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Stereoselective synthesis of chiral thiol-containing 1,2-aminoalcohols via SmI_2-mediated coupling

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ABSTRACT

The stereoselective synthesis of highly functionalized aminohydroxythiols represents a synthetic challenge as the oxidation sensitivity and coordinating property of the thiol group interferes with many established synthetic methods. The SmI_2/LiBr-mediated reductive coupling between Ellman *N*-sulfinylimines, containing thiol groups protected either as trityl thioether or dihydrothiazolidine, and aldehydes enables the synthesis of chiral aminohydroxythiols in high enantio- and diastereoselectivity. The scope of this reaction has been established for 18 examples and applied for the synthesis of a complex intermediate needed for a biosynthesis study.

1. Introduction

In the course of a biosynthetic study [1] we faced the challenge in synthesizing the highly functionalized chiral thiol-containing 1,2-aminoalcohol compound **A** (Fig. 1).

While there are excellent methods for the synthesis of chiral 1,2-aminoalcohols available, such as nucleophilic addition at an α-amino carbonyl or α-hydroxy imine [2–14], ring opening reactions of epoxide [14–21] or aziridine [14,22–29] precursors, as well as the addition of both heteroatoms to α,β-unsaturated double bonds via Sharpless asymmetric aminohydroxylation [14,30–33], the presence of a thiol group limits the applicability of these methods as we found out when trying several of these methods as thiols (or thioethers) are incompatible with oxidative conditions and coordinate to metal reagents.

One of the first methods we considered for the synthesis of the highly functionalized intermediate **A** was the Sharpless asymmetric aminohydroxylation (SAA). To the best of our knowledge the SAA had been attempted for sulfur containing heterocycles (thiophene)

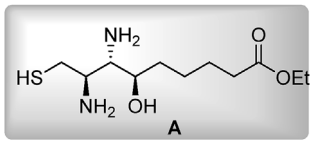

Fig. 1. Intermediate **A** designed for a biosynthetic study.

[34,35], but not yet for thiol or thioether containing substrates. These functional groups represent a special challenge due to their oxidation sensitivity and metal coordinating properties. However, with trityl protected substrate **3** an aminohydroxylation product **4** was generated in 42% yield (Scheme 1). Unfortunately, the produced amino-alcohol **4** showed a regiochemistry contrary to the intended one. Apparently, in our reaction the regioselectivity of the SAA was dominated by the trityl protecting group and therefore opposite to the established rule about the regioselectivity of the SAA [36,37]. Since this undesired regioselectivity of the SAA could not be changed, we turned to a pinacol type C-C coupling of an aldehyde with an imine [38], for which SmI_2 [39,40] has proved as a very powerful and chemoselective reagent whose activity and

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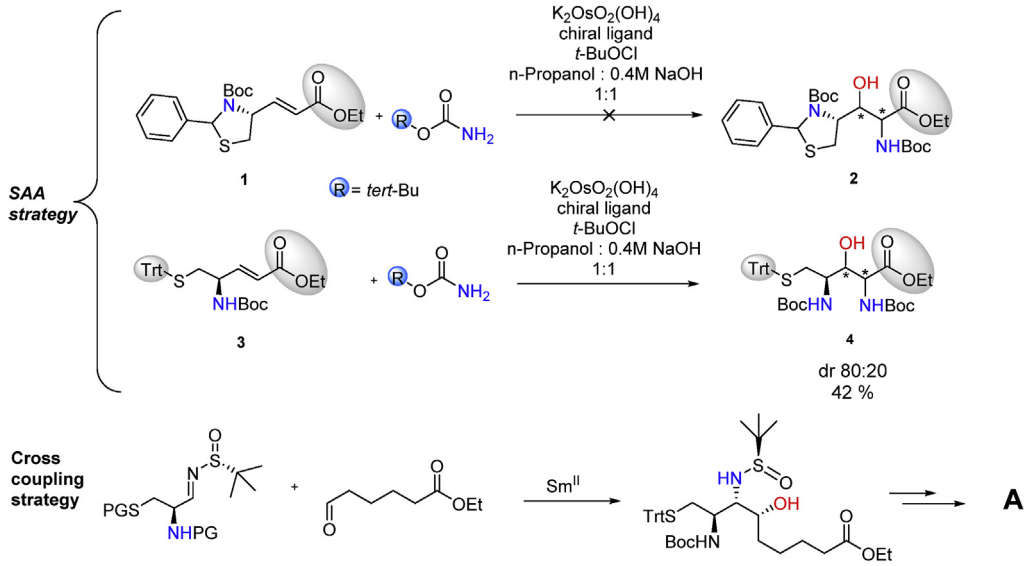


