, the amino acids bearing the side chains of His and Met have been shown to be incompatible with the types of reactions (cf. treatment with CH_2N_2 or with I–CH_2CN) used for the solid-phase synthesis of peptide thioesters;[68] therefore the corresponding β^2-homoamino acids had to be incorporated in the decapeptide **3** with the terminal β^{2}hCys residue (Figs. 15 and 16).
- The β^{2}hPro residue was necessary to be placed in position 20 (i.e., first on the Wang resin), because this amino acid with its secondary piperidine-amino group does not fit into a 3_{14}-helix; rather it is a hairpin-turn structural element.[69]

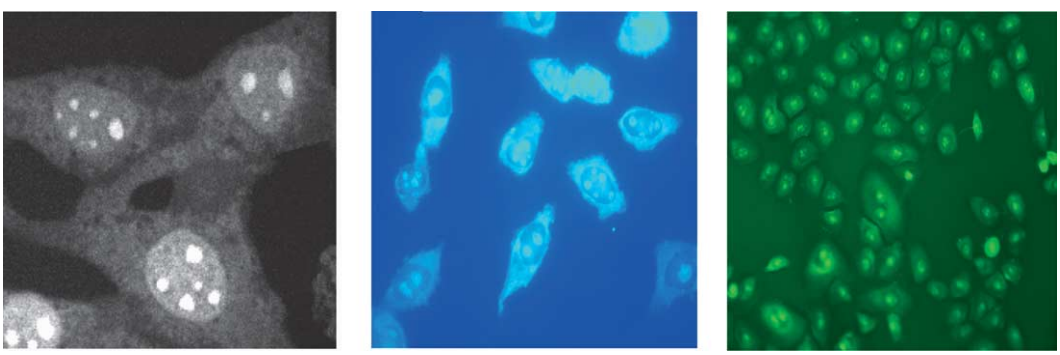

Figure 11. Fluorescence microscopy of mouse fibroblast (left), HeLa (center), and human keratinocyte cells (right) after treatment with fluoresceinylated β^3-oligoarginines consisting of 7, 8 or 10 β^{3}hArg residues. This Figure has, in part, been reproduced by permission of the Verlag Helvetica Chimica Acta. [Seebach, D.; Namoto, K.; Mahajan, Y. R.; Bindschädler, P.; Sustmann, R.; Kirsch, M.; Ryder, N. S.; Weiss, M.; Sauer, M.; Roth, C.; Werner, S.; Beer, H.-D.; Munding, C. *Chem. Biodiversity*, **2004**, *1*, 65.]

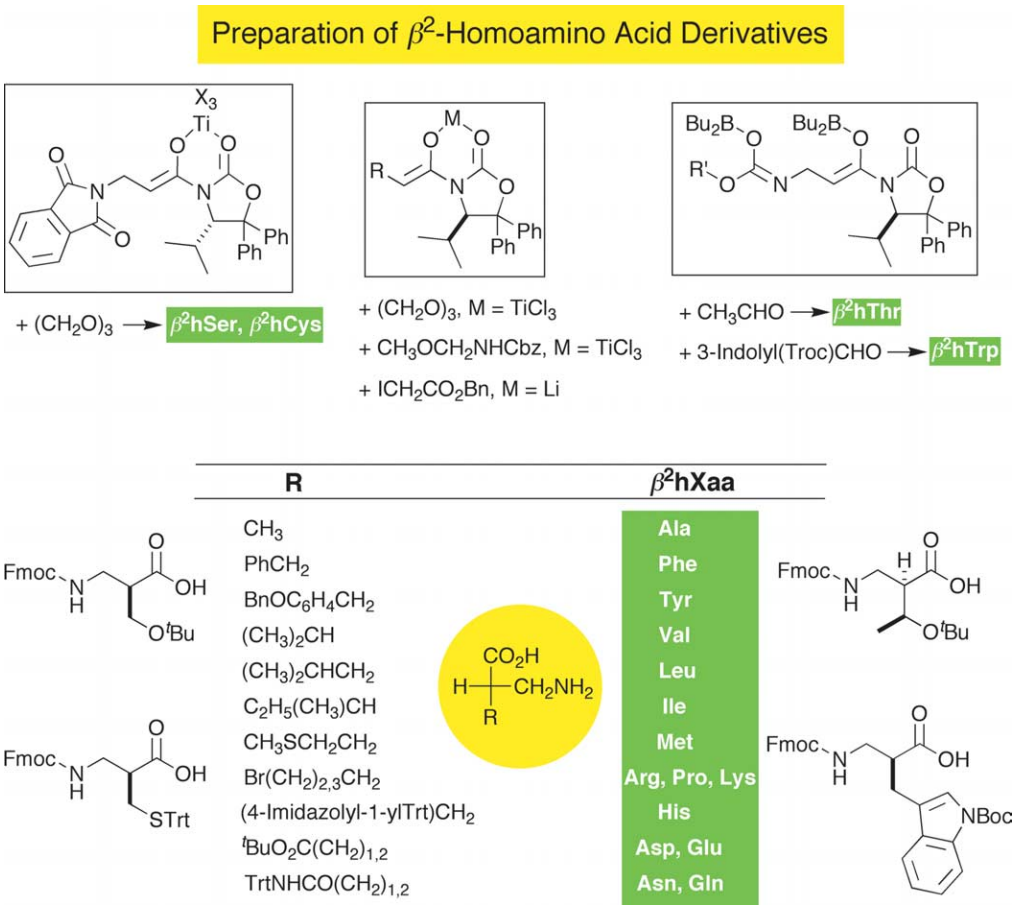

Figure 12. Preparation of 19 β[2]-homoamino acid derivatives with the proteinogenic side chains, using enolates derived from the chiral auxiliary DIOZ. For the preparation of Fmoc-(*S*)β[2]hTrp(Boc)-OH, the classical Evans auxiliary (without the geminal Ph groups) gives better results.

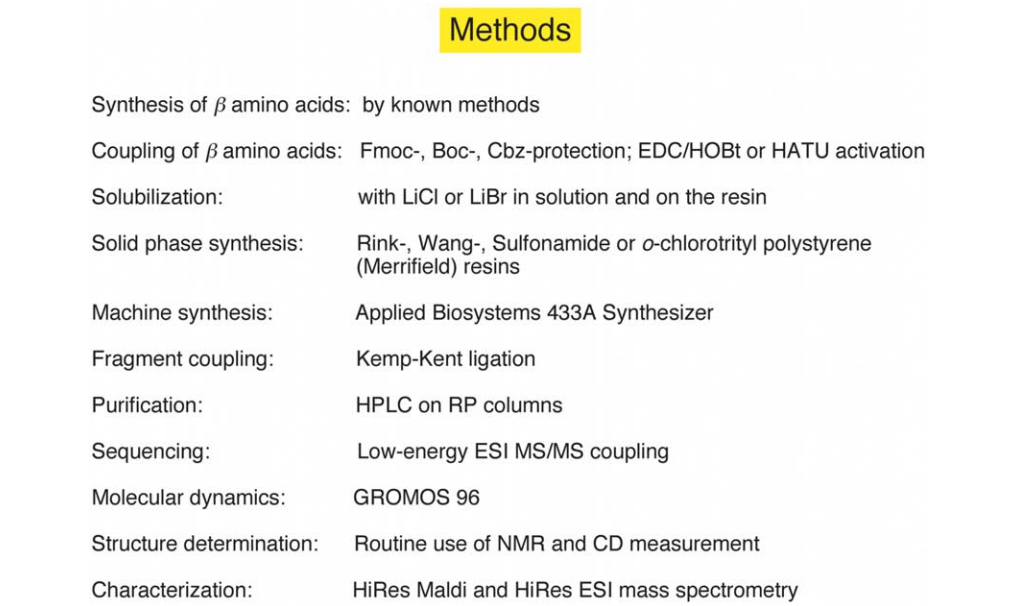

Figure 13. The synthesis and analysis of β-peptides from the Fmoc-β[2]- or -β[3]hXaa(PG)-OH is accomplished by the well established methods of α-peptide chemistry (see text books and monographs).

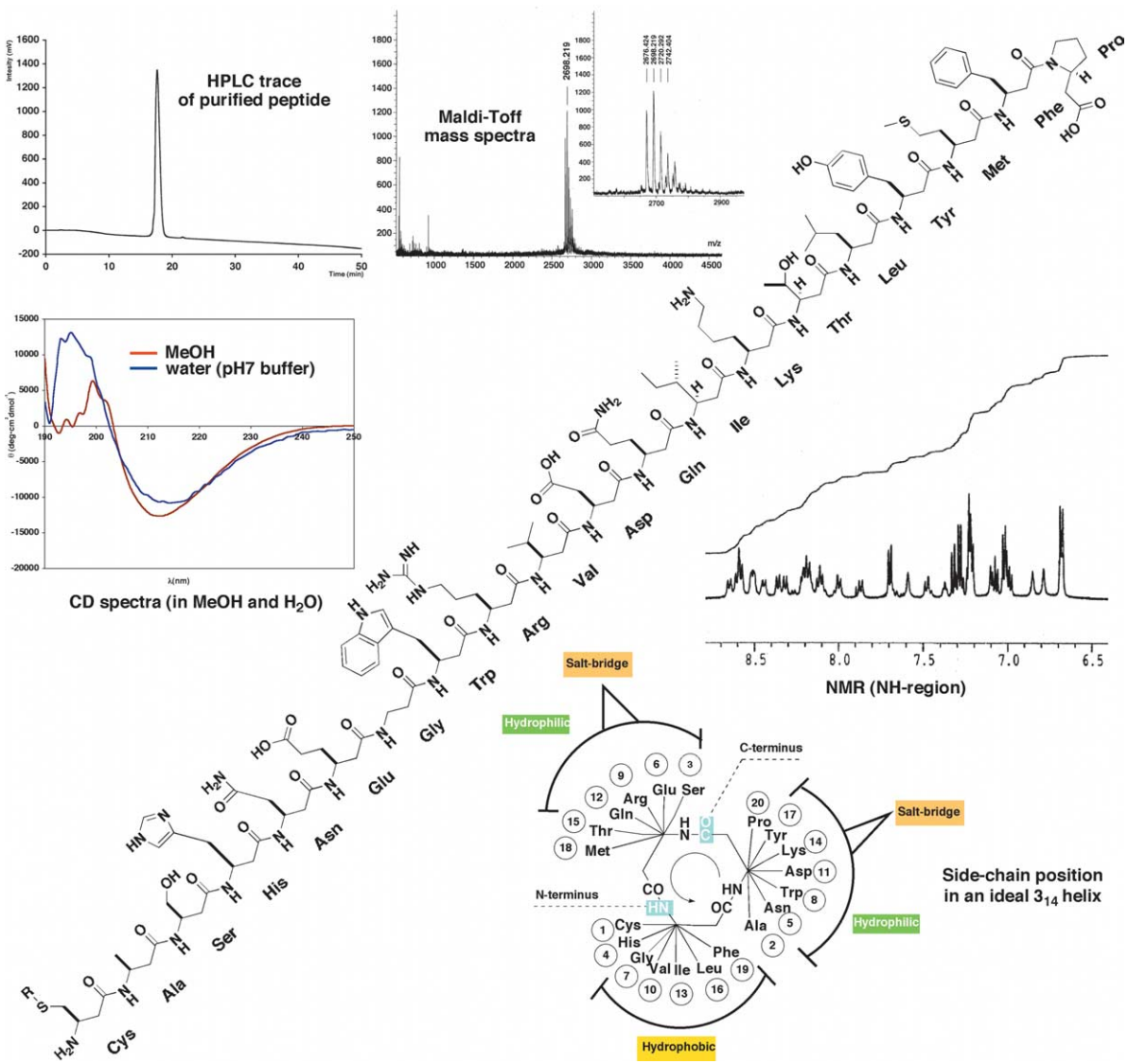

Figure 14. A β^3-eicosapeptide containing the 20 homologated proteinogenic amino acids. The compound was prepared on solid support and purified by preparative HPLC. MS, HPLC of purified sample, CD (normalized) and NMR spectra, and helical-wheel presentation of an (*M*)-3_{14}-helix, which might be formed by the β^3-eicosapeptide.

- The β^2hGly in position 1 was chosen in order to have a sterically unbiased *N*-terminus for derivatization.
- Furthermore, we employed β^2-dipeptide-fragment coupling, to make sure that the two β^2-decapeptide fragments **2** and **3** would be easy to purify in case of failure of a coupling step (a decamer is expected to be separated more easily from an octamer than from a nonamer); the β^2-dipeptide building blocks **4**–**12** could readily be isolated in diastereomerically pure form.
- The sequence of the dimer segments was, wherever possible, chosen such that the less epimerization-prone β^2-homoamino acid was at the *C*-, and the more 'dangerous' one (Phe, Asp, His, Cys, Tyr, Asn side chains) at the *N*-end; in this way, activation of the carboxylic acid group as active ester would involve less risk of epimerization.

The formulae of the suitably protected dipeptide derivatives are shown in Figure 18, and their preparations are outlined in the experimental part, where the not previously described intermediates **13**–**25**, are fully characterized, including specific references to their β^2hXaa-precursors. The dipeptide-coupling steps are preceded by numerous protection, deprotection and protective-group interchange operations. The enantiomer purities of all β^2hXaa starting materials were checked by HPLC analysis on chiral columns and/or by NMR spectroscopy of diastereomeric Pd-complexes.[70] Likewise, the diastereomer purity of the Fmoc-β^2-dipeptide acids was confirmed by NMR and RP-HPLC analysis before use in the solid-phase coupling steps, to make sure that no epimerization has occurred during dipeptide coupling or, else, that any epimer, which might have been formed, had actually been removed in the chromatographic purification procedure.

For the synthesis of β^2-decapeptide **3** bearing an *N*-terminal β^2hCys, by the Fmoc/^{t}Bu solid-phase strategy on Wang resin, the first dipeptide **4** was attached to the resin using the

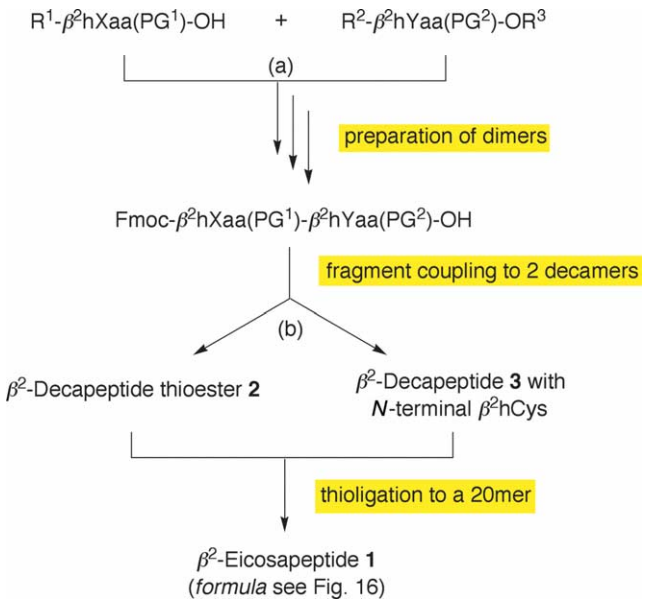

Figure 15. Strategy for the synthesis of a β^2-eicosapeptide through two β^2-decapeptides by dimer-fragment solid-phase coupling on sulfonamide (**2**) and Wang (**3**) resin, with subsequent thioligation.

MSNT/MeIm method[71] and the resin loading determined (after treatment with piperidine, 20% in DMF), by measuring the absorbance of the dibenzofulvene-piperidine adduct at 290 nm (we use the common abbreviations of peptide chemistry[72]). The unreacted OH groups were then 'capped' by acetylation (Ac_2O and DMAP). Chain elongation on solid support was performed with HATU and 3 equiv. of the Fmoc-protected β^2-dipeptides **5**–**8**, and with piperidine for Fmoc deprotection. After the last coupling, the peptide was cleaved from the resin and the side chains deprotected by treatement with CF_3COOH/EDT/TIS/H_2O. Finally purification by reverse-phase HPLC yielded the β^2-peptide **3**, which was analysed by high-resolution mass spectrometry (ESI HRMS).

The β^2-peptide **2** bearing a *C*-terminal thioester was prepared using the methodology developed by Ingenito et al.[68] and based on Kenner's acylsulfonamide safety-catch linker.[73,74] The loading of the resin was achieved with 4 equiv. of the Fmoc-protected β^2-dipeptide **9**, and DIPCDI/MeIm in DCM/DMF. The peptide was then assembled by the standard Fmoc protocol (HATU as coupling reagent and

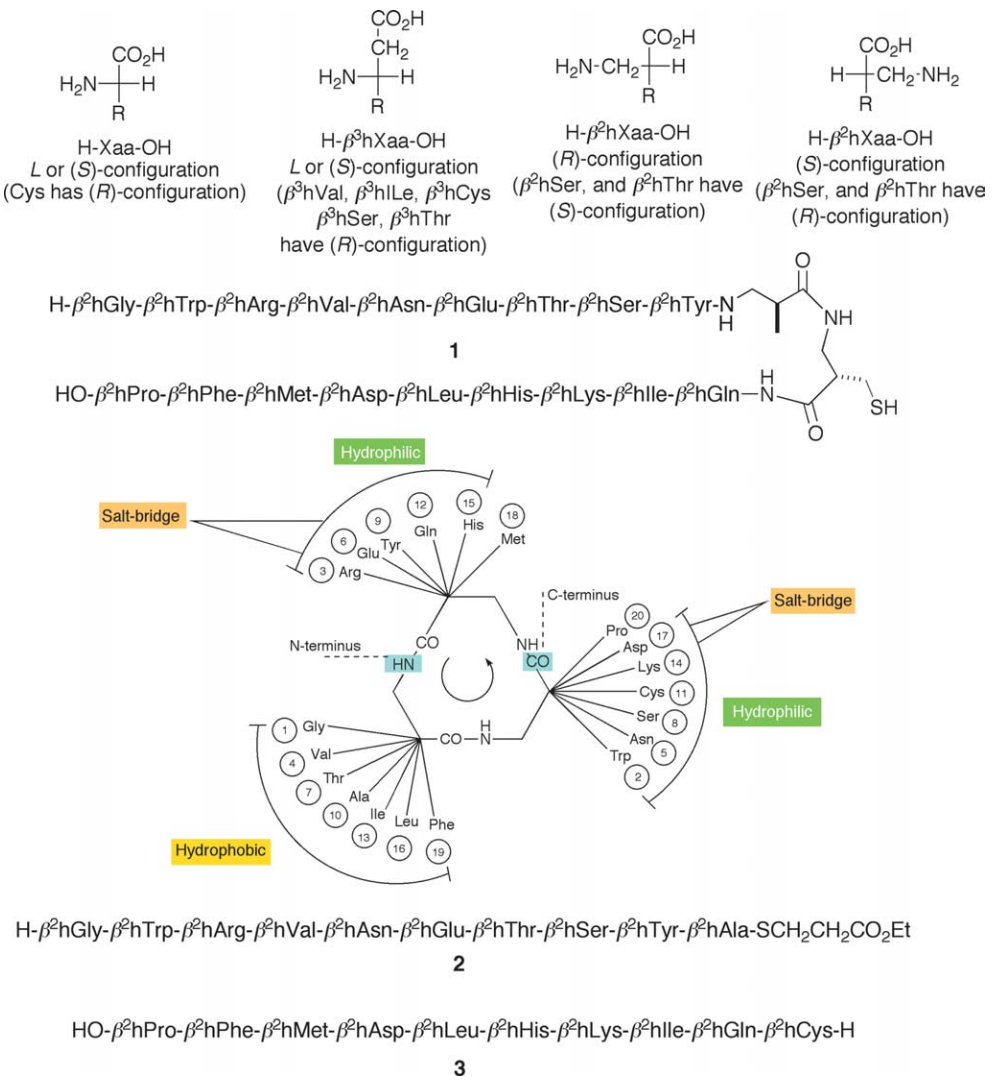

Figure 16. Configurational nomenclature of β-homoamino acids (top), and β^2-eicosapeptide **1** with central β^2hAla and β^2hCys segment, idealized helical-wheel-type presentation of its supposed (*M*)-3_{14}-helix secondary structure (middle), and the two β^2-decapeptide precursors **2** and **3** for thioligation (bottom).

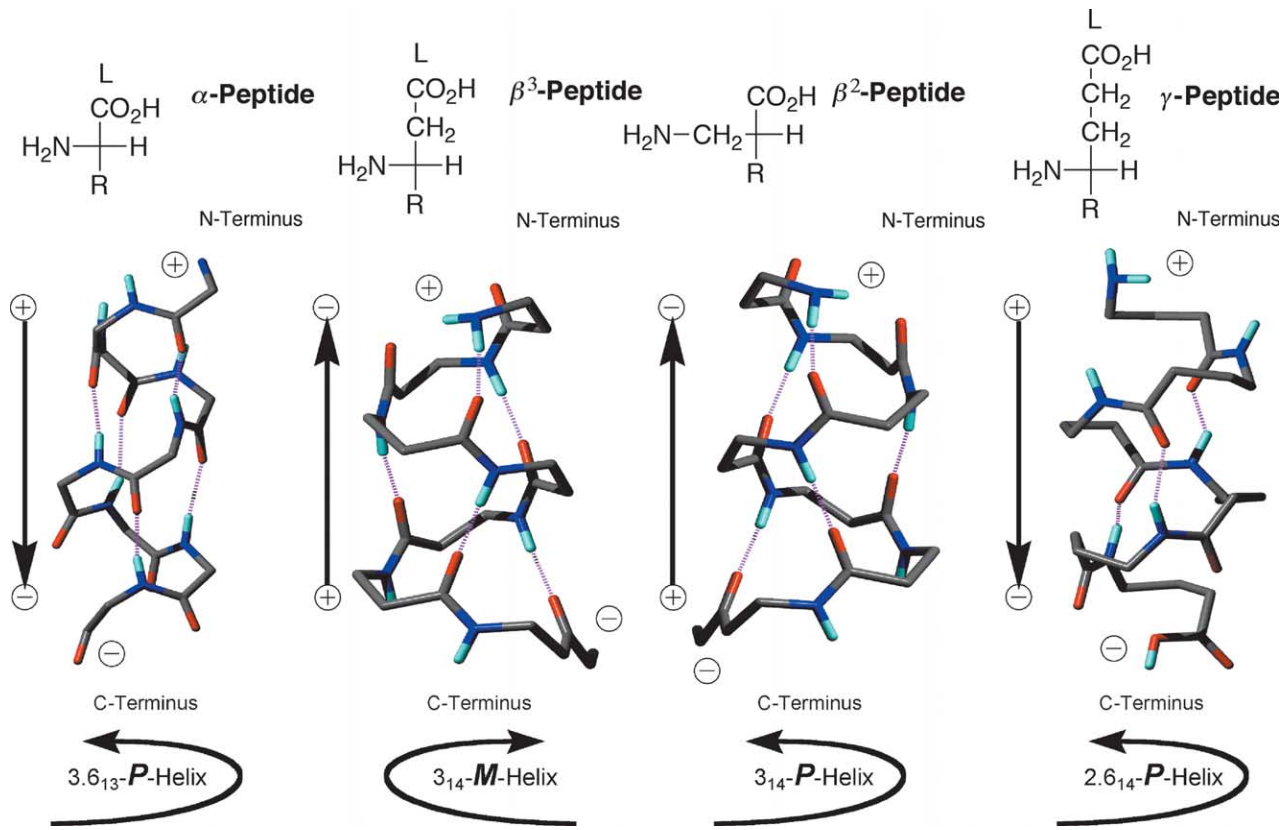

Figure 17. Helicity and direction of macrodipole reverse, as we go from α- to β^3- or β^2- to γ^4-peptides built of homochiral amino acids. The α- and γ-peptidic helices suffer from destabilizing pole-charge interaction, which is a stabilizing effect in the β-peptidic 3_{14}-helix. Furthermore, the resulting macrodipoles (increasing with chain lengths) destabilize the helices, which is counteracted by side chains with opposite charge (⊕ near ⊖ pole and vice versa). Note that helices built of β^2hXaa (shown here) and of the enantiomeric building blocks (Figure 12) have opposite helicity. This Figure has, in part, been reproduced by permission of the Verlag Helvetica Chimica Acta. [Seebach, D.; Schreiber, J. V.; Abele, S.; Daura, X.; van Gunsteren, W. F. *Helv. Chim. Acta*, **2000**, *83*, 34.]

piperidine for Fmoc deprotection). After the last coupling step, activation of the safety-catch linker, treatment with diazomethane followed by a displacement reaction involving $NaSPh/HS(CH_2)_2COOC_2H_5$ led to the still protected decapeptide. Finally, the side chain-protecting groups were removed in solution by treatment with TFA in the presence of an appropriate scavenger. In this way we obtained the β^2-peptide **2**. The displacement reaction did first not work, even in the presence of LiBr.[10,13,14,75,76] However, heating the reaction mixture at 80 °C overnight, and deprotection resulted in the formation of the desired thioester, which was purified by preparative reverse-phase HPLC and identified by high-resolution mass spectrometry. CD Spectra of the two β^2-decapeptides **2** and **3** are shown in Figure 19.

The chemical ligation-methodology, which allows the coupling of unprotected peptide fragment in aqueous solution, has made considerable advance in recent years. It offers a new route for the synthesis of larger peptides and proteins.[77,78] In the thioligation reaction the coupling process starts with a trans thioesterification reaction involving a peptide already bearing a *C*-terminal thioester and the sulfhydryl group of a second peptide bearing an *N*-terminal Cys. The thioester-linked intermediate undergoes a subsequent rapid intramolecular S → N acyl shift, forming the amide bond at the ligation site. In the case of peptides containing a β^2-homocysteine, the intramolecular S → N acyl shift in the ligation reaction proceeds through a 6-membered, rather than a 5-membered heterocycle, which is involved with Cys and β^3hCys as coupling components (Fig. 20).

We applied this method for the final step in the synthesis of the β^2-peptide **1** containing all the β^2-homoamino acids with proteinogenic side chains. The ligation was performed under standard conditions[79] (aqueous solution, pH 7.5 phosphate buffer and 4% (v/v) PhSH). After 4 h, more than 70% conversion had occurred and the reaction was essentially complete after 12 h as evident from the analytical RP-HPLC traces shown in Figure 21.

The crude product **1** was then purified by preparative reverse-phase HPLC and characterised by high-resolution mass spectrometry. The normalized CD spectrum of the β^2-eicosapeptide **1** in methanol shows the familiar negative Cotton effect between 210 and 220 nm with an intensity similar to that observed with the isomeric β^3-eicosapeptide (Fig. 14). However in water the negative Cotton effect (trough) almost vanishes, and an intensive positive Cotton effect (peak) appears at shorter wavelengths. Similar changes of β-peptidic CD patterns upon replacement of MeOH by H_2O as solvent had been observed previously,[58,80–82] and commented with awe ('miraculous');[81] they may suggest an alteration of the secondary structures, or unfolding to a 'totally disordered' backbone conformation. However, only a full NMR investigation will be able to elucidate what is going on (Fig. 22).[62,82]

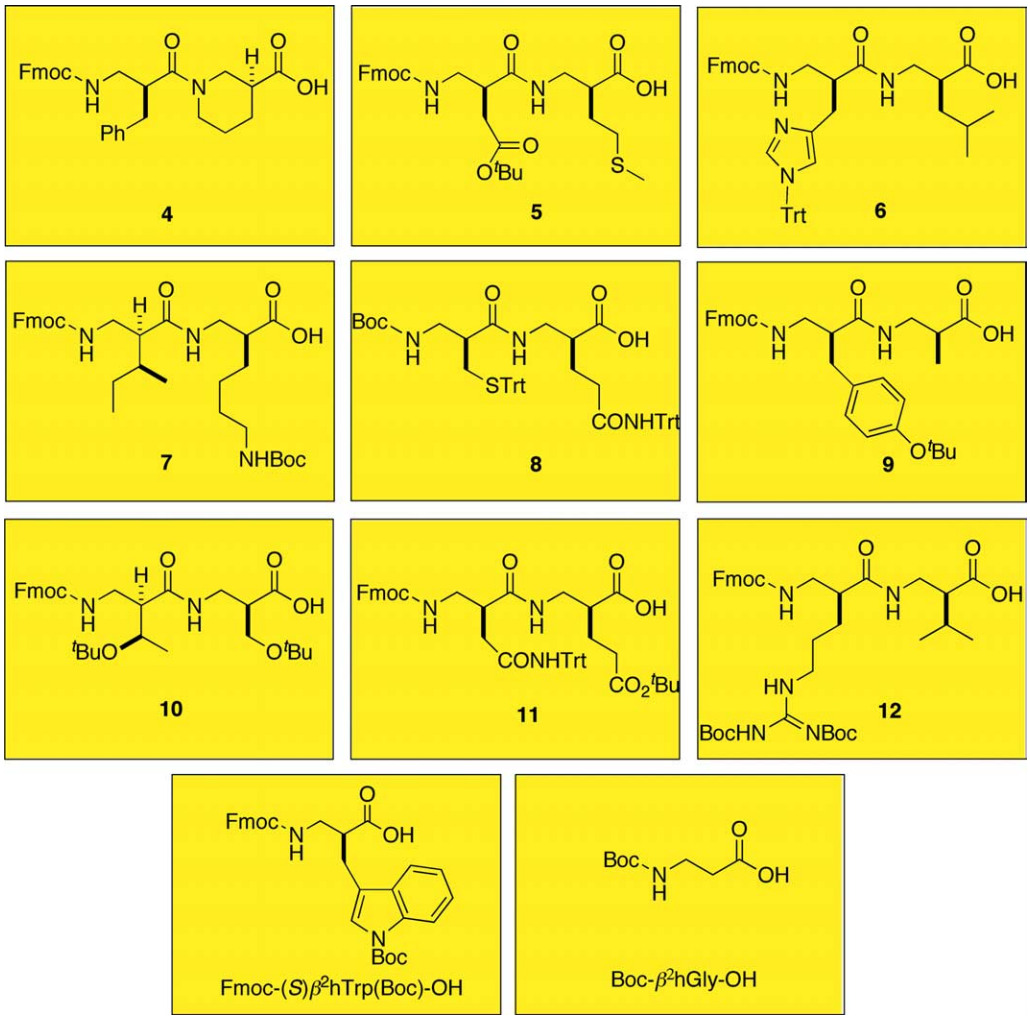

Figure 18. Nine β^2-dipeptide derivatives **4**-**12** and the Fmoc-(*S*)β^{2}hTrp(Boc) and β^{2}hGly components (*N*-terminal in **1** and **2**) for the solid-phase synthesis of the β^2-decapeptides **2** and **3** (Figure 16).

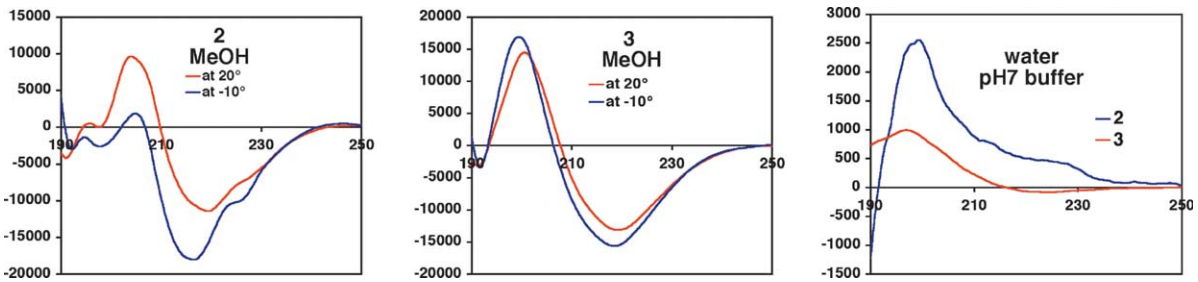

Figure 19. CD Spectra (normalized) of the two β^2-decapeptides **2** and **3** in MeOH at +20 and −10 °C, and in H_2O. The Cotton effect observed between 215 and 220 nm increases with decreasing temperature.[64,65] The pattern obtained with **3** we would consider typical of a 3_{14}-helix. The shoulder near 225 nm and the drastic reduction of intensity of the positive Cotton effect near 205 nm seen with the β^2-decapeptide **2**, however, is totally surprising and can not be interpreted at present. In aqueous pH 7 buffer the β^2-decapeptide **2** shows a positive Cotton effect at 200 nm albeit with low intensity; the β^2-decapeptide **3** does not show any significant Cotton effect. Compare the CD spectra of the β^2-eicosapeptide **1** in H_2O and MeOH in Figure 22 below.

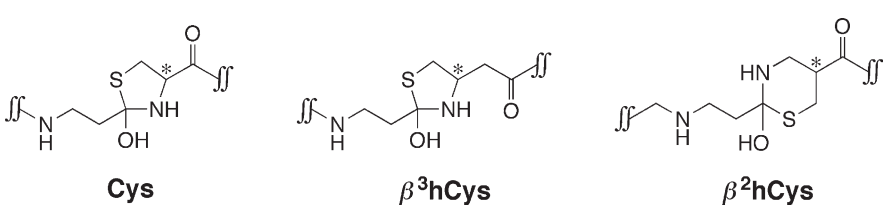

Figure 20. Formulae of the cyclic intermediates formed during the S → N acyl shift in the course of the thioligation reaction involving Cys, β^{3}hCys and β^{2}hCys.

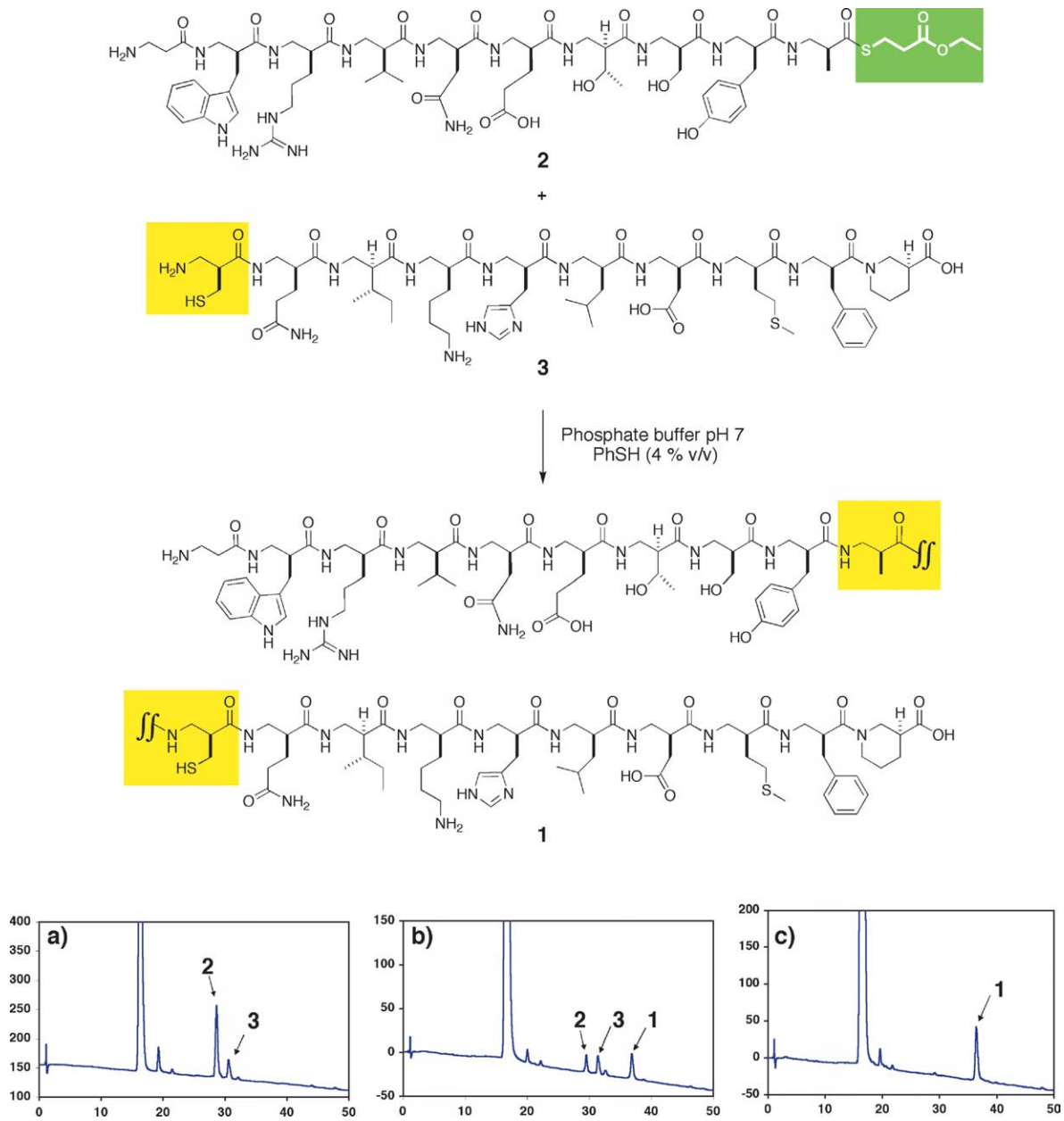

Figure 21. Analytical-HPLC traces of the ligation reaction between β^2-decapeptide **2** with a *C*-terminal thioester group and β^2-decapeptide **3** with an *N*-terminal β^2hCys residue. Samples taken from the reaction mixture at: (a) $t = 10$ min, (b) $t = 2$ h, and (c) $t = 12$ h (chromatographic conditions see Section 2).

The syntheses of the two β-eicosamers may be taken as a demonstration, that any sequence of β^2- or β^3-homoamino acid residues with the proteinogenic side chains can be assembled. This makes us confident that we will be able to construct–by design–β-peptides with tertiary and quaternary structures and, possibly, with catalytic activities. Some evidence for aggregation of long-chain β^3-peptides (consisting of homologated 'natural' α-aminoacid residues) has already emerged from concentration-dependent CD spectra.[58] Also, intramolecular helix–helix interaction has been deduced from CD spectra of a β^3-peptide with proteinogenic side chains.[83]

We should, however, not be too sure of our ability to synthesize any β-peptidic sequence: with the sheet-forming α-branched $\beta^{2,3}$-homoamino-acid residues we[39,84] and others[85] have observed difficulties in the solid-phase synthesis of corresponding β-peptides. On the other hand, we are optimistic, as synthetic organic chemists must be 'by definition', that there will be a solution to any synthetic problem, if we just try hard enough.

Besides construction of more complex architectures with function, the major goal in the field of β-peptides, and also γ-peptides,[86] is the exploitation of their biological, pharmacological, and biomedical potential.[28] Recent experiments with short-chain β-peptides (proteolytically and metabolitically stable!) have involved structure-dependent tissue-specific distributions, gene profiling in brain and lung tissues, affinity to MHC-type-I proteins,

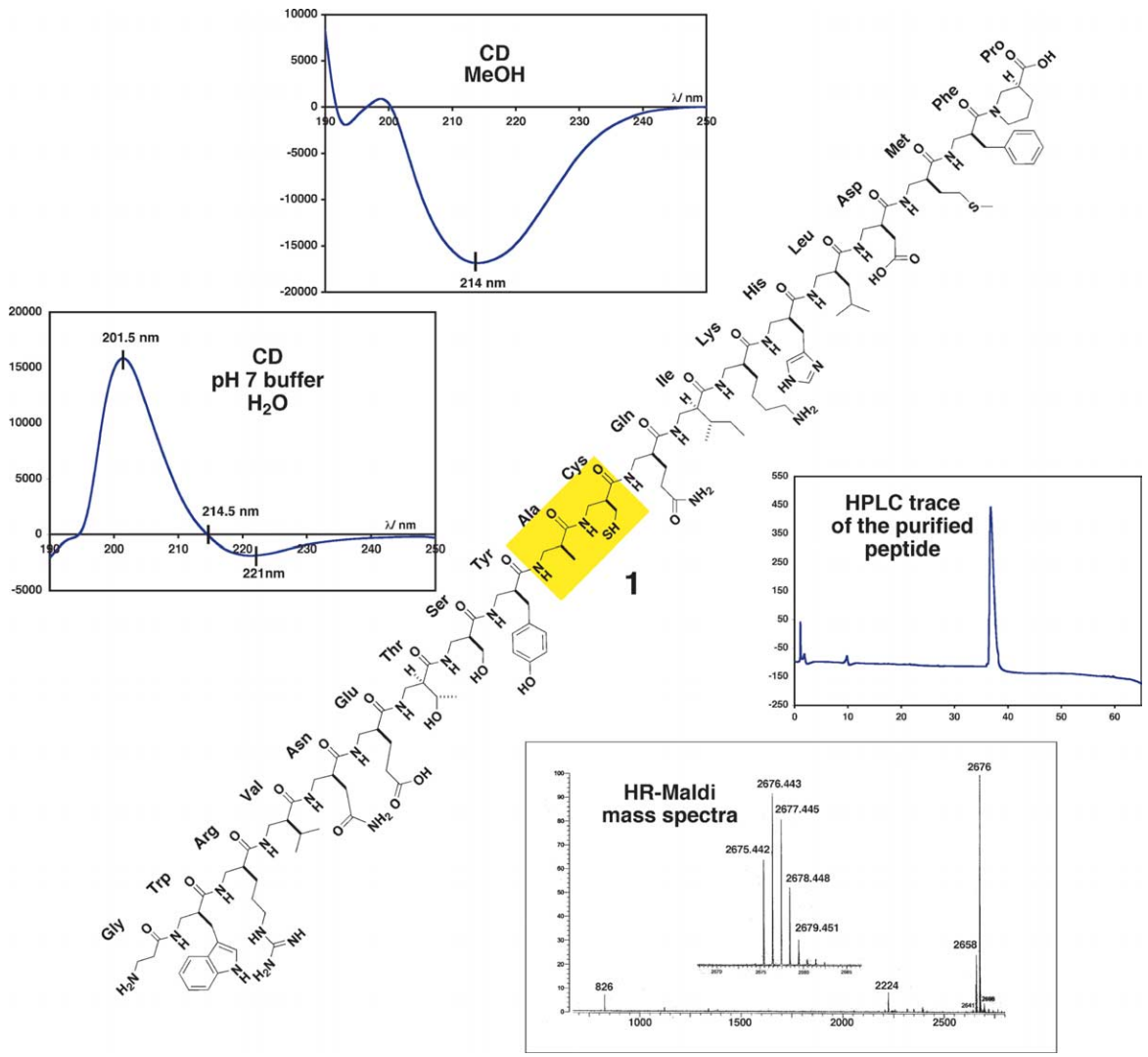

Figure 22. Formula, mass spectra, HPLC of a purified sample, CD spectrum (normalized) in MeOH and in H_2O of β^2-eicosapeptide **1**.

and human-leukocyte-antigen-mediated protection of pig cells against human natural-killer-cell cytotoxicity.[43]

2. Experimental

2.1. General

Abbreviations: The official abbreviations of Peptide Science[72] are used throughout this paper. DMAP (4-(dimethylamino)pyridine), DIPCDI (diisopropylcarbodiimide), DIPEA (diisopropylethylamine), EDC (*N*-(3-dimethylaminopropyl)-*N'*-ethyl-carbodiimide hydrochloride), EDT (ethanedithiol), FC (flash chromatography), FmocOSu (*N*-(9-Fluorenylmethoxycarbonyloxy)succinimide), HATU (*O*-(7-azabenzotriazol-1-yl)-*N*,*N*,*N'*,*N'*-tetramethyluronium hexafluorophosphate), h.v. (high vacuum, 0.01–0.1 Torr), 1-MeIm (1-methylimidazole), NMM (*N*-methylmorpholine), MSNT (1-(mesitylene-2-sulphonyl)-3-nitro-1*H*-1,2,4-triazole), TBAF (tetra-*n*-butylammonium fluoride), TFA (trifluoroacetic acid), TIS (triisopropylsilane), TNBS (2,4,6-trinitrobenzensulfonic acid). Solvents for chromatography were distilled from Sikkon (anh. $CaSO_4$; Fluka), THF was distilled from Na, CH_2Cl_2 and NEt_3 from CaH_2. LiCl was dried in h.v. at 100 °C for 1 h. All other reagents were used as received from Fluka. TLC: Merck silica gel 60 F_{254} plates; detection with UV or 'Mo-stain' solution (25 g phosphormolybdic acid, 10 g $Ce(SO_4)_2{\cdot}H_2O$, 60 mL conc. H_2SO_4, 940 mL H_2O), FC: Fluka silica gel 60 (40–63 μm); at ca. 0.2 bar. Anal HPLC: Merck HPLC system (LaChrom, pump type L-7150, UV detector L-7400, Interface D-7000, HPLC Manager D-7000). Macherey-Nagel C_8-column (Nucleosil 100-5 C_8 250×4 mm); Waters HPLC system (pump type 515, data module type 746, tunable absorbance detector type 484). Chiralcel OD-H column. Prep. HPLC: Merck HPLC system (LaChrom, pump type L-7150, UV detector L-7400, Interface D-7000, HPLC Manager D-7000) Macherey-Nagel C_8 column (Nucleosil 100-7 C_8 (250×21 mm)). Circular dichroism (CD): CD spectra were recorded on a Jasco J-710 spectropolarimeter from 190 to 250 nm with a Jasco PTC-348 WI Peltier System at 20 °C or −10 °C in 1 mm rectangular cells. The optical system was flushed with N_2 at a flow rate of ca. 10 L/min. Parameters: band width 1.0 nm, resolution 0.2–1 nm, sensitivity 100 mdeg, response 0.5 s, speed 50 nm/min, 5 accumulations. All spectra were corrected for the corresponding solvent spectrum and normalized. Peptide concentrations were typically 0.2 mM. The molar ellipticity [θ] in

deg·cm^2·mol^{-1} (λ in nm). Smoothing was done by Jasco software. Solvents: MeOH (HPLC grade), aq. Buffer pH 7.0: 0.1 M KH_2PO_4/0.1 M NaOH. NMR: Bruker AMX 500 (^{1}H 500 MHz, ^{13}C 125 MHz), AMX-400 (^{1}H 400 MHz, ^{13}C 100 MHz) and Varian Gemini (^{1}H 300 MHz, ^{13}C 75 MHz) chemical shifts δ in ppm downfield from internal $SiMe_4$ (0 ppm). Mass Spectra: IonSpec Ultima 4.7 T FT Ion Cyclotron Resonance (ICR, HR-MALDI, in a 2.5-dihydroxybenzoic acid matrix), or Finnigan MAT TSQ 700 (ESI) mass spectrometer; in *m*/*z* (% of basis peak). Melting points: Büchi-510 apparatus; uncorrected. Optical rotations: Perkin–Elmer 241 polarimeter (10 cm, 1 mL cell, room temperature). IR: Perkin–Elmer 1600 FT-IR spectrophotometer. Elemental analyses were performed by the Microanalytical Laboratory of the Laboratorium für Organische Chemie, ETH Zürich.

2.2. General procedures

2.2.1. Peptide coupling to give dimers 4–12: general procedure 1 (GP1). The appropriate *N*-deprotected amino acid (1 equiv.) was dissolved in CH_2Cl_2 (0.1 M) and cooled in an ice-bath. To the mixture was successively added NMM (3 equiv.) and the *N*-protected amino acid (1 equiv.). To this solution either HATU (1.2 equiv.) (GP1a) or EDC (1.2 equiv.) and HOBt (1.2 equiv.) (GP1b) was added and the mixture allowed to warm up to 25 °C and stirred overnight. The mixture was then diluted with CH_2Cl_2 and washed with 1 M HCl, 10% aq. K_2CO_3 and brine solutions. The organic phase was dried ($MgSO_4$) and the solvent removed under reduced pressure. The crude dipeptide was purified by FC.

2.2.2. Hydrogenolysis of Cbz and Bn-ester groups: general procedure 2 (GP2). The corresponding substrate was dissolved in either MeOH or THF (0.02 M) and ca. 10% (w/w) Pd/C (10%) was added. The apparatus was evacuated and flushed with H_2 (3×), and the solution was stirred under an atmosphere of H_2 for the indicated amount of time (monitoring by TLC). Subsequent filtration through Celite and removal of solvent under reduced pressure yielded the product, which was used in the next step without further purification.

2.2.3. Saponifications: general procedure 3 (GP3). The appropriate ester (1 equiv.) was dissolved in MeOH/H_2O 3:1 (0.1 M) at 25 °C. To the resulting solution, LiOH·H_2O (2.5 equiv.) was added and the reaction mixture was stirred 3 h. The mixture was diluted with H_2O and extracted with Et_2O. The aqueous phase was acidified with 1 N HCl to pH~1 and extracted with AcOEt (3×). The combined organic extracts were dried ($MgSO_4$) and the solvent removed under reduced pressure. The crude product was purified by FC.

2.2.4. Fmoc-protection: general procedure 4 (GP4). To a solution of the *N*-deprotected dipeptide in 0.15 M Na_2CO_3 (2 equiv.) was added FmocOSu (1.2 equiv.) in acetone (0.1 M). If necessary, the pH was adjusted to 9–10 with additional aq. Na_2CO_3 solution and the mixture stirred at 25 °C for 4 h. The acetone was carefully removed under reduced pressure at 30 °C and the resulting mixture diluted with H_2O. At this point the pH of the solution was adjusted to 9–10 using 0.6 M aq. Na_2CO_3. The aq. mixture was then extracted with Et_2O (2×). The aq. phase was separated, cooled to 0 °C and AcOEt added. With continuous stirring of the biphasic system at 0 °C, the pH of the aq. phase was adjusted to 4–5 by slow addition of 10% aq. citric acid. The org. layer was separated and the aq. layer extracted with AcOEt (2×). The combined org. layers were washed with brine, then dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by FC.

2.2.5. Preparation of trimethylsilylethyl esters: general procedure 5 (GP5). To a solution of the *C*-unprotected amino acid (1 equiv.) in CH_2Cl_2 (0.1 M) at 0 °C under Ar, was added trimethylsilylethanol (1.5 equiv.), DMAP (0.2 equiv.), and EDC (1.2 equiv.). The resulting mixture was stirred at 0 °C for 16 h then diluted with AcOEt and the org. phase washed with 10% Na_2CO_3 (2×), and brine, then dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was purified by FC.

2.2.6. Trimethylsilylethyl ester deprotection: general procedure 6 (GP6). To a solution of the corresponding Si-ester (1.0 equiv.) in THF (0.1 M) was added TBAF·3H_2O (4 equiv.) and the mixture stirred at 25 °C for 1 d. The reaction mixture was then diluted with AcOEt and the organic phase washed with sat. aq. NH_4Cl, and brine, then dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was purified by FC.

2.2.7. Reversed-phase (RP) HPLC analysis and purification. RP-HPLC analysis was performed on a Macherey-Nagel C_8 column (Nucleosil 100-5 C_8 (250×4 mm)) by using a linear gradient of A (0.1% TFA in H_2O) and B (MeCN) at a flow rate of 1.2 mL/min with UV detection at 220 nm; t_R in min. RP-HPLC purification was performed on

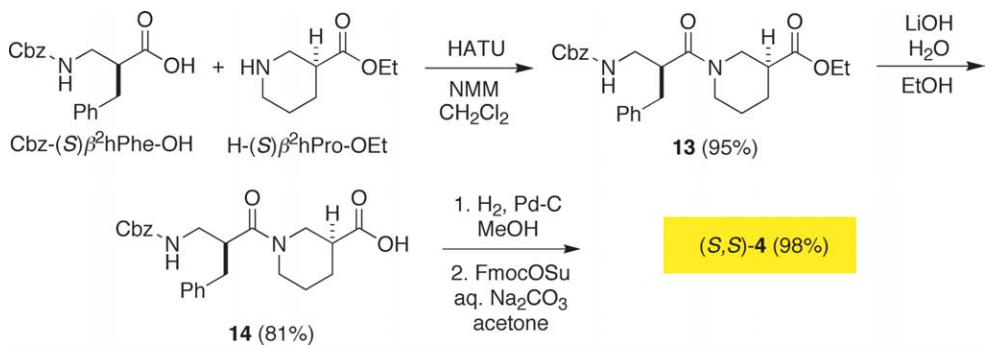

Figure 23. Preparation of Fmoc-(*S*)β^{2}hPhe-(*S*)β^{2}hPro-OH (**4**).

a Macherey-Nagel C_8 column (Nucleosil 100-5 C_8 (250×21 mm)) by using a linear gradient of A and B at a flow rate of 18 mL/min (Merck HPLC system).

2.3. Preparation of Fmoc-protected dipeptides 4–12

2.3.1. Cbz-(*S*)β²hPhe-(*S*)β²hPro-OEt (13). Amino acids Cbz-(*S*)β²hPhe-OH[87] (1.05 g, 3.35 mmol) and H-(*S*)β²hPro-OEt[88] (0.53 g, 3.35 mmol) were coupled according to GP1a. FC (AcOEt/hexane 1:1) gave **13** (1.44 g, 95%) as colorless oil; R_f=0.23 (AcOEt/hexane 1:1); $[\alpha]_D$=+27.5 (c=0.80, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3450 (w), 3007 (m), 2944 (w), 1720 (s), 1626 (s), 1511 (s), 1454 (m), 1139 (m), 1085 (m), 1030 (m), 856 (w) cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) **13**+rotamers δ 0.92–1.14 (m, 2H, CH_2), 1.17 (t, J=6.3 Hz, 3H, CH_3), 1.26–1.50 (m, 2H, CH_2), 1.66–1.84 (m, 2H, CH_2), 2.29 (m, 1H, CH), 2.51–2.90 (m, 4H, CH, CH_2, C*H*H), 3.06–3.19 (m, 2H, CH_2N), 3.67 (t, J=14.4 Hz, 1H, NH), 4.03 (m, 2H, OCH_2), 4.27 (d, J=11 Hz, 1H, CH*H*), 5.01 (m, 2H, OCH_2Ph), 7.07–7.49 (m, 10H, arom.); ^{13}C NMR (125 MHz, DMSO-d_6) **13**+rotamers δ: 13.9, 23.7, 24.4, 26.5, 26.7, 35.8, 36.3, 40.0, 40.5, 40.6, 41.4, 41.9, 42.2, 42.9, 43.1, 43.2, 45.0, 46.8, 59.8, 59.9, 65.1, 126.1, 127.6, 128.1, 128.2, 128.8, 137.2, 139.3, 156.1, 171.0, 172.2, 172.4; MALDI HRMS calcd for $C_{26}H_{32}N_2O_5Na$ $(M+Na)^+$: 475.2203, found: 475.2207. Anal. calcd for $C_{26}H_{32}N_2O_5$: C 69.01, H 7.13, N 6.19; found: C 69.01, H 7.16, N 5.93 (Fig. 23).

2.3.2. Cbz-(*S*)β²hPhe-(*S*)β²hPro-OH (14). Dipeptide ester **13** (1.34 g, 2.96 mmol) was hydrolyzed according to GP3. The resulting crude material was crystallized from $CHCl_3$/hexane to give **14** (1.02 g, 81%) as white crystals; mp 189–190 °C; R_f=0.32 (AcOEt/hexane/AcOH 10:10:1); $[\alpha]_D$=+2.4 (c=0.15, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3446 (w), 3008 (m), 1715 (s), 1627 (s), 1513 (m), 1454 (m), 1082 (m), 1046 (m), 1005 (w), 877 (w) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) **14**+rotamers δ 0.91–1.50 (m, 5H, 2×CH_2 and C*H*H), 1.68–1.91 (m, 2H, CH_2), 2.21–2.86 (m, 3H, NH, CH, CH*H*), 3.06–3.19 (m, 2H, CH_2), 3.54 (m, 1H, CH), 4.20 (d, J=12.9 Hz, 1H, C*H*H), 4.43 (d, J=10.7 Hz, 1H, CH*H*), 5.02 (m, 2H, OCH_2Ph), 7.06–7.39 (m, 10H, arom.), 12.32 (br s, 1H, COOH); ^{13}C NMR (100 MHz, DMSO-d_6) **14**+rotamers δ: 23.9, 24.6, 26.8, 26.9, 36.3, 40.6, 40.7, 41.5, 42.0, 42.1, 42.8, 43.1, 43.2, 45.0, 47.0, 65.1, 126.0, 126.1, 127.5, 126.6, 126.7, 128.1, 128.15, 128.22, 128.24, 128.6, 128.8, 137.1, 137.2, 139.2, 139.3, 156.1, 170.9, 171.1, 174.0, 174.2; MALDI HRMS calcd for $C_{24}H_{28}N_2O_5Na$ $(M+Na)^+$: 447.1890, found: 447.1887. Anal. calcd for $C_{24}H_{28}N_2O_5$: C 67.91, H 6.65, N 6.60; found: C 67.89, H 6.45, N 6.54.

2.3.3. Fmoc-(*S*)β²hPhe-(*S*)β²hPro-OH (4). Cbz-dipeptide **14** was hydrogenolyzed according to GP2 then Fmoc-protected according to GP4. The crude peptide was purified by FC (AcOEt/hexane/AcOH 10:10:0.1) to give **4** (1.13 g, 98%) as a white foam; mp 84–87 °C; R_f=0.35 (AcOEt/hexane/AcOH 10:10:1); $[\alpha]_D$=−1.6 (c=0.73, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3450 (w), 3008 (m), 2949 (m), 2862 (w), 1713 (s), 1625 (s), 1514 (s), 1467 (m), 1450 (s), 1181 (m), 1144 (m), 1084 (m), 1008 (m), 990 (w), 856 (w) cm^{-1}; ^1H NMR (400 MHz, CD_3OD) **4**+rotamers δ 1.02–1.99 (m, 4H, 2×CH_2), 2.27–2.93 (m, 4H, 2×CH and CH_2), 3.21–3.79 (m, 4H, 2×CH_2), 4.21 (m, 2H, CH_2), 4.30–4.53 (m, 3H, OCH_2CH), 7.08–7.79 (m, 13H, arom.); ^{13}C NMR (100 MHz, CD_3OD) **4**+rotamers δ 21.5, 25.35, 25.41, 25.7, 26.4, 28.4, 28.6, 37.8, 38.1, 42.39, 42.48, 42.54, 43.3, 43.5, 43.6, 44.1, 44.5, 44.6, 44.8, 44.83, 44.86, 44.93, 45.1, 45.3, 47.4, 67.6, 67.7, 67.8, 67.9, 121.0, 126.0, 126.1, 126.2, 126.3, 127.5, 127.6, 127.7, 128.2, 128.8, 129.3, 129.5, 129.6, 129.7, 130.0, 130.3, 140.3, 140.7, 142.7, 145.4, 158.9, 174.2, 174.3, 174.4, 176.2, 176.6, 176.9; MALDI HRMS calcd for $C_{31}H_{32}N_2O_5Na$ $(M+Na)^+$: 535.2203; found: 535.2199. Anal. calcd for $C_{31}H_{32}N_2O_5$: C 72.64, H 6.29, N 5.46; found: C 72.71, H 6.43, N 5.24 (Fig. 23).

2.3.4. Boc-(*S*)β²hMet-OCH_2CCl_3 (15). The crude H-(*S*)β²hMet-OH[55] (2.42 mmol) was dissolved in H_2O (2.5 mL) and aq. 1 M NaOH (5 mL) at 5 °C (ice bath). To the resulting solution Boc_2O (0.63 g, 2.90 mmol, 1.2 equiv.) in dioxane (5 mL), was added and the mixture stirred for 30 min at 25 °C. The solution was concentrated to half of its original volume, cooled again in an ice bath, covered with a layer of AcOEt and acidified with a dilute solution of $KHSO_4$ to pH 2–3. The aqueous phase was extracted with AcOEt (2×). The combined organic extracts were washed with H_2O, dried ($MgSO_4$) and the solvent removed under reduced pressure. The crude product (0.45 g, 1.71 mmol)

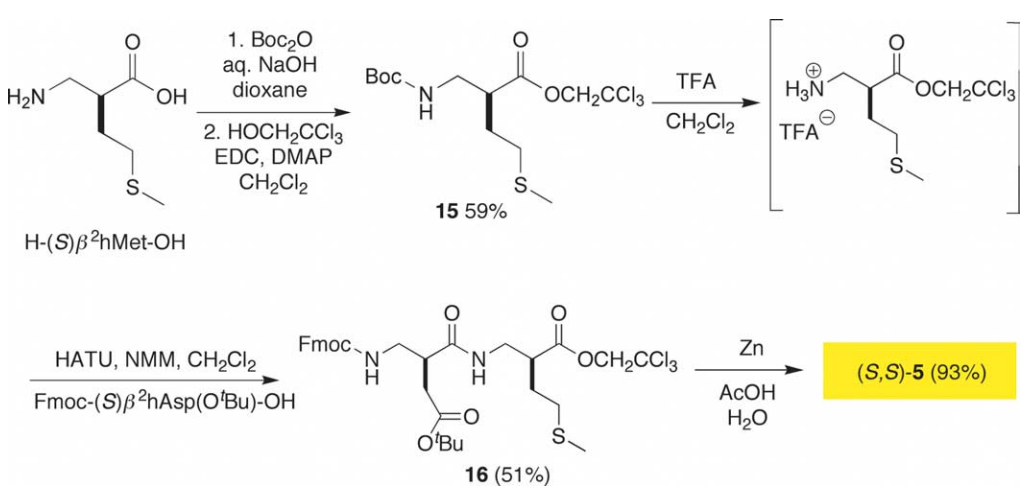

Figure 24. Preparation of Fmoc-(*S*)β²hAsp(O′Bu)-(*S*)β²hMet-OH (**5**).

and DMAP (42 mg, 0.34 mmol, 20 mol%) were dissolved in CH_2Cl_2 (20 mL) and Cl_3CCH_2OH (0.19 mL, 0.28 g, 1.88 mmol, 1.1 equiv.) was added. The resulting solution was cooled in an ice bath then EDC (0.39 g, 2.05 mmol, 1.2 equiv.) added and the reaction mixture stirred for 18 h at 25 °C. Sat. aq. NH_4Cl was added and the organic phase washed with 0.1 N HCl, 0.1 M K_2CO_3 and brine then dried ($MgSO_4$) and solvent removed under reduced pressure. The crude product was purified by FC (AcOEt/hexane 3:7) to give **15** (0.56 g, 59%) as colorless oil; R_f=0.61 (AcOEt/hexane 1:1); $[\alpha]_D$=+3.1 (c=0.26, $CHCl_3$); IR (neat) ν_{max} 3344 (w), 3054 (w), 2976 (w), 2140 (m), 1752 (s), 1710 (s), 1513 (m), 1445 (m), 1366 (m), 1272 (m), 1250 (m), 1167 (s), 789 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.43 (s, 9H, ^{t}Bu), 1.86 (m, 1H, C*H*HS), 2.03 (m, 1H, CH*H*S), 2.10 (s, 3H, SCH_3), 2.60 (t, J=7.5 Hz, 2H, CH_2), 2.95 (m, 1H, CHCO), 3.39 (m, 2H, CH_2N), 4.78 (s, 2H, OCH_2), 4.89 (br s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.4, 28.5, 28.6, 31.6, 41.3, 44.7, 74.0, 79.7, 94.8, 155.7, 172.6; MALDI HRMS calcd for $C_{13}H_{22}Cl_3NO_4SNa$ $(M+Na)^+$: 416.0227; found: 416.0233.

2.3.5. Fmoc-(*S*)β²hAsp(O^{t}Bu)-(*S*)β²hMet-OCH$_2$CCl$_3$ (16). To a solution of compound **15** (0.63 g, 1.60 mmol) in CH_2Cl_2 (6 mL), was added slowly TFA (6 mL) and the mixture stirred for 2 h at 25 °C. After removal of solvent under reduced pressure, the amino ester was coupled with Fmoc-(*S*)β²hAsp(O^{t}Bu)-OH[56] (0.68 g, 1.60 mmol) according to GP1a. FC (AcOEt/hexane 1:1) yielded **16** (0.57 g, 51%) as a white solid. R_f=0.33 (AcOEt/hexane 1:1); $[\alpha]_D$=+12.8 (c=0.49, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3445 (w), 3008 (w), 2974 (w), 2923 (w), 1720 (s), 1667 (m), 1513 (m), 1450 (m), 1368 (m), 1153 (s), 1077 (w), 1046 (w), 841 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.44 (s, 9H, ^{t}Bu), 1.80 (m, 1H, C*H*HS), 2.03 (m, 1H, CH*H*S), 2.08 (s, 3H, CH_3S), 2.37 (m, 1H, CH), 2.54 (m, 3H, CH and CH_2), 2.81–3.05 (m, 2H, CH_2), 3.29–3.57 (m, 4H, 2×CH_2N), 4.20 (t, J=6.2 Hz, 1H, C*H*CH_2O), 4.39 (d, J=6.2 Hz, 2H, CHC*H*$_2$O), 4.67–4.83 (m, 2H, CH_2CCl_3), 5.46 (br s, 1H, NH), 6.57 (br s, 1H, NH), 7.26–7.42 (m, 4H, arom.), 7.59 (d, J=7.1 Hz, 2H, arom.), 7.76 (d, J=7.2 Hz, 2H, arom.); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.4, 28.1, 28.7, 31.4, 35.7, 39.9, 42.2, 42.6, 44.1, 47.3, 66.7, 68.4, 74.1, 81.4, 119.9, 125.0, 126.9, 127.6, 141.2, 143.7, 156.4, 171.3, 172.2, 173.6; MALDI HRMS calcd for $C_{32}H_{39}Cl_3N_2O_7SNa$ $(M+Na)^+$: 723.1436; found: 723.1444.

2.3.6. Fmoc-(*S*)β²hAsp(O^{t}Bu)-(*S*)β²hMet-OH (5). Dipeptide ester **16** (0.86 g, 1.22 mmol) was dissolved in a mixture of AcOH (50 mL) and H_2O (5 mL). To the cooled solution (ice bath), Zn powder (3.99 g, 61 mmol, 50 equiv.) was added in portions over 2 h. The reaction mixture was allowed to warm up to 25 °C and stirred for 3 h. Zn was removed by filtration and the filtrate diluted with H_2O and extracted with AcOEt (3×). The combined organic extracts were dried ($MgSO_4$) and the solvent removed under reduced pressure. FC (AcOEt/hexane/AcOH 10:10:0.1) of the crude product yielded **5** (0.65 g, 93%) as a white solid; mp 143–144 °C; R_f=0.37 (AcOEt/hexane/AcOH 10:10:1); $[\alpha]_D$=+15.9 (c=0.43, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3436 (w), 3005 (m), 2974 (m), 1720 (s), 1667 (m), 1512 (m), 1450 (m), 1368 (m), 1154 (m), 1077 (w), 841 (w) cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 1.43 (s, 9H, ^{t}Bu), 1.84 (m, 2H, CH_2S), 2.05 (s, 3H, CH_3S), 2.32 (m, 1H, CH); 2.47–2.58 (m, 3H, CH and CH_2), 2.77 (m, 2H, CH_2), 3.15–3.43 (m, 4H, 2×CH_2), 4.21 (t, J=6.6 Hz, 1H, C*H*CH_2O), 4.36 (d, J=6.5 Hz, 2H, CHC*H*$_2$O), 7.11 (m, 1H, NH), 7.28–7.40 (m, 4H, arom), 7.64 (d, J=7.2 Hz, 2H, arom.), 7.79 (d, J=7.5 Hz, 2H, arom.), 8.05 (br s, 1H, NH); ^{13}C NMR (75 MHz, CD_3OD) δ 15.0, 28.1, 29.9, 32.1, 36.0, 41.2, 43.6, 44.0, 45.3, 47.8, 67.5, 81.6, 120.5, 125.8, 127.7, 128.3, 142.1, 144.8, 144.9, 172.0, 175.0, 176.8; MALDI HRMS calcd for $C_{30}H_{38}N_2O_7SNa$ $(M+Na)^+$ 593.2292, found 593.2299 (Fig. 24).

2.3.7. Fmoc-(*S*)β²hHis(Trt)-(*S*)β²hLeu-OBn (17). Fmoc-(*S*)β²hHis(Trt)-OH[57] (0.72 g, 1.34 mmol) and *p*TsOH·H-(*S*)β²hLeu-OBn[65] (0.49 g, 1.41 mmol) were coupled according to GP1a in the presence of 4 equiv. of NMM. The crude product was purified by FC (AcOEt/hexane 3:1) to yield 0.96 g (84%) of **17** as an amorphous solid. R_f=0.12 (AcOEt/hexane 3:1). $[\alpha]_D$=−2.5 (c=0.75, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3734 (w), 3628 (w), 3063 (w), 2923 (w), 2853 (w), 1718 (s), 1652 (m), 1539 (m), 1495 (w), 1448 (s), 1169 (m), 1245 (m), 1139 (m), 1085 (w), 843 (m) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 0.76 (d, J=6.3 Hz, 3H, Me); 0.77 (d, J=6.3 Hz, 3H, Me) 1.18–1.23 (m, 1H, CH*H*(*i*-Pr)), 1.37–1.47 (m, 2H, C*H*H(*i*-Pr), Me_2CH); 2.52–2.62 (m, 4H, 2×CHCO and CH_2Ar), 2.66–2.73 (m, 1H, CH*H*N); 2.97–3.06 (m, 1H, C*H*HN), 3.08–3.15 (m, 1H, C*H*HN), 3.20–3.26 (m, 1H, CH*H*N), 4.16–4.25 (m, 3H, OCH_2CH), 5.00–5.10 (m, 2H, CH_2Ph), 6.60 (s, 1H, arom.), 7.05–7.07 (m, 6H, arom.), 7.21 (s, 1H, arom.), 7.27–7.41 (m, 19H, 18 arom., NH), 7.66–7.68 (m, 2H, arom.), 7.88–7.99 (m, 2H, arom.), 8.02 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.7, 22.7, 25.5, 28.6, 38.3, 40.6, 42.1, 43.2, 45.7, 46.6, 65.5, 74.3, 118.3, 120.0, 125.1, 125.1, 126.9, 127.5, 127.8, 127.8, 128.0, 128.3, 129.1, 136.0, 137.2, 138.4, 140.6, 142.2, 143.7, 156.0, 173.0, 173.9. MALDI HRMS calcd for $C_{55}H_{54}N_4O_5Na$ $(M+Na)^+$: 873.3992; found: 873.3986.

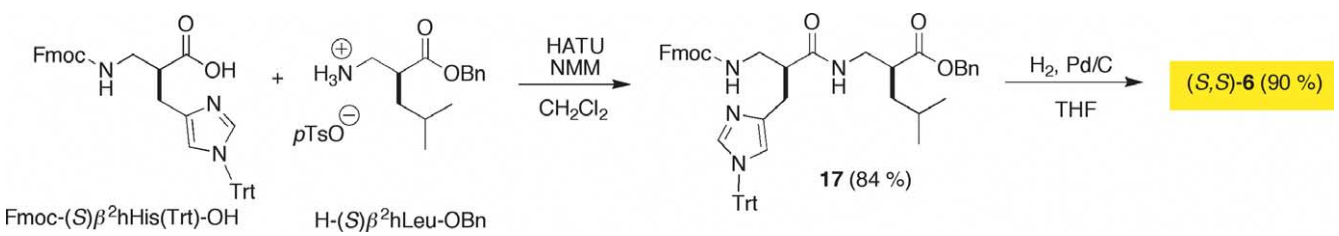

Figure 25. Preparation of Fmoc-(*S*)β²hHis(Trt)-(*S*)β²hLeu-OH (**6**).

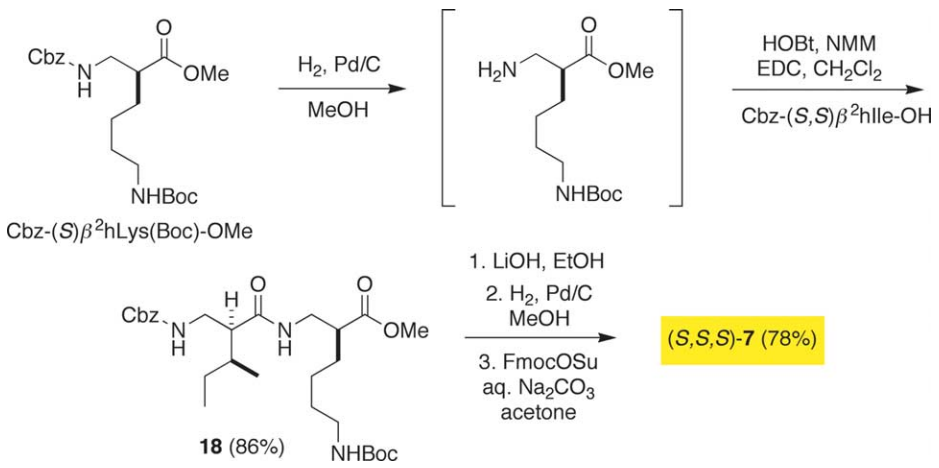

Figure 26. Preparation of Fmoc-(*S*,*S*)β^{2}hIle-(*S*)β^{2}hLys(Boc)-OH (**7**).

2.3.8. Fmoc-(*S*)β^{2}hHis(Trt)-(*S*)β^{2}hLeuOH (6). The *C*-terminus of the fully protected dipeptide **17** (0.96 g, 1.14 mmol) was deprotected according to GP2 in THF for 8 h. The crude product was purified by FC (CH_2Cl_2/MeOH 9:1) to yield 0.78 g (90%) of **6** as an amorphous solid. R_f=0.18 (CH_2Cl_2/MeOH 9:1); $[\alpha]_D$=+10.6 (*c*=0.43, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3297 (w), 3061 (w), 2922 (w), 2854 (w), 1719 (s), 1649 (s), 1551 (s), 1449 (s), 1245 (m), 1132 (m), 1001 (w), 842 (m) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.77 (d, *J*=6.4 Hz, 3H, Me); 0.79 (d, *J*=6.4 Hz, 3H, Me) 1.12–1.14 (m, 1H, C*H*H(*i*-Pr)); 1.36–1.44 (m, 1H, CH*H*(*i*-Pr)), 1.52–1.53 (m, 1H, Me_2CH), 2.40–2.46 (m, 1H, CHCO), 2.52–2.69 (m, 3H, CH_2Ar, CHCO), 2.96–3.17 (m, 4H, 2×CH_2N), 4.16–4.25 (m, 3H, OCH_2CH), 6.64 (s, 1H, arom.), 7.05–7.07 (m, 6H, arom.), 7.21 (s, 1H, arom.), 7.28–7.44 (m, 14H, 13 arom., NH), 7.67–7.68 (m, 2H, arom.), 7.86–7.88 (m, 2H, arom.), 7.97 (s, NH), 12.35 (br s, 1H, OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.8, 22.8, 25.5, 28.4, 38.5, 40.9, 41.8, 45.4, 46.6, 54.8, 65.3, 74.4, 119.9, 121.3, 127.0, 127.2, 127.5, 127.8, 128.0, 128.8, 129.2, 138.1, 140.6, 140.6, 142.2, 143.8, 156.0, 172.8; MALDI HRMS calcd for $C_{48}H_{48}N_4O_5Na$ (M+Na)$^+$: 783.3523; found: 783.3517 (Fig. 25).

2.3.9. Cbz-(*S*,*S*)β^{2}hIle-(*S*)β^{2}hLys(Boc)-OMe (18). The Cbz-protecting group of Cbz-(*S*)β^{2}hLys(Boc)-OMe[54] (1.01 g, 2.47 mmol) was hydrogenated according to GP2 and the resulting crude H-(*S*)β^{2}hLys(Boc)-OMe was coupled with Cbz-(*S*,*S*)β^{2}hIle-OH[55] (0.69 g, 2.47 mmol) according to GP1b. The crude product was purified by FC (hexane/AcOEt 8:2→5:5) to yield **18** (1.13 g, 86%) as a colorless solid; mp 93–96 °C; R_f=0.18 (AcOEt/hexane 1:1); $[\alpha]_D$=+30.3 (*c*=1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3450 (w), 3007 (w), 2968 (m), 2872 (w), 1713 (s), 1666 (m), 1509 (s), 1456 (m), 1367 (m), 1170 (m), 1064 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.87 (t, *J*=7.4 Hz, 3H, Me), 0.91 (d, *J*=6.9 Hz, 3H, Me), 1.08–1.19 (m, 1H, CH), 1.30–1.37 (m, 2H, CH_2), 1.43 (s, 9H, ^{t}Bu), 1.42–1.51 (m, 2H, CH_2), 1.52–1.58 (m, 2H, CH_2),1.59–1.67 (m, 2H, CH_2), 2.22–2.26 (m, 1H, CH), 2.60–2.66 (m, 1H, CH), 3.07 (d, *J*=6.0 Hz, 2H, CH_2), 3.26–3.35 (m, 2H, CH_2), 3.42–3.54 (m, 2H, CH_2), 3.68 (s, 3H, MeO), 4.55 (br s, 1H, NH), 5.07 (q, *J*=12.4 Hz, 2H, CH_2Ph), 5.35 (br s, 1H, NH), 6.10 (br s, 1H, NH), 7.30–7.36 (m, 5H, arom.); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.4, 15.9, 23.7, 27.2, 28.4, 28.9, 29.4, 29.7, 29.9, 35.2, 39.9, 40.2, 40.4, 44.8, 45.1, 51.9, 52.0, 58.5, 66.6, 72.3, 79.2, 128.0, 128.5, 136.6, 156.1, 156.5, 174.4, 175.4; MALDI HRMS calcd for $C_{28}H_{45}N_3O_7Na$ (M+Na)$^+$: 558.3150, found: 558.3157. Anal. calcd for $C_{28}H_{45}N_3O_7$: C 62.78, H 8.47, N 7.84; found: C 62.80, H 8.28, N 7.71.

2.3.10. Fmoc-(*S*,*S*)β^{2}hIle-(*S*)β^{2}hLys(Boc)-OH (7). The methyl ester- and the Cbz-protecting group of compound **18** (1.06 g, 1.98 mmol) were removed according to GP3 and GP2 respectively, and the resulting amino acid Fmoc-protected according to GP4. FC (CH_2Cl_2/MeOH 100:1→CH_2Cl_2/MeOH/AcOH 20:1:0.2) yielded **7** (0.94 g, 78%) colorless solid; mp 114–117 °C; R_f=0.30 (CH_2Cl_2/MeOH/AcOH 20:1:0.2); $[\alpha]_D$=+29.4 (*c*=1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3449 (w), 3344 (w), 3007 (w), 2969 (m), 2933

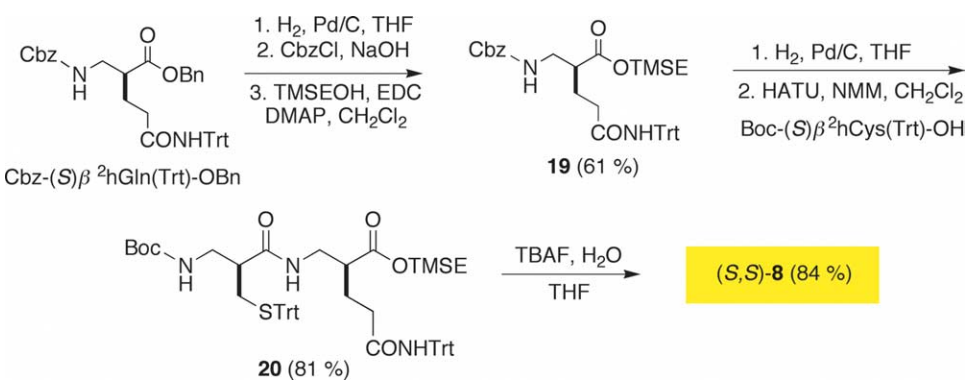

Figure 27. Preparation of Boc-(*S*)β^{2}hCys(Trt)-(*S*)β^{2}hGln(Trt)-OH (**8**).

(m), 2872 (w), 1710 (s), 1662 (m), 1510 (s), 1451 (m), 1368 (m), 1167 (m), 1078 (w), 990 (w) cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 0.89 (t, J=7.4 Hz, 3H, Me), 0.94 (t, J=6.8 Hz, 3H, Me), 1.10–1.57 (m, 2H, CH_2), 1.29–1.39 (m, 2H, CH_2), 1.41 (s, 9H, ^{t}Bu), 1.42–1.49 (m, 2H, CH_2), 1.51–1.63 (m, 4H, 2×CH_2), 2.29–2.34 (m, 1H, CH), 2.58–2.62 (m, 1H, CH), 3.00 (d, J=6.9 Hz, 2H, CH_2), 3.20–3.28 (m, 2H, CH_2), 3.32–3.39 (m, 2H, CH_2), 4.19 (t, J=6.9 Hz, 2H, CH_2), 4.31 (d, J=7.1 Hz, 2H, CH_2), 6.89 (t, J=5.9 Hz, 1H, NH), 7.29–7.80 (m, 8H, arom.); ^{13}C NMR (125 MHz, CD_3OD) δ 11.7, 16.5, 25.3, 28.3, 28.8, 30.7, 30.9, 36.5, 41.1, 41.8, 42.0, 46.6, 48.5, 53.4, 67.9, 73.6, 79.8, 121.0, 126.2, 126.3, 128.2, 128.8, 142.6, 145.3, 145.4, 158.6, 158.7, 176.9, 178.2; MALDI HRMS calcd for $C_{34}H_{47}N_3O_7Na$ $(M+Na)^+$: 632.3306; found: 632.3313. Anal. calcd for $C_{34}H_{47}N_3O_7$: C 66.97, H 7.77, N 6.89; found: C 66.97, H 7.66, N 6.64 (Fig. 26).

2.3.11. Cbz-(*S*)β²hGln(Trt)-OTMSE (19). Cbz-(*S*)β²hGln(Trt)-OBn[56] (2.45 g, 3.9 mmol) was transformed to compound **19** in three steps. The first transformation involved hydrogenolysis in MeOH for 1.5 h according to GP2 to yield the amino acid (H-β²hGln(Trt)-OH), which without purification was *N*-Cbz protected using the following procedure: to an aqueous solution of the free amino acid in 0.5 M NaOH (1.1 equiv.) at 0 °C was added with continuous stirring BnO_2CCl (1.3 equiv.). The pH was kept basic by periodic addition of 1 M NaOH. After the addition was completed, the reaction mixture was stirred for one additional hour then extracted with AcOEt after adjusting the pH to 3 using 1 M HCl. The organic layer was washed with brine, dried ($MgSO_4$) and the solvent evaporated under reduced pressure to give a yellow oil. Unreacted BnO_2CCl and BnOH were removed from the mixture by passing the mixture through a short column, and the crude product treated according to GP5. The purification by FC (Et_2O/pentane 1:3) yielded **19** (1.52 g, 61%) as a white solid; mp 135–136 °C; R_f=0.42 (Et_2O/pentane 1:3); $[\alpha]_D$=−6.8 (c=1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3439 (w), 3007 (w), 2956 (w), 1716 (s), 1516 (m), 1490 (m), 1448 (w), 860 (w), 839(w) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 0.01 (s, 9H, $SiMe_3$), 0.90–0.95 (m, 2H, CH_2Si); 1.56–1.65 (m, 2H, CH_2CH$_2$CON), 2.24–2.27 (m, 2H, CH_2CON), 2.44–2.47 (m, 1H, CHCO), 3.06–3.19 (m, 2H, CH_2N), 4.06–4.11 (m, 2H, OCH_2), 4.95–5.02 (m, 2H, CH_2Ph), 7.14–7.35 (m, 21H, 20 arom., NH), 8.53 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ−1.5, 16.8, 25.0, 33.2, 42.0, 44.9, 62.0, 65.2, 69.2, 126.2, 127.4, 127.6, 127.7, 128.3, 128.5, 137.1, 144.9, 156.1, 171.2, 173.5; MALDI HRMS calcd for $C_{38}H_{44}N_2O_5SiNa$ $(M+Na)^+$: 659.2917; found: 659.2912.

2.3.12. Boc-(*S*)β²hCys(Trt)-(*S*)β²hGln(Trt)-OTMSE (20). Compound **19** (1.00 g, 1.57 mmol) was hydrogenated in THF to give H-(*S*)β²hGln(Trt)-OTMSE according to GP2, then coupled with Boc-(*S*)β²hCys(Trt)-OH[57] (0.75 g, 1.57 mmol) according to GP1a. The crude product was purified by FC (CH_2Cl_2/*i*-PrOH 96:4) to yield **20** (1.22 g, 81%) as an amorphous solid; R_f=0.32 (CH_2Cl_2/*i*-PrOH 96:4); $[\alpha]_D$=+11.4 (c=1.0, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3436 (w), 3026 (w), 1708 (s), 1681 (m), 1492 (s), 1446 (w), 1251 (m), 1164 (m), 1041 (w) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 0.00 (s, 9H, $SiMe_3$) 0.93 (t, J=8.5 Hz, 2H, CH_2Si), 1.31 (s, 9H, ^{t}Bu), 1.61–1.64 (m, 2H, CH_2CH$_2$CON), 2.01–2.03 (m, 1H,CH*H*S), 2.25–2.28 (m, 2H, CH_2CON), 2.30–2.33 (m, 2H, C*H*HS and CHCO), 2.47–2.50 (m, 1H, CHCO), 2.86–2.90 (m, 2H, CH_2N), 3.11–3.25 (m, 2H, CH_2N), 4.00–4.14 (m, 2H, OCH_2), 6.49 (s, 1H, NH), 7.15–7.30 (m, 30H, arom.), 7.93 (s, 1H, NH), 8.54 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ −1.6, 16.8, 25.1, 28.1, 31.1, 33.1, 39.9, 42.0, 44.3, 45.4; 61.9, 65.8, 69.1, 77.5, 126.2, 126.5, 127.3, 127.8, 128.4, 129.0, 144.3, 144.8, 155.2, 171.1, 171.6, 173.5; MALDI HRMS calcd for $C_{58}H_{67}N_3O_6SSiNa$ $(M+Na)^+$: 984.4418; found: 984.4400.

2.3.13. Boc-(*S*)β²hCys(Trt)-(*S*)β²hGln(Trt)-OH (8). The *C*-terminus of the fully protected dipeptide **20** (1.32 g, 1.37 mmol) was deprotected according to GP2. The crude product was purified by FC (AcOEt/Hexane/AcOH 20:10:0.1) to yield **8** (1.00 g, 85%) as an amorphous solid. R_f=0.10 (AcOEt/hexane/AcOH 20:10:0.1); $[\alpha]_D$=−6.3 (c=0.9, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3432 (w), 3058 (w), 3009 (w), 2980 (w), 1706 (s), 1667 (m), 1494 (s), 1445 (m), 1366 (w), 1228 (m), 1164 (m) cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.31 (s, 9H, ^{t}Bu), 1.62–1.66 (m, 2H, CH_2CH$_2$CON), 2.02–2.05 (m, 1H, CH*H*S), 2.28–2.33 (m, 4H, C*H*HS, CH_2CON, and CHCO), 2.37–2.43 (m, 1H, CHCO), 2.84–2.88 (m, 2H, CH_2N), 3.06–3.10 (m, 1H, CH*H*N), 3.25–3.31 (m, 1H, C*H*HN), 6.50 (t, J=5.8 Hz, 1H, NH), 7.15–7.32 (m, 30H, arom.), 7.89 (t, J=5.8 Hz, 1H, NH), 8.57 (s, 1H, NH), 12.30 (br s, 1H, OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 25.1, 28.1, 31.1, 33.4, 41.3, 42.1, 44.3, 45.4, 65.8, 69.1, 77.5, 126.2, 126.5, 127.3, 127.8, 128.4, 129.0, 144.3, 144.8, 155.3, 171.3, 171.6, 175.2; MALDI HRMS calcd for $C_{53}H_{55}N_3O_6SNa$ $(M+Na)^+$: 884.3708; found: 884.3704 (Fig. 27).

2.3.14. Cbz-(*S*)β²hTyr(^{t}Bu)-(*S*)β²hAla-OBn (21). H-(*S*)β²hAla-OH[89] was dissolved in toluene, BnOH and *p*TsOH were added and the mixture was heated at reflux for 18 h using a Dean–Stark trap to azeotropically remove H_2O. The reaction mixture was cooled to 25 °C, toluene was evaporated and the residue washed several times with Et_2O. The resulting benzyl ester (0.92 g, 2.52 mmol) was coupled with Cbz-(*S*)β²hTyr(^{t}Bu)-OH[55] (0.97 g, 2.52 mmol) according to GP1a. FC (AcOEt/hexane 1:1) yielded **21** (1.17 g, 83%) as a white solid; mp 74–76 °C; R_f=0.18 (AcOEt/hexane 1:1); $[\alpha]_D$=+14.8 (c=0.54, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3443 (w), 2980 (m), 1719 (s), 1667 (m), 1507 (s), 1456 (m), 1367 (m), 1160 (m), 894 (m) cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 0.96 (d, J=7.1 Hz, 3H, Me), 1.28 (s, 9H, ^{t}Bu), 2.54 (q, J=7.0 Hz, 1H, CHCO), 2.66–2.93 (m, 3H, $CHCH_2Ph$), 3.11–3.29 (m, 4H, 2×CH_2N), 5.05 (s, 2H, OCH_2Ph), 5.07 (AB, J=12.6 Hz, 2H, OCH_2Ph), 6.85 (d, J=8.4 Hz, 2H, arom.), 7.04 (d, J=8.4 Hz, 2H, arom.), 7.26–7.34 (m, 10H, arom.); ^{13}C NMR (100 MHz, CD_3OD) δ 15.2, 29.2, 36.5, 40.8, 42.9, 44.1, 50.4, 67.4, 67.5, 79.4, 125.2, 128.8, 129.0, 129.1, 129.2, 129.5, 129.6, 130.4, 135.5, 137.6, 138.3, 155.0, 158.8, 176.0; MALDI HRMS calcd for $C_{33}H_{40}N_2O_6Na$ $(M+Na)^+$ 583.2779, found 583.2785. Anal. calcd for $C_{33}H_{40}N_2O_6$: C 70.69, H 7.19, N 5.00; found: C 70.52, H 7.34, N 5.14.