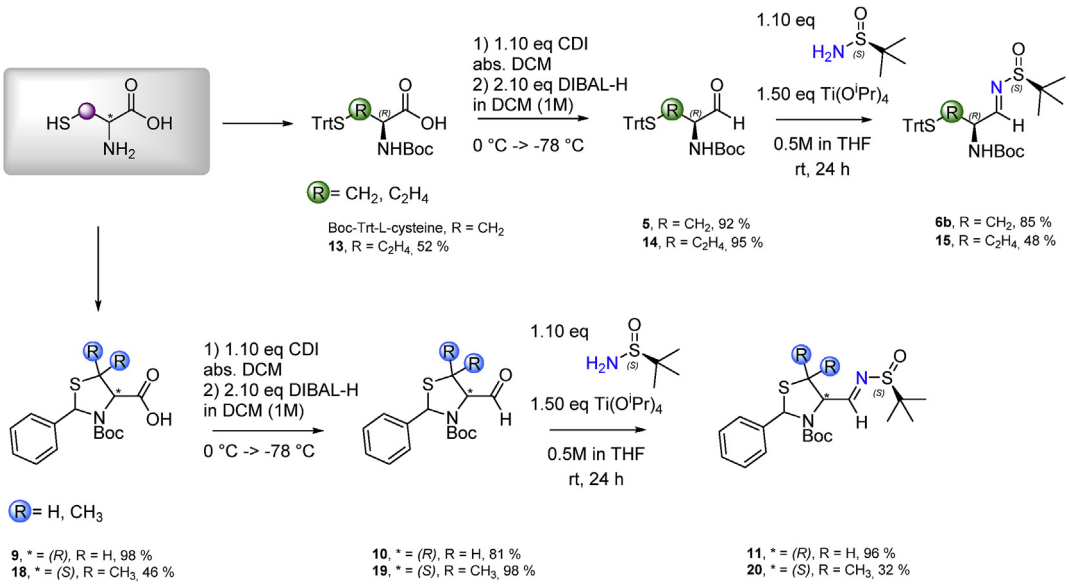
Scheme 1. Illustration of failed SAA strategy and envisioned Sm^{II}-mediated cross coupling strategy (Success of the SAA-reaction was strongly depending on the thiol protection).

selectivity towards functional groups can be finetuned by the use of appropriate additives and ligands [41–46]. The SmI_2 reagent was originally introduced by Kagan et al. [47]. Besides cross coupling reactions SmI_2 was also frequently used to perform various reduction reactions [46]. Preparation of vicinal amino-alcohols via Sm^{II}-mediated pinacol type reactions was achieved by coupling different imine derivatives (i.e. nitrones) with aldehydes or ketones [48–59]. The stereoselectivity of this Sm^{II}-mediated pinacol type reaction could be significantly increased by coupling a *N-tert*-butane sulfinimine derived from Ellman's auxillary with carbonyl moieties [38,51–56]. Various further examples for the utilization of Sm^{II}-mediated cross couplings in synthetic strategies can be found in the literature [40,57,58]. Employment of this strategy in the synthesis of **A** was envisioned to be achieved by the Sm^{II}-mediated coupling of a suitably protected *tert*-butylsulfinimine derivative of cysteine with ethyl-6-oxohexanoate (Scheme 1).

Here, we report that the Sm^{II}-mediated coupling between aldehydes and aldimines can be extended to the synthesis of chiral 1,2-aminoalcohol-thiols when using suitable protecting groups for the mercapto moiety.

2. Results and discussion

In our synthetic strategy the use of *(R)*- or *(S)*-*tert*-butane sulfinimine ("Ellman reagent" [59]) as chiral auxiliary at the imine moiety allowed the stereoselective formation of a vicinal amino-alcohol moiety next to an already existing chiral amine via a pinacol-type cross coupling reaction. Therefore, within a short reaction sequence highly functionalized small molecule intermediates could be synthesized in high enantio- and diastereoselectivities when the thiol group was protected either as a trityl thioether or dihydrothiazolidine thioaminal. To test the Sm^{II}-induced coupling reaction on thiol protected aldimines we started from both easily accessible compounds such as cysteine and methionine as well as the structurally more demanding D-penicillamine (Scheme 2). For the imine substrates both the trityl-Boc



Scheme 2. Synthesis of imine substrates (Boc-Trt-L-cysteine is commercially available; Syntheses of **13**, **9** and **18** are described in the experimental section).

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protecting group strategy as well as the thioaminal-Boc protecting group strategy was used. The reduction of the protected chiral amino acid compounds to the aldehyde was performed via our recently developed protocol of in situ activation with 1,1′-carbonyldiimidazole (CDI) followed by reduction with DIBAL-H [60]. For the protected cysteine and methionine substrates the reduction to the aldehyde was high yielding (92%–95%) and did not lead to any racemization of those compounds. The protected D-penicillaminal (**19**) could be isolated in 98% yield after the CDI mediated DIBAL-H reduction of the carboxylic acid moiety. The aldehyde substrates were converted to the respective imine substrates (compounds **6b**, **15**, **11**, **20**) via $Ti(O^iPr)_4$-mediated condensation with *(S)-tert*-butane sulfinamide (Ellman-reagent) in 32%–96% yield after column chromatography (Scheme 2).

The Sm^{II}-mediated reductive coupling reaction was optimized for the test reaction of **6b** with isovaleraldehyde [38]. Under standard reaction conditions (entry 1) the desired product **7c** could be isolated in only 36% yield, but with excellent diastereomeric ratio (dr) of 98:2 using 2.0 eq *t*-BuOH as proton source (Table 1). A slight improvement of the reaction outcome could be observed, when the aldehyde and aldimine substrate solutions were prepared separately (each of them 0.16M) and added via syringe pump over a period of 15 min to the SmI_2*THF solution at −78 °C (entry 3). In this case 2.0 eq of the proton source were added to the aldimine solution before the addition. The reaction was cleaner but no increase in dr was recognized. However, due to the observed positive effect also for the following screening reactions the substrate solutions were added separately via syringe pump at a concentration of 0.16M each.

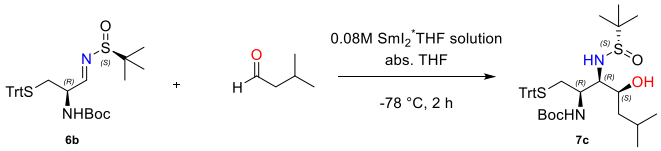
By increasing the reduction potential of Sm^{II}-metal a positive influence on the reaction outcome could be noticed. The use of the nontoxic HMPA surrogate tris-(*N*,*N*-tetramethylene)phosphoric acid triamide (TPPO) [61,62] led to 53% yield accompanied by a drop in dr from 98:2 to 95:5 (entries 5&6), which made this modification less attractive. The use of more acidic alcohols as alternative proton sources did not lead to the desired increase in yield (entries 9–12). Fortunately, through in situ formation of the much more reactive "$SmBr_2$"-species by addition of 16 eq LiBr, an increase in yield (73%) and diastereoselectivity of the reaction (99:1) could be achieved (entry 13). The observed positive effect of LiBr addition to the SmI_2 reagent is in accordance to reported investigations concerning Sm^{II}-mediated coupling reactions [63–70]. Therefore, the found optimum reaction conditions were used to explore the substrate scope of this reaction (Scheme 3).

The SmI_2-LiBr induced reductive coupling was tested with 6 different aldehyde substrates furnishing **7a**-**7f** in good to moderate yields (Scheme 3). Aliphatic aldehydes (piv-, isobutyr- and isovaleraldehyde) gave slightly better yields than their aromatic counterparts or penten-4-al bearing an unsaturated double bond. The diastereomeric excess of the reaction was excellent for all aldehyde substrates with the exception of the sterically less hindered penten-4-al (dr 95:5). While the diastereoselectivity of the reaction is mainly controlled by the absolute configuration of the used Ellman reagent, it might also be influenced by the steric hindrance of the aldehyde substrate, as observed for the SmI_2-mediated reductive coupling of non-thiol containing aldimines and aliphatic aldehydes [38].

The absolute configuration of the coupling products of the reductive coupling reactions could be unambiguously proven by X-ray spectroscopy for compound **7a** (c.f. molecular structure shown in Scheme 3, for crystallographic details see SI). According to this data, the two newly formed stereogenic centres are introduced with the *(S)-N-tert*-butane sulfinimines in (*R*,*S*)-configuration. This is in accordance with the literature for this type of coupling reactions [38].