2.3.15. Fmoc-(*S*)β²hTyr(^{t}Bu)-(*S*)β²hAla-OH (9). The dipeptide derivative **21** was hydrogenated according to

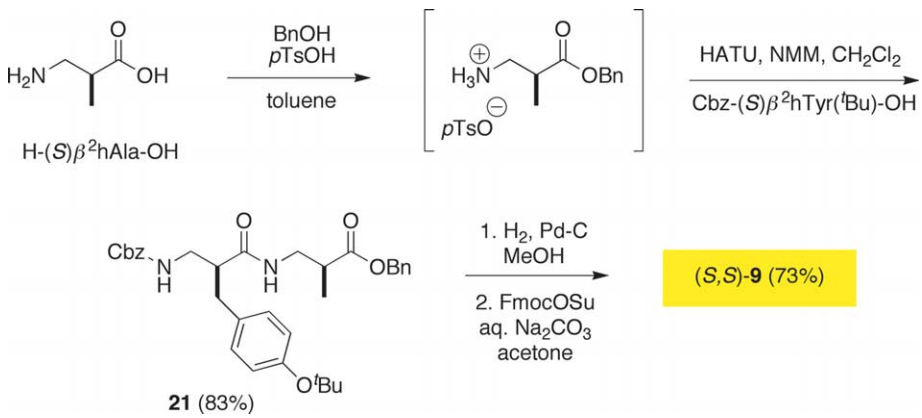

Figure 28. Preparation of Fmoc-(*S*)β^{2}hTyr(^{t}Bu)-(*S*)β^{2}hAla-OH (**8**).

GP2 and Fmoc-protected according to GP4. The crude peptide was purified by FC (AcOEt/hexane/AcOH 10:10:0.1) to give **9** (0.72 g, 73%) as a white solid; mp 143–144 °C; R_f=0.16 (AcOEt/hexane/AcOH 10:10:1); $[\alpha]_D$=+7.3 (*c*=0.55, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3442 (w), 3005 (m), 2980 (m), 1717 (s), 1683 (m), 1508 (s), 1467 (m), 1450 (m), 1368 (m), 1157 (m), 1082 (w), 891 (m) cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 0.98 (d, *J*=7.1 Hz, 3H, Me), 1.29 (s, 9H, ^{t}Bu), 2.45 (q, *J*=7.1 Hz, 1H, CHMe), 2.67–2.80 (m, 3H, C*H*HN, CH_2Ph), 3.15 (dd, *J*=7.0, 13.4 Hz, 1H, CH), 3.26 (m, 3H, CH_2N, CH*H*N), 4.19 (t, *J*=6.8 Hz, 1H, C*H*CH_2O), 4.34 (d, *J*=6.9 Hz, 2H, CHCH_2O), 6.87 (d, *J*=8.5 Hz, 2H, arom.), 7.07 (d, *J*=8.4 Hz, 2H, arom.), 7.29 (m, 2H, arom.), 7.37 (m, 2H, arom.), 7.63 (d, *J*=7.5 Hz, 2H, arom.), 7.77 (m, 2H, arom.); ^{13}C NMR (100 MHz, CD_3OD) δ 15.4, 29.2, 36.5, 40.6, 43.0, 44.2, 48.5, 50.4, 67.8, 79.5, 121.0, 125.3, 126.2, 128.2, 128.8, 130.5, 135.7, 142.7, 145.4, 155.0, 158.9, 176.1, 178.4; MALDI HRMS calcd for $C_{33}H_{38}N_2O_6Na$ $(M+Na)^+$: 581.2622, found: 581.2629. Anal. calcd for $C_{33}H_{38}N_2O_6$: C 70.95, H 6.86, N 5.01; found: C 70.99, H 6.87, N 4.89 (Fig. 28).

2.3.16. Cbz-(*R*,*S*)β^{2}hThr(^{t}Bu)-(*R*)β^{2}hSer(^{t}Bu)-OBn (22). Cbz-(*R*,*S*)β^{2}hThr(^{t}Bu)-OH[57] (0.70 g, 2.16 mmol) and H-(*R*)β^{2}hSer(^{t}Bu)-OBn[57] (0.6 g, 2.27 mmol) were coupled according to GP1a. The crude product was purified by FC (AcOEt/hexane 3:4) to obtain 0.97 g (79%) of **22** as an amorphous solid. R_f=0.35 (AcOEt/hexane 3:4); $[\alpha]_D$=+27.6 (*c*=0.41, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3323 (w), 2972 (m), 2925 (w), 1726 (s), 1653 (m), 1534 (m), 1457 (m), 1233 (m), 1193 (m), 1091 (w) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.97 (d, *J*=4.8 Hz, 3H, Me); 1.05 (s, 9H, ^{t}Bu), 1.10 (s, 9H, ^{t}Bu), 2.36–2.40 (m, 1H, CHCO), 2.74–2.79 (m, 1H, CHCO), 3.10–3.27 (m, 3H, CH_2N, OCH*H*), 3.33–3.37 (m, 1H, OC*H*H), 3.44–3.51 (m, 2H, CH_2N), 3.68–3.70 (m, 1H, OCH), 4.95–5.17 (m, 4H, 2×CH_2Ph), 7.03 (t, *J*=4.6 Hz, 1H, NH) 7.27–7.37 (m, 10H, arom.); 7.72 (t, *J*=4.6 Hz, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.1, 27.0, 28.2, 37.3, 39.7, 46.1, 52.6, 60.3, 65.0, 65.2, 66.2, 72.0, 73.2, 127.4, 127.6, 127.6, 127.8, 128.2, 128.2, 136.1, 137.2, 155.9, 171.7, 172.2; MALDI HRMS calcd for $C_{32}H_{46}N_2O_7Na$: 593.3203; found: 593.3197.

2.3.17. Fmoc-(*R*,*S*)β^{2}hThr(^{t}Bu)-(*R*)β^{2}hSer(^{t}Bu)-OH (10). The fully protected dipeptide **22** (0.9 g, 1.58 mmol) was hydrogenolyzed in MeOH for 16 h according to GP2. The resulting amino acid was Fmoc-protected according to GP4. The crude product was purified by FC (AcOEt/Hexane/AcOH 10:10:0.1) to obtain 0.73 g (81%) of **22** as colorless oil. R_f=0.20 (AcOEt/hexane/AcOH 10:10:0.1). $[\alpha]_D$=+12.7 (*c*=0.52, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3312 (w), 2971 (m), 2925 (w), 1718 (s), 1653 (m), 1539 (m), 1450 (m), 1363 (m), 1249 (m), 1193 (m), 1091 (w) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.00 (*d*, *J*=4.8 Hz, 3H, Me), 1.08 (s, 9H, ^{t}Bu), 1.12 (s, 9H, ^{t}Bu), 2.36–2.43 (m, 1H, CHCO), 2.53–2.60 (m, 1H, CHCO), 3.12–3.22 (m, 3H, CH_2N, OCH*H*), 3.35–3.41 (m, 1H, OC*H*H), 3.45 (d, *J*=4.6 Hz, 2H, CH_2N); 3.69–3.74 (m, 1H, OCH), 4.18–4.27 (m, 3H, OCH_2CH), 7.12 (t, *J*=4.5 Hz, 1H, NH), 7.30–7.34 (m, 2H, arom.), 7.39–7.43 (m, 2H, arom.), 7.62 (t, *J*=4.5 Hz, 1H, NH), 7.67 (d, *J*=5.8 Hz, 2H, arom.), 7.88 (d, *J*=6.1 Hz, 2H, arom.), 12.22 (br s, 1H, OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 20.1, 27.1, 28.1, 37.4, 39.9, 46.0, 46.6, 52.4, 60.4, 65.4, 66.3, 72.2, 73.3, 120.0, 125.1, 126.9, 127.5, 140.6, 143.8, 155.9, 171.6, 173.8; MALDI HRMS calcd for $C_{32}H_{44}N_2O_7Na$: 591.3047; found: 591.3041 (Fig. 29).

2.3.18. Cbz-(*S*)β^{2}hGlu(O^{t}Bu)-OTMSE (23). Cbz-(*S*)β^{2}hGlu(O^{t}Bu)-OH[56] (0.9 g, 2.56 mmol) was treated according to GP5. Purification of the crude product by FC (Et_2O/pentane 1:1) gave **23** (1.06 g, 92%) as a colorless oil. R_f=0.43 (Et_2O/pentane 1:1). $[\alpha]_D$=+4.7 (*c*=0.9, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3446 (w), 3025 (w), 2954 (w), 1718 (s), 1508 (m), 1451 (w), 1364 (w), 1246 (m), 1148 (m), 1056

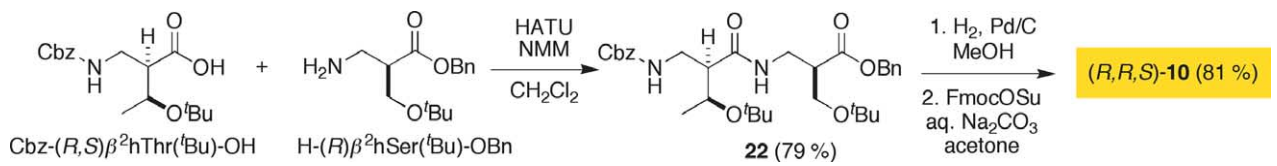

Figure 29. Preparation of Fmoc-(*R*,*S*)β^{2}hThr(^{t}Bu)-(*R*)β^{2}hSer(^{t}Bu)-OH (**10**).

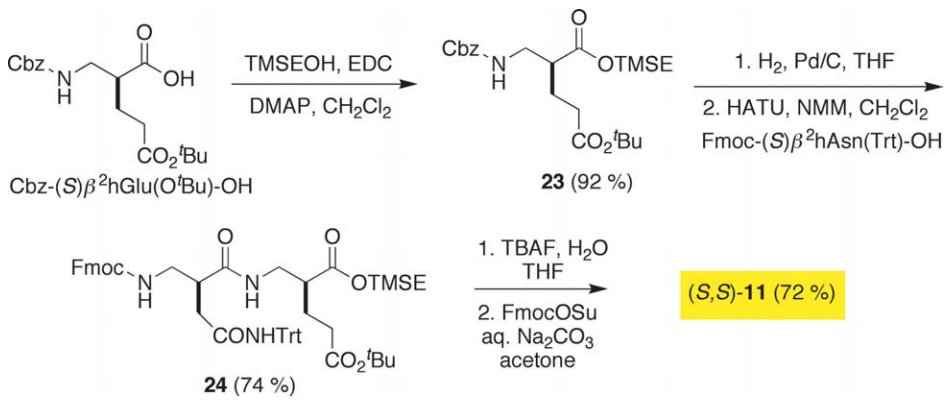

Figure 30. Preparation of Fmoc-(*S*)β^{2}hAsn(Trt)-(*S*)β^{2}hGlu(O^{t}Bu)-OH (**11**).

(w), 856 (w) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.02 (s, 9H, SiMe$_3$), 0.91–0.95 (m, 2H, CH$_2$Si), 1.39 (s, 9H, ^{t}Bu), 1.62–1.73 (m, 2H, C*H*$_2$CH$_2$CO), 2.11–2.26 (m, 2H, CH$_2$CO), 2.24–2.27 (m, 2H, CH$_2$CON), 2.51–2.55 (m, 1H, CHCO), 3.07–3.23 (m, 2H, CH$_2$N), 4.07–4.11 (m, 2H, OCH$_2$), 5.00 (s, 2H, CH$_2$Ph), 7.28–7.40 (m, 6H, 5 arom., NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ −1.6, 16.7, 24.2, 27.6, 32.1, 41.7, 44.4, 62.0, 65.1, 79.6, 127.5, 127.7, 128.2, 137.0, 156.0, 171.4, 173.2; MALDI HRMS calcd for $C_{23}H_{37}NO_6SiNa$ (M+Na)$^+$: 474.2388; found: 474.2382.

2.3.19. Fmoc-(*S*)β^{2}hAsn(Trt)-(*S*)β^{2}hGlu(O^{t}Bu)-OTMSE (24). Compound **23** (0.93 g, 2.06 mmol) was hydrogenated according to GP2 in THF. Coupling with Fmoc-(*S*)β^{2}hAsn(Trt)-OH[56] (1.26 g, 2.06 mmol) according to GP1a give a crude product, which was purified by FC (AcOEt/hexane 1:1) to yield **24** (1.39 g, 74%) as an amorphous solid. R_f=0.23 (AcOEt/hexane 1:1). $[\alpha]_D$=−16.0 (*c*=0.43, CHCl$_3$); IR (CHCl$_3$) ν_{max} 3436 (w), 3019 (w), 1716 (s), 1677 (m), 1504 (m), 1445 (w), 1248 (w), 1154 (m) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ −0.01 (s, 9H, SiMe$_3$), 0.89–0.94 (m, 2H, CH$_2$Si), 1.34 (s, 9H, ^{t}Bu), 1.64–171 (m, 2H, C*H*$_2$CH$_2$CO), 2.07–2.21 (m, 2H, CH$_2$CO), 2.27–2.33 (m, 1H, CHCO), 2.52–2.59 (m, 2H, CH*H*CON and CHCO), 2.71–2.75 (m, 1H, C*H*HCON), 2.99–3.05 (m, 1H, CH*H*N), 3.06–3.08 (m, 2H, CH$_2$N), 3.33–3.39 (m, 1H, C*H*HN), 4.03–4.13 (m, 2H, OCH$_2$), 4.18–4.29 (m, 3H, OCH$_2$CH), 7.13–7.41 (m, 20H, 19 arom., NH), 7.66 (d, *J*=7.5 Hz, 2H, arom.), 7.87 (d, *J*=7.6 Hz, 2H, arom.), 7.89 (s, 1H, NH), 8.52 (s, 1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ −1.6, 16.7, 24.1, 27.6, 32.0, 33.1, 36.0, 40.1, 42.3, 42.4, 43.9, 46.6, 62.0, 65.4, 69.2, 79.5, 119.9, 121.3, 125.1, 126.9, 127.2, 127.3, 128.4, 140.6, 143.8, 144.8, 155.9, 170.1, 171.5, 172.7, 173.4; MALDI HRMS calcd for $C_{54}H_{63}N_3O_8SiNa$ (M+Na)$^+$: 932.4282; found: 932.4277.

2.3.20. Fmoc-(*S*)β^{2}hAsn(Trt)-(*S*)β^{2}hGlu(O^{t}Bu)-OH (11). The *C*-terminus of dipeptide derivative **24** (1.15 g, 1.27 mmol) was deprotected according to GP6; however, considerable amounts of Fmoc-deprotection took place during the reaction. For this reason, the crude reaction mixture was evaporated under reduced pressure and treated in situ with FmocOSu (1.2 equiv.) according to GP4. The crude product was purified by FC (AcOEt/CH$_2$Cl$_2$ 1:7→1:3) to give **11** (0.74 g, 72%) as an amorphous solid. R_f=0.23 (AcOEt/hexane 1:1); $[\alpha]_D$=−11.2 (*c*=0.75, CHCl$_3$); IR (CHCl$_3$) ν_{max} 3426 (w), 3343 (w), 3015 (w), 2985 (w), 1718 (s), 1677 (m), 1508 (m), 1492 (m), 1446 (w), 1369 (w), 1246 (m), 1154 (m) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.35 (s, 9H, ^{t}Bu), 1.62–1.74 (m, 2H, C*H*$_2$CH$_2$CO), 2.11–2.25 (m, 2H, CH$_2$CO), 2.28–2.32 (m, 1H, CHCO), 2.43–2.48 (m, 1H, CHCO), 2.55–2.60 (m, 1H, CH*H*CON), 2.72–2.78 (m, 1H, C*H*HCON), 2.99–3.06 (m, 1H, CH*H*N), 3.07–3.14 (m, 2H, CH$_2$N), 3.35–3.41 (m, 1H, C*H*HN), 4.19–4.29 (m, 3H, OCH$_2$CH), 7.13–7.42 (m, 21H, 19 arom., 2×NH), 7.68 (d, *J*=6.0 Hz, 2H, arom.), 7.88 (d, *J*=5.8 Hz, 2H, arom.),

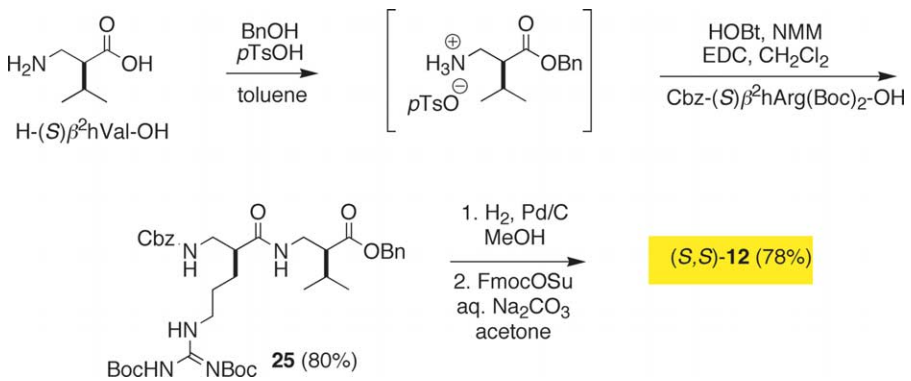

Figure 31. Preparation of Fmoc-(*S*)β^{2}hArg(Boc)$_2$-(*S*)β^{2}hVal-OH (**8**).

8.53 (s, 1H, NH), 12.30 (br s, 1H, OH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.2, 27.6, 32.2, 36.1, 40.0, 42.4, 42.4, 43.8, 46.6, 65.4, 69.2, 79.5, 120.0, 125.1, 126.2, 127.0, 127.3, 127.5, 128.4, 140.6, 143.8, 144.8, 156.0, 170.1, 171.6, 172.7, 175.0; MALDI HRMS calcd for $C_{49}H_{51}N_3O_8Na$ $(M+Na)^+$: 832.3598; found: 832.3568 (Fig. 30).

2.3.21. Cbz-(*S*)β^{2}hArg(Boc)$_2$-(*S*)β^{2}hVal-OBn (25). H-(*S*)β^{2}hVal-OH[89] was dissolved in toluene, BnOH and *p*TsOH were added and mixture was refluxed for 18 h using a Dean–Stark trap to azeotropically remove H_2O. The reaction mixture was cooled to 25 °C, and the toluene removed under reduced pressure. The crude product was purified by recrystallization from toluene/hexane to give the *p*TsOH-salt of H-(*S*)β^{2}hVal-OBn (0.72 g, 1.82 mmol) which was coupled with Cbz-(*S*)β^{2}hArg(Boc)$_2$-OH[48] (0.95 g, 1.82 mmol) according to GP1b. FC (AcOEt/hexane 3:7) yielded **25** (1.06 g, 80%) as white solid; mp 45–47 °C; R_f=0.22 (AcOEt/hexane 1:1); $[\alpha]_D$=+16.8 (c=0.37, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3446 (w), 3328 (w), 3007 (m), 2974 (m), 2933 (w), 1719 (s), 1636 (s), 1615 (s), 1574 (m), 1509 (m), 1418 (m), 1369 (m), 1332 (m), 1282 (m), 1136 (s), 1051 (m), 1027 (m), 872(w), 648(w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (d, J=6.8 Hz, 3H, Me), 0.94 (d, J=6.8 Hz, 3H, Me), 1.41 (m, 2H, CH_2), 1.47 (s, 9H, ^{t}Bu), 1.49 (s, 9H, ^{t}Bu), 1.55 (m, 1H, C*H*H), 1.78 (m, 1H, CH*H*), 1.93 (m, 1H, C*H*(Me)$_2$), 2.47 (m, 1H, CHCO), 2.50 (m, 1H, CHCO), 3.21–3.38 (m, 5H, 2×CH_2 and C*H*H), 3.60 (m, 1H, CH*H*), 5.04 (d, J=12.2 Hz, 1H, OC*H*HPh), 5.08 (s, 2H, OCH_2Ph), 5.15 (d, J=12.2 Hz, 1H, OCH*H*Ph), 5.32 (br s, 1H, NH), 6.30 (br s, 1H, NH), 7.28–7.52 (m, 10H, arom.), 8.32 (br s, 1H, NH), 11.48 (br s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 20.3, 26.6, 27.1, 28.1, 28.3, 28.9, 31.3, 38.8, 40.1, 42.8, 45.8, 51.9, 66.3, 66.6, 79.3, 83.2, 128.0, 128.1, 128.4, 128.5, 128.6, 135.8, 136.6, 153.3, 156.3, 156.6, 163.4, 174.2, 174.4; MALDI HRMS calcd for $C_{38}H_{55}N_5O_9Na$ $(M+Na)^+$: 748.3892; found: 748.3901. Anal. calcd for $C_{38}H_{55}N_5O_9$: C 62.88, H 7.64, N 9.65; found: C 62.92, H 7.68, N 9.51.

2.3.22. Fmoc-(*S*)β^{2}hArg(Boc)$_2$-(*S*)β^{2}hVal-OH (12). Dipeptide derivative **25** (1.06 g) was hydrogenated according to GP2. Subsequent Fmoc-protection according to GP4 and FC (AcOEt/hexane 1:1→1:0) yielded **12** (0.99 g, 78%) as white solid; mp 93–96 °C; R_f=0.46 (AcOEt/hexane/AcOH 10:10:1); $[\alpha]_D$=+29.3 (c=0.91, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3446 (w), 3326 (w), 3007 (m), 2972 (m), 2934 (m), 1719 (s), 1643 (s), 1615 (s), 1513 (m), 1450 (m), 1416 (m), 1369 (m), 1333 (m), 1282 (m), 1138 (s), 1053 (m), 872 (w), 650 (w) cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.87 (d, J=6.8 Hz, 3H, Me), 0.91 (d, J=6.8 Hz, 3H, Me), 1.35–1.61 (m, 4H, CH_2CH_2), 1.39 (s, 9H, ^{t}Bu), 1.46 (s, 9H, ^{t}Bu), 1.79 (m, 1H, C*H*(Me)$_2$), 2.30 (m, 1H, CHCO), 2.38 (br s, 1H, NH), 2.49 (m, 1H, CH), 2.99–3.10 (m, 3H, C*H*H, CH_2), 3.23 (m, 2H, CH_2), 3.35 (m, 1H, CH*H*), 4.17–4.28 (m, 3H, $CHCH_2O$), 7.13–7.36 (m, 3H, 2 arom., NH), 7.41 (t, J=7.4 Hz, 2H, arom.), 7.68 (d, J=7.4 Hz, 2H, arom.), 7.88 (d, J=7.5 Hz, 2H, arom.), 7.94 (br s, 1H, NH), 8.24 (br s, 1H, NH), 11.48 (br s, 1H, COOH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.5, 19.7, 20.2, 20.9, 26.1, 26.2, 26.8, 27.5, 27.9, 28.0, 31.2, 38.7, 42.6, 78.0, 82.8, 109.6, 119.9, 121.3, 127.2, 128.8, 137.3, 139.3, 142.5, 152.0, 155.1, 163.0, 173.1, 173.2; MALDI HRMS calcd for $C_{38}H_{53}N_5O_9Na$ $(M+Na)^+$: 746.3736, found: 746.3728. Anal. calcd for $C_{38}H_{53}N_5O_9$: C 63.05, H 7.38, N 9.67; found: C 63.17, H 7.40, N 9.44 (Fig. 31).

2.4. Solid-phase synthesis of 2 and 3 and their ligation to eicosapeptide 1

2.4.1. H-β^{2}hGly-(*S*)β^{2}hTrp-(*S*)β^{2}hArg-(*S*)β^{2}hVal-(*S*)β^{2}hAsn-(*S*)β^{2}hGlu-(*R*,*S*)β^{2}hThr-(*R*)β^{2}hSer-(*S*)β^{2}hTyr-(*S*)β^{2}hAla-*S*-Ethylpropionate (2). The loading of the sulfamylbutyryl resin was performed according to a procedure found in the literature.[90] A solution of Fmoc-(*S*)β^{2}hTyr(^{t}Bu)-(*S*)β^{2}hAla-OH (**9**) (502 mg, 0.9 mmol), DIPCDI (0.5 mL, 3.6 mmol) and 1-MeIm (0.2 mL, 3.6 mmol) in CH_2Cl_2/DMF (4:1) was added to the resin (205 mg, 0.225 mmol) that had been preswelled in CH_2Cl_2 for 1 h. The suspension was gently stirred using Ar bubbling for 18 h at 25 °C. Consequently, the resin was filtered off, washed with DMF (4 mL, 4×1 min), CH_2Cl_2 (4 mL, 4×1 min), and dried under h.v. overnight. Resin loading was measured using the absorbance of the benzofulvene–piperidine adduct according to Schreiber and Seebach[80] and was determined to be 0.66 mmol/g, which corresponds to 0.133 mmol of **9**. The Fmoc group was removed using 20% piperidine in DMF (4 mL, 4×10 min) under Ar bubbling. After filtration, the resin was washed with DMF (4mL, 4×1 min). Solid phase synthesis was continued by sequential incorporation of *N*-Fmoc-protected dipeptides or *N*-Fmoc protected β^2-homoamino acids building blocks (**10**, **11**, **12**, Fmoc-(*S*)β^{2}hTrp(Boc)-OH, Boc-β^{2}hGly-OH). For each coupling step, the resin was treated with a solution of Fmoc-protected building block (3 equiv.), HATU (2.9 equiv.) and DIPEA (6 equiv.) in DMF. The suspension was then gently stirred using Ar bubbling for 45–60 min. Monitoring of the coupling reaction was performed with TNBS.[91] In the case of a positive TNBS test (indicating incomplete coupling), the suspension was filtrated, and treated again with a freshly prepared solution of the same *N*-Fmoc protected building block (2 equiv.) and coupling reagents. The resin was then filtered off and washed with DMF (4 mL, 4×1 min) prior to the subsequent Fmoc deprotection step using 20% piperidine in DMF (4 mL, 4×10 min). After filtration, the resin was washed with DMF (4 mL, 3×1 min) and solid-phase synthesis was continued by sequential incorporation of *N*-Fmoc protected building blocks. For each coupling step, the resin was treated as described above. After the last coupling the resin was filtered off, washed with DMF (4 mL, 4×1 min), CH_2Cl_2 (4 mL, 4×1 min), and activated for the cleavage according to Ingenito et al.[68] After swelling the resin in THF (4 mL), a solution of TMS–CHN_2 (2 M in hexane) was added, and the suspension was gently stirred using Ar bubbling for 2 h. Subsequently, the resin was filtered off, washed with THF (4 mL, 4×1 min) and DMF (4 mL, 4×1 min), to prepare it for the displacement reaction. The activated *N*-acylsulfonamide resin was swollen in DMF and filtered off. A solution of ethyl-3-mercaptopropionate (0.86 mL, 6.65 mmol) and sodium thiophenolate (9 mg, 0.066 mmol) in DMF (5 mL) was added and the resulting mixture heated at 80 °C for 24 h. Removal of side-chain protecting groups was accomplished in solution by treating the protected β-peptide thioester with a solution of TFA/H_2O/TIS

(95/2.5/2.5). The solvents were removed under reduced pressure and the precipitate, which formed upon addition of cold Et_2O to the oily residue, was collected by centrifugation. Purification by RP-HPLC (10–50% B in 50 min, C_8) yielded **2** (10 mg, 10%) as a colorless fluffy solid. Anal. RP-HPLC: t_R 28.34 (10–40% B in 50 min, 40–95% B in 10 min C_8). CD (0.2 mM in MeOH, 20 °C): −11387.9 (219.5 nm); 0 (210 nm); +9643.96 (204 nm); CD (0.2 mM in MeOH, −10 °C): −17955.4 (216 nm); 0 (206.5 nm);+1895.45 (205 nm). ESI MS (positive mode): 1437.9 (15, $(M+H)^+$), 730.5 (40, $(M+Na+H)^{2+}$), 719.7 (100, $(M+2H)^{2+}$), 480.0 (32, $(M+3H)^{3+}$).

2.4.2. H-(*S*)β²hCys-(*S*)β²hGln-(*S*,*S*)β²hIle-(*S*)β²hLys-(*S*)β²hHis-(*S*)β²hLeu-(*S*)β²hAsp-(*S*)β²hMet-(*S*)β²hPhe-(*S*)β²hPro-OH (3). Esterification of the Wang resin was performed according to Chan and White.[71]To a soln. of Fmoc-(*S*)β²hPhe-(*S*)β²hPro-OH (**4**) (461 mg, 0.9 mmol) in dry CH_2Cl_2 (4 mL) was added 1-MeIm (0.05 mL, 0.675 mmol) followed by MSNT (267 mg, 0.90 mmol). The mixture was stirred until all MSNT had dissolved. The solution was then transferred to a vessel containing the preswelled resin (200 mg, 0.18 mmol), and mixed under Ar bubbling for 1 h at 25 °C. The resin was then filtered off, washed with DMF (4 mL, 4×1 min), CH_2Cl_2 (4 mL, 4×1min), and dried under h.v. overnight. The loading of the resin was determined by measuring the absorbance of the benzofulvene–piperidine adduct according to Schreiber and Seebach[80] and was found to be 0.61 mmol/g (68%), corresponding to 0.122 mmol of anchored **4**. The unreacted hydroxy groups were capped using Ac_2O (0.12 mL, 1.22 mmol) in DMF (4 mL) and DMAP (5 mg, 0.04 mmol, added in 0.5 mL DMF) for 30 min. The Fmoc group was removed using 20% piperidine in DMF (4 mL, 4×10 min) under Ar bubbling. After filtration, the resin was washed with DMF (4 mL, 4×1 min). Solid-phase synthesis was continued by sequential incorporation of *N*-Fmoc-protected dipeptides building blocks (**5**, **6**, **7**, **8**). For each coupling step, the resin was treated with a solution of Fmoc building block (3 equiv.), HATU (2.9 equiv.) and DIPEA (6 equiv.) in DMF. The suspension was then gently stirred using Ar bubbling for 45–60 min. Monitoring of the coupling reaction was performed with TNBS.[91] In the case of a positive TNBS test (indicating incomplete coupling), the suspension was filtered, and treated again with a freshly prepared solution of the same *N*-Fmoc protected building blocks (2 equiv.) and coupling reagents. The resin was then filtered off and washed with DMF (4 mL, 4×1 min) prior to the subsequent Fmoc deprotection step using 20% piperidine in DMF (4 mL, 4×10 min). After filtration, the resin was washed with DMF (4 mL, 3×1 min) and solid-phase synthesis was continued by sequential incorporation of *N*-Fmoc protected building block. For each coupling step, the resin was treated as described above. After the last coupling the resin was filtered off, washed with DMF (4 mL, 4×1 min), CH_2Cl_2 (4 mL, 4×1 min), MeOH (4 mL, 4×1 min) and dried under h.v. for 24 h. The dry peptide resin was treated for 2 h with a TFA/H_2-O/EDT/TIS (94:2.5:2.5:1) solution (10 mL). The resin was removed by filtration, washed with TFA, and the organic phase containing the peptide was concentrated under reduced pressure. The precipitate, which formed upon addition of cold Et_2O to the oily residue, was collected by centrifugation. The crude peptide was purified by RP-HPLC (15–50% B in 40 min, 50–95% B in 20 min, C_8) to yield the TFA salt of **3** (65 mg, 38%) as a colorless fluffy solid. Homogeneity >95% (RP-HPLC). Anal. RP-HPLC: t_R 28.44 (10–40% B in 40 min, 40–95% B in 5 min, C_8). CD (0.2 mM in MeOH, 20 °C): −13128.5 (219 nm); 0 (207.5 nm);+14495.7 (200.5 nm); CD (0.2 mM in MeOH, −10 °C): −15643.1 (218.5 nm); 0 (206 nm);+16894.2 (199.5 nm). ESI HRMS (positive mode): 708.3576 (100, $(M+2Na)^{2+}$, $C_{65}H_{106}N_{14}Na_2O_{14}S_2^{2+}$; calcd 708.3625), 697.3718 (70, $(M+H+Na)^{2+}$, $C_{65}H_{107}N_{14}NaO_{14}S_2^{2+}$; calcd 697.3715), 686.3795 (10, $(M+2H)^{2+}$, $C_{65}H_{108}N_{14}O_{14}S_2^{2+}$; calcd 686.3805).

2.4.3. H-β²hGly-(*S*)β²hTrp-(*S*)β²hArg-(*S*)β²hVal-(*S*)β²hAsn-(*S*)β²hGlu-(*R*,*S*)β²hThr-(*R*)β²hSer-(*S*)β²hTyr-(*S*)β²hAla-(*S*)β²hCys-(*S*)β²hGln-(*S*,*S*)β²hIle-(*S*)β²hLys-(*S*)β²hHis-(*S*)β²hLeu-(*S*)β²hAsp-(*S*)β²hMet-(*S*)β²Phe-(*S*)β²hPro-OH (1). β²-Peptide fragment **3** (5.2 mg, 3.1 μmol) and the *C*-terminal thioester β²-peptide **2** (4.8 mg, 3.1 μmol) were ligated in an aqueous buffer (100 mM phosphate, pH 7.5) (3 mL) containing thiophenol (4% v/v). The ligation reaction was performed at 25 °C and monitored using anal. RP-HPLC (see Fig. 21 above). Following completion of the ligation, the reaction mixture was diluted with H_2O (1 mL) containing 0.1% TFA and purified by preparative RP-HPLC (10–50% B in 40 min, 50–99% B in 10 min, C_8) to yield the TFA salt of **1** (5.12 mg, 54%) as a colorless fluffy solid. Anal. RP-HPLC: t_R 36.82 (10–50% B in 40 min, 50–99% B in 10 min, C_8). CD (0.2 mM in MeOH): −16849.8 (214 nm); 0 (200 nm); CD (0.2 mM in H_2O, pH 7): −1863.85 (220 nm); 0 (214.5 nm);+15824.65 (201.5 nm). MALDI HRMS: 2697.428 (10, $(M+Na)^+$, $C_{127}H_{199}N_{29}NaO_{30}S_2^+$; calcd 2697.428), 2675.442 (60, $(M+H)^+$, $C_{127}H_{199}N_{29}O_{30}S_2^+$; calcd 2675.445).

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References and notes

1. Seebach, D. *Chimia* **2000**, *54*, 751–758.
2. Seebach, D. On the occasion of the 10 year anniversary LONZA Japan on October 5, 1990, in Tokyo Nohrin Nenkin Kaikan, PastoraleLonza Brochure, Lonza Ltd. Basel, 1990.
3. Seebach, D. *Aldrichim. Acta* **1992**, *25*, 59–66.
4. Seebach, D.; Geiss, K. H.; Kolb, M.; Beck, A. K. *Modern*

Synthetic Methods, Scheffold, R., Ed.; Sauerländer, AG: Aarau, 1976; Vol. 1, pp 173–299.
5. Gfeller, J. C.; Beck, A. K.; Seebach, D. *Helv. Chim. Acta* **1980**, *63*, 728–732.
6. Seebach, D.; Bossler, H.; Gründler, H.; Shoda, S.-i.; Wenger, R. *Helv. Chim. Acta* **1991**, *74*, 197–224.
7. Köck, M.; Kessler, H.; Seebach, D.; Thaler, A. *J. Am. Chem. Soc.* **1992**, *114*, 2676–2686.
8. Seebach, D.; Beck, A. K.; Bossler, H.; Gerber, C.; Ko, S. Y.; Murtiashaw, C. W.; Naef, R.; Shoda, S.-i.; Thaler, A.; Krieger, U.; Wenger, R. *Helv. Chim. Acta* **1993**, *76*, 1564–1590.
9. Seebach, D.; Bossler, H.; Flowers, R.; Arnett, E. M. *Helv. Chim. Acta* **1994**, *77*, 291–305.
10. Seebach, D.; Beck, A. K.; Studer, A. *Modern Synthetic Methods*, Ernst, B., Leumann, C., Eds.; VHCA Verlag Helvetica Chimica Acta/VCH: Basel/Weinheim, 1995; Vol. 7, pp 1–178.
11. Miller, S. A.; Griffiths, S. L.; Seebach, D. *Helv. Chim. Acta* **1993**, *76*, 563–595.
12. Seebach, D.; Bezençon, O.; Jaun, B.; Pietzonka, T.; Matthews, J. L.; Kühnle, F. N. M.; Schweizer, W. B. *Helv. Chim. Acta* **1996**, *79*, 588–608.
13. Seebach, D.; Thaler, A.; Beck, A. K. *Helv. Chim. Acta* **1989**, *72*, 857–867.
14. Thaler, A.; Seebach, D.; Cardinaux, F. *Helv. Chim. Acta* **1991**, *74*, 628–643.
15. Seebach, D.; Ko, S. Y.; Kessler, H.; Köck, M.; Reggelin, M.; Schmieder, P.; Walkinshaw, M. D.; Bölsterli, J. J.; Bevec, D. *Helv. Chim. Acta* **1991**, *74*, 1953–1990.
16. Bürger, H. M.; Seebach, D. *Angew. Chem.* **1994**, *106*, 459–460, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 442–444.
17. Matt, T.; Seebach, D. *Helv. Chim. Acta* **1998**, *81*, 1845–1895.
18. Seebach, D.; Charczuk, R.; Gerber, C.; Renaud, P.; Berner, H.; Schneider, H. *Helv. Chim. Acta* **1989**, *72*, 401–425.
19. Podlech, J.; Seebach, D. *Angew. Chem.* **1995**, *107*, 507–509, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 471–472.
20. Guibourdenche, C.; Podlech, J.; Seebach, D. *Liebigs Ann.* **1996**, 1121–1129.
21. Guibourdenche, C.; Seebach, D.; Natt, F. *Helv. Chim. Acta* **1997**, *80*, 1–13.
22. Seebach, D.; Wasmuth, D. *Helv. Chim. Acta* **1980**, *63*, 197–200.
23. Seebach, D.; Aebi, J. D.; Wasmuth, D. *Org. Synth.* **1985**, *63*, 109–120.
24. Seebach, D.; Wasmuth, D. *Angew. Chem.* **1981**, *93*, 1007–1008, *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 971–972.
25. Aebi, J. D.; Seebach, D. *Helv. Chim. Acta* **1985**, *68*, 1507–1518.
26. Estermann, H.; Seebach, D. *Helv. Chim. Acta* **1988**, *71*, 1824–1839.
27. Seebach, D.; Sifferlen, T.; Bierbaum, D. J.; Rueping, M.; Jaun, B.; Schweizer, W. B.; Schaefer, J.; Mehta, A. K.; O'Connor, R. D.; Meier, B. H.; Ernst, M.; Glättli, A. *Helv. Chim. Acta* **2002**, *85*, 2877–2917.
28. Seebach, D.; Beck, A. K.; Bierbaum, D. J. *Chem. Biodiversity* **2004**. in press.
29. Laube, T.; Dunitz, J. D.; Seebach, D. *Helv. Chim. Acta* **1985**, *68*, 1373–1393.
30. Seebach, D.; Sting, A. R.; Hoffmann, M. *Angew. Chem.* **1996**, *108*, 2880–2921, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2708–2748.
31. Seebach, D.; Boog, A.; Schweizer, W. B. *Eur. J. Org. Chem.* **1999**, 335–360.
32. Seebach, D.; Fritz, M. G. *Int. J. Biol. Macromol.* **1999**, *25*, 217–236.
33. Gademann, K.; Häne, A.; Rueping, M.; Jaun, B.; Seebach, D. *Angew. Chem.* **2003**, *115*, 1573–1575, *Angew. Chem. Int. Ed.* **2003**, *42*, 1534–1537.
34. Claridge, T. D. W.; Goodman, J. M.; Moreno, A.; Angus, D.; Barker, S. F.; Taillefumier, C.; Watterson, M. P.; Fleet, G. W. J. *Tetrahedron Lett.* **2001**, *42*, 4251–4255.
35. Seebach, D.; Gademann, K.; Schreiber, J. V.; Matthews, J. L.; Hintermann, T.; Jaun, B.; Oberer, L.; Hommel, U.; Widmer, H. *Helv. Chim. Acta* **1997**, *80*, 2033–2038.
36. Appella, D. H.; Christianson, L. A.; Klein, D. A.; Powell, D. R.; Huang, X. L.; Barchi, J. J.; Gellman, S. H. *Nature* **1997**, *387*, 381–384.
37. Seebach, D.; Overhand, M.; Kühnle, F. N. M.; Martinoni, B.; Oberer, L.; Hommel, U.; Widmer, H. *Helv. Chim. Acta* **1996**, *79*, 913–941.
38. Appella, D. H.; Christianson, L. A.; Karle, I. L.; Powell, D. R.; Gellman, S. H. *J. Am. Chem. Soc.* **1996**, *118*, 13071–13072.
39. Seebach, D.; Abele, S.; Gademann, K.; Jaun, B. *Angew. Chem.* **1999**, *111*, 1700–1703, *Angew. Chem. Int. Ed.* **1999**, *38*, 1595–1597.
40. Daura, X.; Gademann, K.; Jaun, B.; Seebach, D.; van Gunsteren, W. F.; Mark, A. E. *Angew. Chem.* **1999**, *111*, 249–253, *Angew. Chem. Int. Ed.* **1999**, *38*, 236–240.
41. Frackenpohl, J.; Arvidsson, P. I.; Schreiber, J. V.; Seebach, D. *ChemBioChem* **2001**, *2*, 445–455.
42. Wiegand, H.; Wirz, B.; Schweitzer, A.; Camenisch, G. P.; Perez, M. I. R.; Gross, G.; Woessner, R.; Voges, R.; Arvidsson, P. I.; Frackenpohl, J.; Seebach, D. *Biopharm. Drug Dispos.* **2002**, *23*, 251–262.
43. Wiegand, H.; Puls, K. L.; Hoyer, D.; Kimmerlin, T.; Sebesta, R.; Seebach, J. D.; Baumann, B. C.; Seebach, D., hitherto unpublished results: Novartis Pharma AG, Basel, ETH Zürich and Medical School of Zürich University.
44. Greenhow, D.; Perry, S.; Lind, R.; Kimmerlin, T.; Seebach, D., hitherto unpublished results: Syngenta (GB Jealotts Hill) and ETH Zürich.
45. Schreiber, J. V.; Frackenpohl, J.; Moser, F.; Fleischmann, T.; Kohler, H. P.; Seebach, D. *ChemBioChem* **2002**, *3*, 424–432.
46. Gademann, K.; Kimmerlin, T.; Hoyer, D.; Seebach, D. *J. Med. Chem.* **2001**, *44*, 2460–2468.
47. Nunn, C.; Rueping, M.; Langenegger, D.; Schuepbach, E.; Kimmerlin, T.; Micuch, P.; Hurth, K.; Seebach, D.; Hoyer, D. *Naunyn-Schmiedeberg's Arch. Pharmacol.* **2003**, *367*, 95–103.
48. Seebach, D.; Namoto, K.; Mahajan, Y. R.; Bindschädler, P.; Sustmann, R.; Kirsch, M.; Ryder, N. S.; Weiss, M.; Sauer, M.; Roth, C.; Werner, S.; Beer, H.-D.; Munding, C.; Walde, P.; Voser, M. *Chem. Biodiversity* **2004**, *1*, 65–97.
49. Rossi, F.; Lelais, G.; Seebach, D. *Helv. Chim. Acta* **2003**, *86*, 2653–2661.
50. Gaul, C.; Schweizer, B. W.; Seiler, P.; Seebach, D. *Helv. Chim. Acta* **2002**, *85*, 1546–1566.
51. Brenner, M.; La Vecchia, L.; Leutert, T.; Seebach, D. *Org. Synth.* **2003**, *80*, 57–65.
52. Hintermann, T.; Seebach, D. *Helv. Chim. Acta* **1998**, *81*, 2093–2126.
53. Micuch, P.; Seebach, D. *Helv. Chim. Acta* **2002**, *85*, 1567–1577.
54. Seebach, D.; Schaeffer, L.; Gessier, F.; Bindschädler, P.; Jäger, C.; Josien, D.; Kopp, S.; Lelais, G.; Mahajan, Y. R.;

Micuch, P.; Sebesta, R.; Schweizer, B. W. *Helv. Chim. Acta* **2003**, *86*, 1852–1861.
55. Sebesta, R.; Seebach, D. *Helv. Chim. Acta* **2003**, *86*, 4061–4072.
56. Lelais, G.; Campo, M. A.; Seebach, D. *Helv. Chim. Acta* **2004**, 1545–1560.
57. Lelais, G.; Micuch, P.; Josien, D.; Rossi, F.; Seebach, D. *Helv. Chim. Acta* **2004**. in press.
58. Kimmerlin, T.; Seebach, D.; Hilvert, D. *Helv. Chim. Acta* **2002**, *85*, 1812–1826.
59. Kimmerlin, T.; Seebach, D. *Helv. Chim. Acta* **2004**. in press.
60. Aurora, R.; Rose, G. D. *Prot. Sci.* **1998**, *7*, 21–38.
61. Kimmerlin, T.; Seebach, D. *Helv. Chim. Acta* **2003**, *86*, 2098–2103.
62. Seebach, D.; Kimmerlin, T.; Jaun, B.; Mathad, R.; Wüthrich, K.; Hilty, C. Unpublished results, ETH Zürich.
63. Guichard, G.; Seebach, D. *Chimia* **1997**, *51*, 315–318.
64. Hintermann, T.; Seebach, D. *Synlett* **1997**, 437–438.
65. Seebach, D.; Abele, S.; Gademann, K.; Guichard, G.; Hintermann, T.; Jaun, B.; Matthews, J. L.; Schreiber, J. V.; Oberer, L.; Hommel, U.; Widmer, H. *Helv. Chim. Acta* **1998**, *81*, 932–982.
66. Seebach, D.; Schreiber, J. V.; Abele, S.; Daura, X.; van Gunsteren, W. F. *Helv. Chim. Acta* **2000**, *83*, 34–57.
67. Hart, A.; Bahador, A. B. F.; Matthews, E. E.; Qui, X. J.; Schepartz, A. *J. Am. Chem. Soc.* **2003**, *125*, 4022–4023.
68. Ingenito, R.; Bianchi, E.; Fattori, D.; Pessi, A. *J. Am. Chem. Soc* **1999**, *121*, 11369–11374.
69. Chung, Y. J.; Huck, B. R.; Christianson, L. A.; Stanger, H. E.; Krauthäuser, S.; Powell, D. R.; Gellman, S. H. *J. Am. Chem. Soc.* **2000**, *122*, 3995–4004, correction: *J. Am. Chem. Soc.* **2001**, *123*, 5851.
70. Böhm, A.; Seebach, D. *Helv. Chim. Acta* **2000**, *83*, 3262–3278.
71. Chan, W. C.; White, P. D. In *Fmoc Solid Phase Peptide Synthesis: A Practical Approach*. Chan, W. C., White, P. D., Eds.; Oxford University Press: Oxford, 2000; pp 41–74.
72. Jones, J. H. *J. Pept. Sci.* **2003**, *9*, 1–8.
73. Backes, B. J.; Ellman, J. A. *J. Org. Chem.* **1999**, *64*, 2322–2330.
74. Kenner, G. W.; McDermott, J. R.; Sheppard, R. C. *J. Chem. Soc.,Chem. Commun.* **1971**, 636–637.
75. Quaderer, R.; Hilvert, D. *Org. Lett.* **2001**, *3*, 3181–3184.
76. Thaler, A.; Seebach, D.; Cardinaux, F. *Helv. Chim. Acta* **1991**, *74*, 617–627.
77. Dawson, P. E.; Kent, S. B. H. *Annu. Rev. Biochem.* **2000**, *69*, 923–960.
78. Tam, J. P.; Yu, Q.; Miao, Z. *Biopolymers* **2000**, *51*, 311–332.
79. Dawson, P. E.; Churchill, M. J.; Ghadiri, M. R.; Kent, S. B. H. *J. Am. Chem. Soc.* **1996**, *119*, 4325–4329.
80. Schreiber, J. V.; Seebach, D. *Helv. Chim. Acta* **2000**, *83*, 3139–3152.
81. Seebach, D.; Schreiber, J. V.; Arvidsson, P. I.; Frackenpohl, J. *Helv. Chim. Acta* **2001**, *84*, 271–279.
82. Etezady-Esfarjani, T.; Hilty, C.; Wüthrich, K.; Rueping, M.; Schreiber, J. V.; Seebach, D. *Helv. Chim. Acta* **2002**, *85*, 1197–1209.
83. Cheng, R. P.; DeGrado, W. F. *J. Am. Chem. Soc.* **2002**, *124*, 11564–11565.
84. Abele, S. Dissertation, ETH-Zürich, No. 13203.
85. Langenhan, J. M.; Gellman, S. H. *Org. Lett.* **2004**, *6*, 937–940.
86. Seebach, D.; Schaeffer, L.; Brenner, M.; Hoyer, D. *Angew. Chem.* **2003**, *115*, 730–736, *Angew. Chem. Int. Ed.* **2003**, *115*, 776–778.
87. Arvanitis, E.; Ernst, H.; Ludwig, A. A.; Robinson, A. J.; Wyatt, P. B. *J. Chem. Soc., Perkin Trans. 1* **1998**, 521–528.
88. Abele, S.; Vögtli, K.; Seebach, D. *Helv. Chim. Acta* **1999**, *82*, 1539–1558.
89. Guichard, G.; Abele, S.; Seebach, D. *Helv. Chim. Acta* **1998**, *81*, 187–206.
90. Calbiochem-Novabiochem; Resins, S.B. S.-C. Novabiochem Inovation 4/99, 1999.
91. Hancock, W. S.; Battersby, J. E. *Anal. Biochem.* **1976**, *71*, 260–264.