The substrate scope was further investigated by testing different aldimines (**6b, 11, 15, 20**) in the established cross coupling reaction. In substrate **11** the amino thiol group is protected as an *N*-Boc-2-phenylthiazolidine leading to a more rigid substrate when compared to the *S*-trityl protected substrate **6b** (Table 2). Coupling

Table 1
Reaction optimization conditions.



Entry	Isoveraldehyde	SmI_2*THF	Substrate solution	Comments	Isolated yield	dr
1	1.50 eq	2.00 eq	0.08M	addition at once	36 %[a]	98:2
2	1.50 eq	2.00 eq	0.08M	aldehyde freshly distilled	36 %[a]	98:2
3	1.50 eq	2.00 eq	0.08M		40 %[a,b]	98:2
4	1.50 eq	2.00 eq	0.50M		21%[a,b]	97:3
5	1.50 eq	2.00 eq	0.08M	2 eq TPPO	37%[a,b]	94:6
6	1.50 eq	2.00 eq	0.08M	8 eq TPPO	53%[a,b]	95:5
7	3.00 eq	2.00 eq	0.08M		53%[a,b]	99:1
8	1.50 eq	3.00 eq	0.08M		30%[a,b]	96:4
9	1.50 eq	2.00 eq	0.08M	2 eq trifluoroethanol	37%[b]	98:2
10	1.50 eq	2.00 eq	0.08M	2 eq phenol	37%[b]	98:2
11	1.50 eq	2.00 eq	0.08M	2 eq HFIP	43%[b]	99:1
12	1.50 eq	2.00 eq	0.08M	8 eq deionized H_2O	19%[b]	95:5
13	1.50 eq	2.00 eq	0.08M	16 eq LiBr	73%[b]	99:1
14	1.50 eq	2.00 eq	0.08M	8 eq abs. MeOH	no product formation[b]	/
15	3.00 eq	2.00 eq	0.08M	8 eq TPPO	47%[a,b]	97:3
16	3.00 eq	2.00 eq	0.08M	16 eq LiBr	64%[b]	99:1

dr was determined via HPLC-MS.
[c] Isolated via preparative HPLC. HFIP: hexafluoroisopropanol.
[a] Reaction conditions: 2.00 eq *t*-BuOH as proton source.
[b] Reaction conditions: aldehyde/imine solutions were added separately via syringe pump.

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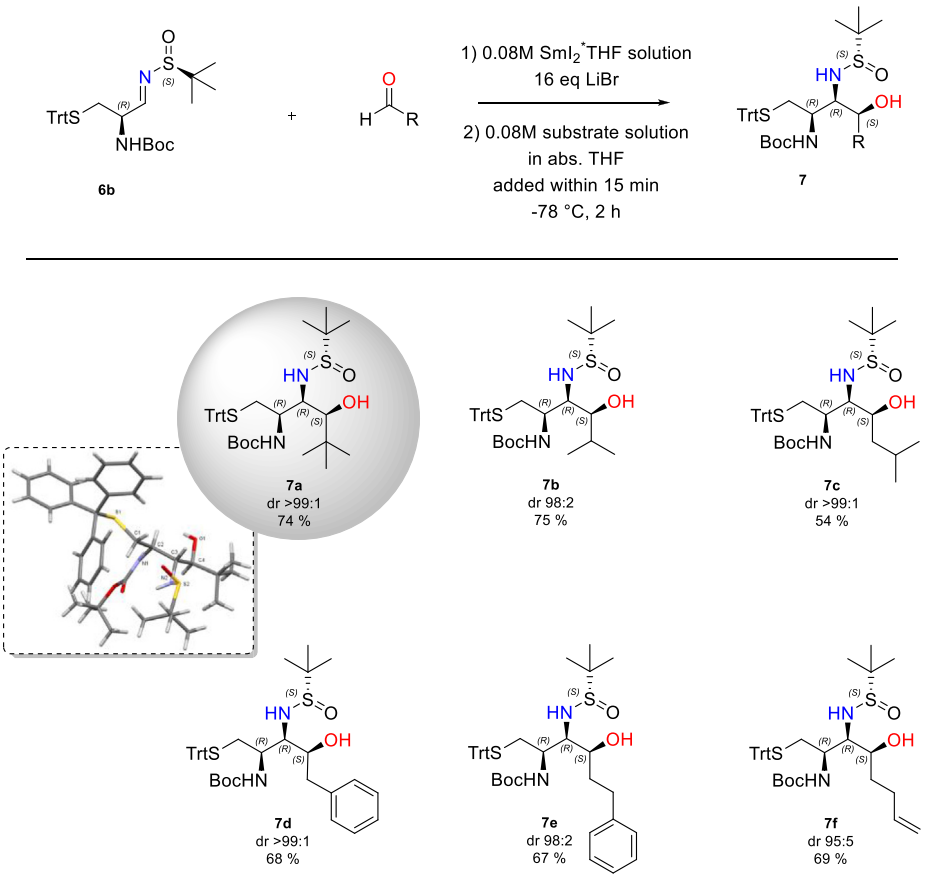

Scheme 3. SmI_2-LiBr-mediated reductive coupling with substrate **6b**.

compound **11** with sterically more demanding aldehyde substrates such as pivaldehyde or 2-phenylacetaldehyde subsequently led to a dramatic decrease of the dr (82:18 and 77:23 for compound **12a** and **12d** respectively) of the reaction. Whereas the reductive cross coupling with sterically less hindered aliphatic aldehyde substrates proceeded in excellent dr's of 98:2 for **12c** and **12d**, a minor decrease of the dr for 3-phenylpropionaldehyde (dr 93:7; **12e**) and penten-4-al (95:5; **12f**) was observed.

The SmI_2-LiBr-mediated reductive cross coupling with the aldimine compound **15** delivered products in quite consistent yield. As sterically more demanding aldehyde substrates such as pivaldehyde showed a decrease in yield to 58% (Table 2), the also very demanding 2-phenylacetaldehyde showed a yield in the same range as obtained for the other aldehyde substrates. However, steric effects seem to exert a strong influence on the diastereomeric excess of the reaction. The dr of reactions with sterically more demanding aldehydes was the highest (compound **16a** and **16d**), whereas more flexible aldehydes show a decreased dr (compounds **16c**, **16e** and **16f**).

The substrate screening revealed that for the flexible aldimine substrates **6b** and **15** dr's are better for sterically demanding aldehyde substrates such as pivaldehyde or 2-phenylacetaldehyde. This is in contrast to rigid aldimine substrate **11**, which showed poor dr for the reaction with sterically demanding aldehyde compounds.

For the SmI_2-LiBr-mediated reductive coupling reaction with the sterically very demanding and rigid aldimine substrate **20** derived from D-penicillamine, the reaction led to the formation of many side products and only little product formation could be indicated with HPLC-MS. Compounds **21d** and **21e** could be isolated in poor yield of 6% and 2% (Table 2).

The substrate screening revealed, that the level of diastereoselectivity for this transformation is not only influenced by the configuration of the *N*-*tert*-butane sulfinimine. Also, the steric bulk of the aldehyde substrates slightly influences the stereo-selective outcome of the reaction. For the D-pencillimine substrate **20** nearly no product formation could be detected. This substrate is the most sterically demanding imine substrate tested for the reductive coupling reactions. Very likely the increased steric repulsion led to the poor product formation for this imine substrate.

Finally, with the optimized reaction conditions for the Sm^{II}-mediated reductive coupling reaction, the synthesis of target compound **A** could be attempted (Scheme 4). For the synthesis of intermediate **A** we started from commercially available *N*-Boc-*S*-trityl-L-cysteine. After two reaction steps the corresponding imine substrate **6a** could be isolated in moderate yield of 48%. The SmI_2-LiBr-mediated reductive coupling reaction with the C_5-aldehyde compound **22** proceeded well in presence of 16 eq LiBr as additive. Compound **23** could be isolated as single diastereomer in 67% yield.

For this coupling reaction a (*R*)-*tert*-butylsulfinylimine was used as substrate contrary to the previous described screening reactions, where (*S*)-*tert*-butylsulfinylimines were used. The steric inversion of the auxiliary group changed the spatial arrangement of the central 2,3-diamino-alcohol moiety formed by the cross coupling reaction. This means that while the 1,2-aminoalcohol moiety was still formed in *trans* fashion, its overall orientation relative to the protected 3-amino group was inverted. The observed high diastereoselectivity in the formation of **63** (dr = 98:2), alongside with the fact, that also in couplings with (*S*)-*tert*-butylsulfinylimines many products could be formed with high diastereoselectivity (Table 2), shows that the stereoselectivity of the SmI_2-LiBr