Further Reading

List of Publications

1. Seebach, D. Diplomarbeit, Zur Reaktion von Bleitetraacetat mit 1,1-Diphenyl-2-hydroperoxy-propiomesitylen, Technische Hochschule Karlsruhe, 1961.
2. Seebach, D. Dissertation, 2.5-Dihydro-Furan-Peroxyde, Technische Hochschule Karlsruhe, 1964.
3. Criegee, R.; Seebach, D. Ein Bishydroperoxyd mit ungewöhnlicher Bildungstendenz. *Chem. Ber.* **1963**, *96*, 2704–2711.
4. Seebach, D. Die Reaktion von 2.5-Dimethyl-furan mit Wasserstoffperoxyd. *Chem. Ber.* **1963**, *96*, 2712–2722.
5. Seebach, D. Die Reaktion von Pentamethylpyrrol mit Wasserstoffperoxyd. *Chem. Ber.* **1963**, *96*, 2723–2729.
6. Criegee, R.; Zirngibl, U.; Furrer, H.; Seebach, D.; Freund, G. Photosynthese substituierter Cyclobutene. *Chem. Ber.* **1964**, *97*, 2942–2948.
7. Seebach, D. Über ein sehr labiles Bicyclo(2.2.0)hexen-Derivat. *Chem. Ber.* **1964**, *97*, 2953–2958.
8. Seebach, D. Gespannte polycyclische Systeme aus Drei-und Vierring-Bausteinen. *Angew. Chem.* **1965**, *77*, 119–129, *Angew. Chem. Int. Ed. Engl.* **1965**, *4*, 121–131.
9. Criegee, R.; Kristinsson, H.; Seebach, D.; Zanker, F. Eine neuartige Synthese von Bicyclo(2.2.0)hexen-(2)-Derivaten. *Chem. Ber.* **1965**, *98*, 2331–2338.
10. Criegee, R.; Seebach, D.; Winter, R. E.; Börretzen, B.; Brune, H.-A. Valenzisomerisierungen von Cyclobutenen. *Chem. Ber.* **1965**, *98*, 2339–2352.
11. Corey, E. J.; Seebach, D. Carbanionen der 1,3-Dithiane, Reagentien zur C–C-Verknüpfung durch nucleophile Substitution oder Carbonyl-Addition. *Angew. Chem.* **1965**, *77*, 1134–1135, *Angew. Chem. Int. Ed. Engl.* **1965**, *4*, 1075–1077.
12. Corey, E. J.; Seebach, D. Synthese von 1,*n*-Dicarbonylverbindungen mit Carbanionen der 1,3-Dithiane. *Angew. Chem.* **1965**, *77*, 1135–1136, *Angew. Chem. Int. Ed. Engl.* **1965**, *4*, 1077–1078.
13. Corey, E. J.; Seebach, D. Phenylthiomethyllithium and Bis(phenylthio)methyllithium. *J. Org. Chem.* **1966**, *31*, 4097–4099.
14. Seebach, D.; Erickson, B. W.; Singh, G. Synthesis of 1-Deuterioaldehydes. Benzaldehyde-1-d. *J. Org. Chem.* **1966**, *31*, 4303–4304.
15. Corey, E. J.; Seebach, D.; Freedmann, R. Synthesis of α-silyl ketones via 1,3-dithianes. *J. Am. Chem. Soc.* **1967**, *89*, 434–436.
16. Seebach, D. Metallierte Ortho-trithioameisensäureester.

Angew. Chem. **1967**, *79*, 468–469, *Angew. Chem. Int. Ed. Engl.* **1967**, *6*, 442–443.
17. Seebach, D. Bis(phenylthio)carben. *Angew. Chem.* **1967**, *79*, 469–470, *Angew. Chem. Int. Ed. Engl.* **1967**, *6*, 443–444.
18. Seebach, D.; Jones, N. R.; Corey, E. J. A new synthetic route to cyclic mono- and diketone derivatives via bisthio carbanions. *J. Org. Chem.* **1967**, *33*, 300–305.
19. Seebach, D.; Graf, B. 1-Methyl-2,3,4-trimethylen-cyclobutenid-ion. *Angew. Chem.* **1968**, *80*, 532–533, *Angew. Chem. Int. Ed. Engl.* **1968**, *7*, 538–539.
20. Crouse, D. M.; Seebach, D. Erzeugung und Reaktion von α-Li-N.N-Dimethyl-acetamid und-propion-amid und von α-Li-Acetonitril. *Chem. Ber.* **1968**, *101*, 3113–3121.
21. Seebach, D.; Steinmüller, D. Herstellung von (*S*)-(2-Methylbutyl)- und (*S*)-(sek.Butyl)-ketonen aus optisch aktivem 2-Methylbutanol nach der Dithian-Methode. *Angew. Chem.* **1968**, *80*, 617–618, *Angew. Chem. Int. Ed. Engl.* **1968**, *7*, 619–620.
22. Seebach, D.; Steinmüller, D.; Demuth, F. Synthese von (R)- und (S)-konfigurierten Aldehyden und Ketonen aus chiralen sek.-Alkylhalogeniden. *Angew. Chem.* **1968**, *80*, 618–619, *Angew. Chem. Int. Ed. Engl.* **1968**, *7*, 620–621.
23. Seebach, D. Die 'Woodward-Hoffmann-Regeln' Orbitalsymmetriebetrachtungen bei synchron ablaufenden Valenzisomerisierungen und Cycloadditionen. *Fortschritte der chemischen Forschung* **1968**, *11*, 177–215.
24. Seebach, D. Buchbesprechung: Carbonium Ions, an Introduction, von D. Bethell und V. Gold. *Angew. Chem.* **1969**, *81*, 125. *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 85.
25. Seebach, D.; Beck, A. K. Kinetic evidence for the existence of free bis(phenylthio)methylene in solution. *J. Am. Chem. Soc.* **1969**, *91*, 1540–1542.
26. Seebach, D.; Peleties, N. Mono-, Bis- und Tris(phenylseleno)methyllithium (selenstabilisierte Carbanionen). *Angew. Chem.* **1969**, *81*, 465–466, *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 450–451.
27. Seebach, D. Habilitationsschrift, Metallierte *ortho*-Trithioameisensäureester, Nachweis von freien Bis-(arylthio)-carbenen in Lösung, Selen-stabilisierte Carbanionen, Universität Karlsruhe (T.H.), Juli 1969.
28. Seebach, D. Methoden und Möglichkeiten der nucleophilen Acylierung. *Angew. Chem.* **1969**, *81*, 690–700, *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 639–649.
29. Seebach, D. Nucleophile Acylierung mit 2-Lithium-1,3-dithianen bzw.-1,3,5-trithianen. *Synthesis* **1969**, *1*, 17–36.
30. Seebach, D.; Dörr, H.; Bastani, B.; Ehrig, V. Asymmetrische Lösungsmittelkatalyse; 1,4-Bis(dimethylamino)-2,3-dimethoxybutan, ein neues chirales Medium. *Angew. Chem.* **1969**, *81*, 1002–1003, *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 982–983.
31. Seebach, D.; Leitz, H. F. 1,4-Addition von 2-Lithium-1,3-dithianen an substituierte ω-Nitrostyrole. *Angew. Chem.* **1969**, *81*, 1047–1048, *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 983–984.
32. Seebach, D.; Beck, A. K.; Stegmann, H. B. Tris(phenylthio)-methyl und Bis(phenylthio)methan durch Pyrolyse von Tetrakis-(phenylthio)methan und Hexakis(phenylthio)äthan. *Tetrahedron Lett.* **1970**, 1933–1936.
33. Corey, E. J.; Seebach, D. 1,3-Dithiane (*m*-dithiane). *Org. Synth.* **1970**, *72*, 74. Collect. Vol. VI, 1988, 556–559.
34. Seebach, D. Buchbesprechung: Modern Reactions in Organic Synthesis von C. J. Timmons. *Angew. Chem.* **1971**, *83*, 51. *Angew. Chem. Int. Ed. Engl.* **1971**, *10*, 82.
35. Seebach, D.; Daum, H. Asymmetric induction of photopinacolization in a chiral aminoether. *J. Am. Chem. Soc.* **1971**, *93*, 2795–2796.
36. Seebach, D. Methoden zur Herstellung und Umwandlung isocyclischer Vierring-Verbindungen. In *Methoden der Organischen Chemie* (Houben-Weyl), Herausgegeben von Eugen Müller, Georg Thieme: Stuttgart, 1971; Band IV/4. S. 1-443.
37. Seebach, D.; Beck, A. K.; Stegmann, H. B. Homolyse der Äthan-C–C-Bindung, Nachweis von Tris(phenylthio)methyl durch ^{13}C-Markierung. *Angew. Chem.* **1971**, *83*, 534–535, *Angew. Chem. Int. Ed. Engl.* **1971**, *10*, 500–501.
38. Seebach, D.; Leitz, H. F. Michael-Addition von metallierten Carbonsäureamiden an Nitrostyrole., Ein vereinfachter Zugang zu Tryptaminen. *Angew. Chem.* **1971**, *83*, 542–544, *Angew. Chem. Int. Ed. Engl.* **1971**, *10*, 501–503.
39. Seebach, D.; Beck, A. K. Aldehydes from *sym*-trithiane: *n*-pentadecanal. *Org. Synth.* **1971**, *51*, 39–43, Collect. Vol. VI, 1988, 869–872.
40. Seebach, D.; Beck, A. K. Cyclic ketones from 1,3-dithiane: cyclobutanone. *Org. Synth.* **1971**, *51*, 76–81, Collect. Vol. VI, 1988, 316-319.
41. Seebach, D.; Braun, M. Solvolyseversuche mit 7,7-Bis(alkylthio)norcaranen. Eine neue Methode der Homologisierung. *Angew. Chem.* **1972**, *84*, 60–61, *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 49–50.
42. Seebach, D.; Ehrig, V. Synthese des Lithiumenolates von (*S*)-(+)-sek.-Butyl-methyl-keton und Acylierung zu chiralen 1,3-Diketonen. *Angew. Chem.* **1972**, *84*, 107–108, *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 127–128.
43. Seebach, D. Buchbesprechung: Spektroskopie: Spektroskopische Methoden in der organischen Chemie von D. H. Williams und I. Fleming. *Chemie in unserer Zeit* **1972**, *6*, 31.
44. Seebach, D. Tris-phenylmercapto-methyllithium Ein ungewöhnliches Carbenoid. *Chem. Ber.* **1972**, *105*, 487–510.
45. Seebach, D. Neoklis Peleties, α-Phenylseleno-methyllithiumverbindungen. *Chem. Ber.* **1972**, *105*, 511–520.
46. Seebach, D.; Enders, D. C–C-Verknüpfungen in α-Stellung zum Stickstoff sekundärer Amine, Lithium-dimethylnitrosamin. *Angew. Chem.* **1972**, *84*, 350–351, *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 301–302.
47. Seebach, D.; Gröbel, B.-T.; Beck, A. K.; Braun, M.; Geiβ, K.-H. Ketenthioacetale durch 'Peterson-Carbonylolefinierung' mit metallierten Formyltrimethylsilyl-thioacetalen. *Angew. Chem.* **1972**, *84*, 476–477, *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 443–444.
48. Seebach, D.; Geiβ, K.-H.; Beck, A. K.; Graf, B.; Daum, H. Herstellung von Polyalkylmercapto- und Polyarylmercaptomethanen, -äthanen und -äthylenen aus metallierten Orthotrithioameisensäureestern. *Chem. Ber.* **1972**, *105*, 3280–3300.
49. Seebach, D.; Beck, A. K. Einfache Darstellung von Hexakis(organylthio)äthanen Pyrolyse von Hexakis(arylthio)äthanen, Hinweise auf eine C–C-Dissoziation. *Chem. Ber.* **1972**, *105*, 3892–3904.
50. Seebach, D.; Stegmann, H. B.; Scheffler, K.; Beck, A. K.; Geiβ, K.-H. ESR-Spektroskopischer Beweis für die C–C-Dissoziation von Hexakis- (organylthio)äthanen und die S–C-Dissoziation von Tetrakis(organylthio)- methanen, Tris-(organylthio)methyl-Radikale. *Chem. Ber.* **1972**, *105*, 3905–3914.
51. Seebach, D.; Enders, D. Metallierung am primären, sekundären und tertiären C-Atom offenkettiger und cyclischer

Nitrosamine. *Angew. Chem.* **1972**, *84*, 1186–1187, *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 1101–1102.
52. Seebach, D.; Enders, D. Reaktion metallierter Nitrosamine mit Nitrilen, Eine neue Methode zur Darstellung von v-Triazolen. *Angew. Chem.* **1972**, *84*, 1187. *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 1102–1103.
53. Seebach, D.; Kolb, M.; Gröbel, B.-T. 'Michael-artige' Addition an konjugierte Keten-thioacetale. *Angew. Chem.* **1973**, *85*, 42–43, *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 69–70.
54. Seebach, D.; Enders, D.; Renger, B.; Brügel, W. Isolierung und Identifizierung von v-Tetrazinderivaten aus dem Zerfall von Nitrosamin-Anionen. *Angew. Chem.* **1973**, *85*, 504. *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 495.
55. Seebach, D. Buchbesprechung: Organic Reactions and Orbital Symmetry von T. L. Gilchrist, R. C. Storr. *Angew. Chem.* **1973**, *85*, 594.
56. Seebach, D.; Kolb, M.; Gröbel, B.-T. Umsetzung metallierter Trimethylsilylformaldehyd-thioacetale mit Carbonylverbindungen Eine einfache Methode grosser Anwendungsbreite zur Herstellung von Keten-thioacetalen. *Chem. Ber.* **1973**, *106*, 2277–2290.
57. Seebach, D.; Braun, M.; Du Preez, N. Ringöffnung von Cyclopropanon Bis-methylthio-Acetalen zu Ketonen und Dimethyldisulfid in Trifluoressigsäure, Br/SCH_3-Austausch in Dibromcarbenaddukten. *Tetrahedron Lett.* **1973**, 3509–3512.
58. Seebach, D.; Teschner, M. Thiolierung von Aldeyd- und Keton-Lithiumenolaten. *Tetrahedron Lett.* **1973**, 5113–5116.
59. Enders, D.; Seebach, D. Nucleophile Thioacylierung mit Lösungen von Dimethyl-thiocarbamoyl-lithium. *Angew. Chem.* **1973**, *85*, 1104. *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 1014–1015.
60. Seebach, D.; Meyer, H. Ergiebige Synthese von (±)-Pestalotin und (±)-Epipestalotin. Optisch reines (−)-Pestalotin durch asymmetrische Synthese. *Angew. Chem.* **1974**, *86*, 40–41, *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 77–78.
61. Seebach, D.; Gröbel, B.-T. Bequeme Darstellung von Vinylsilanen und deren Verwendung zur Ketonsynthese. *Angew. Chem.* **1974**, *86*, 102–103, *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 83–84.
62. Roelofsen, G.; Kanters, J. A.; Seebach, D. Kristall- und Molekülstruktur von Hexakis(phenylthio)äthan. *Chem. Ber.* **1974**, *107*, 253–262.
63. Seebach, D.; Corey, E. J.; Beck, A. K. Lithio-1,3,5-trithiane, Erzeugung, Umsetzung mit Elektrophilen und Verwendung als nucleophile Acylierungsmittel. *Chem. Ber.* **1974**, *107*, 367–379.
64. Seebach, D.; Neumann, H. Brom-Lithium-Austausch an Vinyl- und Aryl-bromiden mit *tert*-Butyllithium. Zur Ringerweiterung über Dibromcarbenaddukte. *Chem. Ber.* **1974**, *107*, 847–853.
65. Seebach, D.; Geiß, K.-H. Doppelt metallierter Thiobenzylalkohol.-Thiobenzaldehyd-Dianion. *Angew. Chem.* **1974**, *86*, 202–203, *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 202–203.
66. Seebach, D.; Braun, M. Cyclobutanone aus 1-Brom-1-lithiocyclopropanen und Ketonen. *Angew. Chem.* **1974**, *86*, 279–280, *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 277–278.
67. Seebach, D.; Daum, H. Asymmetrische Hydrierungen mit 1,4-Bis((dimethylamino)-(2*S*,3*S*)- und-(2*R*,3*R*)-butan-2,3-diol(DBD)/Lithiumaluminiumhydrid. *Chem. Ber.* **1974**, *107*, 1748–1763.
68. Bock, H.; Wagner, G.; Wittel, K.; Sauer, J.; Seebach, D. n/π-Konjugation in heterosubstituierten Äthylenen. *Chem. Ber.* **1974**, *107*, 1869–1881.
69. Seebach, D.; Ehrig, V. Addition von Oxoalkan-Polyanionen an Nitroolefine, Neue Synthese von Cyclohexanonen. *Angew. Chem.* **1974**, *86*, 446–447, *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 401–402.
70. Geiß, K.-H.; Seuring, B.; Pieter, R.; Seebach, D. Doppelt metalliertes 2-Propen-1-thiol -Thioacrolein-Dianon. *Angew. Chem.* **1974**, *86*, 484–486, *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 479–480.
71. Seebach, D.; Kolb, M.; Gröbel, B.-T. Homologative transformation of aldehydes and ketones to, α,β-unsaturated ketones through metalated ketene thioacetals. *Tetrahedron Lett.* **1974**, 3171–3174.
72. Seebach, D.; Kolb, M. Umpolung (dipole inversion) of carbonyl reactivity. *Chem. Ind. (London)* **1974**, 687–692.
73. Seebach, D.; Enders, D. Synthesis of α-heterosubstituted nitrosamines. Novel test substances for cancer and mutagenesis reasearch? *J. Med. Chem.* **1974**, *17*, 1225–1227.
74. Seebach, D.; Beck, A. K. Sekundäre und tertiäre Phenylthio- und Phenylseleno-alkyllithiumverbindungen als neuartige Reagentien zur C–C-Verknüpfung. *Angew. Chem.* **1974**, *86*, 859–860, *Angew. Chem. Int. Ed. Engl.* **1974**, *13*, 806–807.
75. Seebach, D.; Enders, D. Umpolung der Reaktivität von Aminen, Nucleophile α-sek.-Aminoalkylierung über metallierte Nitrosamine. *Angew. Chem.* **1975**, *87*, 1–18, *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 15–32.
76. Seebach, D.; Bürstinghaus, R. Michael-Additionen metallierter Thioacetale an cyclische Enone. *Angew. Chem.* **1975**, *87*, 37–38, *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 57–58.
77. Stegmann, H. B.; Scheffler, K.; Seebach, D. Spindichte-Verteilung in Tris(organylthio)methyl-Radikalen. *Chem. Ber.* **1975**, *108*, 64–70.
78. Seebach, D.; Beck, A. K. Mono-und Bis(phenyltelluro)-methyllithium. *Chem. Ber.* **1975**, *108*, 314–321.
79. Seebach, D.; Corey, E. J. Generation and synthetic applications of 2-lithio-1,3-dithianes. *J. Org. Chem.* **1975**, *40*, 231–237.
80. Seebach, D.; Enders, D. Lithiierte Methylnitrosamine. Nucleophile α-sek.-Aminomethylierung. *Chem. Ber.* **1975**, *108*, 1293–1320.
81. Seebach, D.; Leitz, H. F.; Ehrig, V. Michael-Additionen von Lithiumenolaten und schwefelsubstituierten Lithiumorganylen an Nitroolefine. *Chem. Ber.* **1975**, *108*, 1924–1945.
82. Seebach, D.; Ehrig, V.; Leitz, H. F.; Henning, R. Umwandlungen von Michael-Addukten an Nitroolefine in Carbonylverbindungen, 1,4-Diaminobutane, Indole und Isochinoline. *Chem. Ber.* **1975**, *108*, 1946–1960.
83. Ehrig, V.; Seebach, D. Reaktionen polymetallierter Carbonylverbindungen mit Nitroolefinen, Eine neue Ringschluss- und Anellierungsmethode. *Chem. Ber.* **1975**, *108*, 1961–1973.
84. Bischof, P.; Gleiter, R.; Dach, R.; Enders, D.; Seebach, D. Zur Wechselwirkung einsamer Elektronenpaare in Δ^2 Tetrazenen. Photoelektronenspektroskopische Untersuchungen. *Tetrahedron* **1975**, *31*, 1415–1417.
85. Seebach, D.; Bürstinghaus, R. *S*-Methyl thiocarboxylates from aldehydes and ketones through ketene thioacetals. Reductive nucleophile thiocarbonylation. *Synthesis* **1975**, 461–462.
86. Braun, M.; Dammann, R.; Seebach, D. Umsetzung von 1-Brom-1-lithiocyclopropanen mit Ketonen und Aldehyden.

Oxaspiropentane, Cyclobutanone, Cyclopropylketone und Lactone. *Chem. Ber.* **1975**, *108*, 1368–1390.
87. Seebach, D.; Oei, H.-A. Zum Mechanismus der elektrochemischen Pinakolisierung. Die erste asymmetrische Elektrosynthese in chiralem Medium. *Angew. Chem.* **1975**, *87*, 629–630, *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 634–636.
88. Seebach, D. Neue links- und rechtshändige Werkzeuge für den Chemiker. In *Schriftenreihe des Verbands der Chemischen Industrie, Fonds der Chemischen Industrie, 25 Jahre Fonds der Chemischen Industrie 1950–1975, Frankfurt*, 1975; S.13-29.
89. Seebach, D. Neue Wege in der Organischen Synthese? In *Schriftenreihe des Verbands der Chemischen Industrie, Fonds der Chemischen Industie, 25 Jahre Fonds der Chemischen Industrie 1950–1975, Frankfurt*, 1975; S. 57-63.
90. Kalinowski, H.-O.; Seebach, D.; Crass, G. Alkylierung von Tl^{I} -Alkoholaten. Eine nützliche Variante der Williamson-Synthese. *Angew. Chem.* **1975**, *87*, 812–813, *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 762–764.
91. Meyer, H.; Seebach, D. Synthese einiger Pilzmetabolite mit 4-Methoxy-5,6-dihydro-2-pyron-Struktur. *Liebigs Ann. Chem.* **1975**, 2261–2278.
92. Braun, M.; Seebach, D. Darstellung und 'disproportionierende Hydrolyse' von Cyclopropanonthioacetalen. Eine neue Homologisierungsmethode. *Chem. Ber.* **1976**, *109*, 669–691.
93. Gröbel, B.-T.; Bürstinghaus, R.; Seebach, D. Preparation of α-haloesters by homologation of aldehydes and ketones through α-trimethylsilylvinyl sulfides and ketene thioacetals. *Synthesis* **1976**, 121–124.
94. Seebach, D.; Lubosch, W.; Enders, D. Nucleophile Thioacylierung mit Thiocarbamoyllithium-Derivaten von sek. Aminen. *Chem. Ber.* **1976**, *109*, 1309–1323.
95. Kalinowski, H.-O.; Renger, B.; Seebach, D. Die magnetische Nichtäquivalenz der C-Atome prochiraler Diphenylmethylgruppen in der ^{13}C-NMR-Spektroskopie. *Angew. Chem.* **1976**, *88*, 256–257, *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 234–235.
96. Yamaguchi, H.; Kawada, K.; Okamoto, T.; Egert, E.; Lindner, H. J.; Braun, M.; Dammann, R.; Liesner, M.; Neumann, H.; Seebach, D. Stereospezifische Br/OAc-Substitution an syn- und anti-11-Brom-2,3-benzotricyclo[4.4.1.0]undecen-4-onen. Die Retentive Substitution am Dreiring. *Chem. Ber.* **1976**, *109*, 1589–1600.
97. Seebach, D.; Teschner, M. Herstellung α-thiolierter Carbonylverbindungen. *Chem. Ber.* **1976**, *109*, 1601–1616.
98. Seebach, D.; Lubosch, W. Nucleophile Aminoalkylierung. Lithiiertes N,N-Dimethyl-thiopivalamid. *Angew. Chem.* **1976**, *88*, 339–340, *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 313.
99. Seebach, D.; Geiß, K. -H. New Applications of Organometallic Reagents in Organic Synthesis. In *Proceedings of a Symposium at the ACS National Meeting in New York City, April 6–9th, 1976.* Seyferth, D., Eds.; J. Organometallic Chemistry, Library 1, Elsevier: Amsterdam, 1976; 1–92.
100. Seebach, D.; Geiβ, K.-H.; Pohmakotr, M. Das Magnesium-Derivat des Thioacrolein-Dianions. Ein einfacher Zugang zu Vinyl- und Divinyloxiranen. *Angew. Chem.* **1976**, *88*, 449–450, *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 437–438.
101. Seebach, D.; Wilka, E.-M. Alkylation of 2-lithio-1,3-dithianes with arenesulfonates of primary alcohols. *Synthesis* **1976**, 476–478.
102. Gray, R. W.; Chapleo, C. B.; Vergnani, T.; Dreiding, A.; Liesner, M.; Seebach, D. Contribution to the problem of nucleophilic substitution reactions at small-ring carbon atoms occurring with retention of configuration. *Helv. Chim. Acta* **1976**, *59*, 1547–1552.
103. Seebach, D.; Meyer, N. Doppelt metalliertes Methanol, ein nucleophiles, Hydroxymethylierungsreagens. *Angew. Chem.* **1976**, *88*, 484. *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 438.
104. Enders, D.; Hassel, T.; Pieter, R.; Renger, B.; Seebach, D. Reductive denitrosation of nitrosamines to secondary amines with hydrogen/Raney nickel. *Synthesis* **1976**, 548–550.
105. Seebach, D.; Lehr, F. α,α-Doppeldeprotonierte Nitroalkane. Erhöhung der Nitronat-C-Nucleophilie. *Angew. Chem.* **1976**, *88*, 540–541, *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 505–506.
106. Seebach, D.; Ehrig, V.; Teschner, M. Erzeugung und Reaktionen des chiralen Lithiumenolats von (+)-(*S*)-3-Methyl-2-pentanon. *Liebigs Ann. Chem.* **1976**, 1357–1369.
107. Seebach, D.; Kalinowski, H.-O. Enantiomerenreine Naturstoffe und Pharmaka aus billigen Vorläufern (Chiral Pool).-Zur Frage der chiral ökonomischen und ökologischen Totalsynthese. *Nachr. Chem. Techn.* **1976**, *24*, 415–418.
108. Seebach, D.; Geiβ, K.-H.; Kolb, M.; Beck, A. K. Verwendung von Schwefel- und Selenderivaten in der Organischen Synthese. In *Modern Synthetic Methods*, Scheffold, R., Ed.; Sauerländer AG: Aarau, 1976; Vol. 1, pp 173–299.
109. Henning, R.; Lehr, F.; Seebach, D. α,β-Doppeldeprotonierte nitroalkane: Super-enamine? *Helv. Chim. Acta* **1976**, *59*, 2213–2217.
110. Seebach, D. *Verbotene Reaktionen*. *Studienführer Chemie*, VAC (Vereinigung der Assistenten an den chemischen Laboratorien der ETH Zürich): ETH-Zentrum, Zürich, 1976; pp 108–115.
111. Dammann, R.; Braun, M.; Seebach, D. γ-Lakton-*cis*-anellierung an Δ^3-und Δ^2-Cholesten. *Helv. Chim. Acta* **1976**, *59*, 2821–2829.
112. Neumann, H.; Seebach, D. Stereospecific preparation of terminal vinyllithium derivatives by Br/Li-exchange with *t*-butyllithium. *Tetrahedron Lett.* **1976**, 4839–4842.
113. Seebach, D. Buchbesprechung: 'Frontier Orbitals and Organic Chemical Reactions' von I. Fleming. *Nachr. Chem. Techn.* **1976**, *25*, 33.
114. Bürstinghaus, R.; Seebach, D. 1,4-Additionen lithiierter Bis(methylthio)methane an cyclische Enone. *Chem. Ber.* **1977**, *110*, 841–851.
115. Gröbel, B.-T.; Seebach, D. Erzeugung von und Olefinierung mit α-S-, -Se-, -Si- und -Sn-per-heterosubstituierten (Trimethylsilyl)methyllithium-Verbindungen. *Chem. Ber.* **1977**, *110*, 852–866.
116. Gröbel, B.-T.; Seebach, D. Erzeugung und Reaktionen von α-(Trimethylsilyl)-, α-(Phenylthio)- und α-(Phenylseleno) vinyllithium-Verbindungen. *Chem. Ber.* **1977**, *110*, 867–877.
117. Seebach, D.; Kalinowski, H.-O.; Bastani, B.; Crass, G.; Daum, H.; Dörr, H.; Du Preez, N. P.; Ehrig, V.; Langer, W.; Nüssler, C.; Oei, H.-A.; Schmidt, M. Herstellung von Hilfsstoffen für die asymmetrische Synthese aus Weinsäure. Addition von Butyllithium an Aldehyde in chiralem Medium. *Helv. Chim. Acta* **1977**, *60*, 301–325.
118. Seebach, D.; Henning, R.; Lehr, F.; Gonnermann, J. Carbon alkylations of α,α-and α,β-doubly deprotonated nitroalkanes. *Tetrahedron Lett.* **1977**, 1161–1164.
119. Beck, A. K.; Hoekstra, M. S.; Seebach, D. 1,3-Diketones by 1:1-reactions of Li-enolates with acid chlorides generation of

kinetic enolates with mesityl lithium. *Tetrahedron Lett.* **1977**, 1187–1190.
120. Seebach, D.; Seuring, B.; Kalinowski, H.-O.; Lubosch, W.; Renger, B. Synthese und Bestimmung der absoluten Konfiguration von Pyrenophorin und Vermiculin. *Angew. Chem.* **1977**, *89*, 270–271, *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 264–265.
121. Pohmakotr, M.; Seebach, D. Doppelt deprotoniertes Allylacetophenon. Erstes Beispiel für einen 'direkten E5-Synthesebaustein'. *Angew. Chem.* **1977**, *89*, 333–334, *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 320–321.
122. Seebach, D.; Hoekstra, M. S.; Protschuk, G. 4-Hydroxy-2-cyclopenten-1-one aus Ketonen und 3-Nitropropionylchlorid. Eine einfache Methode zum Aufbau von Fünfringen. *Angew. Chem.* **1977**, *89*, 334–335, *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 321–322.
123. Geiβ, K.-H.; Seebach, D.; Seuring, B. Doppelmetallierung von Benzyl- und Allylmercaptanen; das Thiobenzaldehyd- und Thioacrolein-Dianion. *Chem. Ber.* **1977**, *110*, 1833–1851.
124. Seebach, D.; Enders, D.; Renger, B. Lithiierung und elektrophile Substitution an α-Methylengruppen von Nitrosaminen. Umpolung der Reaktivität sekundärer Amine. *Chem. Ber.* **1977**, *110*, 1852–1865.
125. Renger, B.; Kalinowski, H.-O.; Seebach, D. Regio- und stereochemischer Verlauf der Reaktionen von substituierten 2-Lithio-*N*-nitrosopiperidinen. *Chem. Ber.* **1977**, *110*, 1866–1878.
126. Seebach, D.; Enders, D.; Dach, R.; Pieter, R. Reaktion metallierter Nitrosamine mit Nitrilen. Eine neue Methode zur Darstellung von *ν*-Triazolen. *Chem. Ber.* **1977**, *110*, 1879–1886.
127. Lindner, H. J.; Kitschke, B.; Liesner, M.; Seebach, D. Neues über den Mechanismus der retentiven Substitution am Dreiring von Propellanen. *Helv. Chim. Acta* **1977**, *60*, 1151–1154.
128. Seuring, B.; Seebach, D. Synthese von vier chiralen, elektrophilen C_3- und C_4-Synthesebausteinen aus Hydroxycarbonsäuren. *Helv. Chim. Acta* **1977**, *60*, 1175–1181.
129. Seebach, D.; Oei, H.-A.; Daum, H. Asymmetrische Synthese bei Photo-, Elektro- und Alkalimetall-Pinakolisierungen von Benzaldehyd und Phenonen im chiralen Medium DDB. *Chem. Ber.* **1977**, *110*, 2316–2333.
130. Renger, B.; Seebach, D. Reaktionen von 1-Nitrosaminoallyllithiumverbindungen. Reversibilität der Carbonyladdition. *Chem. Ber.* **1977**, *110*, 2334–2354.
131. Gröbel, B.-T.; Seebach, D. Umpolung of the reactivity of carbonyl compounds through sulfur containing reagents. *Synthesis* **1977**, 357–402.
132. Seebach, D.; Kolb, M. Zur Umpolung der Carbonylreaktivität; Deprotonierung von Keten-thioacetalen zu 1,1-dithiosubstituierten Allyl- und Pentadienyl-lithiumverbindungen sowie deren Reaktionen mit Elektrophilen. *Liebigs Ann. Chem.* **1977**, 811–829.
133. Seebach, D.; Bürstinghaus, R.; Gröbel, B.-T.; Kolb, M. Zur Umpolung der Carbonylreaktivität; N^2/E^1- und N^4/E^1-Reaktion von 1,1-diheterosubstituierten Olefinen und Dienen. *Liebigs Ann. Chem.* **1977**, 830–845.
134. Seebach, D.; Meyer, N.; Beck, A. K. α-Heterosubstituierte Organyllithiumverbindungen durch Selen/Lithium Austausch; gezielte Kopplung von Carbonylverbindungen. *Liebigs Ann. Chem.* **1977**, 846–858.
135. Schlecker, R.; Seebach, D. Generation and reactions of tetrasubstituted *N*-lithiomethyl-succinimides. *Helv. Chim. Acta* **1977**, *60*, 1459–1471.
136. Schlecker, R.; Henkel, U.; Seebach, D. Ueber den Mechanismus des Zerfalls perheterosubstituierter Ethane. Hexakis(alkylthio)- und Tetrakis(methylthio)bis(trimethylsilyl)-ethane. *Chem. Ber.* **1977**, *110*, 2880–2904.
137. Kalinowski, H.-O.; Lubosch, W.; Seebach, D. ^{1}H- und ^{13}C-NMR-spektroskopische Untersuchungen an Thioamidderivaten; Ringstromeffekt in der ^{13}C-NMR-Spektroskopie. *Chem. Ber.* **1977**, *110*, 3733–3744.
138. Schlecker, R.; Seebach, D.; Lubosch, W. CH-Acidität in α-Stellung zum N-Atom in *N*,*N*-Dialkylamiden mit sterisch geschützter Carbonylgruppe, Zur nucleophilen Aminoalkylierung. *Helv. Chim. Acta* **1978**, *61*, 512–526.
139. Seebach, D.; Hassel, T. 2,4,6-Tri-*tert*-butylphenoxy (TBPO) als sterisch wirksame Carbonylschutzgruppe. Ein neues nucleophiles Dimethylaminomethylierungsmittel. *Angew. Chem.* **1978**, *90*, 296–297, *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 274.
140. Seebach, D.; Henning, R.; Lehr, F. Doppelte Deprotonierung von 3-Nitropropen und 4-Nitro-1-buten: Derivate ihrer Dianionen als neuartige Reagentien zur CC-Verknüpfung. *Angew. Chem.* **1978**, *90*, 479–480, *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 458-459.
141. Seebach, D.; Dach, R.; Enders, D.; Renger, B.; Jansen, M.; Brachtel, G. 1,4,5,6-Tetrahydro-*ν*-tetrazin-Derivate. *Helv. Chim. Acta* **1978**, *61*, 1622–1647.
142. Renger, B.; Hügel, H.; Wykypiel, W.; Seebach, D. Drei neue Varianten der C–C-Verknüpfung mit Nitrosaminen. Erzeugung und Herstellung sowie Umsetzungen von Kalium- und Zinn-Derivaten; Acylierung mit α-Ketonitrilen. *Chem. Ber.* **1978**, *111*, 2630–2645.
143. Meyer, N.; Seebach, D. Lithium-*ortho*-lithiobenzylalkoholate. *Angew. Chem.* **1978**, *90*, 553–554, *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 521–522.
144. Neumann, H.; Seebach, D. Brom/Lithium-Austausch an Vinylbromiden mit 2 Moläquivv. *tert*-Butyllithium. Umsetzungen von Vinyllithiumverbindungen mit Hetero- und Kohlenstoff-Elektrophilen. *Chem. Ber.* **1978**, *111*, 2785–2812.
145. Colvin, E. W.; Seebach, D. Silyl nitronates: improved nitroaldol reactions and reductive routes to 2-aminoalcohols. *J. Chem. Soc., Chem. Commun.* **1978**, 689–691.
146. Hassel, T.; Seebach, D. Steric carbonyl protection. Metalation and cleavage of highly hindered ureas. *Helv. Chim. Acta* **1978**, *61*, 2237–2240.
147. Seebach, D.; Willert, I.; Beck, A. K.; Gröbel, B.-T. 2-Stannyl-1,3-dithiane. Herstellung, Sn/Li-Transmetallierung und Verwendung für Cyclisierungen. *Helv. Chim. Acta* **1978**, *61*, 2510–2523.
148. Nitsche, M.; Seebach, D.; Beck, A. K. Kinetische Analyse des Zerfalls von Tris(arylthio)methyllithium-Verbindungen. Beweis für das Vorliegen von freiem Bis(phenylthio)carben in Tetrahydrofuran-Lösung. *Chem. Ber.* **1978**, *111*, 3644–3664.
149. Seebach, D.; Wykypiel, W.; Lubosch, W.; Kalinowski, H.-O. Zum stereochemischen Verlauf der elektrophilen Substitution an CH-Gruppen in α-Stellung zum N-Atom behinderter Amide. *Helv. Chim. Acta* **1978**, *61*, 3100–3102.
150. Seuring, B.; Seebach, D. Synthese und Bestimmung der absoluten Konfiguration von Norpyrenophorin, Pyrenophorin und Vermiculin. *Liebigs Ann. Chem.* **1978**, 2044–2073.

151. Enders, D.; Pieter, R.; Renger, B.; Seebach, D. Nucleophilic α-sec-aminoalkylation: 2(Diphenylhydroxymethyl)pyrrolidine. *Org. Synth.* **1978**, *58*, 113–122, Collect. Vol. VI, 1988, 542–549.
152. Seebach, D.; Henning, R.; Gonnermann, J. Zweifache Deprotonierung von 2-Aryl-1-nitroethanen. Umpolung der Nitroolefin-Reaktivität. *Chem. Ber.* **1979**, *112*, 234–248.
153. Seebach, D.; Colvin, E. W.; Lehr, F.; Weller, T. Nitroaliphatic compounds—ideal intermediates in organic synthesis? *Chimia* **1979**, *33*, 1–18.
154. Pohmakotr, M.; Geiß, K.-H.; Seebach, D. Anwendungen der Magnesiumderivate von Thioacrolein-Dianionen zur Synthese schwefelfreier Verbindungen (Vinyl- und Divinylepoxide, Acylcyclo-pentene). *Chem. Ber.* **1979**, *112*, 1420–1439.
155. Seebach, D.; Pohmakotr, M. Syntheses of (+)-(*S*,*S*)-(*cis*−6-methyltetrahydropyran-2-yl)acetic acid and of (−)-*R*,*R*)-didesoxy-pyrenophorine using a new d^5-reagent. *Helv. Chim. Acta* **1979**, *62*, 843–846.
156. Seebach, D. Methoden der Reaktivitätsumpolung. *Angew. Chem.* **1979**, *91*, 259–278, *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 239–258.
157. Hassel, T.; Seebach, D. Ein metallierter Allylharnstoff mit sterisch geschützter Carbonylgruppe als neuartiges 'd^3-Reagens'. *Angew. Chem.* **1979**, *91*, 427–428, *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 399–400.
158. Dammann, R.; Seebach, D. Ueber die Umlagerung von Bromcyclopropylcarbinolen zu Homoallylderivaten und Cyclobutanonen. *Chem. Ber.* **1979**, *112*, 2167–2176.
159. Seebach, D.; Dammann, R.; Lindner, H. J.; Kitschke, B. Stereoselektive Bildung von Oxaspiropentanen und Spiropentylketonen. Zur Stereochemie der nucleophilen Substitution am Cyclopropan. *Helv. Chim. Acta* **1979**, *62*, 1143–1161.
160. Seebach, D.; Neumann, H.; Dammann, R. Intramolekulare Inversionssubstitution am Dreiring von 7-exo-Brom-bicyclo-[4.1.0]heptan-3-endo-ol unter Bildung eines Tetrahydrofuranringes. *Helv. Chim. Acta* **1979**, *62*, 1162–1170.
161. Pohmakotr, M.; Seebach, D. Dianion derivatives of methyl- and isopropyl-2,4-pentadienedithioate as d^5-reagents. *Tetrahedron Lett.* **1979**, 2271–2274.
162. Seebach, D.; Wykypiel, W. Safe one-pot carbon–carbon bond formation with lithiated nitrosamines including denitrosation by sequential reduction with lithium aluminium hydride and Raney-nickel. *Synthesis* **1979**, 423–424.
163. Seebach, D.; Langer, W. Enantioselektive 1,2-Additonen von Li-, Mg-, Zn- und Cu-organischen Verbindungen und von Li-Enolaten an Carbonylverbindungen im chiralen Medium DDB. *Helv. Chim. Acta* **1979**, *62*, 1701–1709.
164. Langer, W.; Seebach, D. Enantioselektive 1,4-Additionen von metallorganischen Verbindungen an konjugierte Systeme im chiralen Medium DDB. *Helv. Chim. Acta* **1979**, *62*, 1710–1722.
165. Seebach, D.; Siegel, H.; Müllen, K.; Hiltbrunner, K. Direkte ^{13}C-NMR-spektroskopische Beobachtung von Cyclopropyliden- Bromlithiumcarbenoiden. *Angew. Chem.* **1979**, *91*, 844–845, *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 784–785.
166. Siegel, H.; Hiltbrunner, K.; Seebach, D. ^{13}C-NMR-Spektren von Tribrommethyl- und 1,1-Dibromethyllithium. *Angew. Chem.* **1979**, *91*, 845–846, *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 785–786.
167. Seebach, D. H.C. Brown und G. Wittig—Nobelpreis für synthetische organische Chemie. *Neue Zürcher Zeitung* **1979**, *7*(259), 57.
168. Seebach, D.; Lehr, F. Lithium- und Kupfer-Derivate von α,α-doppeldeprotonierten Nitroalkanen-Erzeugung, Eigenschaften und Umsetzungen mit Alkyl- und Allylhalogeniden. *Helv. Chim. Acta* **1979**, *62*, 2239–2257.
169. Lehr, F.; Gonnermann, J.; Seebach, D. Umsetzungen von Dilithio-nitroalkanen und -allylnitroderivaten mit Carbonylverbindungen. *Helv. Chim. Acta* **1979**, *62*, 2258–2275.
170. Seebach, D.; Locher, R. α,β-Ungesättigte Carbonylverbindungen mit sterisch geschützter Carbonylgruppe.-Erzwungene a^3- versus a^1-Reaktivität. *Angew. Chem.* **1979**, *91*, 1024–1025, *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 957–958.
171. Hungerbühler, E.; Seebach, D.; Wasmuth, D. Chirale Reagentien aus Weinsäure.- 1-Benzyloxy-3,4-epoxy-2-butanol, ein vielseitiges Zwischenprodukt für die Enantiomerensynthese. *Angew. Chem.* **1979**, *91*, 1025–1026, *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 860–958.
172. Seebach, D.; Crass, G.; Wilka, E.-M.; Hilvert, D.; Brunner, E. Three new chiral aminoethers from tartaric acid for improved asymmetric syntheses with organolithium reactions. *Helv. Chim. Acta* **1979**, *62*, 2695–2698.
173. Bock, H.; Brähler, G.; Henkel, U.; Schlecker, R.; Seebach, D. Die Oxidation von Hexathioethanen zu Tetrathioethen-Radikalkationen. *Chem. Ber.* **1980**, *113*, 289–301.
174. Lubosch, W.; Seebach, D. Nucleophile Aminoalkylierung mit Thiopivalamiden. *Helv. Chim. Acta* **1980**, *63*, 102–116.
175. Seebach, D.; Wasmuth, D. Herstellung von erythro-2-Hydroxybernsteinsäure-Derivaten aus Aepfelsäureester. *Helv. Chim. Acta* **1980**, *63*, 197–200.
176. Amstutz, R.; Seebach, D.; Seiler, P.; Schweizer, B.; Dunitz, J. D. Kristallstruktur von 2-Lithio-2-methyl-1,3-dithian-Tetramethyl-ethylendiamin (1/1). *Angew. Chem.* **1980**, *92*, 59–60, *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 54.
177. Siegel, H.; Seebach, D. A convenient synthesis of ^{13}C-bromoform and ^{13}C-tetrabromomethane from ^{13}C-iodomethane labelling through $^{13}CBr_2$. *J. Lab. Comp. Radiopharm.* **1980**, *17*, 279–287.
178. Meyer, N.; Seebach, D. Doppelt metalliertes Methanol. Alkohol-d^1- und -d^3-Reagenzien. *Chem. Ber.* **1980**, *113*, 1290–1303.
179. Meyer, N.; Seebach, D. Direkte ortho-Metallierung von Benzylalkoholen. Eine neuartige Herstellung von *ortho*-substituierten Benzylalkoholen. *Chem. Ber.* **1980**, *113*, 1304–1319.
180. Seebach, D. Autoreferat H.C. Brown, G. Wittig und die Umpolung (Berner Chemische Gesellschaft, 16. January 1980). *Chimia* **1980**, *34*, 185–186.
181. Colvin, E. W.; Beck, A. K.; Bastani, B.; Seebach, D.; Kai, Y.; Dunitz, J.-D. Synthesis, properties and crystal structure of silyl nitronates (silyl esters of aci-nitroalkanes): towards the S_N2 reaction path with retention of configuration at silicon. *Helv. Chim. Acta* **1980**, *63*, 697–710.
182. Gfeller, J.-C.; Beck, A. K.; Seebach, D. Erhöhung der Nachweisempfindlichkeit von Cyclosporin A durch Derivatisierung mit 2-Naphthylselenylchlorid. *Helv. Chim. Acta* **1980**, *63*, 728–732.
183. Schmidt, M.; Amstutz, R.; Crass, G.; Seebach, D. Herstellung einiger chiraler Aminodiole aus Weinsäure. Chirale Lithiumalanate für asymmetrische Hydrierungen. *Chem. Ber.* **1980**, *113*, 1691–1707.
184. Paulsen, H.; Sumfleth, E.; Sinnwell, V.; Meyer, N.; Seebach, D. Direkte Hydroxymethylierung zu verzweigten Zuckern mit einem Hydroxymethyl-d^1-Reagenz. *Chem. Ber.* **1980**, *113*, 2055–2061.

185. Wykypiel, W.; Seebach, D. A nitrosamine route to (±)-macrostomine. *Tetrahedron Lett.* **1980**, *21*, 1927–1930.
186. Seebach, D.; Hungerbühler, E. Syntheses of Enantiomerically Pure Compounds (EPC-Syntheses). Tartaric Acid, an Ideal Source of Chiral Building Blocks for Synthesis? In *Modern Synthetic Methods*, Scheffold, E., Ed.; Salle+ Sauerländer: Frankfurt/Aarau, 1980; Vol. 2, pp 91–173.
187. Hungerbühler, E.; Naef, R.; Wasmuth, D.; Seebach, D.; Loosli, H.-R.; Wehrli, A. Synthese optisch aktiver 2-Methyl- und 2-Aethyl-1,6-dioxaspiro[4.4]-nonan- und -[4.5]decan-Pheromone aus einem gemeinsamen chiralen Vorläufer. *Helv. Chim. Acta* **1980**, *63*, 1960–1970.
188. Züger, M.; Weller, T.; Seebach, D. 2,3-Disubstituted γ-butyrolactams from the Michael-additions of doubly deprotonated, optically active β-hydroxycarboxylates to nitroolefins. *Helv. Chim. Acta* **1980**, *63*, 2005–2009.
189. Seebach, D.; Siegel, H.; Gabriel, J.; Hässig, R. Tieftemperatur ^{13}C-NMR-Spektren von ^{13}C- und ^{6}Li-markierten Chlor-, Brom- und Jod-Lithium-Carbenoiden. *Helv. Chim. Acta* **1980**, *63*, 2046–2053.
190. Weidmann, B.; Seebach, D. Methyl-triisopropoxy-titanium, a highly selective nucleophilic methylating reagent. *Helv. Chim. Acta* **1980**, *63*, 2451–2454.
191. Weidmann, B.; Widler, L.; Olivero, A. G.; Maycock, C. D.; Seebach, D. Selectivities in the reactions of alkyl-, aryl- and heterosubstituted organotitanium compounds. *Helv. Chim. Acta* **1981**, *64*, 357–361.
192. Lohmann, J.-J.; Seebach, D.; Syfrig, M. A.; Yoshifuji, M. Lithiiertes *N*-Pivaloyl-tetrahydroisochinolin—ein Supernucleophil. *Angew. Chem.* **1981**, *93*, 125–126, *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 128–129.
193. Kalinowski, H.-O.; Crass, G.; Seebach, D. Veretherungen von Diolen, Triolen und Hydroxycarbonsäurederivaten über Thallium(I)-alkoholate. Eine neue Variante der Williamson-Reaktion. *Chem. Ber.* **1981**, *114*, 477–487.
194. Knochel, P.; Seebach, D. Nitroallylation par le Nitro-2 Pivaloyloxy-3 Propène, Un Réactif $a^2/a^{2'}$. *Nouv. J. Chim.* **1981**, *5*, 75–77.
195. Seebach, D.; Yoshifuji, M. 2-Bis(dimethylamino)phosphinoyl-1-lithio-1,2,3,4-tetrahydroisoquinoline. A highly nucleophilic d^1-reagent for the preparation of 1-substituted tetrahydroisoquinolines. *Helv. Chim. Acta* **1981**, *64*, 643–647.
196. Hungerbühler, E.; Seebach, D. Chirale elektrophile Synthesebausteine mit vier verschiedenen funktionellen Gruppen aus Weinsäure, 2,3-und 3,4-Epoxy-butandiolderivate in allen vier stereoisomeren Formen. *Helv. Chim. Acta* **1981**, *64*, 687–702.
197. Seebach, D.; Weller, T.; Protschuk, G.; Beck, A. K.; Hoekstra, M. S. Herstellung von 1,3-Diketonen und von Nitro-diketonen durch (1:1)-Acylierungen von Lithiumenolaten mit Acylchloriden. *Helv. Chim. Acta* **1981**, *64*, 716–735.
198. Weller, T.; Seebach, D.; Davis, R. E.; Laird, B. B. 3-Hydroxy-4-nitro-cyclohexanone aus Ketonen und 4-Nitrobuttersäurechlorid. Eine ringerweiternde Fünfringanellierung. *Helv. Chim. Acta* **1981**, *64*, 736–760.
199. Seebach, D.; Beck, A. K.; Lehr, F.; Weller, T.; Colvin, E. W. Diastereoselektive Synthese von β-Nitro- und β-Aminoalkoholen. *Angew. Chem.* **1981**, *93*, 422–424, *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 397–399.
200. Amstutz, R.; Dunitz, J. D.; Seebach, D. Kristallstruktur von 2-Lithio-2-phenyl-1,3-dithian-Tetrahydrofuran-Tetramethylethylendiamin (1/1/1); 'X–X'-Elektronendichteverteilung in Lithio-methyl- und Lithio-phenyl-dithian. *Angew. Chem.* **1981**, *93*, 487–488, *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 465–466.
201. Locher, R.; Seebach, D. Michael-Addition von Lithiumacetyliden an Propenyltritylketon. *Angew. Chem.* **1981**, *93*, 614–615, *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 569–570.
202. Wykypiel, W.; Lohmann, J.-J.; Seebach, D. Lithiierung in α-Stellung zum N-Atom von Triphenylacetamiden aus cyclischen sekundären Aminen. Umlagerung metallierter Triphenylacetamide unter 1,3-Verschiebung der Carbonylgruppe. *Helv. Chim. Acta* **1981**, *64*, 1337–1346.
203. Seebach, D.; Golinski, J. Synthesis of open-chain 2,3-disubstituted 4-nitroketones by diastereoselective Michael-addition of (*E*)-enamines to (*E*)-nitroolefins. A topological rule for C,C-bond forming processes between prochiral centres. *Helv. Chim. Acta* **1981**, *64*, 1413–1423.
204. Hungerbühler, E.; Seebach, D.; Wasmuth, D. Doppelt und dreifach funktionalisierte, enantiomerenreine C_4-Synthesebausteine aus β-Hydroxybuttersäure, Aepfelsäure und Weinsäure. *Helv. Chim. Acta* **1981**, *64*, 1467–1487.
205. Weidmann, B.; Maycock, C. D.; Seebach, D. Alkyl-, aryl-, vinyl- and heterosubstituted organozirconium compounds, selective nucleophiles of low basicity. *Helv. Chim. Acta* **1981**, *64*, 1552–1557.
206. Knochel, P.; Seebach, D. Nitroallylation of highly reactive organolithium compounds by 2-nitro-3-pivaloyloxy-1-propene (NPP). *Tetrahedron Lett.* **1981**, *22*, 3223–3226.
207. Colvin, E. W.; Robertson, A. D.; Seebach, D.; Beck, A. K. The reactions of silyl nitronates with organolithium reagents. *J. Chem. Soc., Chem. Commun.* **1981**, 952–953.
208. Amstutz, R.; Hungerbühler, E.; Seebach, D. Revidierte Struktur des Makrodiolids Colletodiol. *Helv. Chim. Acta* **1981**, *64*, 1796–1799.
209. Colvin, E. W.; Beck, A. K.; Seebach, D. Improved nitroaldol reactions and reductive routes to vicinal aminoalcohols. *Helv. Chim. Acta* **1981**, *64*, 2264–2271.
210. Olivero, A. G.; Weidmann, B.; Seebach, D. Enantioselective addition of chiral organotitanium derivatives to aldehydes. *Helv. Chim. Acta* **1981**, *64*, 2485–2488.
211. Seebach, D.; Wasmuth, D. Alkylierung von Aminosäuren ohne Verlust der optischen Aktivität: α- und β-Alkylierung eines Asparaginsäure-Derivates. *Angew. Chem.* **1981**, *93*, 1007–1008, *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 971–972.
212. Seebach, D.; Pohmakotr, M. Generation of dienone and trienone dianion derivatives. *Tetrahedron* **1981**, *37*, 4047–4058, Tetrahedron Symposia-in-Print, No. 2 on 'New General Synthetic Methods'.
213. Naef, R.; Seebach, D. Direkte diasteroselektive Verzweigung der Weinsäure über ein Enolat. *Angew. Chem.* **1981**, *93*, 1113. *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 1030–1031.
214. Amstutz, R.; Schweizer, W. B.; Seebach, D.; Dunitz, J. D. Trameric cubic structures of two solvated lithium enolates. *Helv. Chim. Acta* **1981**, *64*, 2617–2621.
215. Seebach, D.; Amstutz, R.; Dunitz, J. D. Mechanistic implications of the tetrameric cubic structure of lithium enolates. *Helv. Chim. Acta* **1981**, *64*, 2622–2626.
216. Seebach, D.; Naef, R. Enantioselective generation and diastereoselective reactions of chiral enolates derived from α-heterosubstituted carboxylic acids. *Helv. Chim. Acta* **1981**, *64*, 2704–2708.
217. Mali, R. S.; Pohmakotr, M.; Weidmann, B.; Seebach, D. A short synthesis of (*R*,*R*)-(−)-pyrenophorin from (*S*)-propylene,

oxide and a 3-pentenoic acid d^5-reagent. *Liebigs Ann. Chem.* **1981**, 2272–2284.
218. Seidel, W.; Seebach, D. Grahamimycin A1. Synthesis and determination of configuration and chirality. *Tetrahedron Lett.* **1982**, *23*, 159–162.
219. Seebach, D.; Hungerbühler, E.; Naef, R.; Schnurrenberger, P.; Weidmann, B.; Züger, M. Titanate-mediated transesterifications with functionalized substrates. *Synthesis* **1982**, 138–142.
220. Weller, T.; Seebach, D. Synthesis of (±)-1-desoxy-2-lycorinone and of a possible trans-dihydro-lycoricidine precursor. *Tetrahedron Lett.* **1982**, *23*, 935–938.
221. Kai, Y.; Knochel, P.; Kwiatkowski, S.; Dunitz, J. D.; Oth, J. F. M.; Seebach, D. Structure, synthesis, and properties of some persubstituted 1,2-dinitroethanes. In quest of nitrocyclopropyl-anion derivatives. *Helv. Chim. Acta* **1982**, *65*, 137–161.
222. Wasmuth, D.; Arigoni, D.; Seebach, D. Zum stereochemischen Verlauf der Biosynthese von 2-Oxo-pantolacton:-Synthese von stereospezifisch indiziertem Pantolacton aus Aepfelsäure. *Helv. Chim. Acta* **1982**, *65*, 344–352, Erratum: *Helv. Chim. Acta* **1982**, *65*, 620.
223. Mukhopadhyay, T.; Seebach, D. Substitution of HMPT by the cyclic urea DMPU as a cosolvent for highly reactive nucleophiles and bases. *Helv. Chim. Acta* **1982**, *65*, 385–391.
224. Seebach, D.; Pohmakotr, M.; Schregenberger, C.; Weidmann, B.; Mali, R. S.; Pohmakotr, S. d^5-Reactions of doubly deprotonated γ,δ-unsaturated carbonyl derivatives with electrophiles. A novel approach to the synthesis of tetrahydrofuran and tetrahydropyran derivatives. *Helv. Chim. Acta* **1982**, *65*, 419–450.
225. Seebach, D.; Züger, M. Ueber die Depolymerisierung von Poly-(*R*)-3-hydroxy-buttersäureester (PHB). *Helv. Chim. Acta* **1982**, *65*, 495–503.
226. Seebach, D.; Henning, R.; Mukhopadhyay, T. Doubly deprotonated methyl 3-nitropropanoate, an acrylic ester d^2-reagent. *Chem. Ber.* **1982**, *115*, 1705–1720.
227. Hässig, R.; Siegel, H.; Seebach, D. Herstellung von substituierten Methylencyclopropanen aus geminalen Dibromcyclopropanen und Carbonylverbindungen. *Chem. Ber.* **1982**, *115*, 1990–1997.
228. Widler, L.; Seebach, D. Diastereoselektive Synthese von β-Methyl-homoallylalkoholen durch lk-Addition von (2-Butenyl)triphenoxytitan an Aldehyde. *Helv. Chim. Acta* **1982**, *65*, 1085–1089.
229. Seebach, D.; Beck, A. K.; Mukhopadhyay, T.; Thomas, E. Diastereoselektive synthesis of nitroaldol derivatives. *Helv. Chim. Acta* **1982**, *65*, 1101–1133.
230. Schnurrenberger, P.; Züger, M. F.; Seebach, D. Herstellung von Methylestern durch Umesterung funktionalisierter Substrate mit Titansäureestern als Katalysatoren. *Helv. Chim. Acta* **1982**, *65*, 1197–1201.
231. Blarer, S. J.; Schweizer, W. B.; Seebach, D. Asymmetrische Michael-Additionen. Praktisch vollständig diastereo- und enantioselektive Alkylierung des Enamins aus Cyclohexanon und Prolinylmethyläther durch ω-Nitrostyrole zu u-2-(1′-Aryl-2′-nitro-äthyl)-cyclohexanonen. *Helv. Chim. Acta* **1982**, *65*, 1637–1654.
232. Knochel, P.; Seebach, D. Synthesis and reactions of substituted nitro-allylating reagents. *Tetrahedron Lett.* **1982**, *23*, 3897–3900.
233. Seebach, D.; Prelog, V. Spezifikation des sterischen Verlaufs von asymmetrischen Synthesen. *Angew. Chem.* **1982**, *94*, 696–702, *Angew. Chem. Int. Ed. Engl.* **1982**, 21, 654–660.
234. Seebach, D.; Widler, L. A case of highly diastereoselective addition to unsymmetrical ketones; lk-addition of (2-alkenyl)triphenoxytitanium derivatives. *Helv. Chim. Acta* **1982**, *65*, 1972–1981.
235. Knochel, P.; Seebach, D. Dehydratisierung von Nitroaldolen mit Dicyclohexylcarbodiimid: Herstellung von Nitroolefinen unter milden Bedingungen. *Synthesis* **1982**, 1017–1018.
236. Seebach, D.; Schiess, M. Alkylative amination of non-enolizable aldehydes with alkyl(dialkylamino)titanium derivatives. *Helv. Chim. Acta* **1982**, *65*, 2598–2602.
237. Weidmann, B.; Seebach, D. Organometallverbindungen von Titan und Zirconium als selektive nucleophile Reagentien für die Organische Synthese. *Angew. Chem.* **1983**, *95*, 12–26, *Angew. Chem. Int. Ed. Engl.* **1983**, 22, 31–45.
238. Seebach, D.; Hässig, R.; Gabriel, J. ^{13}C NMR.-Spektroskopie von Organolithiumverbindungen bei tiefen Temperaturen. Strukturinformation aus der ^{13}C, ^{6}Li-Kopplung. *Helv. Chim. Acta* **1983**, *66*, 308–337.
239. Seebach, D.; Kalinowski, H.-O.; Langer, W.; Crass, G.; Wilka, E.-M. Chiral media for asymmetric solvent inductions. (*S*,*S*)-(+)-1,4-Bis-(dimethylamino)-2,3-dimethoxybutane from (*R*,*R*)-(+)-tartaric acid diethyl ester. *Org. Synth.* **1983**, *61*, 24–34, Collect. Vol. VII 1990, 41–50.
240. Seebach, D.; Hidber, A. Enantioselective addition of butyllithium in the presence of the chiral cosolvent DDB. (+)-(*R*)-Phenyl-1-pentanol. *Org. Synth.* **1983**, *61*, 42–47, Collect. Vol. VII 1990, 447–450.
241. Seebach, D.; Weidmann, B.; Widler, L. Titanium and Zirconium Derivatives in Organic Synthesis. A Review with Procedures. *Modern Synthetic Methods*, Scheffold, R., Ed.; Salle+Sauerländer/Wiley: Aarau, Switzerland/New York, USA, 1983; Vol. 3, pp 217–353.
242. Blarer, S. J.; Seebach, D. Asymmetrische Michael-Additionen. Stereoselektive Alkylierungen des (*R*)- und (*S*)-Enamins aus Cyclohexanon und 2-(Methoxymethyl)pyrrolidin durch α-(Methoxycarbonyl)zimtsäure-methylester. *Chem. Ber.* **1983**, *116*, 2250–2260.
243. Sutter, M. A.; Seebach, D. Synthese von (2E,4E,6S,7R,10E,12E,14S,15R)-6,7,14,15-Tetramethyl-16-dioxa-2,4,10,12-cyclohexadecatetraen-1,9-dion. Ein Modellsystem für Elaiophylin. *Liebigs Ann. Chem.* **1983**, 939–949.
244. Seebach, D.; Lohmann, J.-J.; Syfrig, M. A.; Yoshifuji, M. Alkylation of the isoquinoline skeleton in the 1-position. *Tetrahedron* **1983**, *39*, 1963–1974. Tetrahedron Symposia-in-Print, No. 9 on 'Heteroatom-Directed Metallations in Heterocyclic Synthesis'.
245. Seebach, D.; Aebi, J. D. α-Alkylation of threonine. *Tetrahedron Lett.* **1983**, *24*, 3311–3314.
246. Seebach, D.; Weber, T. α-Alkylation of a cysteine derivative without racemization and without the use of a chiral auxiliary. *Tetrahedron Lett.* **1983**, *24*, 3315–3318.
247. Schiess, M.; Seebach, D. *N*-Methyl-*C*-(trichlortitanio)formimidoylchlorid. Ein effizientes Reagenz zur Homologisierung von Aldehyden und Ketonen zu α-Hydroxy-carbonsäureamiden. *Helv. Chim. Acta* **1983**, *66*, 1618–1623.
248. Seebach, D.; Boes, M.; Naef, R.; Schweizer, W. B. Alkylation of amino acids without loss of the optical activity: preparation of α-substituted proline derivates. A case of self-reproduction of chirality. *J. Am. Chem. Soc.* **1983**, *105*, 5390–5398.
249. Blarer, S. J.; Seebach, D. Asymmetrische Michael-Additionen. Regio-, diastereo- und enantioselektive Alkylierungen

der Enamine aus β-Tetralonen und (*S*)-2-(Methoxymethyl)-pyrrolidin ('Prolinolmethylether') durch ω-Nitrostyrole. *Chem. Ber.* **1983**, *116*, 3086–3096.
250. Hässig, R.; Seebach, D. Bestimmung der Struktur von Phenyläthinyllithium in Lösung mittels Tieftemperatur-NMR-Spektroskopie. *Helv. Chim Acta* **1983**, *66*, 2269–2273.
251. Seebach, D.; Beck, A. K.; Schiess, M.; Widler, L.; Wonnacott, A. Some recent advances in the use of titanium reagents for organic synthesis. *Pure Appl. Chem.* **1983**, *55*, 1807–1822.
252. Naef, R.; Seebach, D. Vierstufige EPC-Synthese von (+)- oder (-)-Frontalin aus Milchsäure. Eine erste Anwendung des Prinzips der Selbstreproduktion der Chiralität in der Naturstoffsynthese. *Liebigs Ann. Chem.* **1983**, 1930–1936.
253. Seebach, D.; Hidber, A. Synthese bei Temperaturen unter −80 °C. *Chimia* **1983**, *37*, 449–462.
254. Aebi, J. D.; Sutter, M. A.; Wasmuth, D.; Seebach, D. Enantiomerenreine Synthesebausteine aus verzweigter Aepfelsäure. *Liebigs Ann. Chem.* **1983**, 2114–2126, Berichtigung: *Liebigs Ann. Chem.* **1984**, 407.
255. Thaisrivongs, S.; Seebach, D. Diastereoselective benzyloxymercuration/demercuration of derivatives of γ-alkyl-δ-hydroxy-α,β-unsaturated esters. A new strategy for the synthesis of aldol-type products. *J. Am. Chem. Soc.* **1983**, *105*, 7407–7413.
256. Züger, M. F.; Giovannini, F.; Seebach, D. Herstellung von (*R*)-(-)-3-Hydroxy-2-methyl-propionsäureethylester durch Hefereduktion von α-Formyl-propionsäureethylester. *Angew. Chem.* **1983**, *95*, 1024. *Angew. Chem. Int. Ed. Engl.* **1983**, *22*, 1012.
257. Amstutz, R.; Laube, T.; Schweizer, W. B.; Seebach, D.; Dunitz, J. D. Further investigation of the nature of the C-Li bond. Structures of a phenylthiomethyllithium complex and of a methylthiomethyllithium complex. *Helv. Chim. Acta* **1984**, *67*, 224–236.
258. Seebach, D.; Knochel, P. 2′-Nitro-2′-propen-1′-yl 2,2-dimethylpropanoate (NPP), a multiple coupling reagent. *Helv. Chim. Acta* **1984**, *67*, 261–283.
259. Nájera, C.; Yus, M.; Seebach, D. C-Metallierte chirale Alkoxide als d^2- und d^3-Reagenzien für die Synthese enantiomerenreiner Produkte (EPC-Synthese). *Helv. Chim. Acta* **1984**, *67*, 289–300.
260. Seebach, D.; Züger, M. F.; Giovannini, F.; Sonnleitner, B.; Fiechter, A. Präparative mikrobiologische Reduktion von β-Oxoestern mit Thermoanaerobium brockii. *Angew. Chem.* **1984**, *96*, 155–156, *Angew. Chem. Int. Ed. Engl.* **1984**, 23, 151–152.
261. Seebach, D.; Syfrig, M. A. Diastereoselektive Hydroxyalkylierungen in 1-Stellung von 2-Pivaloyl-1,2,3,4-tetrahydroisochinolin über ein Magnesiumderivat. *Angew. Chem.* **1984**, *96*, 235–236, *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 248–249.
262. Hässig, R.; Seebach, D.; Siegel, H. Herstellung von Allenen aus geminalen Dibromolefinen und Aldehyden. *Chem. Ber.* **1984**, 1877–1884.
263. Schnurrenberger, P.; Hungerbühler, E.; Seebach, D. (+)-Colletodiol-synthesis from (*S*,*S*)-tartaric acid and (*R*)-3-hydroxy-butyric acid. *Tetrahedron Lett.* **1984**, *25*, 2209–2212.
264. Seebach, D.; Naef, R.; Calderari, G. α-Alkylation of α-heterosubstituted carboxylic acids without racemization. EPC-Syntheses of tertiary alcohols and thiols. *Tetrahedron* **1984**, *40*, 1313–1324, Tetrahedron Symposia-in-Print, No. 15 on 'Synthesis of Chiral Non-Racemic Compounds'.
265. Seebach, D.; Aebi, J. D. α-Alkylation of serine with self-reproduction of the center of chirality. *Tetrahedron Lett.* **1984**, *25*, 2545–2548.
266. Gabriel, J.; Seebach, D. Synthese und NMR-Spektren einiger ^{13}C-markierter Thio- und Seleno-äther, -acetale und -orthoester. *Helv. Chim Acta* **1984**, *67*, 1070–1082.
267. Seebach, D.; Gabriel, J.; Hässig, R. Low temperature ^{13}C-NMR spectra of ^{6}Li- and ^{13}C-labelled sulfur- and selenium-substituted organolithium derivatives. *Helv. Chim. Acta* **1984**, *67*, 1083–1099.
268. Nájera, C.; Yus, M.; Hässig, R.; Seebach, D. Fluoro(phenylsulfinyl)methyllithium. Note on the ^{13}C-NMR Spectrum of a Fluorocarbenoid. *Helv. Chim. Acta* **1984**, *67*, 1100–1103.
269. Seebach, D.; Züger, M. F. On the preparation of methyl and ethyl (*R*)-(−)-3-hydroxy-valerate by depolymerization of a mixed PHB/PHV biopolymer. *Tetrahedron Lett.* **1984**, *25*, 2747–2750.
270. Seebach, D.; Bauer, W.; Hansen, J.; Laube, T.; Schweizer, W. B.; Dunitz, J.-D. Crystal and molecular structure of 1-lithio-3,6-diethoxy-2,5-dimethyl-1,2-dihydropyrazine, the lithiated bis-lactim ether of the diketopiperazine from alanine. *J. Chem. Soc., Chem. Commun.* **1984**, 853–854.
271. Seebach, D.; Dust, M.; Naef, R.; Bänziger, M. Synthese und Bestimmung der absoluten Konfiguration von (+)-Delesserin, einem Inhaltsstoff der roten Meeresalge Delesseria sanguinea (Lamouroux). *Angew. Chem.* **1984**, *96*, 498. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 530–531.
272. Häner, R.; Laube, T.; Seebach, D. Reversal of product configuration in Michael additions of lithium enolates to *E*- and *Z*-1-nitro-1-propene. *Chimia* **1984**, *38*, 255–257.
273. Imwinkelried, R.; Seebach, D. Aminierende, reduktive Kupplung aromatischer Aldehyde mit Tris(dialkyl-amino)-methylvanadium (IV) zu N,N,N′,N′,-Tetraalkyl-1,2-diaryl-äthylen-diaminen. *Helv. Chim. Acta* **1984**, *67*, 1496–1502.
274. Seebach, D.; Betschart, C.; Schiess, M. Diastereoselektive Synthese neuartiger Mannich-Basen mittels Titanderivaten. *Helv. Chim. Acta* **1984**, *67*, 1593–1597.
275. Seebach, D.; Weber, T. Hydroxyalkylierungen von Cystein über das Enolat von (2R,5R)-2(tert-Butyl)-1-aza-3-oxa-7-thiabicyclo[3.3.0]octan-4-on und unter Selbstreproduktion des Chiralitätszentrums. *Helv. Chim. Acta* **1984**, *67*, 1650–1661.
276. Seebach, D.; Renaud, P.; Schweizer, W. B.; Züger, M. F.; Brienne, M.-J. Preparation by yeast reduction and determination of the sense of chirality of enantiomerically pure ethyl (-)-4,4,4-trichloro-3-hydroxy- and (+)- 4,4,4-trifluoro-3-hydroxybutanoate. *Helv. Chim. Acta* **1984**, *67*, 1843–1853.
277. Bauer, W.; Seebach, D. Bestimmung des Aggregationsgrads lithiumorganischer Verbindungen durch Kryoskopie in Tetrahydrofuran. *Helv. Chim. Acta* **1984**, *67*, 1972–1988.
278. Seebach, D. Alkylierung von Hydroxy- und Aminosäuren unter Erhaltung oder unter Selbstreproduktion des Chiralitätszentrums. *(Autorenreferat) Mitteilungsblatt der Chemischen Gesellschaft der Deutschen Demokratischen, Republik* **1984**, *31*(Heft 11), 249–251.
279. Seebach, D. Crystal Structures and Stereoselective Reactions of Organic Lithium Derivatives. In *Proceedings of The Robert A. Welch Foundation Conferences on Chemical, Research. XXVII. Stereospecificity in Chemistry and Biochemistry, Nov. 7–9, 1983*. Houston, TX, 1984; pp 93–145.

280. Schregenberger, C.; Seebach, D. Synthesis and determination of the absolute configuration of the macrodiolide (+)-conglobatin. *Tetrahedron Lett.* **1984**, *25*, 5881–5884.
281. Seebach, D.; Sutter, M. A.; Weber, R. H.; Züger, M. F. Yeast reduction of ethyl acetoacetate: (*S*)-(+)-ethyl 3-hydroxybutanoate. *Org. Synth* **1985**, *63*, 1–9. Collect. Vol. VII, **1990**, 215–220.
282. Seebach, D.; Aebi, J.; Wasmuth, D. Diastereoselective α-alkylation of β-hydroxycarboxylic esters through alkoxide enolates: (+)-diethyl (2*S*,3*R*)-3-allyl-2-hydroxysuccinate from (−)-diethyl *S*-malate. *Org. Synth.* **1985**, *63*, 109–120, Collect. Vol. VII **1990**, 153–159.
283. Seebach, D.; Coquoz, M. α-Alkylation of (*S*)-glyceric acid through the tert-butylthioester of (2*R*,4*S*)-2-tert-butyl-1,3-dioxolane-4-carboxylic acid. *Chimia* **1985**, *39*, 20–22.
284. Naef, R.; Seebach, D. Herstellung enantiomerenreiner cis- oder trans-konfigurierter 2-(tert-Butyl)-3-methylimidazolidin-4-one aus den Aminosäuren (*S*)-Alanin, (*S*)-Phenylalanin, (*R*)-Phenylglycin, (*S*)-Methionin und (*S*)-Valin. *Helv. Chim. Acta* **1985**, *68*, 135–143.
285. Seebach, D.; Aebi, J. D.; Naef, R.; Weber, T. α-Alkylation of amino acids without racemization. Preparation of either (*S*)- or (*R*)-α-methyldopa from (*S*)-alanine. *Helv. Chim. Acta* **1985**, *68*, 144–154.
286. Weber, T.; Seebach, D. Alkylierung in der 2-Stellung von (2S,4R)-4-Hydroxyprolin unter Retention, Helv. *Chim. Acta* **1985**, *68*, 155–161.
287. Seebach, D.; Beck, A. K.; Golinski, J.; Hay, J. N.; Laube, T. Ueber den sterischen Verlauf der Umsetzung von Enaminen aus offenkettigen Aldehyden und Ketonen mit Nitroolefinen zu 2,3-disubstituierten 4-Nitro-ketonen. *Helv. Chim. Acta* **1985**, *68*, 162–172.
288. Seebach, D.; Ertas, M.; Locher, R.; Schweizer, W. B. Tritylketone und Tritylenone, Beiträge zur sterisch erzwungenen Michael-addition und zur diastereoselektiven Aldol-Addition. *Helv. Chim Acta* **1985**, *68*, 264–282.
289. Bauer, W.; Laube, T.; Seebach, D. Crystal and molecular structure of a THF-solvated lithium amide enolate dimer. *Chem. Ber.* **1985**, *118*, 764–773.
290. Seebach, D.; Brook, M. A. Reversed stereochemical course of the michael-addition of cyclohexanone to β-nitrostyrenes by using1-(trimethylsiloxy)cyclohexene/dichloro -(diisopropoxy)titanium. *Helv. Chim. Acta* **1985**, *68*, 319–324.
291. Widler, L.; Weber, T.; Seebach, D. d^1- und d^3-selektive Umsetzungen von schwefelsubstituierten Allyl-Titan- Derivaten mit Aldehyden und Ketonen. *Chem. Ber.* **1985**, *118*, 1329–1344.
292. Seebach, D.; Hansen, J.; Seiler, P.; Gromek, J. M. On the steric course of addition of 1-lithio- and 1-magnesio-2-pivaloyl-1,2,3,4-tetrahydroisoquinoline to aldehydes and ketones. An X-ray crystal structure determination of the organomagnesium reagent. *J. Organomet. Chem.* **1985**, *285*, 1–13.
293. Seebach, D. Neue Synthesemethoden aus Röntgenstrukturdaten, Jahresbericht 1984 der ETH (Eidgenössischen Technischen Hochschule), Zürich, Mai 1985, S. 31–33.
294. Eyer, M.; Seebach, D. l-2-Nitro-1,3-alkanediols by stereoselective addition of nitroethanol to aldehydes. On the asymmetric electrophilic addition to double bonds. *J. Am. Chem. Soc.* **1985**, *107*, 3601–3606.
295. Seebach, D.; Miller, D. D.; Müller, S.; Weber, T. The chiral glycine enolate derivative from 1-benzoyl-2-(tert-butyl)-3-methyl-1,3-imidazolidin-4-one is alkylated in the 5-position with relative topicity lk. *Helv. Chim. Acta* **1985**, *68*, 949–952.
296. Seebach, D.; Giovannini, F.; Lamatsch, B. Preparative Asymmetric Reduction of 3-Ketobutyrate and -valerate by Suspended Cells of Thermophilic Bacteria (Thermoanaerobium brockii) in Ordinary Laboratory Equipment. *Helv. Chim. Acta* **1985**, *68*, 958–960.
297. Ertas, M.; Seebach, D. Selektive Herstellung von l- oder u-Aldolen aus Äthyl-trityl-keton und aromatischen Aldehyden über Lithium- bzw. Aluminium-Enolate, *Helv. Chim. Acta* **1985**, *68*, 961–968.
298. Seebach, D.; Calderari, G.; Meyer, W. L.; Merritt, A.; Odermann, L. Stereoselective (3+3)-carbocyclization of enamines with nitroallylating reagents. *Chimia* **1985**, *39*, 183–184.
299. Seebach, D.; Fadel, A. N,O-Acetals from pivalaldehyde and amino acids for the α-alkylation with self-reproduction of the center of chirality. Enolates of 3-benzoyl-2-(*tert*-butyl)-1,3-oxazolidin-5-ones. *Helv. Chim. Acta* **1985**, *68*, 1243–1250.
300. Laube, T.; Dunitz, J. D.; Seebach, D. Ueber die Wechselwirkung zwischen Lithium-Enolaten und sekundären Aminen in Lösung und im Kristall. *Helv. Chim. Acta* **1985**, *68*, 1373–1393.
301. Seebach, D. New applications of organometallic derivates of Li,Mg,B,Al,Si,Ti and V in selective syntheses. In *Organic Synthesis: an interdisciplinary challenge*. *Proceedings of the, 5th IUPAC Conference on Organic Synthesis, Freiburg/-Breisgau, 1984*, Streith, J., Prinzbach, H., Schill, G., Eds.; Blackwell Scientific Publications Ltd: Oxford, GB, 1985; pp 77–99.
302. Seebach, D.; Huber, I. M. P. Herstellung diastereomerenreiner l- oder u-konfigurierter 1-hydroxy-benzylierter Tetrahydroisochinolin-Vorläufer für Aporphin-, Protoberberin, Quettamin- und Phthalid-Alkaloide (Stereoselektive Synthese von (±)-Ushinsunin und (±)-Oliverolin). *Chimia* **1985**, *39*, 233–234.
303. Imwinkelried, R.; Seebach, D. Allylierung von Aldehyden unter Veretherung mit Dialkoxydichlorotitan und Allyltrimethylsilan; eine asymmetrische Variante der Sakurai-Reaktion. *Angew. Chem.* **1985**, *97*, 781–782, *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 765–766.
304. Seebach, D.; Chow, H.-F.; Jackson, R. F. W.; Lawson, K.; Sutter, M.-A.; Thaisrivongs, S.; Zimmermann, J. Total synthesis of (+)-11,11′-di-*O*-methylelaiophylidene: an aglycone of elaiophylin. *J. Am. Chem. Soc.* **1985**, *107*, 5292–5293.
305. Seebach, D.; Beck, A. K.; Roggo, S.; Wonnacott, A. Enantioselektive Addition von Arylgruppen an aromatische Aldehyde mit Aryltitan-Binaphthol-Derivaten. *Chem. Ber.* **1985**, *118*, 3673–3682.
306. Seebach, D.; Schiess, M.; Schweizer, W. B. On the stereochemical course of asymmetric mannich reactions. *Chimia* **1985**, *39*, 272–273.
307. Aebi, J. D.; Seebach, D. Enantioselektive α-Alkylierung von Asparagin- und Glutaminsäure über die Dilithium-enolatocarboxylate von 2-[3-Benzoyl-2-(tert-butyl)-1-methyl-5-oxoimidazolidin-4-yl]essigsäure und 3-[3-Benzoyl-2-(tert-butyl)-1-methyl-5-oxoimidazolidin-4-yl]propionsäure. *Helv. Chim. Acta* **1985**, *68*, 1507–1518.
308. Calderari, G.; Seebach, D. Asymmetrische Michael-Additionen. Stereoselektive Alkylierung chiraler, nicht racemischer Enolate durch Nitroolefine. Herstellung enantiomerenreiner

γ-Aminobuttersäure- und Bernsteinsäure-Derivate. *Helv. Chim. Acta* **1985**, *68*, 1592–1604.
309. Häner, R.; Laube, T.; Seebach, D. Regio- and diastereoselective preparation of aldols from α-branched ketone enolates generated from BHT ester enolates and organolithium reagents—in situ generation and trapping of ketenes from ester enolates. *J. Am. Chem. Soc.* **1985**, *107*, 5396–5403.
310. Seebach, D.; Amstutz, R.; Laube, T.; Schweizer, W. B.; Dunitz, J. D. Structures of three lithium ester enolates by X-ray diffraction: derivation of reaction path for cleavage into ketene and alcoholate. *J. Am. Chem. Soc.* **1985**, *107*, 5403–5409.
311. Wuthier, U.; Pham, H. V.; Pretsch, E.; Ammann, D.; Beck, A. K.; Seebach, D.; Simon, W. Zur Anionenselektivität von Distannylderivaten in Membranen. *Helv. Chim. Acta* **1985**, *68*, 1822–1827.
312. Heinzer, J.; Oth, J. F. M.; Seebach, D. Quantitative lineshape analysis of temperature- and concentration-dependent ^{13}C-NMR spectra of ^{6}Li- and ^{13}C-labelled organolithium compounds. *Helv. Chim. Acta* **1985**, *68*, 1848–1862.
313. Seebach, D.; Calderari, G.; Knochel, P. Trifluoroacetoxyphenylselenation of nitroolefins. Regioselective preparation of nitroallylic alcohol derivatives and their use as multiple coupling reagents. *Tetrahedron* **1985**, *41*, 4861–4872, Tetrahedron Symposia-in-Print No. 23 on 'Recent Aspects of Organoselenium Chemistry'.
314. Häner, R.; Seebach, D. Nitration of the DHBA cyclopropanecarboxylate enolate—a new and efficient route to 1-aminocyclopropane-1-carboxylic acid. *Chimia* **1985**, *39*, 356–357.
315. Jackson, R. F. W.; Sutter, M. A.; Seebach, D. Preparation of (2*E*,4*E*,6*S*,7*S*,10*E*,12*E*,14*S*,15*S*,1′(*S*)-7,15-Bis (1′-hydroxymethylethyl)-6,14-dimethyl-8,16-dioxa-2,4,10,12-cyclohexadecatetraene-1,9-dione. A building block for the synthesis of elaiophylin. *Liebigs Ann. Chem.* **1985**, 2313–2327.
316. Seebach, D.; Renaud, P. Chirale Synthesebausteine durch Kolbe-Elektrolyse enantiomerenreiner β-Hydroxy-carbonsäurederivate. (*R*)- und (S)-Methyl- sowie (*R*)-Trifluormethyl-γ-butyrolactone und-δ-valerolactone. *Helv. Chim. Acta* **1985**, *68*, 2342–2349.
317. Raubenheimer, H. G.; Seebach, D. Convenient in situ generation of an active titanium (III)-reagent for stereoselective pinacolization of aromatic aldehydes. *Chimia* **1986**, *40*, 12–13.
318. Seebach, D.; Beck, A. K.; Renaud, P. Di- und trifluorsubstituierte Dilithium Verbindungen für die Organische Synthese. *Angew. Chem.* **1986**, *98*, 96–97, *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 98–99.
319. Seebach, D.; Eberle, M. (*R*)-Ethyl 4-*t*-butoxy-3-hydroxybutanote, a versalite chiral buildingblock for EPC (enantiomerically pure compound) syntheses, by yeast reduction of ethyl 4-*t*-butoxy-3-oxobutanoate. *Synthesis* **1986**, 37–40.
320. Amstutz, R.; Dunitz, J. D.; Laube, T.; Schweizer, W. B.; Seebach, D. Die Geometrie von Lithium-Komplexen mit koordinativ gebundenen Carbonylverbindungen und die Struktur eines Lithiumdienolates. *Chem. Ber.* **1986**, *119*, 434–443.
321. Brändli, U.; Eyer, M.; Seebach, D. Regioselektive Erzeugung und diastereoselektive Umsetzungen in β-Stellung zur Nitrogruppe sekundärer Nitroalkane über α,β-doppelt deprotonierte Derivate (Super-enamine). *Chem. Ber.* **1986**, *119*, 575–588.
322. Seebach, D.; Imwinkelried, R.; Stucky, G. Optisch aktive Alkohole aus 1,3-Dioxan-4-onen; eine praktikable Variante der asymmetrischen Synthese unter nucleophiler Substitution an Acetalzentren. *Angew. Chem.* **1986**, *98*, 182–183, *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 178–180.
323. Meyer, W. L.; Brannon, M. J.; Merritt, A.; Seebach, D. Annulation of 2-formyl-2-cyclohexenones by reaction with enamines. *Tetrahedron Lett.* **1986**, *27*, 1449–1452.
324. Häner, R.; Schweizer, W. B.; Seiler, P.; Seebach, D. Aldol addition of a lithium ketone enolate with persubstituted double bond—a reversal of the usual stereochemical course. *Chimia* **1986**, *40*, 97–98.
325. Seebach, D.; Imwinkelried, R.; Weber, T. EPC Syntheses with C,C Bond Formation via Acetals and Enamines. In *Modern Synthetic Methods*, Scheffold, R., Ed.; Springer: Berlin, 1986; Vol. 4, pp 125–259.
326. Fitzi, R.; Seebach, D. Enantiomerentrennung von (*R*,*S*)-2-(*tert*-Butyl)-3-methyl-4-imidazolidinon, einem chiralen Baustein für die Aminosäuresynthese. *Angew. Chem.* **1986**, *98*, 363–364, Berichtigung: ibid **1986**, *98*, 842; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 345–346; Erratum: ibid **1986**, *25*, 766.
327. Chow, H.-F.; Seebach, D. Diastereoselective aldol addition using boron trichloride or alkoxydichloroborane. *Helv. Chim. Acta* **1986**, *69*, 604–614.
328. Renaud, P.; Seebach, D. Electrochemical decarboxylation of hydroxyproline: a simple three-step conversion of (2S,4R)-4-hydroxy-proline to (R)-γ-amino-β-hydroxy -butanoic acid (GABOB). *Synthesis* **1986**, 424–426.
329. Ehrler, J.; Giovannini, F.; Lamatsch, B.; Seebach, D. Stereoselectivity of yeast reductions-an improved procedure for the preparation of ethyl (*S*)-3-hydroxybutanoate and (*S*)-hydroxymethyl-butanoate. *Chimia* **1986**, *40*, 172–173.
330. Dunitz, J. D.; Seebach, D. Prelog Symposium, Israel, March 16–19 (Report from the Conference at the Weizmann Institute, Rehovot). *Chimia* **1986**, *40*, 174.
331. Seebach, D.; Chow, H.-F.; Jackson, R. F. W.; Sutter, M. A.; Thaisrivongs, S.; Zimmermann, J. (+)-11,11′-Di-*O*-methylelaiophylidene-preparation from elaiophylin and total synthesis from (*R*)-3-hydroxybutyrate and (*S*)-malate. *Liebigs Ann. Chem.* **1986**, 1281–1308.
332. Seebach, D.; Zimmermann, J. 1,3-Dioxanone derivates from β-hydroxy-carboxylic acids and pivalaldehyde. Versatile building blocks for syntheses of enantiomerically pure compounds. A chiral acetoacetic acid derivative. *Helv. Chim. Acta* **1986**, *69*, 1147–1152.
333. Seebach, D. Vladimir Prelog-Jahrgang 1906. *Nachr. Chem. Tech. Lab.* **1986**, *34*, 810–811.
334. Weber, T.; Aeschimann, R.; Maetzke, T.; Seebach, D. Methionin als Vorläufer zur enantioselektiven Synthese α-verzweigter Vinylglycine und anderer Aminosäuren. *Helv. Chim. Acta* **1986**, *69*, 1365–1377.
335. Renaud, P.; Seebach, D. Herstellung chiraler Synthesebausteine aus Aminosäuren und Peptiden durch oxidative elektrolytische Decarboxylierung und $TiCl_4$-induzierte Umsetzung mit Nucleophilen. *Angew. Chem.* **1986**, *98*, 836–838, *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 843–844.
336. Seebach, D.; Eberle, M. Enantioselective cleavage of *meso*-nitrodiol diacetates by an esterase concentrate from fresh pig liver: preparation of useful nitroaliphatic building blocks for EPC syntheses. *Chimia* **1986**, *40*, 315–318.
337. Häner, R.; Maetzke, T.; Seebach, D. Generation and

reactions of lithiated *tert*-butyl and 2,6-Di(*tert*-butyl)-4-methylphenyl cyclopropanecarboxylates. *Helv. Chim. Acta* **1986**, *69*, 1655–1665.
338. Renaud, P.; Seebach, D. Enantiomerenreine Pyrrolidin-Derivate aus trans-4-Hydroxy-L-prolin durch elektrochemische oxidative Decarboxylierung und Titantetrachlorid-vermittelte Umsetzung mit Nukleophilen. *Helv. Chim. Acta* **1986**, *69*, 1704–1710.
339. Schregenberger, C.; Seebach, D. Totalsynthese des Makrodiolids (+)-Conglobatin. *Liebigs Ann. Chem.* **1986**, 2081–2103.
340. Seebach, D.; Roggo, S.; Zimmermann, J. Biological-Chemical Preparation of 3-Hydroxycarboxylic Acids and Their Use in EPC-Syntheses. In *Stereochemistry of Organic and Bioorganic Transformations, Workshop Conferences Hoechst*, Bartmann, W., Sharpless, K. B., Eds.; Chemie: Weinheim, 1987; Vol. 17, pp 85–126.
341. Seebach, D.; Häner, R. C-alkylation of phenylthio aziridine carboxylates. *Chem. Lett. Jpn* **1987**, 49–52.
342. Seebach, D.; Juaristi, E.; Miller, D. D.; Schickli, C.; Weber, T. Addition of chiral glycine, methionine, and vinylglycine enolate derivatives to aldehydes and ketones in the preparation of enantiomerically pure α-amino-β-hydroxy acids. *Helv. Chim. Acta* **1987**, *70*, 237–261.
343. Meyer, W. L.; Schweizer, W. B.; Beck, A. K.; Scheifele, W.; Seebach, D.; Schreiber, S. L.; Kelly, S. E. Revised structure of the fungal germination self-inhibitor gloeosporone. *Helv. Chim. Acta* **1987**, *70*, 281–291.
344. Renaud, P.; Hürzeler, M.; Seebach, D. Elektrochemische Oxidation von (*S*)-Äpfelsäurederivaten: ein Weg zu enantiomerenreinen alkylierten Malonaldehydsäure-estern. *Helv. Chim. Acta* **1987**, *70*, 292–298.
345. Seebach, D.; Imwinkelried, R.; Stucky, G. Optisch aktive Alkohole aus 1,3-Dioxan-4-onen: eine praktikable Variante der enantioselektiven Synthese unter nucleophiler Substitution an Acetal-Zentren, Helv. *Chim. Acta* **1987**, *70*, 448–464.
346. Brook, M. A.; Seebach, D. Cyclic nitronates from the diastereoselective addition of 1-tri-methylsilyloxy-cyclohexene to nitroolefins. Starting materials for stereoselective Henry-reactions and 1,3-dipolar cycloadditions. *Can. J. Chem.* **1987**, *65*, 836–850.
347. Imwinkelried, R.; Schiess, M.; Seebach, D. Diisopropyl (2*S*,3*S*)-2,3-0-isopropylidenetartrate. *Organic Syntheses* **1987**, *65*, 230–235, Collect. Vol. VIII, **1993**, 201–204.
348. Seebach, D.; Estermann, H. α-Alkylation of β-aminobutanoates with *lk*−1.2-induction. *Tetrahedron Lett.* **1987**, *28*, 3103–3106.
349. Seebach, D.; Beck, A. K.; Imwinkelried, R.; Roggo, S.; Wonnacott, A. Chirale Alkoxytitan(IV)-Komplexe für enantioselektive nucleophile Additionen an Aldehyde und als Lewis-Säuren in Diels–Alder-Reaktionen. *Helv. Chim. Acta* **1987**, *70*, 954–974.
350. Zimmermann, J.; Seebach, D. Brominations of cyclic acetals from α-amino acids and α- or β-hydroxy acids with *N*-bromosuccinimide. *Helv. Chim. Acta* **1987**, *70*, 1104–1114.
351. Seebach, D.; Aebi, J. D.; Gander-Coquoz, M.; Naef, R. Stereoselektive Alkylierung an C(α) von Serin. Glycerinsäure, Threonin und Weinsäure über heterocyclische Enolate mit exocyclischer Doppelbindung. *Helv. Chim. Acta* **1987**, *70*, 1194–1216.
352. Seebach, D.; Herradon, B. Diastereoselective elaboration of the carbon skeleton of β-hydroxyesters from yeast reductions. Preparation of (2*S*)-2-hydroxy-cyclohexane carboxylic acids with three contiguous stereogenic centers. *Tetrahedron Lett.* **1987**, *28*, 3791–3794.
353. Griesbeck, A.; Seebach, D. Einfache Umwandlung von (−)-(*R*)-3-Hydroxybuttersäure in das (+)-(*S*)-Enantiomere und dessen Lacton (−)-(*S*)-4-Methyloxetan-2-on. *Helv. Chim. Acta* **1987**, *70*, 1320–1325.
354. Griesbeck, A.; Seebach, D. Herstellung enantiomerenreiner Derivate von 3-Amino- und 3-Mercapto-buttersäure durch S_N2-Ringöffnung des β-Lactons und eines 1,3-Dioxanons aus der 3-Hydroxybuttersäure. *Helv. Chim. Acta* **1987**, *70*, 1326–1332.
355. Seebach, D.; Huber, I. M. P.; Syfrig, M. A. Diastereoselektive Hydroxyalkylierungen in 1-Stellung von Tetrahydro -isochinolinen und Synthese von Aporphin-, Protoberberin- und Phthalid Alkaloiden. *Helv. Chim. Acta* **1987**, *70*, 1357–1379.
356. Seebach, D.; Häner, R.; Vettiger, T. Nucleophile Ringöffnung von α-Nitrocyclopropancarbonsäure-arylestern mit sterisch geschützter, aber elektronisch wirksamer Carbonyl- und Nitro-Gruppe. Ein neues Prinzip der α-Aminosäure-Synthese (Aminobutansäure-a^4-Synthon). *Helv. Chim. Acta* **1987**, *70*, 1507–1515.
357. Seebach, D.; Roggo, S.; Maetzke, T.; Braunschweiger, H.; Cercus, J.; Krieger, M. Diastereo- und enantioselektive Reduktion von β-Ketoestern mit Cyclopentanon-, Cyclohexanon-, Piperidon- und Tetralon-Struktur durch nicht fermentierende Bäcker-Hefe. *Helv. Chim. Acta* **1987**, *70*, 1605–1615.
358. Adam, G.; Zibuck, R.; Seebach, D. Total synthesis of (+)-gloeosporone: assignment of absolute configuration. *J. Am. Chem. Soc.* **1987**, *109*, 6176–6177.
359. Schnurrenberger, P.; Hungerbühler, E.; Seebach, D. Total synthesis of (+)-colletodiol from (*S*,*S*)-tartrate and (*R*)-3-hydroxy butanoate. *Liebigs Ann. Chem.* **1987**, 733–744.
360. Häner, R.; Olano, B.; Seebach, D. Preparation and C-alkylation of enantiomerically pure *S*-phenyl aziridin-carbothioates. On the structure of small-ring ester lithium enolates. *Helv. Chim. Acta* **1987**, *70*, 1676–1693.
361. Polt, R.; Seebach, D. Alkylation of imidazolidinone dipeptide derivatives: preparation of enantiomerically pure di- and tripeptides by 'chirality transfer' via a pivalaldehyde *N*,*N*-acetal center. *Helv. Chim. Acta* **1987**, *70*, 1930–1936.
362. Huber, I. M. P.; Seebach, D. EPC-synthesis of tetrahydroisoquinolines by diastereoselective alkylation at the 1-position of phenylalanine-derived precursors. Synthesis of the alkaloid (+)-corlumine. *Helv. Chim. Acta* **1987**, *70*, 1944–1954.
363. Krause, N.; Seebach, D. Zur Chemie acetylenischer Titan-Verbindungen. *Chem. Ber.* **1987**, *120*, 1845–1851.
364. Noda, Y.; Seebach, D. Reactions of chiral 2-(*tert*-butyl)-2*H*,4*H*−1,3-dioxin-4-ones bearing functional groups in the 6-position and diastereoselective catalytic hydrogenation to *cis*−2,6-disubstituted 1,3-dioxan-4-ones. *Helv. Chim. Acta* **1987**, *70*, 2137–2145.
365. Betschart, C.; Seebach, D. Aminierende reduktive Kupplung aromatischer Aldehyde mit niedervalenten Titan-Reagentien zu 1,2-Diarylethylendiaminen. *Helv. Chim. Acta* **1987**, *70*, 2215–2231.
366. Seebach, D. Geburtstagsadresse, Commemoration of Prof. Dr. Teruaki Mukaiyama's 60th birthday, Kokenkai, Tokyo University, 1987.
367. Eberle, M.; Egli, M.; Seebach, D. Enantioselektive Verseifung der Diacetate von 2-Nitro-1,3-diolen mit Schweineleber-Esterase und Herstellung enantiomerenreiner Derivate

von 2-Nitro-allylalkoholen (chirale Verknüpfungsreagenzien). *Helv. Chim. Acta* **1988**, *71*, 1–23.
368. Seebach, D.; Brändli, U.; Schnurrenberger, P.; Przybylski, M. High-yield synthesis of 20-, 24-, and 28-membered Macropentolide, -hexolide, and -heptolide, respectively, from (*R*)- or (*S*)-3-hydroxy-butanoic acid under Yamaguchi's macrolactonization conditions. *Helv. Chim. Acta* **1988**, *71*, 155–167.
369. Gander-Coquoz, M.; Seebach, D. Herstellung enantiomerenreiner, α-alkylierter Lysin-, Ornithin- und Tryptophan-Derivate. *Helv. Chim. Acta* **1988**, *71*, 224–236.
370. Zibuck, R.; Seebach, D. Note on the preparation of 1,2-diketones from acetylenes. *Helv. Chim. Acta* **1988**, *71*, 237–240.
371. Seebach, D.; Adam, G.; Gees, T.; Schiess, M.; Weigand, W. Scope and limitations of the $TiCl_4$-mediated additions of isocyanides to aldehydes and ketones with formation of α-hydroxycarboxylic acid amides. *Chem. Ber.* **1988**, *121*, 507–517.
372. Seebach, D.; Maetzke, T.; Haynes, R. K.; Paddon-Row, M. N.; Wong, S. S. Low-temperature X-ray crystal-structure analysis of the thermally unstable lithiated 2-butenyl *tert*-butyl sulfide: a comparison with model ab initio MO calculations. *Helv. Chim. Acta* **1988**, *71*, 299–311.
373. Adam, G.; Seebach, D. (2*S*,3*R*)-2-Benzyloxy-3,4-epoxybutan-1-ol; a versatile synthetic building block formally derived from (u)-tartaric acid. *Synthesis* **1988**, 373–376.
374. Seebach, D. Editorial, Revolution der Publikationstechnik aus der Sicht eines Konsumenten. *Chimia* **1988**, *42*, 122.
375. Beck, A. K.; Seebach, D. Large-scale preparation of (*S*)-α-methylmethionine from the parent amino acid. *Chimia* **1988**, *42*, 142–144.
376. Seebach, D.; Stucky, G.; Renaud, P. Chirale Synthesebausteine aus Aminosäuren über einen elektrochemischen Schlüsselschritt: Herstellung von (*R*)-2-*tert*-Butyl-3-methoxycarbonyl-1,3-oxazolinen aus (*S*)-Serin und (*S*)-Threonin. *Chimia* **1988**, *42*, 176–178.
377. Krause, N.; Seebach, D. The ring opening of unsymmetrical allylic, benzylic, propargylic, and Si-substituted epoxides by titanium acetylides: a convenient access to certain 2-substituted 3-butyn-1-ols. *Chem. Ber.* **1988**, *121*, 1315–1320.
378. Seebach, D.; Zimmermann, J.; Gysel, U.; Ziegler, R.; Ha, T.-K. Totally stereoselective additions to 2,6-disubstituted 1,3-dioxin-4-ones (chiral acetoacetic acid derivatives). Synthetic and mechanistic aspects of remote stereoselectivity. *J. Am. Chem. Soc.* **1988**, *110*, 4763–4772.
379. Zimmermann, J.; Seebach, D.; Ha, T.-K. α-Alkylierung von β-Hydroxycarbonsäuren über 1,3-Dioxan-4-on-Enolate. *Helv. Chim. Acta* **1988**, *71*, 1143–1155.
380. Seebach, D.; Müller, S. G.; Gysel, U.; Zimmermann, J. Präparative chromatographische Enantiomerentrennung von synthetisch nützlichen cyclischen Acetalen. *Helv. Chim. Acta* **1988**, *71*, 1303–1318.
381. Fitzi, R.; Seebach, D. Resolution and use in α-amino acid synthesis of imidazolidinone glycine derivatives. *Tetrahedron* **1988**, *44*, 5277–5292, Tetrahedron Symposia-in-Print No. 33 on 'α-Amino Acid Synthesis'.
382. Seebach, D. In *In Memory of Prof. Dr. Gen-ichi Tsuchihashi. Memorial Writings for Prof. Dr. Gen-ichi Tsuchihashi*, Aramaki, K., Iwata, S., Ohta, H., Ogawa, S., Ogura, K., Kaya, K., Kinoshita, M., Kondo, K., Saito, Y., Shizusato, Y., Suehiro, T., Sugai, T., Suzuki, K., Tatsuta, K., Honda, H., Morita, S., Yamamura, S., Eds.; Keio University: Yokohama, Japan, 1988.
383. Seebach, D.; Stucky, G. Reaktivität von (*R*)-2-*tert*-Butyldihydrooxazol-Derivaten aus Serin und Threonin-neuartige und vielseitig einsetzbare chirale Synthesebausteine. *Angew. Chem.* **1988**, *100*, 1398–1404, *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1351–1353.
384. Estermann, H.; Seebach, D. Diastereoselektive Alkylierung von 3-Aminobutansäure in der 2-Stellung. *Helv. Chim. Acta* **1988**, *71*, 1824–1839.
385. Betschart, C.; Schmidt, B.; Seebach, D. Anwendungsbreite der reduktiven Kupplung aromatischer Aldimin-Derivate mit niedervalenten Titan-Reagenzien zu 1,2-Diarylethylendiaminen. *Helv. Chim. Acta* **1988**, *71*, 1999–2021.
386. Seebach, D. Struktur und Reaktivität von Lithiumenolaten vom Pinakolon zur selektiven C-Alkylierung von Peptiden-Schwierigkeiten und Möglichkeiten durch komplexe Strukturen. *Angew. Chem.* **1988**, *100*, 1685–1715, *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1624–1654.
387. Amberg, W.; Seebach, D. Direkte Michael-Additionen von Silylgruppen an α,β-ungesättigte β-Aryl-ketone und ein α-Benzylidenlakton mit Mischungen aus Kupfer(I)-cyanid Butyllithium und Chlorsilanen. *Angew. Chem.* **1988**, *100*, 1786–1787, *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1718–1719.
388. Brook, M. A.; Faggiani, R.; Lock, C. J. L.; Seebach, D. *u*,*l*−4a,5,6,7,8,8a-Hexahydro-4-phenyl-8a-(trimethylsiloxy)-4*H*−1,2-benzoxazine 2-oxide. *Acta Crystallogr.* **1988**, *44*, 1981–1984.
389. Imwinkelried, R.; Seebach, D. 3′Nitro-1-phenylethanol by addition of methyltriisopropoxytitanium to *m*-nitrobenzaldehyde. *Org. Synth.* **1989**, *67*, 180–185.
390. Egli, M.; Polt, R.; Seebach, D. Diastereoselective cyclization of a glycyl-alanine azomethine to an imidazolidinone: determination of the product configuration by X-ray analysis. *Chimia* **1989**, *43*, 4–5.
391. Betschart, C.; Seebach, D. Anwendungen niedervalenter Titan-Reagentien in der Organischen Synthese. *Chimia* **1989**, *43*, 39–49.
392. Polt, R.; Seebach, D. Stereoselektive alkylation of glycine units in dipeptide derivatives: 'chirality transfer' via a pivalaldehyde *N*,*N*-acetal center. *J. Am. Chem. Soc.* **1989**, *111*, 2622–2632.
393. Seebach, D.; Charczuk, R.; Gerber, C.; Renaud, P.; Berner, H.; Schneider, H. Elektrochemische Decarboxylierung von L-Threonin- und Oligopeptid-Derivaten unter Bildung von *N*-Acyl-*N*,*O*-acetalen: Herstellung von Oligopeptiden mit Carboxamid- oder Phosphonat-C-Terminus. *Helv. Chim. Acta* **1989**, *72*, 401–425.
394. Maetzke, T.; Seebach, D. Röntgenstrukturanalyse von 2,4,6-Tri(tert-butyl)phenyllithium. *N*,*N*,*N*′,*N*′-Tetramethylpropan-1,2-diamin: eine monomere Organolithium-Verbindung. *Helv. Chim. Acta* **1989**, *72*, 624–630.
395. Seebach, D.; Mißlitz, U.; Uhlmann, P. Das Dienolat von (*R*)-2-*tert*-Butyl-6-methyl-1,3-dioxin-4(2*H*)-on - ein chirales Acetessigester-d^4-Reagens. *Angew. Chem.* **1989**, *101*, 484–485, *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 472–473.
396. Herradon, B.; Seebach, D. Mono- and dialkylation of derivatives of (1R,2S)-2-hydroxycyclo-pentanecarboxylic acid and -cyclohexanecarboxylic acid via bicyclic dioxanones: selective generation of three contiguous stereogenic centers on a cyclohexane ring. *Helv. Chim. Acta* **1989**, *72*, 690–714.

397. Ehrler, J.; Seebach, D. Notiz über mikrobiologische Umsetzungen mit Halobacterium halobium: Reduktion von 3-Oxobutansäure-ethylester und Hydrolyse von 3-Hydroxybutansäure-ethylester. Cooperative Effekte von Reduktase und Hydrolase. *Helv. Chim. Acta* **1989**, *72*, 793–799.
398. Seebach, D.; Thaler, A.; Beck, A. K. Solubilization of peptides in non-polar organic solvents by the addition of inorganic salts: facts and implications. *Helv. Chim. Acta* **1989**, *72*, 857–867.
399. Seebach, D.; Jeanguenat, A.; Schmidt, J.; Maetzke, T. Chirale Synthesebausteine aus Aminosäuren: Dihydrothiazol-Derivate (Δ^4-Thiazoline) aus Cystein. *Chimia* **1989**, *43*, 314–317.
400. Seebach, D.; Brändli, U.; Müller, H.-M.; Dobler, M.; Egli, M.; Przybylski, M.; Schneider, K. On the macrolactonization of β-hydroxy acids. Crystal structure of the pentolide and the hexolide from (*R*)-3-hydroxybutanoic acid. Molecular modeling studies of the tetrolide. *Helv. Chim. Acta* **1989**, *72*, 1704–1717.
401. Haag, T.; Arslan, T.; Seebach, D. Preparative β-ketoester reductions and ester hydrolyses by yeast, using free cells in organic media. *Chimia* **1989**, *43*, 351–353.
402. Stucky, G.; Seebach, D. Substitutionen und Additionen an (*R*)-2-*tert*-Butyl-Δ^4−1,3-oxazolin-3-carbonsäure-methylester. *Chem. Ber.* **1989**, *122*, 2365–2375.
403. Seebach, D.; Stucky, G.; Pfammatter, E. Cycloadditionen an die Doppelbindung von (*R*)-2-*tert*-Butyl-Δ^4−1,3-oxazolin-3-carbonsäure-methylestern. *Chem. Ber.* **1989**, *122*, 2377–2389.
404. Seebach, D.; Dziadulewicz, E.; Behrendt, L.; Cantoreggi, S.; Fitzi, R. Synthesis of nonproteinogenic (*R*)- or (*S*)-amino acids. Analogues of phenylalanine, isotopically labelled and cyclic amino acids from *tert*-butyl 2-(*tert*-butyl)-3-methyl-4-oxo-1-imidazolidinecarboxylate (Boc-BMI). *Liebigs Ann. Chem.* **1989**, 1215–1232.
405. Seebach, D.; Adam, G.; Zibuck, R.; Simon, W.; Rouilly, M.; Meyer, W. L.; Hinton, J. F.; Privett, T. A.; Templeton, G. E.; Heiny, D. K.; Gisi, U.; Binder, H. Gloeosporone—a macrolide fungal germination self-inhibitor. Total synthesis and activity. *Liebigs Ann. Chem.* **1989**, 1233–1240.
406. Vettiger, T.; Seebach, D. Nucleophile Ringöffnung von 1-Nitro-1-cyclopropancarbonsäure-arylestern mit sterisch geschützter, aber elektronisch wirksamer Carbonyl- und Nitrogruppe. Ein neues Prinzip der Aminosäuresynthese. *Liebigs Ann. Chem.* **1990**, 195–201.
407. Ehrler, J.; Seebach, D. Enantioselektive Verseifungen substituierter, achiraler 3-Acyloxy-propylester mit Lipasen: Herstellung chiraler Derivate von 'Tris(hydroxymethyl)-methan'. *Liebigs Ann. Chem.* **1990**, 379–388.
408. Acs, M.; von dem Bussche, C.; Seebach, D. An efficient method of preparing (*R*)- and (*S*)-4,4,4-trifluoro-3-hydroxybutanoic acid: resolution with (*R*)- or (*S*)-1-phenylethylamine. *Chimia* **1990**, *44*, 90–92.
409. Seebach, D.; Beck, A. K.; Brändli, U.; Müller, D.; Przybylski, M.; Schneider, K. Partial depolymerization and solubilization of poly[(*R*)-3-hydroxy-butanoate] (PHB) and its copolymer with (*R*)-3-hydroxyvalerate (BIOPOL®) by treatment with Li-amides/LiCl in tetrahydrofuran at low temperature. *Chimia* **1990**, *44*, 112–116.
410. Breitschuh, R.; Seebach, D. Herstellung von (*S*)-4-Methyloxetan-2-on (β-Butyrolacton) durch Lactonisierung von (*R*)-3-Hydroxybuttersäure mit Orthoessigsäuretriethylester. *Chimia* **1990**, *44*, 216–218.
411. Kessler, H.; Gehrke, M.; Lautz, J.; Köck, M.; Seebach, D.; Thaler, A. Complexation and medium effects on the conformation of cyclosporin A studied by NMR spectroscopy and molecular dynamics calculations. *Biochem. Pharmacol.* **1990**, *40*, 169–173, erratum ibid. *40*, 2185–2186.
412. Seebach, D.; Vettiger, T.; Müller, H.-M.; Plattner, D.; Petter, W. Stereoselective hydroxy alkylations of (*S*)-2-azetidine carboxylic acid. *Liebigs Ann. Chem.* **1990**, 687–695.
413. Beck, A. K.; Gautschi, M.; Seebach, D. Die Geschichte einer Acetalisierung und die überraschende Dimerisierung eines 1,3-Dioxan-4-ons zu einem Zwölfring [2-(tert-Butyl)-6-(trifluoro-methyl)-1,3-dioxan-4-on und 2,8-D(tert-butyl)-6,12-bis(trifluoromethyl)-1,3,7,9-tetraoxacyclodecan-4,10-dion aus rac-, (R)- und (S)-4,4,4-Trifluoro-3-hydroxybutansäure und Pivalaldehyd]. *Chimia* **1990**, *44*, 291–295.
414. Seebach, D. How I became a Peptide Chemist, On the occasion of the 10 year anniversary LONZA Japan on October 5, 1990, in Tokyo Nohrin Nenkin Kaikan, Pastorale, Lonza Brochure, Lonza Ltd. Basel, 1990.
415. Hahn, E.; Maetzke, T.; Plattner, D. A.; Seebach, D. Röntgenstrukturanalyse des dimeren 2,2-Diphenylcyclopropanthiocarbonsäure-*S*-*tert*-butylester-Lithium-Enolat·TMEDA-Komplexes: ein 'ganz normales' Ester-Enolat und ein 'ganz normales' Methylencyclopropan-Derivat. *Chem. Ber.* **1990**, *123*, 2059–2064.
416. Eberle, M.; Missbach, M.; Seebach, D. Enantioselective Saponification with pig liver esterase (PLE): (1S,2S,3R)-3-hydroxy-2-nitrocyclohexyl acetate. *Org. Synth.* **1990**, *69*, 19–30.
417. Seebach, D.; Missbach, M.; Calderari, G.; Eberle, M. [3+3]-Carbocyclizations of nitroallylic esters and enamines with stereoselective formation of up to six new stereogenic centers. *J. Am. Chem. Soc.* **1990**, *112*, 7625–7638.
418. Seebach, D.; Adam, G.; von dem Bussche-Hünnefeld, C.; Gisi, U.; Binder, H. EPC—synthesis and fungistatic acitivity of a gloeosporone analog with an ω-hydroxybutyl instead of the pentyl side chain on the macrocyclic ring. *Liebigs Ann. Chem.* **1990**, 1007–1012.
419. Maetzke, T.; Hidber, C. P.; Seebach, D. X-ray crystal structure analysis of (*N*-isopropylbenzamide)lithium tetrahydrofuran: an aza analogous ketone lithium enolate. *J. Am. Chem. Soc.* **1990**, *112*, 8248–8250.
420. Seebach, D. Ein Chemie-Nobelpreis für die Organische Synthese. *Neue Zürcher Zeitung* **1990**, *14*(265), 65.
421. Seebach, D. Organische Synthese-wohin? *Angew. Chem.* **1990**, *102*, 1363–1409, *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1320–1367.
422. Maetzke, T.; Seebach, D. X-ray crystal structure analysis of an octameric lithium, *N*-isopropylbenzamide aza enolate complex. *Organometallics* **1990**, *9*, 3032–3037.
423. Amberg, W.; Seebach, D. (*E*,*R*,*R*)-5-Alkyliden-2-*tert*-butyl-6-methyl-1,3-dioxan-4-one: Herstellung aus (*R*)-3-Hydroxybuttersäure, Cuprat-Additionen und Hydrolysen zu 3-Hydroxycarbonsäuren mit chiralen sekundären Alkylgruppen in 2-Stellung. *Chem. Ber.* **1990**, *123*, 2413–2428.
424. Amberg, W.; Seebach, D. (2*R*)-5-Alkyl-2-*tert*-butyl-6-methyl-4*H*−1,3-dioxin-4-one als Zwischenprodukte zur Herstellung von α,β,β-trisubstituierten β-Hydroxycarbonsäuren unter Selbstregeneration des stereogenen Zentrums von (*R*)-3-Hydroxybuttersäure. *Chem. Ber.* **1990**, *123*, 2429–2438.

425. Amberg, W.; Seebach, D. Direkte Michael-artige Addition von Si-Gruppen an β-Aryl-α,β-ungesättigte Carbonylverbindungen mit $R_3SiCl/Bu_2Cu(CN)Li_2$. *Chem. Ber.* **1990**, *123*, 2439–2444.
426. Seebach, D.; Bossler, H.; Gründler, H.; Shoda, S.-i.; Wenger, R. C-alkylation of peptides through polylithiated and LiCl-solvated derivatives containing sarcosine Li-enolate units. *Helv. Chim. Acta* **1991**, *74*, 197–224.
427. Schmidt, B.; Seebach, D. Katalytische und stöchiometrische enantioselektive Additionen von Diethylzink an Aldehyde mit Hilfe eines neuartigen chiralen Spirotitanats. *Angew. Chem.* **1991**, *103*, 100–101, *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 99–101.
428. Seebach, D.; Maetzke, T.; Petter, W.; Klötzer, B.; Plattner, D. A. Pyramidalization and reactivity of trigonal centers. X-ray crystal structure analysis of two silyl enol ethers from 1-benzoyl- and 1-(methoxycarbonyl)-2-*tert*-butyl-3,5-dimethyl-4-imidazolidinone (reagents for amino acid synthesis). *J. Am. Chem. Soc.* **1991**, *113*, 1781–1786.
429. Juaristi, E.; Quintana, D.; Lamatsch, B.; Seebach, D. Asymmetric synthesis of β-amino acids. 1. Highly diastereoselective addition of a racemic β-alanine enolate derivative to electrophiles. *J. Org. Chem.* **1991**, *56*, 2553–2557.
430. Seebach, D.; Gysel, U.; Kinkel, J. N. Hoch effiziente, präparative chromatographische Enantiomerentrennung von 2-Phenyl-1,3-dioxin-4-onen an Cellulose-triacetat und Cuprat-Additionen zu β-Hydroxycarbonsäure-Derivaten. *Chimia* **1991**, *45*, 114–117.
431. Thaler, A.; Seebach, D.; Cardinaux, F. Lithium-salt effects in peptide synthesis. Part I: conditions for the use of lithium-salts in coupling reactions. *Helv. Chim. Acta* **1991**, *74*, 617–627.
432. Thaler, A.; Seebach, D.; Cardinaux, F. Lithium-salt effects in peptide synthesis. Part II: improvement of degree of resin swelling and of efficiency of coupling in solid-phase synthesis. *Helv. Chim. Acta* **1991**, *74*, 628–643.
433. Seebach, D. (*R*)-Polyhydroxybutyrate in the Hands of a Synthetic Organic Chemist, Thirty-Second National Organic Chemistry Symposium, The Division of Organic, Chemistry of the American Chemical Society, June 16–20, 1991, *Program and Abstracts*, The University of Minnesota, Minneapolis, Minnesota, USA, 1991; pp 181–195.
434. Schickli, C. P.; Seebach, D. Herstellung chiraler elektrophiler Glycin- und (*E*)-2,3-Dehydroamino-, säure-Derivate aus 2-*t*-Butyl-3-methyl-4-oxo-1-imidazolidincarbonsäure-*t*-butylester (Boc-BMI). *Liebigs Ann. Chem.* **1991**, 655–668.
435. Seebach, D.; Bürger, H. M.; Schickli, C. P. Stereoselektive Umsetzungen von rac-, (*R*)- oder (*S*)-5-Alkyliden-, 2-t-butyl-3-methyl-4-oxo-1-imidazolidincarbonsäure-t-butylestern, (chirale 2,3-Dehydroaminosäure-Derivate) und Herstellung einiger nichtproteinogener Aminosäuren. *Liebigs Ann. Chem.* **1991**, 669–684.
436. Seebach, D.; Thaler, A.; Blaser, D.; Ko, S. Y. Transesterifications with 1,8-diazabicyclo[5.4.0]undec-7-ene/lithium bromide (DBU/LiBr)—also applicable to cleavage of peptides from resins in Merrifield syntheses. *Helv. Chim. Acta* **1991**, *74*, 1102–1118.
437. Seebach, D.; Behrendt, L.; Felix, D. Titanat-katalysierte enantioselektive Addition von in situ aus Grignard-Reagentien in Ether erzeugten Alkylzinkverbindungen an Aldehyde. *Angew. Chem.* **1991**, *103*, 991–992, *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1008–1009.
438. Pietzonka, T.; Seebach, D. Alkylations of (*R*,*R*)-2-*t*-butyl-6-methyl-1,3-dioxan-4-ones which are, not possible with lithium amides may be achieved with a Schwesinger P 4 base. *Chem. Ber.* **1991**, *124*, 1837–1843.
439. Seebach, D.; Miβlitz, U.; Uhlmann, P. Reaktionen von Dienolaten des (*R*)-2-*tert*-Butyl-6-methyl-4*H*−1,3-dioxin-4-ons mit Aldehyden und Ketonen - ein chirales Acetessigester-d^4-Reagens. *Chem. Ber.* **1991**, *124*, 1845–1853.
440. Beck, A. K.; Bastani, B.; Plattner, D. A.; Petter, W.; Seebach, D.; Braunschweiger, H.; Gysi, P.; La Vecchia, L. Grossansätze zur Herstellung von α,α,α′,α′-Tetraaryl-1,3-dioxolan-4,5-dimethanolen (TADDOLe): Nützliche Hilfsstoffe für die EPC-Synthese und ihre Struktur im Festkörper. *Chimia* **1991**, *45*, 238–244.
441. Blaser, D.; Ko, S. Y.; Seebach, D. A stereoselective synthesis of MeBmt employing a new chiral glycine enolate derivative. *J. Org. Chem.* **1991**, *56*, 6230–6233.
442. Blaser, D.; Seebach, D. Benzyl (*R*)- and (*S*)-2-*tert*-butyl-5-oxo-oxazolidine-3-carboxylate for convenient preparation of D- and L-threonine analogs from aldehydes. *Liebigs Ann. Chem.* **1991**, 1067–1078.
443. Jeanguenat, A.; Seebach, D. Stereoselective chain elongation at C-3 of cysteine through 2,3-dihydrothiazoles, without racemization. Preparation of, 2-amino-5-hydroxy-3-mercapto-alkanoic acid derivatives. *J. Chem. Soc. Perkin Trans. 1* **1991**, 2291–2298.
444. Schmidt, B.; Seebach, D. 2,2-Dimethyl-α,α,α′,α′-tetra-(naphth-2-yl)-1,3-dioxolan-4,5-dimethanol (DINOL) für die Titanat-vermittelte, enantioselektive Addition von Diethylzink an Aldehyde. *Angew. Chem.* **1991**, *103*, 1383–1385, *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1321–1323.
445. Gerber, C.; Seebach, D. Dipeptide derivatives with a phosphonate instead of carboxylate terminus by C-Alkylation of protected (decarboxy-dipeptidyl)phosphonates. *Helv. Chim. Acta* **1991**, *74*, 1373–1385.
446. Kinkel, J. N.; Gysel, U.; Blaser, D.; Seebach, D. Preparative resolution of heterocyclic acetals derived from glycine, mercaptoacetic acid, β-alanine, and formyl- or acetylacetic acid by recycling chromatography on chiraspher and temperature dependence, of separation factors. *Helv. Chim. Acta* **1991**, *74*, 1622–1635.
447. Seebach, D.; Ko, S. Y.; Kessler, H.; Köck, M.; Reggelin, M.; Schmieder, P.; Walkinshaw, M. D.; Bölsterli, J. J.; Bevec, D. Thiocyclosporins: preparation, solution and crystal structure, and immunosuppressive activity. *Helv. Chim. Acta* **1991**, *74*, 1953–1990.
448. Seebach, D.; Maestro, M. A.; Sefkow, M.; Neidlein, A.; Sternfeld, F.; Adam, G.; Sommerfeld, T. A highly convergent total synthesis of (+)-myxovirescine M_2. *Helv. Chim. Acta* **1991**, *74*, 2112–2118.
449. Müller, H.-M.; Dobler, M.; Zbinden, P.; Seebach, D. Bildung 12- bis 40-gliedriger Oligolide aus enantiomerenreinen, 3-Hydroxybuttersäure-Derivaten-Bausteine für eine 2_1- und eine, 3_1-Helix. *Chimia* **1991**, *45*, 376–378.
450. Beck, A. K.; Brunner, A.; Montanari, V.; Seebach, D. 6-Chloromethylierte 2-(*tert*-Butyl)-1,3-dioxan- und-1,3-dioxin-4-one, aus (*R*)- oder (*S*)-4,4,4-Trichloro-3-hydroxybuttersäure. *Chimia* **1991**, *45*, 379–382.
451. Beck, A. K.; Seebach, D. Aldol- und Michael-Additionen fluorierter Nitroalkane an Aldehyde, Ketone und α,β-ungesättigte Carbonylverbindungen. *Chem. Ber.* **1991**, *124*, 2897–2911.
452. Pfammatter, E.; Seebach, D. Preparation of (*R*)- and (*S*)-2-alkyl-2-amino-3-(methylamino)propanoic and other

2,3-diaminoalkanoic acid derivatives from a chiral imidazoline. *Liebigs Ann. Chem.* **1991**, 1323–1336.
453. Suzuki, K.; Seebach, D. *threo*−3-Alkyl- and -arylglutamic acid derivatives by Michael additions, of Boc-BMI Li-enolates to 2,6-di-*t*-butyl-4-methoxyphenyl alkenoates. On the diastereo-selectivity of the coupling of trigonal centers involving heterocyclic Li-enolates. *Liebigs Ann. Chem.* **1992**, 51–61.
454. Weber, B.; Seebach, D. Enantiomerenreine tertiäre Alkohole durch TADDOL-vermittelte Additionen an Ketone-oder wie man ein Grignard-Reagens enantioselektiv macht. *Angew. Chem.* **1992**, *104*, 96–97, *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 84–86.
455. Seebach, D.; Gysel, U.; Job, K.; Beck, A. K. Modified preparation of (2*R*)-2-*tert*-butyl-6-methyl-4*H*−1,3-dioxin-4-one; a chiral acetylacetic acid derivative for the synthesis of enantiopure compounds. *Synthesis* **1992**, 39–40.
456. Breitschuh, R.; Seebach, D. Herstellung von stereoisomeren 3-Sulfinylbuttersäuren aus (*R*)- und, (*S*)-4-Methyl-2-oxetanon. *Synthesis* **1992**, 83–89.
457. von dem Bussche-Hünnefeld, C.; Beck, A. K.; Lengweiler, U.; Seebach, D. α,α,α′,α′-Tetraaryl-1,3-dioxolane-4,5-dimethanols (TADDOLs) for Resolution of alcohols and as chiral solvating agents in NMR spectroscopy. *Helv. Chim. Acta* **1992**, *75*, 438–441.
458. Köck, M.; Kessler, H.; Seebach, D.; Thaler, A. Novel backbone conformation of cyclosporin A: the complex with lithium chloride. *J. Am. Chem. Soc.* **1992**, *114*, 2676–2686.
459. Seebach, D.; Müller, H.-M.; Bürger, H. M.; Plattner, D. A. Das Triolid von (*R*)-3-Hydroxybuttersäure - direkte Herstellung aus Polyhydroxybutyrat und Bildung eines Kronen-Estercarbonyl-Komplexes mit Na-Ionen. *Angew. Chem.* **1992**, *104*, 443–444, *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 434–435.
460. Müller, W.; Lowe, D. A.; Neijt, H.; Urwyler, S.; Herrling, P. L.; Blaser, D.; Seebach, D. Synthesis and *N*-methyl-D-aspartate (NMDA) antagonist properties of, the enantiomers of α-amino-5-(phosphonomethyl)[1,1′-biphenyl]-3-propanoic acid. Use of a new chiral glycine derivative. *Helv. Chim. Acta* **1992**, *75*, 855–864.
461. Seebach, D.; Lamatsch, B.; Amstutz, R.; Beck, A. K.; Dobler, M.; Egli, M.; Fitzi, R.; Gautschi, M.; Herradon, B.; Hidber, P. C.; Irwin, J. J.; Locher, R.; Maestro, M.; Maetzke, T.; Mourino, A.; Pfammatter, E.; Plattner, D. A.; Schickli, C.; Schweizer, W. B.; Seiler, P.; Stucky, G.; Petter, W.; Escalante, J.; Juaristi, E.; Quintana, D.; Miravitlles, C.; Molins, E. Structure and reactivity of five- and six-ring *N*,*N*-, *N*,*O*-, and, *O*,*O*-acetals: a lesson in allylic 1,3-strain ($A^{1,3}$ strain). *Helv. Chim. Acta* **1992**, *75*, 913–934.
462. von dem Bussche-Hünnefeld, C.; Seebach, D. Herstellung und Umsetzungen von (*R*,*R*)- und (*S*,*S*)-3-Trifluor-methyloxiran-2-carbonsäure-ethylester, einem vielseitigen, leicht zugänglichen CF_3-haltigen Synthesebaustein. *Chem. Ber.* **1992**, *125*, 1273–1281.
463. Juaristi, E.; Escalante, J.; Lamatsch, B.; Seebach, D. Enantioselective synthesis of β-amino acids. 2. Preparation of the like stereoisomers of 2-methyl- and 2-benzyl-3-aminobutanoic acid. *J. Org. Chem.* **1992**, *57*, 2396–2398.
464. Lamatsch, B.; Seebach, D.; Ha, T.-K. ab initio-Studien an *N*-Acyliminium-Ionen. *Helv. Chim. Acta* **1992**, *75*, 1095–1110.
465. von dem Bussche-Hünnefeld, J. L.; Seebach, D. Enantioselective preparation of sec. alcohols from aldehydes and, dialkyl zinc compounds, generated in situ from Grignard reagents, using substoichiometric amounts of TADDOL-titanates. *Tetrahedron* **1992**, *48*, 5719–5730, Tetrahedron Symposia-in-Print No. 47 on 'Organotitanium Reagents in Organic Chemistry'.
466. Gautschi, M.; Seebach, D. Herstellung von (*R*)- und (*S*)-2-*tert*-Butyl-6-trifluormethyl-1,3-dioxin-4-on, Umsetzungen zu 3-Hydroxy-3-trifluormethylalkanoaten und überraschende Reaktivitätsunterschiede zwischen CH_3- und CF_3-substituierten Verbindungen. *Angew. Chem.* **1992**, *104*, 1061–1062, *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1083–1085.
467. Seebach, D.; Plattner, D. A.; Beck, A. K.; Wang, Y. M.; Hunziker, D.; Petter, W. On the mechanisms of enantioselective reactions using α,α,α′,α′-tetra-aryl-1,3-dioxolane-4,5-dimethanol(TADDOL)-derived titanates: differences between C_2- and C_1-symmetrical TADDOLs—facts, implications and generalizations. *Helv. Chim. Acta* **1992**, *75*, 2171–2209.
468. Breitschuh, R.; Seebach, D. Herstellung enantiomerenreiner Sulfoxide aus Milchsäure und 3-Hydroxy buttersäure: Isopropenyl-tolyl-sulfoxid und 2-(Phenylsulfinyl)acrylester. *Synthesis* **1992**, 1170–1178.
469. Pietzonka, T.; Seebach, D. N-Perbenzylierung von Oligopeptiden mit der P4-Phosphazenbase; eine neue Schutzgruppentechnik zur Modifikation und Solubilisierung von Peptiden in unpolaren organischen Lösungsmitteln. *Angew. Chem.* **1992**, *104*, 1543–1545, *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1481–1482.
470. Seebach, D.; Pfammatter, E.; Gramlich, V.; Bremi, T.; Kühnle, F.; Portmann, S.; Tironi, I. Diastereoselective Michael additions of chiral imidazolidines to trityl enones. *Liebigs Ann. Chem.* **1992**, 1145–1151.
471. Seebach, D.; Beck, A. K.; Breitschuh, R.; Job, K. Direct degradation of the biopolymer poly[(*R*)-3-hydroxybutyric acid] to (*R*)-3-hydroxybutanoic acid and its methyl ester. *Org. Synth.* **1992**, *71*, 39–47, Collect. Vol. IX, **1998**, 483–487.
472. Seebach, D. How we stumbled into peptide chemistry. *Aldrichim. Acta* **1992**, *25*(3), 59–66.
473. Seebach, D.; Schäfer, H.; Schmidt, B.; Schreiber, M. C,C-Kupplung am vinylischen Kohlenstoffatom unter NO_2-/Alkyl-substitution bei der Umsetzung von 2-Aryl-1-nitro-1-alkenen mit Dialkylzinkverbindungen—Eine neue Reaktion. *Angew. Chem.* **1992**, *104*, 1680–1681, *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1587–1588.
474. von dem Bussche-Hünnefeld, C.; Cescato, C.; Seebach, D. Ergiebige Herstellung von (*R*)- und (*S*)-3,3,3-Trifluormilchsäure und von (*R*)- und (*S*)-(Trifluormethyl)oxiran. *Chem. Ber.* **1992**, *125*, 2795–2802.
475. Seebach, D. Poly-β-hydroxybutyrate in the hands of a synthetic chemist. *FEMS Microbiol. Rev.* **1992**, *103*, 215.
476. Seebach, D.; Lapierre, J.-M.; Jaworek, W.; Seiler, P. A simple procedure for the preparation of chiral 'tris(hydroxymethyl)methane' derivatives. *Helv. Chim. Acta* **1993**, *76*, 459–475.
477. Miller, S.; Griffiths, S. L.; Seebach, D. C-alkylation of sarcosine residues in cyclic tetrapeptides via lithium enolates. *Helv. Chim. Acta* **1993**, *76*, 563–595.
478. Seebach, D.; Hayakawa, M.; Sakaki, J.-i.; Schweizer, W. B. Derivatives of α,α,α′,α′-Tetraaryl-2,2-dimethyl-1,3-dioxolan-4,5-dimethanol (TADDOL) containing nitrogen, sulfur, and phosphorus atoms. New ligands and auxiliaries for enantioselective reactions. *Tetrahedron* **1993**, *49*, 1711–1724, Tetrahedron Symposia-in-Print No. 49 on

'Synthesis of Optically Active Compounds—Prospects for the 21st Century'.
479. Riddell, F. G.; Seebach, D.; Müller, H.-M. Solid-state CP/MAS ^{13}C-NMR spectra of oligolides derived from 3-hydroxybutanoic acid. *Helv. Chim. Acta* **1993**, *76*, 915–923.
480. Müller, H.-M.; Seebach, D. Poly(hydroxyfettsäureester), eine fünfte Klasse von physiologisch bedeutsamen organischen Biopolymeren? *Angew. Chem.* **1993**, *105*, 483–509, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 477–502.
481. Seebach, D. Poly[(R)-3-hydroxyalkanoates]—The Fourth Family of Biopolymers: Contributions of an Organic Chemist. International Bioorganic Symposium, Interlaken, April 14–16, 1993, Abstracts 38-39. *Chimia* **1993**, *47*, 102–103.
482. Pietzonka, T.; Seebach, D. Die P4-Phosphazenbase als Teil eines metallfreien Initiatorsystems für die anionische Polymerisation von Methacrylsäuremethylester. *Angew. Chem.* **1993**, *105*, 741–742, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 716–717.
483. Seebach, D.; Beck, A. K.; Bossler, H. G.; Gerber, C.; Ko, S. Y.; Murtiashaw, C. W.; Naef, R.; Shoda, S.-i.; Thaler, A.; Krieger, M.; Wenger, R. Modification of cyclosporin A (CS): generation of an enolate at the sarcosine residue and reactions with electrophiles. *Helv. Chim. Acta* **1993**, *76*, 1564–1590.
484. Sommerfeld, T.; Seebach, D. Dehydroalanine-containing peptides by AcOH—elimination from *O*-acetylserine residues with DBU/$LiClO_4$ in tetrahydrofuran. *Helv. Chim. Acta* **1993**, *76*, 1702–1714.
485. Seebach, D.; Gees, T.; Schuler, F. Herstellung von α-verzeigten Phenylalaninen und von 1,1-disubstituierten Ethylendiaminen über chirale Imidazolidinone und Oxazolidinone aus Glycin-präparative und mechanistische Aspekte. *Liebigs Ann. Chem.* **1993**, 785–799, Erratum: ibid **1994**, 529.
486. Plattner, D. A.; Brunner, A.; Dobler, M.; Müller, H.-M.; Petter, W.; Zbinden, P.; Seebach, D. Cyclische Oligomere von (*R*)-3-Hydroxybuttersäure: Herstellung und strukturelle Aspekte. *Helv. Chim. Acta* **1993**, *76*, 2004–2033.
487. Blank, S.; Seebach, D. Herstellung von (*R*,*R*)- oder (*S*,*S*)-2-Amino-3-hydroxycarbonsäuren (allo-Threonin-Analoge) durch Acylierung/Reduktion von 2-t-Butyl-3-methyl-4-oxo-imidazolidin-1-carbonsäure-t-butylester (Boc-BMI). *Liebigs Ann Chem.* **1993**, 889–896.
488. Bürger, H. M.; Müller, H.-M.; Seebach, D.; Börnsen, K. O.; Schär, M.; Widmer, H. M. Matrix-assisted laser desorption and ionization as a mass spectrometric tool for the analysis of poly[(*R*)-3-hydroxybutanoates]. Comparison with gel permeation chromatography. *Macromolecules* **1993**, *26*, 4783–4790.
489. Lapierre, J.-M.; Skobridis, K.; Seebach, D. Preparation of chiral building blocks for starburst dendrimer synthesis. *Helv. Chim. Acta* **1993**, *76*, 2419–2432.
490. Bürger, H. M.; Seebach, D. Cation transport across bulk liquid organic membranes with oligomers of (*R*)-3-hydroxybutanoic Acid. *Helv. Chim. Acta* **1993**, *76*, 2570–2580.
491. Seebach, D.; Bürger, H. M.; Plattner, D. A.; Nesper, R.; Fässler, T. Complexes of the triolide from (*R*)-3-hydroxybutanoic acid with sodium, potassium, and barium salts: crystal structures, ester chelates and ester crowns, crystal packing, bonding, and electron-localization functions. *Helv. Chim. Acta* **1993**, *76*, 2581–2601.
492. Gees, T.; Schweizer, W. B.; Seebach, D. An unusual rearrangement of a lithiated *N*-acyl-tetrahydroisoquinoline to an amino-indan skeleton and structural comparison of 3-amino-2-methyl-indan- and -tetrahydronaphthalene-2-carboxylic acids as possible building blocks for peptide-turn mimics. *Helv. Chim. Acta* **1993**, *76*, 2640–2653.
493. Sakaki, J.-i.; Schweizer, W. B.; Seebach, D. Catalytic enantioselective hydrosilylation of aromatic ketones using rhodium complexes of TADDOL-derived cyclic phosphonites and phosphites. *Helv. Chim. Acta* **1993**, *76*, 2654–2665.
494. Lapierre, J.-M.; Gautschi, M.; Greiveldinger, G.; Seebach, D. Reaction of 6-(CF_3)- and 6-(CH_3)-2-(*tert*-butyl)-1,3-dioxan-4-one Li enolate with two equivalents of an aldehyde—unusual reorganizations of aldolates. *Chem. Ber.* **1993**, *126*, 2739–2746.
495. Juaristi, E.; Murer, P.; Seebach, D. Use of *N*,*N*′-dimethylpropyleneurea (DMPU) as solvent in the efficient preparation of enantiomerically pure secondary amines. *Synthesis* **1993**, 1243–1246.
496. Juaristi, E.; Beck, A. K.; Hansen, J.; Matt, T.; Mukhopadhyay, T.; Simson, M.; Seebach, D. Enantioselective aldol and Michael additions of achiral enolates in the presence of chiral lithium amides and amines. *Synthesis* **1993**, 1271–1290.
497. Blank, S.; Seebach, D. (*R*) und-(*S*)-4-Alkoxy-2-tert-butyl-2,5-dihydroimidazol-1-carbonsäure-ester - neue chirale Glycinderivate für die Aminosäuresynthese. *Angew. Chem.* **1993**, *105*, 1780–1781, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1765–1766.
498. Seebach, D.; Bossler, H. G.; Flowers, R.; Arnett, E. M. Calorimetric measurements of the complexation of cyclosporin A, ascomycin, fujimycin, and rapamycin with lithium chloride and with an immunophilin. *Helv. Chim. Acta* **1994**, *77*, 291–305.
499. Bossler, H. G.; Waldmeier, P.; Seebach, D. Herstellung und C-Alkylierungen von Peptiden mit Aminomalonsäure-Bausteinen. *Angew. Chem.* **1994**, *106*, 455–456, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 439–440.
500. Seebach, D.; Lapierre, J.-M.; Skobridis, K.; Greiveldinger, G. Chirale Tris(hydroxymethyl)methan-Derivate als Synthesebausteine für chirale Dendrimere. *Angew. Chem.* **1994**, *106*, 457–458, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 440–442.
501. Bürger, H. M.; Seebach, D. Cyclosporin-ein Li- und Ca-spezifischer Ionophor!. *Angew. Chem.* **1994**, *106*, 459–460, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 442–444.
502. Gautschi, M.; Schweizer, W. B.; Seebach, D. In 2- und 3-Stellung verzweigte, enantiomerenreine 4,4,4-Trifluor-3-hydroxybuttersäure-Derivate aus 6-Trifluormethyl-1,3-dioxan- und -dioxin-4-onen. *Chem. Ber.* **1994**, *127*, 565–579.
503. Seebach, D.; Beck, A. K.; Schmidt, B.; Wang, Y. M. Enantio- and diastereoselective titanium-TADDOlate catalyzed addition of diethyl and bis(3-buten-1-yl) zinc to aldehydes. A full account with preparative details. *Tetrahedron* **1994**, *50*, 4363–4384, Tetrahedron Symposia-in-Print No. 54 on 'Catalytic Asymmetric Addition Reactions'.
504. Weber, B.; Seebach, D. Highly enantioselective addition of primary alkyl Grignard reagents to carbocyclic and heterocyclic arylketones in the presence of magnesium TADDOlate. Preparative and mechanistic aspects. *Tetrahedron* **1994**, *50*, 6117–6128, Tetrahedron Symposia-in-Print No. 55 on 'Mechanistic Aspects of Polar Organometallic Chemistry'.
505. Plattner, D. A.; Petter, W.; Seebach, D. Kristallstrukturanalyse von lösungsmittelfreiem Lithium-benzoat. Relevanz für die Materialeigenschaften von Lithiumcarboxylaten? *Chimia* **1994**, *48*, 138–141.
506. Weber, B.; Seebach, D. Ti-TADDOLate-catalyzed highly

enantioselective addition of alkyl- and aryl-titanium derivatives to aldehydes. *Tetrahedron* **1994**, *50*, 7473–7484.
507. Seebach, D.; Bürger, H. M.; Müller, H.-M.; Lengweiler, U. D.; Beck, A. K.; Sykes, K. E.; Barker, P. A.; Barham, P. J. Synthesis of linear oligomers of (*R*)-3-hydroxybutyrate and solid-state structural investigations by electron microscopy and X-ray scattering. *Helv. Chim. Acta* **1994**, *77*, 1099–1123.
508. Bossler, H. G.; Seebach, D. Peptide enolates. C-alkylation of glycine residues in linear tri-, tetra-, and pentapeptides via dilithium azadienediolates. *Helv. Chim. Acta* **1994**, *77*, 1124–1165.
509. Seebach, D.; Maestro, M. A.; Sefkow, M.; Adam, G.; Hintermann, S.; Neidlein, A. Total synthesis of myxovirescins, 1. Strategy and construction of the 'Southeastern' Part [O(1)–C(14)]. *Liebigs Ann. Chem.* **1994**, 701–717.
510. Sefkow, M.; Neidlein, A.; Sommerfeld, T.; Sternfeld, F.; Maestro, M. A.; Seebach, D. Total synthesis of myxovirescins, 2. Assembly of the 'Northwestern' Part [C(15)–C(28)]. *Liebigs Ann. Chem.* **1994**, 719–729.
511. Maestro, M. A.; Sefkow, M.; Seebach, D. Total synthesis of myxovirescins, 3. Coupling of the two key fragments and last steps to myxovirescins A_1 and M_2. *Liebigs Ann. Chem.* **1994**, 731–738.
512. Seebach, D.; Sommerfeld, T. L.; Jiang, Q.; Venanzi, L. M. Preparation of oxazolidine-containing peptides: unusual effects in Rh^{III}-catalyzed acetalizations of aldehydes with urethane-protected serine and threonine esters and with dipeptides containing serine or threonine residues at the N-terminus. *Helv. Chim. Acta* **1994**, *77*, 1313–1330.
513. Seebach, D.; Brunner, A.; Bürger, H. M.; Schneider, J.; Reusch, R. N. Isolation and ^{1}H-NMR spectroscopic identification of poly(3-hydroxy-butanoate) from prokaryotic and eukaryotic organisms. Determination of the absolute configuration (*R*) of the monomeric unit 3-hydroxybutanoic acid from *Escherichia coli* and spinach. *Eur. J. Biochem.* **1994**, *224*, 317–328.
514. Seebach, D.; Lapierre, J.-M.; Greiveldinger, G.; Skobridis, K. Synthesis of chiral starburst dendrimers from PHB-derived triols as central cores. *Helv. Chim. Acta* **1994**, *77*, 1673–1688.
515. Seebach, D.; Hoffmann, T.; Kühnle, F. N. M.; Lengweiler, U. D. Preparation and structure of oligolides from (*R*)-3-hydroxypentanoic acid and comparison with the hydroxybutanoic-acid derivatives: a small change with large consequences. *Helv. Chim. Acta* **1994**, *77*, 2007–2034.
516. Seebach, D.; Studer, A.; Pfammatter, E.; Widmer, H. Synthesis of tri-, penta-, and heptapeptides containing an (*R*)-2-alkyl-2-amino-3-(methylamino)-propionic acid residue in the central position. *Helv. Chim. Acta* **1994**, *77*, 2035–2050.
517. Seebach, D.; Rheiner, P. B.; Beck, A. K.; Kühnle, F. N. M.; Jaun, B. Preparation and cationic rearrangements of *ortho*- and *para*-methoxy-TADDOLs. *Pol. J. Chem.* **1994**, *68*, 2397–2413.
518. Ito, Y. N.; Ariza, X.; Beck, A. K.; Bohác, A.; Ganter, C.; Gawley, R. E.; Kühnle, F. N. M.; Tuleja, J.; Wang, Y. M.; Seebach, D. Preparation and structural analysis of several new $\alpha,\alpha,\alpha',\alpha'$-tetraaryl-1,3-dioxolane-4,5-dimethanols (TADDOLs) and TADDOL analogs, their evaluation as titanium ligands in the enantioselective addition of methyltitanium and diethylzinc reagents to benzaldehyde, and refinement of the mechanistic hypothesis. *Helv. Chim. Acta* **1994**, *77*, 2071–2110.
519. Murer, P.; Rheiner, B.; Juaristi, E.; Seebach, D. Enantioselective synthesis of β-amino acids, 5. stereoselective reaction of chiral pyrimidinone enolates with aldehydes. *Heterocycles* **1994**, *39*, 319–344.
520. Beck, A. K.; Blank, S.; Job, K.; Seebach, D.; Sommerfeld, T. Synthesis of (*S*)-2-methylproline: a general method for the preparation of α-branched amino acids. *Org. Synth.* **1995**, *72*, 62–73, Collect. Vol. IX **1998**, 626–632.
521. Studer, A.; Seebach, D. Enantioselective synthesis of α-branched α-amino acids with bulky substituents. *Liebigs Ann. Chem.* **1995**, 217–222.
522. Studer, A.; Seebach, D. Preparation of either enantiomer of 1,2-diaminoalkane-2-phosphonic acid derivatives. *Heterocycles* **1995**, *40*, 357–378.
523. Schäfer, H.; Seebach, D. Enantioselective conjugate addition of primary dialkylzinc reagents to 2-aryl- and 2-heteroaryl-nitroolefins mediated by titanium-TADDOLates. Preparation of enantioenriched 2-aryl-alkylamines. *Tetrahedron* **1995**, *51*, 2305–2324.
524. Podlech, J.; Seebach, D. Die Arndt-Eistert-Reaktion in der Peptidchemie: ein einfacher Zugang zu Homopeptiden. *Angew. Chem.* **1995**, *107*, 507–509, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 471–472.
525. Sommerfeld, T. L.; Seebach, D. Herstellung von ψ[SCH_2]–ψ[$SOCH_2$]- und ψ[SO_2CH_2]-Peptid-Isosteren. *Angew. Chem.* **1995**, *107*, 622–623, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 553–554.
526. Sykes, K. E.; McMaster, T. J.; Miles, M. J.; Barker, P. A.; Barham, P. J.; Seebach, D.; Müller, H.-M.; Lengweiler, U. D. Direct imaging of the surfaces of poly(β)hydroxybutyrate and hydroxy-butyrate oligomers by atomic force microscopy. *J. Mater. Sci.* **1995**, *30*, 623–627.
527. Seebach, D.; Dahinden, R.; Marti, R. E.; Beck, A. K.; Plattner, D. A.; Kühnle, F. N. M. On the Ti-TADDOLate-catalyzed Diels–Alder addition of 3-butenoyl-1,3-oxazolidin-2-one to cyclopentadiene. General features of Ti-BINOLate- and Ti-TADDOLate-mediated reactions. *J. Org. Chem.* **1995**, *60*, 1788–1799, Correction: *J. Org. Chem.* **1995**, *60*, 5364.
528. Seebach, D.; Beck, A. K.; Studer, A. Some effects of lithium salts, of strong bases, and of the cosolvent DMPU in peptide chemistry, and elsewhere. In *Modern Synthetic Methods*, Ernst, B., Leumann, C., Eds.; VHCA Verlag Helvetica Chimica Acta/VCH: Basel/Weinheim, 1995; Vol. 7, pp 1–178.
529. Marti, R. E.; Heinzer, J.; Seebach, D. Preparation and reactions of silyl nitronates derived from 2,2,2-trifluoronitroethane. Diastereoselective synthesis of trifluoromethyl-substituted aminoethanols and -propanols. *Liebigs Ann.* **1995**, 1193–1215.
530. Podlech, J.; Seebach, D. On the preparation of β-amino acids from α-amino acids using the Arndt-Eistert reaction: Scope, limitations and stereoselectivity. Application to carbohydrate peptidation. Stereoselective α-alkylations of some β-amino acids. *Liebigs Ann.* **1995**, 1217–1228.
531. Brandl, H.; Aeberli, B.; Bachofen, R.; Schwegler, I.; Müller, H.-M.; Bürger, M. H.; Hoffmann, T.; Lengweiler, U. D.; Seebach, D. Biodegradation of cyclic and substituted linear oligomers of poly(3-hydroxybutyrate). *Can. J. Microbiol.* **1995**, *41*(Suppl. 1), 180–186.
532. Studer, A.; Hintermann, T.; Seebach, D. Synthesis and first applications of a new chiral auxiliary (*tert*-butyl-2-(*tert*-butyl)-5,5-dimethyl-4-oxoimidazolidine-1-carboxylate). *Helv. Chim. Acta* **1995**, *78*, 1185–1206.

533. Podlech, J.; Seebach, D. Azetidin-3-ones from (S)-α-amino acids and their reactions with nucleophiles: preparation of some azetidine-containing amino-alcohol and amino-acid derivatives. *Helv. Chim. Acta* **1995**, *78*, 1238–1246.
534. Seebach, D. Foreword in *Enzyme Catalysis in Organic Synthesis*, Drauz, K., Waldmann, H., Eds.; VCH: Weinheim, 1995; Vol. 1.
535. Seebach, D.; Hoffmann, T.; Kühnle, F. N. M.; Kinkel, J. N.; Schulte, M. Preparation, structure, and properties of all possible cyclic dimers (diolides) of 3-hydroxybutanoic acid. *Helv. Chim. Acta* **1995**, *78*, 1525–1540.
536. Stamm, T.; Kouvenhoven, H. W.; Seebach, D.; Prins, R. Zeolite-catalyzed isomerization of aromatic amines to methyl-aza-aromatics. *J. Catal.* **1995**, *155*, 268–282.
537. Studer, A.; Seebach, D. 1-Benzoyl-2-*t*-butyl-3,5-dimethyl-4-imidazolidinone. *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L., Ed.; Wiley: Chichester, 1995; Vol. 1, pp 306–308.
538. Studer, A.; Seebach, D. (2*S*,4*S*)-3-Benzoyl-2-*t*-butyl-4-methyl-1,3-oxazolidin-5-one. *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L., Ed.; Wiley: Chichester, 1995; Vol. 1, pp 308–330.
539. Studer, A.; Seebach, D. *t*-Butyl 2-*t*-butyl-3-methyl-4-oxo-1-imidazolidinecarboxylate. *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L., Ed.; Wiley: Chichester, 1995; Vol. 2, pp 852–854.
540. Beck, A. K.; Seebach, D. (*R*)-2-*t*-Butyl-6-methyl-4*H*−1,3-dioxin-4-one. *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L., Ed.; Wiley: Chichester, 1995; Vol. 2, pp 929–993.
541. Sting, A. R.; Seebach, D. (*R*,*R*)-2-*t*-Butyl-5-methyl-1,3-dioxolan-4-one. *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L., Ed.; Wiley: Chichester, 1995; Vol. 2, pp 931–933.
542. Marti, R. E.; Seebach, D. *O*,*O*-Dilithio-1-nitropropene. *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L., Ed.; Wiley: Chichester, 1995; Vol. 2, pp 1946–1948.
543. Beck, A. K.; Seebach, D. *N*,*N*′-Dimethylpropyleneurea. *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L., Ed.; Wiley: Chichester, 1995; Vol. 3, pp 2123–2127.
544. Dahinden, R.; Beck, A. K.; Seebach, D. 2,2-Dimethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanolatotitanium diisopropoxide. *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L., Ed.; Wiley: Chichester, 1995; Vol. 3, pp 2167–2217.
545. Marti, R. E.; Seebach, D. Lithium-α-lithiomethanenitronate. *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L., Ed.; Wiley: Chichester, 1995; Vol. 5, pp 3138–3314.
546. Beck, A. K.; Dahinden, R.; Seebach, D. Mesityllithium. *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L., Ed.; Wiley: Chichester, 1995; Vol. 5, pp 3275–3276.
547. Podlech, J.; Seebach, D. (*R*)-Methyl 2-*t*-butyl-3(2*H*)-oxazolecarboxylate. *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L., Ed.; Wiley: Chichester, 1995; Vol. 5, pp 3452–3453.
548. Beck, A. K.; Dahinden, R.; Seebach, D. Methyl 4-nitrobutanoate. *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L., Ed.; Wiley: Chichester, 1995; Vol. 5, pp 3549–3550.
549. Beck, A. K.; Marti, R. E.; Seebach, D. Methyl 3-nitropropanoate. *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L., Ed.; Wiley: Chichester, 1995; Vol. 5, pp 3351–3352.
550. Beck, A. K.; Seebach, D. Trimethylsilyl methanenitronate. *Encyclopedia of Reagents for Organic Synthesis*, Paquette, L., Ed.; Wiley: Chichester, 1995; Vol. 5, pp 5270–5273.
551. Murer, P.; Seebach, D. Synthese und Eigenschaften von Dendrimeren erster bis dritter Generation mit zwei- und dreifach verzweigenden chiralen Bausteinen. *Angew. Chem.* **1995**, *107*, 2297–2300, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2116–2119.
552. Juaristi, E.; Anzorena, J. L.; Boog, A.; Madrigal, D.; Seebach, D.; García-Barradas, E. V.; García-Barradas, O.; Gordillo, B.; Kramer, A.; Steiner, I.; Zürcher, S. Highly diastereoselective alkylation of 1-benzoyl-2-alkyl-3-(1(-methylbenzyl)imidazolidin-4-ones. *J. Org. Chem.* **1995**, *60*, 6408–6415.
553. Seebach, D.; Devaquet, E.; Ernst, A.; Hayakawa, M.; Kühnle, F. N. M.; Schweizer, W. B.; Weber, B. Preparation of the $PdCl_2$ complex of TADDOP, the bis(diphenylphosphinite) of TADDOL: use in enantioselective 1,3-diphenylallylations of nucleophiles and discussion of the mechanism. *Helv. Chim. Acta* **1995**, *78*, 1636–1650.
554. Seebach, D.; Jaeschke, G.; Wang, Y. M. Hoch enantioselektive Oeffnung cyclischer meso-Anhydride zu Isopropylhalbestern mit Diisopropoxytitan-TADDOLaten. *Angew. Chem.* **1995**, *107*, 2605–2606, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2395–2396.
555. Lubec, G.; Labudova, O.; Seebach, D.; Beck, A.; Hoeger, H.; Hermon, M.; Weninger, M. Alpha-methyl-proline restores normal levels of bone collagen type I synthesis in ovariectomized rats. *Life Sci.* **1995**, *57*, 2245–2252.
556. Seebach, D.; Brunner, A.; Bachmann, B. M.; Hoffmann, T.; Kühnle, F. N. M.; Lengweiler, U. D. *Biopolymers and -oligomers of (R)-3-Hydroxyalkanoic Acids-Contributions of Synthetic Organic Chemists*, Ernst Schering Research Foundation, 1995; Vol. 28. pp 7–98.
557. Sting, A. R.; Seebach, D. Synthesis of (2R),3S)- or (2S,3R)-2-amino-3-trifluoromethyl-3-hydroxy-alkanoic acid derivatives (threonine and allo-threonine analogs) from enantiopure 4,4,4-trifluoro-3-hydroxybutanoic acid. *Tetrahedron* **1996**, *52*, 279–290, Tetrahedron Symposia-in-Print No. 58 on 'Fluoroorganic Chemistry: Synthetic Challenges and Biomedicinal Rewards'.
558. Götzö, S. P.; Seebach, D. Preparation of (*R*)- and (*S*)-3-hydroxy-2-(trifluoromethyl)propionic acid by resolution with (*R*,*R*)- and (*S*,*S*)-2-amino-1-phenylpropane-1,3-diol. *Chimia* **1996**, *50*, 20–23.
559. Schmidt, B.; Seebach, D. Coupling of an aromatic iminium salt by a low-valent titanium reagent. In *Synthetic Methods of Organometallic and Inorganic Chemistry (Herrmann/-Brauer). Literature, Laboratory Techniques and Common Starting Materials*, Herrmann, W. A., Salzer, A., Eds.; George Thieme: Stuttgart, 1996; Vol. 1, pp 99–100.
560. Sommerfeld, T.; Seebach, D. Selective transesterification of a carboxylate in the presence of a phosphonate.[1] In *Synthetic Methods of Organometallic and Inorganic Chemistry (Herrmann/Brauer). Literature, Laboratory Techniques and Common Starting Materials*, Herrmann, W. A., Salzer, A., Eds.; George Thieme: Stuttgart, 1996; Vol. 1, pp 100–101.
561. Wang, Y. M.; Seebach, D. Diastereoselective synthesis of u-3-methyl-2-(2-naphthyl)-4-penten-2-ol. In *Synthetic Methods of Organometallic and Inorganic Chemistry (Herrmann/-Brauer). Literature, Laboratory Techniques and Common Starting Materials*, Herrmann, W. A., Salzer, A., Eds.; George Thieme: Stuttgart, 1996; Vol. 1, pp 101–103.
562. Behrendt, L.; Seebach, D. Enantioselective alkylation of

aldehydes by titanate-catalyzed addition of dialkylzinc reagents: preparation of (*S*)-4-methyl-1-phenylpentanol. In *Synthetic Methods of Organometallic and Inorganic Chemistry (Herrmann/Brauer). Literature, Laboratory Techniques and Common Starting Materials*, Herrmann, W. A., Salzer, A., Eds.; George Thieme: Stuttgart, 1996; Vol. 1, pp 103–104.

563. Brunner, A.; Kühnle, F. N. M.; Seebach, D. Preparation, structure, and reactivity of thioxo and imino derivatives of the triolide (and pentolide) from (*R*)-3-hydroxybutanoic acid. *Helv. Chim. Acta* **1996**, *79*, 319–345.
564. Seebach, D.; Brunner, A.; Bürger, H. M.; Reusch, R. N.; Bramble, L. L. Channel-forming activity of 3-hydroxybutanoic-acid oligomers in planar lipid bilayers. *Helv. Chim. Acta* **1996**, *79*, 507–517.
565. Seebach, D.; Bezençon, O.; Jaun, B.; Pietzonka, T.; Matthews, J. L.; Kühnle, F. N. M.; Schweizer, W. B. Further C-alkylations of cyclotetrapeptides via lithium and phosphazenium (P4) enolates: discovery of a new conformation. *Helv. Chim. Acta* **1996**, *79*, 588–608.
566. Lengweiler, U. D.; Fritz, M. G.; Seebach, D. Synthese monodisperser linearer und cyclischer Oligomere der, (*R*)-3-Hydroxybuttersäure mit bis zu 128 Einheiten. *Helv. Chim. Acta* **1996**, *79*, 670–701.
567. Ramón, D. J.; Guillena, G.; Seebach, D. Nonreductive enantioselective ring opening of *N*-(methylsulfonyl)-dicarboximides with diisopropoxytitanium α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanolate. *Helv. Chim. Acta* **1996**, *79*, 875–894.
568. Seebach, D.; Overhand, M.; Kühnle, F. N. M.; Martinoni, B.; Oberer, L.; Hommel, U.; Widmer, H. β-Peptides: synthesis by Arndt-Eistert homologation with concomitant peptide coupling. Structure determination by NMR and CD spectroscopy and by X-ray crystallography. Helical secondary structure of a β-hexapeptide in solution and its stability towards pepsin. *Helv. Chim. Acta* **1996**, *79*, 913–941.
569. Guibourdenche, C.; Podlech, J.; Seebach, D. Selective acylations of multifunctional nucleophiles, including carbohydrates and nucleosides, with intermediates generated by Wolff rearrangement of amino acid derived diazo ketones: preparation of β-amino acid derivatives. *Liebigs Ann.* **1996**, 1121–1129.
570. Seebach, D.; Beck, A. K.; Dahinden, R.; Hoffmann, M.; Kühnle, F. N. M. Reduction of ketones with $LiAlH_4$ complexes of α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanols (TADDOLs). A combination of enantioselective reduction and clathrate formation with a discussion of LAH reagents bearing C_2-symmetrical ligands. *Croat. Chem. Acta* **1996**, *69*, 459–484.
571. Bezençon, O.; Seebach, D. Alkylations of chiral imidazolidinones derived from di- and triglycine and attempts at cyclisations to give cycloisodityrosines. *Liebigs Ann.* **1996**, 1259–1276.
572. Hoffmann, T.; Seebach, D. Preparation of 12- and 16-membered macrolactones (oligolides) from (*S*)-malic acid—low molecular-mass analogs of the biopolymer poly[(*S*)-malic acid] (PMA). *Liebigs Ann.* **1996**, 1277–1282.
573. Seebach, D.; Marti, R. E.; Hintermann, T. Polymer- and dendrimer-bound Ti-TADDOLates in catalytic (and stoichiometric) enantioselective reactions: are pentacoordinate cationic Ti complexes the catalytically active species? *Helv. Chim. Acta* **1996**, *79*, 1710–1740.
574. Krohn, K.; Knauer, B.; Küpke, J.; Seebach, D.; Beck, A. K.; Hayakawa, M. Zirconium alkoxide catalyzed oppenauer oxidation using chloral as the hydride acceptor. *Synthesis* **1996**, 1341–1344.
575. Seebach, D.; Ciceri, P. E.; Overhand, M.; Jaun, B.; Rigo, D.; Oberer, L.; Hommel, U.; Amstutz, R.; Widmer, H. Probing the helical secondary structure of short-chain β-peptides. *Helv. Chim. Acta* **1996**, *79*, 2043–2066.
576. Seebach, D.; Sting, A. R.; Hoffmann, M. Die Selbstregeneration von Stereozentren (SRS)—Anwendungen, Grenzen und Preisgabe eines Syntheseprinzips. *Angew. Chem.* **1996**, *108*, 2880–2921, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2708–2748.
577. Seebach, D.; Herrmann, G. F.; Lengweiler, U. D.; Bachmann, B. M.; Amrein, W. Synthese und enzymatischer Abbau von Dendrimeren aus (*R*)-3-Hydroxybuttersäure und Trimesinsäure. *Angew. Chem.* **1996**, *108*, 2969–2972, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2795–2797.
578. Seebach, D. In *Principles of Asymmetric Synthesis*. *Tetrahedron Organic Chemistry Series*, Gawley, R. E., Aubé, J., Eds.; Pergamon: Oxford, 1996; Vol. 14.
579. Guibourdenche, C.; Seebach, D.; Natt, F. Use of the Wolff rearrangement of diazo ketones from amino acids as a synthetic method for the formation of oligonucleo-peptides: a novel approach to chimeric biomolecules. *Helv. Chim. Acta* **1997**, *80*, 1–13.
580. Seebach, D.; Matthews, J. L.; Meden, A.; Wessels, T.; Baerlocher, C.; McCusker, L. B. Cyclo-β-peptides: structure and tubular stacking of cyclic tetramers of 3-aminobutanoic acid as determined from powder diffraction data. *Helv. Chim. Acta* **1997**, *80*, 173–182.
581. Matthews, J. L.; Braun, C.; Guibourdenche, C.; Overhand, M.; Seebach, D. Preparation of enantiopure β-amino acids from α-amino acids using the Arndt–Eistert homologation. In *Enantioselective Synthesis of β-Amino Acids*. Juaristi, E., Ed.; Wiley-VCH: New York, 1997; pp 105–126 Chapter 5.
582. Juaristi, E.; Seebach, D. Enantioselective synthesis of α-substituted and α,β-disubstituted β-amino acids via chiral derivatives of 3-aminopropionic acid. In *Enantioselective Synthesis of β-Amino Acids*. Juaristi, E., Ed.; Wiley-VCH: New York, 1997; pp 261–277 Chapter 13.
583. Hoffmann, M.; Seebach, D. Synthesis of non-proteinogenic amino-acid methyl esters with acid-sensitive side chains from a chiral glycine derivative. *Chimia* **1997**, *51*, 90–92.
584. Hintermann, T.; Seebach, D. The biological stability of β-peptides: no interactions between α- and β-peptidic structures? *Chimia* **1997**, *51*, 244–247.
585. Hintermann, T.; Seebach, D. Synthesis of a β-hexapeptide from (*R*)-2-aminomethyl-alkanoic acids and structural investigations. *Synlett* **1997**, 437–438.
586. Seebach, D.; Jaeschke, G.; Gottwald, K.; Matsuda, K.; Formisano, R.; Chaplin, D. A.; Breuning, M.; Bringmann, G. Resolution of racemic carboxylic acid derivatives by Ti-TADDOLate mediated esterification reactions—a general method for the preparation of enantiopure compounds. *Tetrahedron* **1997**, *53*, 7539–7556.
587. Seebach, D.; Beck, A. K. Catalytic Enantioselective Reactions from Research to Application. Diarylmethanol-Containing Auxiliaries as a Study Case, Spring Meeting of the New Swiss Chemical Society on the Occasion of '100 Years of Progress with Lonza', April 10 and 11, 1997, Visp, Switzerland Organized by: NSCS-Section Industrial Chemistry, *Chimia* **1997**, *51*, 293–297.
588. Guichard, G.; Seebach, D. Solid-phase synthesis of β-oligopeptides. *Chimia* **1997**, *51*, 315–318.

589. Seebach, D.; Herrmann, G. F.; Lengweiler, U. D.; Amrein, W. Synthesis of monodisperse macromolecular bicyclic and dendritic compounds from (*R*)-3-hydroxybutanoic acid and benzene-1,3,5-tricarboxylic acid and analysis by fragmenting MALDI-TOF mass spectroscopy. *Helv. Chim. Acta* **1997**, *80*, 989–1026.
590. Seebach, D.; Beck, A. K.; Hayakawa, M.; Jaeschke, G.; Kühnle, F. N. M.; Nägeli, I.; Pinkerton, A. B.; Rheiner, B. P.; Duthaler, R. O.; Rothe, P. M.; Weigand, W.; Wünsch, R.; Dick, S.; Nesper, R.; Wörle, M.; Gramlich, V. TADDOLs on their way to late transition metal complexes-synthesis and crystal structure of N- and S-containing TADDOL-derived compounds. *Bull. Soc. Chim. Fr.* **1997**, *134*, 315–331.
591. Matthews, J. L.; Overhand, M.; Kühnle, F. N. M.; Ciceri, P. E.; Seebach, D. β-Peptides: oligo-β-homoalanines—the amide analogues of poly(3-hydroxybutanoate). *Liebigs Ann./Recueil* **1997**, 1371–1379.
592. Jaun, B.; Tanaka, M.; Seiler, P.; Kühnle, F. N. M.; Braun, C.; Seebach, D. Studies on the conformation of Boc-protected (*S*)-(+)-isovaline homopeptide methyl esters in the solid state and in solution. *Liebigs Ann./Recueil* **1997**, 1697–1710.
593. Murer, P. K.; Lapierre, J.-M.; Greiveldinger, G.; Seebach, D. Synthesis and properties of first and second generation chiral dendrimers with triply branched units: a spectacular case of diastereoselectivity. *Helv. Chim. Acta* **1997**, *80*, 1648–1681.
594. Daura, X.; van Gunsteren, W. F.; Rigo, D.; Jaun, B.; Seebach, D. Studying the stability of a helical β-heptapeptide by molecular dynamics simulations. *Chem. Eur. J.* **1997**, *3*, 1410–1417.
595. Das, S.; Lengweiler, U. D.; Seebach, D.; Reusch, R. N. Proof for a nonproteinaceous calcium-selective channel in *Escherichia coli* by total synthesis from (*R*)-3-hydroxybutanoic acid and inorganic polyphosphate. *Proc. Natl. Acad. Sci. U. S. A.* **1997**, *94*, 9075–9079.
596. Seebach, D.; Matthews, J. L. β-Peptides: a surprise at every turn. *Chem. Commun.* **1997**, 2015–2022.
597. Rheiner, P. B.; Sellner, H.; Seebach, D. Dendritic styryl TADDOLs as novel polymer cross-linkers: first application in an enantioselective Et_2Zn addition mediated by a polymer-incorporated titanate. *Helv. Chim. Acta* **1997**, *80*, 2027–2032.
598. Seebach, D.; Gademann, K.; Schreiber, J. V.; Matthews, J. L.; Hintermann, T.; Jaun, B.; Oberer, L.; Hommel, U.; Widmer, H. 'Mixed' β-peptides: a unique helical secondary structure in solution. *Helv. Chim. Acta* **1997**, *80*, 2033–2038.
599. Kuball, H.-G.; Weiβ, B.; Beck, A. K.; Seebach, D. TADDOLs with unprecedented helical twisting power in liquid crystals. *Helv. Chim. Acta* **1997**, *80*, 2507–2514.
600. Seebach, D.; Jaeschke, G.; Pichota, A.; Audergon, L. Enantioselective 1,4-addition of aliphatic Grignard reagents to enones catalyzed by readily available copper(I) thiolates derived from TADDOL. *Helv. Chim. Acta* **1997**, *80*, 2515–2519.
601. Rheiner, P. B.; Seebach, D. High-molecular-weight and polymer-bound dendritic TADDOLs for membrane reactors and heterogeneous enantioselective Lewis acid catalysis. *Polym. Mater. Sci. Engng* **1997**, *77*, 130–131.
602. Butz, T.; Murer, P.; Seebach, D. Chiral dendritically expanded diamines as catalysts in enantioselective protonation reactions. *Polym. Mater. Sci. Engng* **1997**, *77*, 132–133.
603. Greiveldinger, G.; Seebach, D. Fluorine containing chiral dendrimers: synthesis and ^{19}F NMR spectroscopic investigations. *Polym. Mater. Sci. Engng* **1997**, *77*, 134–135.
604. Comina, P. J.; Beck, A. K.; Seebach, D. A simple batch reactor for the efficient multiple use of polymer-bound α,α,α',α'-tetraaryl-1,3-dioxolane-4,5-dimethanol titanates in the nucleophilic addition of dialkylzinc reagents to aldehydes. *Org. Process Res. Dev.* **1998**, *2*, 18–26.
605. Guichard, G.; Abele, S.; Seebach, D. Preparation of *N*-Fmoc-protected β^2- and β^3-amino acids and their use as building blocks for the solid-phase synthesis of β-peptides. *Helv. Chim. Acta* **1998**, *81*, 187–206.
606. Hoffmann, M.; Blank, S.; Seebach, D.; Küsters, E.; Schmid, E. Separation of (*R*)-and (*S*)-*tert*-butyl 2-*tert*-butyl-4-methoxy-2,5-dihydro-1,3-imidazole-1-carboxylate (building block for amino acid synthesis) by preparative high performance liquid chromatography on a polysaccharide stationary phase. *Chirality* **1998**, *10*, 217–222.
607. Jaeschke, G.; Seebach, D. Highly enantioselective ring opening of cyclic meso-anhydrides to isopropyl hemiesters with Ti-TADDOLates: an alternative to hydrolytic enzymes? *J. Org. Chem.* **1998**, *63*, 1190–1197.
608. Seebach, D.; Hoffmann, M.; Sting, A. R.; Kinkel, J. N.; Schulte, M.; Küsters, E. Chromatographic resolution of synthetically useful chiral glycine derivatives by high-performance liquid chromatography. *J. Chromatogr. A* **1998**, *796*, 299–307.
609. Seebach, D.; Gottwald, K.; Jaeschke, G.; Audergon, L.; Pichota, A. Ti-TADDOLates and related complexes in asymmetric synthesis: ring-opening and Cu-catalyzed conjugate additions of Grignard reagents. In *Selective Reactions of Metal-Activated Molecules. Proceedings of the Third Symposium held in Würzburg, September 17–19, 1997*, Werner, H., Schreier, P., Eds.; Vieweg and Sohn: Braunschweig, 1998; 1997, pp 61–64.
610. Bringmann, G.; Breuning, M.; Busemann, S.; Hinrichs, J.; Pabst, T.; Stowasser, R.; Tasler, S.; Wuzik, A.; Schenk, W. A.; Kümmel, J.; Seebach, D.; Jaeschke, G. Metal-assisted synthesis and application of axially chiral biaryl systems. In *Selective Reactions of Metal-Activated Molecules. Proceedings of the Third Symposium held in Würzburg, September 17–19, 1997*, Werner, H., Schreier, P., Eds.; Vieweg and Sohn: Braunschweig, 1998; 1998, pp 141–145.
611. Murer, P.; Seebach, D. Synthesis and properties of monodisperse chiral dendrimers (up to fourth generation) with doubly branched building blocks): an intriguing solvent effect. *Helv. Chim. Acta* **1998**, *81*, 603–631.
612. Seebach, D.; Abele, S.; Gademann, K.; Guichard, G.; Hintermann, T.; Jaun, B.; Matthews, J. L.; Schreiber, J. V.; Oberer, L.; Hommel, U.; Widmer, H. β^2- and β^3-Peptides with proteinaceous side chains: synthesis and solution structures of constitutional isomers, a novel helical secondary structure and the influence of solvation and hydrophobic interactions on folding. *Helv. Chim. Acta* **1998**, *81*, 932–982.
613. Hintermann, T.; Gademann, K.; Jaun, B.; Seebach, D. γ-Peptides forming more stable secondary structures than α-peptides: synthesis and helical NMR-solution structure of the γ-hexapeptide analog of H-(Val-Ala-Leu)$_2$-OH. *Helv. Chim. Acta* **1998**, *81*, 983–1002.
614. Greiveldinger, G.; Seebach, D. Second-generation trifluoromethyl-substituted chiral dendrimers containing triply branched building blocks: CF_3 as sensitive NMR probe for 'remote' diastereotopicity. *Helv. Chim. Acta* **1998**, *81*, 1003–1022.

615. Seebach, D.; Hoffmann, M. Preparation and use in amino acid synthesis of a new chiral glycine derivative-(*R*)- and (*S*)-*tert*-butyl 2-*tert*-butyl-4-methoxy-2,5-dihydroimidazole-1-carboxylate (BDI). *Eur. J. Org. Chem.* **1998**, 1337–1351.
616. Seebach, D.; Poenaru, S.; Folkers, G.; Rognan, D. Synthesis of oligo(3-hydroxybutanoate)(OHB)-containing peptides with high binding affinity to a class-I-MHC protein. *Helv. Chim. Acta* **1998**, *81*, 1181–1200.
617. Seebach, D.; Rheiner, P. B.; Greiveldinger, G.; Butz, T.; Sellner, H. Chiral dendrimers. *Topics in Current Chemistry: Dendrimers*, Vögtle, F., Ed.; Springer: Berlin, 1998; Vol. 197, pp 125–164.
618. Krebs, S.; Lamas, J. R.; Poenaru, S.; Folkers, G.; López de Castro, J. A.; Seebach, D.; Rognan, D. Substituting nonpeptidic spacers for the T-cell receptor-binding part of class I major histocompatibility complex-binding peptides. *J. Biol. Chem.* **1998**, *273*, 19072–19079.
619. Daura, X.; Jaun, B.; Seebach, D.; van Gunsteren, W. F.; Mark, A. E. Reversible peptide folding in solution by molecular dynamics simulation. *J. Mol. Biol.* **1998**, *280*, 925–932.
620. Matt, T.; Seebach, D. C-alkylation of peptides containing aminomalonate and (amino)(cyano)acetate residues. *Helv. Chim. Acta* **1998**, *81*, 1845–1895.
621. Matthews, J. L.; Gademann, K.; Jaun, B.; Seebach, D. Linear and cyclic β^3-oligopeptides with functionalised side-chains ($-CH_2OBn$, $-CO_2Bn$, $-CH_2CH_2CO_2Bn$) derived from serine and from aspartic and glutamic acid. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3331–3340.
622. Hintermann, T.; Mathes, C.; Seebach, D. Polylithiated β-peptides: like-selective C-terminal alkylation of Boc-β-HVal-β-HAla-β-HLeu-OMe. *Eur. J. Org. Chem.* **1998**, 2379–2387.
623. Hintermann, T.; Seebach, D. A useful modification of the Evans auxiliary: 4-isopropyl-5,5-diphenyloxazolidin-2-one. *Helv. Chim. Acta* **1998**, *81*, 2093–2126.
624. Seebach, D.; Abele, S.; Schreiber, J. V.; Martinoni, B.; Nussbaum, A. K.; Schild, H.; Schulz, H.; Hennecke, H.; Woessner, R.; Bitsch, F. Biological and pharmacokinetic studies with β-peptides. *Chimia* **1998**, *52*, 734–739.
625. Abele, S.; Guichard, G.; Seebach, D. (*S*)-β^3-Homolysine- and (*S*)-β^3-homoserine-containing β-peptides: CD spectra in aqueous solution. *Helv. Chim. Acta* **1998**, *81*, 2141–2156.
626. Seebach, D.; Abele, S.; Sifferlen, T.; Hänggi, M.; Gruner, S.; Seiler, P. Preparation and structure of β-peptides consisting of geminally disubstituted $\beta^{2,2}$- and $\beta^{3,3}$-amino acids: a turn motif for β-peptides. *Helv. Chim. Acta* **1998**, *81*, 2218–2243.
627. Fritz, M. G.; Seebach, D. Synthesis of amino-acid-, carbohydrate-, coumarin-, and biotin-labelled oligo [(*R*)-3-hydroxybutanoic acids] (OHB). *Helv. Chim. Acta* **1998**, *81*, 2414–2429.
628. Bachmann, B. M.; Seebach, D. Synthesis and structure of linear and cyclic oligomers of 3-hydroxybutanoic acid with specific sequences of (*R*)- and (*S*)-configurations. *Helv. Chim. Acta* **1998**, *81*, 2430–2461.
629. Gottwald, K.; Seebach, D. Ring opening with kinetic resolution of azlactones by Ti-TADDOLates. *Tetrahedron* **1999**, *55*, 723–738.
630. Seebach, D.; Boog, A.; Schweizer, W. B. EPC-Synthesis of β-amino acid derivatives through lithiated hydropyrimidines. *Eur. J. Org. Chem.* **1999**, 335–360.
631. Daura, X.; Gademann, K.; Jaun, B.; Seebach, D.; van Gunsteren, W. F.; Mark, A. E. Peptidfaltung: Wenn die Simulation das Experiment erreicht. *Angew. Chem.* **1999**, *111*, 249–253, *Angew. Chem. Int. Ed.* **1999**, *38*, 236–240.
632. Gademann, K.; Jaun, B.; Seebach, D.; Perozzo, R.; Scapozza, L.; Folkers, G. Temperature-dependent NMR and CD spectra of β-peptides: on the thermal stability of β-peptide helices - is the folding process of β-peptides non-cooperative? *Helv. Chim. Acta* **1999**, *82*, 1–11.
633. Fritz, M. G.; Walde, P.; Seebach, D. Oligoesters of (*R*)-3-hydroxybutanoic acid: transmembrane transport of Ca^{2+} across vesicle bilayers. *Macromolecules* **1999**, *32*, 574–580.
634. Bachmann, B. M.; Seebach, D. Investigation of the enzymatic cleavage of diastereomeric oligo(3-hydroxybutanoates) containing two to eight HB units. A model for the stereoselectivity of PHB depolymerase from *Alcaligenes faecalis* T_1. *Macromolecules* **1999**, *32*, 1777–1784.
635. Gademann, K.; Ernst, M.; Hoyer, D.; Seebach, D. Synthese und biologische Evaluation eines Cycloβtetrapeptids als Somatostatin-Analogon. *Angew. Chem.* **1999**, *111*, 1302–1304, *Angew. Chem. Int. Ed.***1999**, *38*, 1223–1226.
636. Seebach, D.; Abele, S.; Gademann, K.; Jaun, B. Faltblätter und Schleifen von β-Peptiden mit proteinogenen Seitenketten. *Angew. Chem.* **1999**, *111*, 1700–1703, *Angew. Chem. Int. Ed.* **1999**, *38*, 1595–1597.
637. Gademann, K.; Seebach, D. Preparation and NMR structure of the cyclo-β-tripeptide $[\beta^3\text{-HGlu}]_3$ in aqueous solution: a new class of enterobactin-type C_3-symmetrical ligands? *Helv. Chim. Acta* **1999**, *82*, 957–962.
638. Seebach, D.; Pichota, A.; Beck, A. K.; Pinkerton, A. B.; Litz, T.; Karjalainen, J.; Gramlich, V. Preparation of TADDOL derivatives for new applications. *Org. Lett.* **1999**, *1*, 55–58.
639. Beck, A. K.; Gysi, P.; La Vecchia, L.; Seebach, D. (4*R*,5*R*)-2,2-dimethyl-α,α,α′,α′-tetra(naphth-2-yl)-1,3-dioxolane-4,5-dimethanol from dimethyl tartrate and 2-naphthyl-magnesium bromide. *Org. Synth.* **1999**, *76*, 12–22.
640. Seebach, D.; Fritz, M. G. Detection, synthesis, structure, and function of oligo(3-hydroxy-alkanoates): contributions by synthetic organic chemists. *Int. J. Biol. Macromol.* **1999**, *25*, 217–236.
641. S. Abele, R. Wössner, F. Bitsch, D. Seebach, New Secondary Structures of β-Peptides and First Animal Experiments, In *Peptides, 1998: Proceedings of the Twenty-Fifth European Peptide Symposium*, Bajusz, S., Hudecz, F. (Eds.), Akadémiai Kiadó, Budapest, 1999, 408-409.
642. Gademann, K.; Hintermann, T.; Jaun, B.; Seebach, D. Folding of β- and γ-peptides. The influence of substitution patterns on the formation of hydrogen bonds. In *Peptides, 1998. Proceedings of the Twenty-Fifth European Peptide Symposium*, Bajusz, S., Hudecz, F., Eds.; Akadémiai Kiadó: Budapest, 1999; pp 422–423.
643. Heldmann, D. K.; Seebach, D. Catalytic enantioselective hydrosilylation of ketones with rhodium-phosphite complexes containing a TADDOLate and a dihydrooxazole unit. *Helv. Chim. Acta* **1999**, *82*, 1096–1110.
644. Sellner, H.; Seebach, D. Dendritisch quervernetzende chirale Liganden-hohe Standfestigkeit eines polystyrolgebundenen Ti-TADDOLat-Katalysators unter Diffusionskontrolle. *Angew. Chem.* **1999**, *111*, 2039–2041, *Angew. Chem. Int. Ed.* **1999**, *38*, 1918–1920.
645. Poenaru, S.; Lamas, J. R.; Folkers, G.; López de Castro, J. A.; Seebach, D.; Rognan, D. Nonapeptide analogues containing (*R*)-3-hydroxybutanoate and β-homoalanine oligomers: synthesis and binding affinity to a class I major histocompatibility complex protein. *J. Med. Chem.* **1999**, *42*, 2318–2331.

646. Jacobi, A.; Seebach, D. How to stabilize or break β-peptidic helices by disulfide bridges: synthesis and CD investigation of β-peptides with cysteine and homocysteine side chains. *Helv. Chim. Acta* **1999**, *82*, 1150–1172.
647. Hermann, B. A.; Hubler, U.; Jess, P.; Lang, H. P.; Güntherodt, H.-J.; Greiveldinger, G.; Rheiner, P. B.; Murer, P.; Sifferlen, T.; Seebach, D. Chiral dendrimers on a Pt(100) surface investigated by scanning tunnelling microscopy. *Surf. Interf. Anal.* **1999**, *27*, 507–511.
648. Dedier, S.; Krebs, S.; Lamas, J. R.; Poenaru, S.; Folkers, G.; Lopez de Castro, J. A.; Seebach, D.; Rognan, D. Structure-based design of nonnatural ligands for the HLA-B27 protein. *J. Receptor & Signal Transduction Research* **1999**, 645-657.
649. Götzö, S. P.; Seebach, D.; Sanglier, J.-J. EPC syntheses of trifluorocitronellol and of hexafluoropyrenophorin—a comparison of their physiological properties with the nonfluorinated analogs. *Eur. J. Org. Chem.* **1999**, 2533–2544.
650. Abele, S.; Vögtli, K.; Seebach, D. Oligomers of β^2- and of β^3-homoproline: what are the secondary structures of β-peptides lacking H-bonds? *Helv. Chim. Acta* **1999**, *82*, 1539–1558.
651. Abele, S.; Seiler, P.; Seebach, D. Synthesis, crystal structures, and modelling of β-oligopeptides consisting of 1-(aminomethyl)cyclopropanecarboxylic acid: ribbon-type arrangement of eight-membered H-bonded rings. *Helv. Chim. Acta* **1999**, *82*, 1559–1571.
652. Werder, M.; Hauser, H.; Abele, S.; Seebach, D. β-Peptides as inhibitors of small-intestinal cholesterol and fat absorption. *Helv. Chim. Acta* **1999**, *82*, 1774–1783.
653. Rheiner, P. B.; Seebach, D. Dendritic TADDOLs: synthesis, characterization and use in the catalytic enantioselective addition of Et_2Zn to benzaldehyde. *Chem. Eur. J.* **1999**, *5*, 3221–3236.
654. Seebach, D.; Lyapkalo, I. M.; Dahinden, R. Dichloro[TADDOLato(2-)-*O*,*O*′]titanium/dichlorobis[1-methylethoxy]-titanium-mediated highly diastereo- and enantioselective additions of silyl enol ethers to nitro olefins and [3+2] cycloadditions of primary adducts to acetylenes. *Helv. Chim. Acta* **1999**, *82*, 1829–1842.
655. Schreiber, J. V.; Quadroni, M.; Seebach, D. Sequencing of β-peptides by mass spectrometry. *Chimia* **1999**, *53*, 621–626.
656. Sifferlen, T.; Rueping, M.; Gademann, K.; Jaun, B.; Seebach, D. β-Thiopeptides: synthesis, NMR solution structure, CD spectra, and photochemistry. *Helv. Chim. Acta* **1999**, *82*, 2067–2093.
657. Brenner, M.; Seebach, D. Enantioselective preparation of γ-amino acids and γ-lactams from nitro olefins and carboxylic acids, with the valine-derived 4-isopropyl-5,5-diphenyl-1,3-oxazolidin-2-one as an auxiliary. *Helv. Chim. Acta* **1999**, *82*, 2365–2379.
658. Abele, S.; Woessner, R.; Bitsch, F.; Seebach, D. New secondary structures of β-peptides and first animal experiments. In *Peptides, 1998. Proceedings of the Twenty-Fifth European Peptide Symposium, Budapest-Hungary*, Bajusz, S., Hudecz, F., Eds.; Akadémiai Kiadò: Budapest, 1999; pp 408–409.
659. Gademann, K.; Hintermann, T.; Jaun, B.; Seebach, D. Folding of β-and γ-peptides. The influence of substitution patterns on the formation of hydrogen bonds. In *Peptides, 1998. Proceedings of the Twenty-Fifth European Peptide Symposium, Budapest-Hungary*, Bajusz, S., Hudecz, F., Eds.; Akadémiai Kiadò: Budapest, 1999; pp 422–423.
660. Pichota, A.; Pregosin, P. S.; Valentini, M.; Wörle, M.; Seebach, D. Röntgenstrukturanalyse, Diffusionsmessungen und NOESY NMR-Untersuchungen chiraler, vierkerniger CuI-Katalysatoren aus einzähnigen Thiol-Derivaten von TADDOL. *Angew. Chem.* **2000**, *112*, 157–160, *Angew. Chem. Int. Ed.* **2000**, *39*, 153–156.
661. Heckel, A.; Seebach, D. Verankerung von TADDOL auf porösem Kieselgel mit hoher Beladung und erste Anwendungen in der enantioselektiven Katalyse. *Angew. Chem.* **2000**, *112*, 165–167, *Angew. Chem. Int. Ed.* **2000**, *39*, 163–165.
662. Abele, S.; Seebach, D. Preparation of achiral and of enantiopure geminally disubstituted β-amino acids for β-peptide synthesis. *Eur. J. Org. Chem.* **2000**, 1–15.
663. Gademann, K.; Ernst, M.; Seebach, D.; Hoyer, D. The cyclo-β-Tetrapeptide (β-HPhe-β-HThr-β-HLys-β-HTrp): synthesis, NMR structure in methanol solution, and affinity for human somatostatin receptors. *Helv. Chim. Acta* **2000**, *83*, 16–33.
664. Seebach, D.; Schreiber, J. V.; Abele, S.; Daura, X.; van Gunsteren, W. F. Structure and conformation of β-oligopeptide derivatives with simple proteinogenic side chains: circular dichroism and molecular dynamics investigations. *Helv. Chim. Acta* **2000**, *83*, 34–57.
665. Seebach, D. TADDOLs-from enantioselective catalysis to dendritic cross linkers to cholesteric liquid crystals. *Chimia* **2000**, *54*, 60–62.
666. Krell, C. M.; Seebach, D. Preparation of free and of specifically protected oligo[β-malic acids] for enzymatic degradation studies. *Eur. J. Org. Chem.* **2000**, 1207–1218.
667. Gaul, C.; Seebach, D. A valine-derived lithiated 3-methylthiomethyl-1,3-oxazolidin-2-one for enantioselective nucleophilic hydroxymethylation, formylation, and alkoxycarbonylation of aldehydes. *Org. Lett.* **2000**, *2*, 1501–1504.
668. Seebach, D.; Jacobi, A.; Rueping, M.; Gademann, K.; Ernst, M.; Jaun, B. Synthesis of β-hexa- and β-heptapeptides containing novel $\beta^{2,3}$-amino acids with two serine or two cysteine side chains CD- and NMR-spectroscopic evidence for 3_{14}-helical secondary structures in water. *Helv. Chim. Acta* **2000**, *83*, 2115–2140; and In *Hominatio—An International Tribute to Albert Eschenmoser*. Kisakürek, M. V., Ed.; Wiley-VCH: Weinheim, 2001.
669. Gasslmaier, B.; Krell, C. M.; Seebach, D.; Holler, E. Synthetic substrates and inhibitors of β-poly(L-malate)-hydrolase (polymalatase). *Eur. J. Biochem.* **2000**, *267*, 5101–5105.
670. Sellner, H.; Faber, C.; Rheiner, P. B.; Seebach, D. Immobilization of BINOL by cross-linking copolymerization of styryl derivatives with styrene, and applications in enantioselective Ti and Al Lewis acid mediated additions of Et_2Zn and Me_3SiCN to aldehydes and of diphenyl nitrone to enol ethers. *Chem. Eur. J.* **2000**, *6*, 3692–3705.
671. Rueping, M.; Jaun, B.; Seebach, D. NMR structure in methanol of a β-hexapeptide with a disulfide clamp. *Chem. Commun.* **2000**, 2267–2268.
672. Seebach, D.; Sifferlen, T.; Mathieu, P. A.; Häne, A. M.; Krell, C. M.; Bierbaum, D. J.; Abele, S. CD spectra in methanol of β-oligopeptides consisting of β-amino acids with functionalized side chains, with alternating configuration, and with geminal backbone substituents-fingerprints of new secondary structures? *Helv. Chim. Acta* **2000**, *83*, 2849–2864.
673. Seebach, . D. Forschung-eine Fahrt ins Blaue. *Chimia* **2000**, *54*, 751–758.
674. Schreiber, J. V.; Seebach, D. Solid-phase synthesis of a β-dodecapeptide with seven functionalized side chains and

CD-spectroscopic evidence for a dramatic structural switch when going from water to methanol solution. *Helv. Chim. Acta* **2000**, *83*, 3139–3152.
675. Cuenca, A.; Medio-Simón, M.; Aguilar, G. A.; Weibel, D.; Beck, A. K.; Seebach, D. Highly enantioselective protonation of the 3,4-dihydro-2-methyl-naphthalen-1(2*H*)-one Li-enolate by TADDOLs. *Helv. Chim. Acta* **2000**, *83*, 3153–3162.
676. Böhm, A.; Seebach, D. Determination of enantiomer purity of β- and γ-amino acids by NMR analysis of diastereoisomeric palladium complexes. *Helv. Chim. Acta* **2000**, *83*, 3262–3278.
677. Seebach, D. From Peroxides to Synthetic Methodology and Stereoselectivity to β- and γ-Peptide Helices, Articles in Medicine and Science I, *The 1999 and 2000 King Faisal International Prize, King Faisal Centre for Research and Islamic Studies, Riyad, Saudi Arabia*, **2000**, 53-72.
678. Seebach, D.; Beck, A. K.; Heckel, A. TADDOLe, ihre Derivate und Analoga-vielseitige chirale Hilfsstoffe. *Angew. Chem.* **2001**, *113*, 96–142, *Angew. Chem. Int. Ed.* **2001**, *40*, 92–138.
679. Seebach, D.; Brenner, M.; Rueping, M.; Schweizer, B.; Jaun, B. Preparation and determination of X-ray-crystal and NMR-solution structures of $\gamma^{2,3,4}$-peptides. *Chem. Commun.* **2001**, 207–208.
680. Le, H. C.; Hintermann, T.; Wessels, T.; Gan, Z.; Seebach, D.; Ernst, R. R. Determination of the amide plane orientations in a cyclo-β-peptide by magic-angle-spinning deuterium correlation spectroscopy, and comparison with the powder X-ray structure. *Helv. Chim. Acta* **2001**, *84*, 208–221.
681. Aoki, M.; Seebach, D. Preparation of TADOOH, a hydroperoxide from TADDOL, and use in highly enantioface- and enantiomer-differentiating oxidations. *Helv. Chim. Acta* **2001**, *84*, 187–207.
682. Seebach, D.; Schreiber, J. V.; Arvidsson, P. I.; Frackenpohl, J. The miraculous CD spectra (and secondary structures ?) of β-Peptides as they grow longer. *Helv. Chim. Acta* **2001**, *84*, 271–279.
683. Seebach, D.; Beck, A. K.; Rueping, M.; Schreiber, J. V.; Sellner, H. Excursion of synthetic organic chemists to the world of oligomers and polymers. *Chimia* **2001**, *55*, 98–103.
684. Daura, X.; Gademann, K.; Schäfer, H.; Jaun, B.; Seebach, D.; van Gunsteren, W. F. The β-peptide hairpin in solution: conformational study of a β-hexapeptide in methanol by NMR spectroscopy and MD simulation. *J. Am. Chem. Soc.* **2001**, *123*, 2393–2404.
685. Arvidsson, P. I.; Rueping, M.; Seebach, D. Design, machine synthesis, and NMR-solution structure of a β-heptapeptide forming a salt-bridge stabilised 3_{14}-helix in methanol and in water, Chem. *Commun.* **2001**, 649–650.
686. Seebach, . D.; Albert, M.; Arvidsson, P. I.; Rueping, M.; Schreiber, J. V. From the biopolymer PHB to biological investigations of unnatural β- and γ-peptides. *Chimia* **2001**, *55*, 345–353.
687. Gaul, C.; Schärer, K.; Seebach, D. Lithiated 4-isopropyl-3-(methylthiomethyl)-5,5.diphenyloxazolidin-2-one: a chiral formyl anion equivalent for enantioselective preparations of 1,2-diols, 2-amino alcohols, 2-hydroxy ester, and 4-hydroxy-2-alkenoates. *J. Org. Chem.* **2001**, *66*, 3059–3073.
688. Brenner, M.; Rueping, M.; Seebach, D. Synthesis and structural characterization of γ-peptides. In *Peptides, 2000. Proceedings of the Twenty-Sixth European Peptide Symposium, Montpellier-France*, Martinez, J., Fehrentz, J. A., Eds.; EDK: Paris, 2001; pp 455–456.
689. Mathieu, P. A.; Sifferlen, T.; Häne, A.; Seebach, D. Unexpected circular dichroism of some β-oligopeptides consisting of residues with geminal backbone substitution. In *Peptides, 2000. Proceedings of the Twenty-Sixth European Peptide Symposium, Montpellier-France*, Martinez, J., Fehrentz, J.-A., Eds.; EDK: Paris, 2001; pp 507–508.
690. Schreiber, J. V.; Arvidsson, P. I.; Seebach, D. Structures and conformations of β-dipeptides with simple proteinogenic side chains: circular dichroism and computational investigations. In *Peptides, 2000. Proceedings of the Twenty-Sixth European Peptide Symposium, Montpellier-France*, Martinez, J., Fehrentz, J.-A., Eds.; EDK: Paris, 2001; pp 1003–1004.
691. Brenner, M.; Seebach, D. Synthesis and CD spectra in MeCN, MeOH, and H_2O of γ-oligopeptides with hydroxy groups on the backbone. *Helv. Chim. Acta* **2001**, *84*, 1181–1189.
692. Frackenpohl, J.; Arvidsson, P. I.; Schreiber, J. V.; Seebach, D. The outstanding biological stability of β- and γ-peptides toward proteolytic enzymes: an in vitro investigation with fifteen peptidases. *ChemBioChem* **2001**, *2*, 445–455.
693. Sellner, H.; Karjalainen, J. K.; Seebach, D. Preparation of dendritic and non-dendritic styryl-substituted salens for cross-linking suspension copolymerization with styrene and multiple use of the corresponding Mn and Cr complexes in enantioselective epoxidations and hetero-Diels–Alder reactions. *Chem. Eur. J.* **2001**, *6*, 2873–2887.
694. Gademann, K.; Kimmerlin, T.; Hoyer, D.; Seebach, D. Peptide folding induces high and selective affinity of a linear and small, β-peptide to the human somatostatin receptor 4. *J. Med. Chem.* **2001**, *44*, 2460–2468.
695. Waser, P.; Rueping, M.; Seebach, D.; Duchardt, E.; Schwalbe, H. On the solution structure of PHB: preparation and NMR analysis of isotopically labeled oligo[(*R*)-3-hydroxy-butanoic acids] (OHBs). *Helv. Chim. Acta* **2001**, *84*, 1821–1845.
696. Seebach, D.; Beck, A. K.; Heckel, A. TADDOL and its derivatives—our dream of universal chiral auxiliaries. In *Essays in Contemporary Chemistry: From Molecular Structure towards Biology*. Quinkert, G., Kisakürek, M. V., Eds.; Wiley-VCH: Weinheim, 2001; pp 283–306.
697. Seebach, . D.; Rueping, M. Neuartige Peptide und Proteine: Neue Molekül-Welten mit β-Peptiden. *Bulletin ETH Zürich* **2001**, *282*, 18–21.
698. Brenner, M.; Seebach, D. Design, synthesis, NMR-solution and X-ray crystal structure of *N*-acyl-γ-dipeptide amides that form a βII′-type turn. *Helv. Chim. Acta* **2001**, *84*, 2155–2166.
699. Rueping, M.; Dietrich, A.; Buschmann, V.; Fritz, M. G.; Sauer, M.; Seebach, D. On the structure of poly(3-hydroxybutanoic acid) in solution and phospholipid bilayers. Circular dichroism and fluorescence spectroscopy with oligo(3-hydroxybutanoic acid) derivatives. *Macromolecules* **2001**, *34*, 7042–7048.
700. Arvidsson, P. I.; Frackenpohl, J.; Ryder, N. S.; Liechty, B.; Petersen, F.; Zimmermann, H.; Camenisch, G. P.; Woessner, R.; Seebach, D. On the antimicrobial and hemolytic activities of amphiphilic β-peptides. *ChemBioChem* **2001**, *2*, 771–773.
701. Gaul, C.; Arvidsson, P. I.; Bauer, W.; Gawley, R. E.; Seebach, D. Computational, reactIR-, and NMR-spectroscopic investigations on the chiral formyl anion equivalent *N*-(α-lithiomethylthiomethyl)-4-isopropyl-5,5-diphenyloxazolidin-2-one and related compounds. *Chem. Eur. J.* **2001**, *7*, 4117–4125.

702. Seebach, D.; Beck, A. K.; Brenner, M.; Gaul, C.; Heckel, A. From synthetic methods to γ-peptides-from chemistry to biology. *Chimia* **2001**, *55*, 831–838.
703. Gademann, K.; Seebach, D. Synthesis of cyclo-β-tripeptides and their biological in vitro evaluation as antiproliferatives against the growth of human cancer cell lines. *Helv. Chim. Acta* **2001**, *84*, 2924–2937.
704. Seebach, D.; Rueping, M.; Arvidsson, P. I.; Kimmerlin, T.; Micuch, P.; Noti, C.; Langenegger, D.; Hoyer, D. Linear, peptidase-resistant β^2/β^3-di-and α/β^3-tetrapeptide derivatives with nanomolar affinities to a human somatostatin receptor. *Helv. Chim. Acta* **2001**, *84*, 3503–3510.
705. Rueping, M.; Jaun, B.; Seebach, D. Folding of β- and γ-Peptides—the Influence of Substitution Patterns on the Formation of Secondary Structures. In *Peptides: The Wave of the Future*. Lebl, M., Houghten, R. A., Eds.; American Peptide Society, 2001; pp 383–384.
706. Etezady-Esfarjani, T.; Hilty, C.; Wüthrich, K.; Rueping, M.; Seebach, D. NMR Structural Investigation of a β^3-Dodecapeptide with Proteinogenic Side Chains in MeOH and Water. In *Peptides: The Wave of the Future*. Lebl, M., Houghten, R. A., Eds.; American Peptide Society, 2001; pp 312–313.
707. Seebach, D. Homologs of Amino Acids and Explorations into the Worlds of β- and γ-Peptides. In *Peptides: The Wave of the Future*. Lebl, M., Houghten, R. A., Eds.; American Peptide Society, 2001; pp 569–571.
708. Frackenpohl, J.; Schreiber, J. V.; Arvidsson, P. I.; Seebach, D. Recent Advances in the Solid-Phase Synthesis of Long-Chain β-Peptides. In *Peptides: The Wave of the Future*. Lebl, M., Houghten, R. A., Eds.;, 2001; pp 275–276.
709. Kimmerlin, T.; Hoyer, D.; Seebach, D. Synthesis and Biological Evaluation of Mixed β^2/β^3-Dipeptides as Somatostatin Analogs. In *Peptides: The Wave of the Future*. Lebl, M., Houghten, R. A., Eds.; American Peptide Society, 2001; pp 622–623.
710. Micuch, P.; Seebach, D. Enantioselective Synthesis of β^2-Homotryptophan for a Somatostatin Mimetic. In *Peptides: The Wave of the Future*. Lebl, M, Houghten, R. A., Eds.; American Peptide Society, 2001; pp 32–33.
711. Lelais, G.; Seebach, D. Synthesis and CD-Spectra of β^2-(3-Aza-peptides). In *Peptides: The Wave of the Future*. Lebl, M., Houghten, R. A., Eds.;, 2001; pp 581–582.
712. Sellner, H.; Rheiner, P. B.; Seebach, D. Preparation of polystyrene beads with dendritically embedded TADDOL and use in enantioselective Lewis acid catalysis. *Helv. Chim. Acta* **2002**, *85*, 352–387.
713. Heckel, A.; Seebach, D. Preparation and characterization of TADDOLs immobilized on hydrophobic controlled-pore-glass silica gel and their use in enantioselective heterogeneous catalysis. *Chem. Eur. J.* **2002**, *8*, 559–572.
714. Seebach, D.; Brenner, M.; Rueping, M.; Jaun, B. γ^2-, γ^3-, and $\gamma^{2,3,4}$-Amino acids, coupling to γ-hexapeptides: CD spectra, NMR solution and X-ray crystal structures of γ-peptides. *Chem. Eur. J.* **2002**, *8*, 573–584.
715. Rueping, M.; Mahajan, Y.; Sauer, M.; Seebach, D. Cellular uptake studies with β-peptides. *ChemBioChem* **2002**, *3*, 257–259.
716. Gee, P. J.; Hamprecht, F. A.; Schuler, L. D.; van Gunsteren, W. F.; Duchardt, E.; Schwalbe, H.; Albert, M.; Seebach, D. A molecular dynamics simulation study of the conformational preferences of oligo-(3-hydroxyalkonoic acids) in chloroform solution. *Helv. Chim. Acta* **2002**, *85*, 618–632.
717. Albert, M.; Seebach, D.; Duchardt, E.; Schwalbe, H. Synthesis and NMR analysis in solution of oligo-(3-hydroxyalkonoic acid) derivatives with the side chains of alanine, valine, and leucine (β-depsides)-coming full circle from PHB to β-peptides to PHB. *Helv. Chim. Acta* **2002**, *85*, 633–658.
718. Gaul, C.; Seebach, D. Conjugate addition of lithiated (*S*)-4-isopropyl-3-[(methylthio)methyl]-5,5-diphenyloxazolidin-2-one to cinnamoyl derivatives: preparation of enantiomerically pure 1,4-diols. *Helv. Chim. Acta* **2002**, *85*, 772–787.
719. Heckel, A.; Seebach, D. Enantioselective heterogeneous epoxidation and hetero-Diels–Alder reaction with Mn- and Cr-salen complexes immobilized on silica gel by radical grafting. *Helv. Chim. Acta* **2002**, *85*, 913–926.
720. Das, S.; Seebach, D.; Reusch, R. N. Differential effects of temperature on *E. coli* and synthetic polyhydroxybutyrate/-polyphosphate channels. *Biochemistry* **2002**, *41*, 5307–5312.
721. Schreiber, J. V.; Frackenpohl, J.; Moser, F.; Fleischmann, T.; Kohler, H.-P.; Seebach, D. On the biodegradation of β-peptides. *ChemBioChem* **2002**, *3*, 424–432.
722. Gaul, C.; Seebach, D. Metallations and reactions with electrophiles of 4-isopropyl-5,5-diphenyloxazolidin-2-one (DIOZ) with *N*-allyl and *N*-propargyl substituents: chiral homoenolate reagents. *Helv. Chim. Acta* **2002**, *85*, 963–978.
723. Etezady-Esfarjani, T.; Hilty, C.; Wüthrich, K.; Rueping, M.; Schreiber, J.; Seebach, D. NMR-Structural Investigations of a β^3-dodecapeptide with proteinogenic side chains in methanol and in aqueous solutions. *Helv. Chim. Acta* **2002**, *85*, 1197–1209.
724. Gaul, C.; Schweizer, B. W.; Seiler, P.; Seebach, D. Crystal structures—a manifesto for the superiority of the valine-derived 5,5-diphenyloxazolidinone as an auxiliary in enantioselective organic synthesis. *Helv. Chim. Acta* **2002**, *85*, 1546–1566.
725. Micuch, P.; Seebach, D. Preparation of β^2-homotryptophan derivatives for β-peptide synthesis. *Helv. Chim. Acta* **2002**, *85*, 1567–1577.
726. Kimmerlin, T.; Seebach, D.; Hilvert, D. Synthesis of β^3-peptides and mixed α/β^3-peptides by thioligation. *Helv. Chim. Acta* **2002**, *85*, 1812–1826.
727. Seebach, D.; Mahajan, Y. R.; Senthilkumar, R.; Rueping, M.; Jaun, B. β-Depsipeptides—the effect of a missing and a weakened hydrogen bond on the stability of the β-peptidic 3_{14}-helix. *Chem. Commun.* **2002**, 1598–1599.
728. Adam, W.; Roschmann, K. J.; Saha-Möller, C. R.; Seebach, D. *cis*-Stilbene and (1α,2β,3α)-(2-ethenyl-3-methoxycyclopropyl)benzene as mechanistic probes in the Mn^{III}(salen)-catalyzed epoxidation: influence of the oxygen source and the counterion on the diastereoselectivity of the competitive concerted and radical-type oxygen transfer. *J. Am. Chem. Soc.* **2002**, *124*, 5068–5073.
729. Juaristi, E.; Hernàndes-Rodríguez, M.; López-Ruiz, H.; Avina, J.; Muñoz-Muñiz, O.; Hayakawa, M.; Seebach, D. Synthesis of new chiral derivatives of *N*,*N*′-dimethylpropyleneurea (DMPU) and examination of their influence on the regio- and enantioselectivity of addition of 2-(2,3-dithianyl)-lithium to cyclohex-2-en-1-one. *Helv. Chim. Acta* **2002**, *85*, 1999–2008.
730. Rueping, M.; Schreiber, J. V.; Lelais, G.; Jaun, B.; Seebach, D. Mixed β^2/β^3hexapeptides and β^2/β^3-nonapeptides folding to (*P*)-helices with alternating twelve- and ten-membered hydrogen-bonded rings. *Helv. Chim. Acta* **2002**, *85*, 2577–2593.
731. Seebach, D.; Sifferlen, T.; Bierbaum, D. J.; Rueping, M.;

Jaun, B.; Schweizer, B.; Schaefer, J.; Mehta, A. K.; O'Connor, R. D.; Meier, B. H.; Ernst, M.; Glättli, A. Isotopically labelled and unlabelled β-peptides with geminal dimethyl substitution in 2-position of each residue: synthesis and NMR investigation in solution and in the solid state. *Helv. Chim. Acta* **2002**, *85*, 2877–2917.

732. Wiegand, H.; Wirz, B.; Schweitzer, A.; Camenisch, G. P.; Rodriguez Perez, M. I.; Gross, G.; Woessner, R.; Voges, R.; Arvidsson, P. I.; Frackenpohl, J.; Seebach, D. The outstanding metabolic stability of a ^{14}C-labeled β-nonapeptide in rats in-vitro and in-vivo pharmacokinetic studies. *Biopharm. Drug Dispos.* **2002**, *23*, 251–262.
733. Glättli, A.; Daura, X.; Seebach, D.; van Gunsteren, W. F. Can one derive the conformational preference of a β-peptide from its CD spectrum? *J. Am. Chem. Soc.* **2002**, *124*, 12972–12978.
734. Gessier, F.; Rueping, M.; Seebach, D. Synthesis and structural investigations of an α-hydroxylated β-hexapeptide. In *Peptides, 2002*. Benedetti, E., Pedone, C., Eds.; Edizioni Ziino: Napoli, Italy, 2002; pp 108–109.
735. Kimmerlin, T.; Seebach, D. Synthesis of β-peptides by chemical ligation. *Peptides* 2002, Benedetti, E., Pedone, C., Eds.; Edizioni Ziino: Napoli, Italy, 2002; 2002, pp 162–163.
736. Mahajan, Y. R.; Rueping, M.; Seebach, D. β-Homoarginine-containing β-peptides-structure and cell-penetrating ability. In *Peptides* 2002. Benedetti, E., Pedone, C., Eds.; Edizioni Ziino: Napoli, Italy, 2002; pp 210–211.
737. Schaeffer, L.; Hoyer, D.; Seebach, D. Investigation of *N*-acyl-γ-dipeptide amides as somatostatin analogs: synthesis and receptor-affinity measurement. *Peptides* 2002, Benedetti, E., Pedone, C., Eds.; Edizioni Ziino: Napoli, Italy, 2002; 2002, pp 278–279.
738. Mahajan, Y. R.; Senthilkumar, R.; Rueping, M.; Seebach, D. β-Depsipeptides: synthesis and structural studies. In *Peptides* 2002. Benedetti, E., Pedone, C., Eds.; Edizioni Ziino: Napoli, Italy, 2002; pp 798–799.
739. Seebach, D. Homologs of Amino Acids and Explorations into the Worlds of β-and γ-Peptides. In *Chemistry of Crop Protection, Progress and Prospects in Science and Regulation*. Voss, G., Ramos, G., Eds.; Wiley-VCH: New York, 2003; pp 17–29.
740. Seebach, D.; Schaeffer, L.; Brenner, M.; Hoyer, D. Design and synthesis of γ-dipeptide derivatives with submicromolar affinities for human somatostatin receptors. *Angew. Chem.* **2003**, *115*, 730–736, *Angew. Chem. Int. Ed.* **2003**, *42*, 776–778.
741. Nunn, C.; Rueping, M.; Langenegger, D.; Schuepbach, E.; Kimmerlin, T.; Micuch, P.; Hurth, K.; Seebach, D.; Hoyer, D. β^2/β^3 and α/β^3 Tetrapeptide derivatives as potent agonists at somatostatin sst_4 receptors. *Naunyn-Schmiedeberg's Arch. Pharmacol.* **2003**, *367*, 95–103.
742. Gademann, K.; Häne, A.; Rueping, M.; Jaun, B.; Seebach, D. The fourth helical secondary structure of β-peptides: the (*P*)-2_8-helix of a β-hexapeptide consisting of (2*R*,3*S*)-3-amino-2-hydroxy acid residues. *Angew. Chem.* **2003**, *115*, 1573–1575, *Angew. Chem. Int. Ed.* **2003**, *42*, 1534–1537.
743. Sellner, H.; Hametner, K.; Günther, D.; Seebach, D. Manganese distribution in polystyrene beads prepared by copolymerization with cross-linking dendritic salens using laser ablation inductively coupled plasma mass spectrometry. *J. Catal.* **2003**, *215*, 87–93.
744. Arvidsson, P. I.; Frackenpohl, J.; Seebach, D. Syntheses and CD-spectroscopic investigations of longer-chain β-peptides: preparation by solid-phase couplings of single amino acids, dipeptides and tripeptides. *Helv. Chim. Acta* **2003**, *86*, 1522–1553.
745. Adam, W.; Alsters, P. L.; Neumann, R.; Saha Möller, C. R.; Seebach, D.; Zhang, R. Highly efficient catalytic asymmetric epoxidation of allylic alcohols by an oxovanadium-substituted polyoxometalate with a regenerative TADDOL-derived hydroperoxide. *Org. Lett.* **2003**, *5*, 725–728.
746. Adam, W.; Beck, A. K.; Pichota, A.; Saha-Möller, C. R.; Seebach, D.; Vogl, N.; Zhang, R. Control of enantioselectivity through a hydrogen-bonded template in the vanadium(V)-catalyzed epoxidation of allylic alcools by optically active hydroperoxydes. *Tetrahedron: Asymmetry* **2003**, *14*, 1355–1361.
747. Seebach, D.; Schaeffer, L.; Gessier, F.; Bindschädler, P.; Jäger, C.; Josien, D.; Kopp, S.; Lelais, G.; Mahajan, Y.; Micuch, P.; Sebesta, R.; Schweizer, B. W. Enantioselective preparation of (*S*)-2-aminomethyl-carboxylic acid derivatives: solving the β^2-amino-acid problem with the chiral auxiliary 4-isopropyl-5,5-diphenyloxazolidin-2-one (DIOZ). *Helv. Chim. Acta* **2003**, *86*, 1852–1861.
748. Gessier, F.; Noti, C.; Rueping, M.; Seebach, D. Synthesis and CD-spectra of fluoro- and hydroxy-substituted β-peptides. *Helv. Chim. Acta* **2003**, *86*, 1862–1870.
749. Kimmerlin, T.; Seebach, D. Solid-phase synthesis of a β^3-eicosapeptide containing the homologs of the twenty common proteinaceous amino acids. *Helv. Chim. Acta* **2003**, *86*, 2098–2103.
750. Kimmerlin, T.; Namoto, K.; Seebach, D. Evidence from circular dichroism and from melting behavior for helix-inducing complexation of a designed β^3-pentadecapeptide with DNA-duplexes. *Helv. Chim. Acta* **2003**, *86*, 2104–2109.
751. Rossi, F.; Lelais, G.; Seebach, D. Zn^{2+}-complexation by a β-peptidic helix and hairpin containing β^3hCys and β^3hHis building blocks - evidence from CD measurements. *Helv. Chim. Acta* **2003**, *86*, 2653–2661.
752. Arvidsson, P. I.; Ryder, N. S.; Weiss, M. H.; Gross, G.; Kretz, O.; Woessner, R.; Seebach, D. Antibiotic and hemolytic activity of a β^2/β^3-peptide capable of folding to a 12/10-helical secondary structure. *ChemBioChem* **2003**, *4*, 1345–1347.
753. Sebesta, R.; Seebach, D. Preparation of (S,S)-Fmoc-β^2hlle-OH, (S)-Fmoc-β^2hMet-OH, and (S)-Fmoc-β^2hTyr(tBu)-OH for Solid-Phase Syntheses of β^2- and β^2/β^3-Peptides), Helv. *Chim. Acta* **2003**, *86*, 4061–4072.
754. Lelais, G.; Seebach, D. Synthesis, CD spectra and enzymatic stability of β^2-oligoazapeptides prepared from (*S*)-2-hydrazino carboxylic acids carrying the side chains of Val, Ala, Leu. *Helv. Chim. Acta* **2003**, *86*, 4152–4168.
755. Peter, C.; Rueping, M.; Wörner, H. J.; Jaun, B.; Seebach, D.; van Gunsteren, W. F. Molecular dynamics simulations of small peptides: can one derive conformational preferences from ROESY spectra? *Chem. Eur. J.* **2003**, *9*, 5838–5849.
756. Brenner, M.; La Vecchia, L.; Leutert, T.; Seebach, D. (4*S*)-4-(1-Methylethyl)-5,5-diphenyl-2-oxazolidinone. *Org. Synth.* **2003**, *80*, 57–65.
757. Adam, W.; Alsters, P. L.; Neumann, R.; Saha-Möller, C. R.; Seebach, D.; Beck, A. K.; Zhang, R. Chiral hydroperoxides as oxygen source in the catalytic stereoselective epoxidation of allylic alcohols by sandwich-type polyoxometalates: control of enantioselectivity through a metal-coordinated template. *J. Org. Chem.* **2003**, *68*, 8222–8231.

758. Daura, X.; Bakowies, D.; Seebach, D.; Fleischhauer, J.; van Gunsteren, W. F.; Krüger, P. Circular dichroism spectra of β-peptides: sensitivity to molecular structure and effects of motional averaging. *Eur. Biophys J.* **2003**, *32*, 661–670.
759. Belokon, Y. N.; Harutynyan, S.; Vorontsov, E. V.; Peregudov, A. S.; Chrustalev, V. N.; Kochetkov, K. A.; Pripadchev, D.; Sagyan, A. S.; Beck, A. K.; Seebach, D. Nucleophilic addition to an achiral dehydroalanine Schiff Base Ni(II) complex as a route to amino acids. A case of stereodetermining asymmetric protonation in the presence of TADDOL. *ARKIVOC* **2004**(iii), 132–150, http://www.arkat-usa.org/ark/journal/2004/Makosza/MM-853G/853G.htm, http://www.arkat-usa.org/ark/journal/2004/Makosza/MM-853G/853G.pdf.
760. Seebach, D.; Namoto, K.; Mahajan, Y. R.; Bindschädler, P.; Sustmann, R.; Kirsch, M.; Ryder, N. S.; Weiss, M.; Sauer, M.; Roth, C.; Werner, S.; Beer, H.-D.; Munding, C.; Walde, P.; Voser, M. Chemical and biological investigations of β-oligoarginines. *Chem. Biodivers.* **2004**, *1*, 65–97.
761. Rueping, M.; Mahajan, Y. R.; Jaun, B.; Seebach, D. Design, synthesis and structural investigations of a β-peptide forming a 3_{14}-helix stabilized by electrostatic interactions. *Chem. Eur. J.* **2004**, *10*, 1607–1615.