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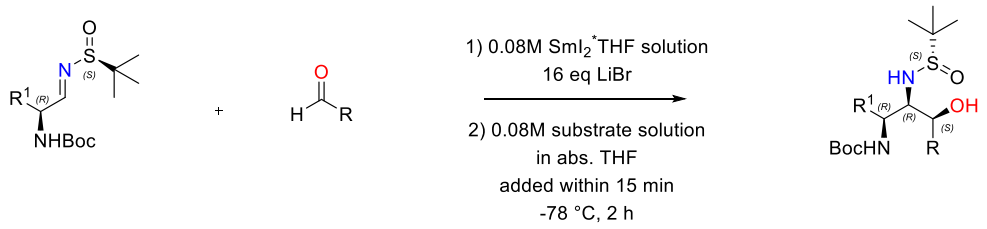
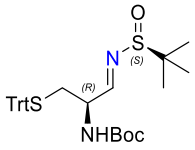
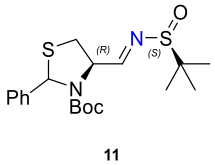
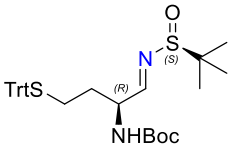
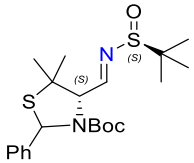
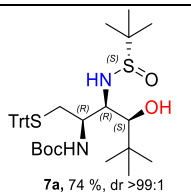
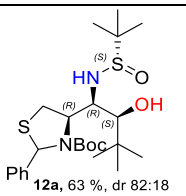
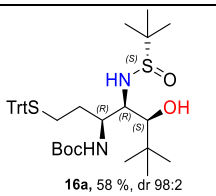
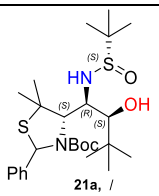
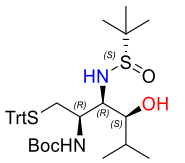
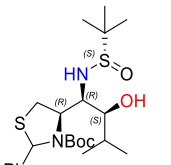
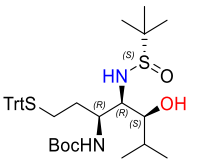
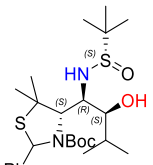
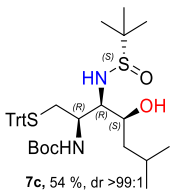
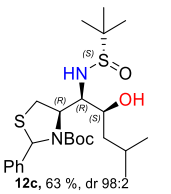
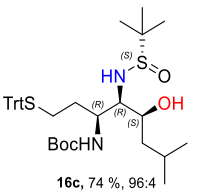
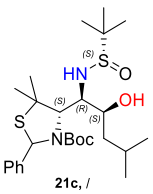
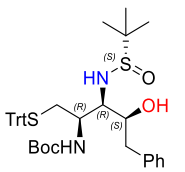
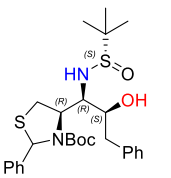
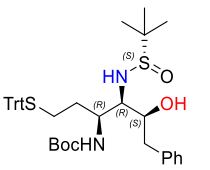
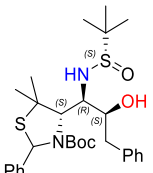
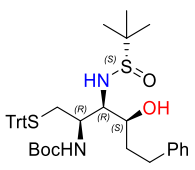
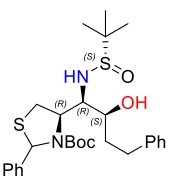
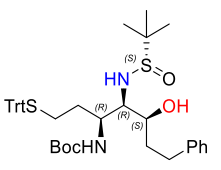
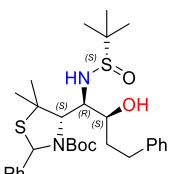
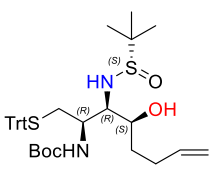
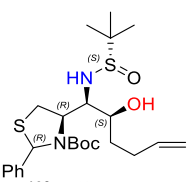
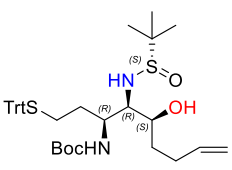
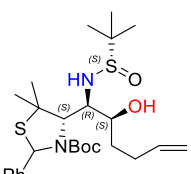
Table 2
Substrate screening of SmI_2-LiBr-mediated reductive coupling reactions.



 **6b**	 **11**	 **15**	 **20**
 **7a,** 74 %, dr >99:1	 **12a,** 63 %, dr 82:18	 **16a,** 58 %, dr 98:2	 **21a,** /
 **7b,** 75 %, dr 98:2	 **12b,** 69 %, dr 98:2	 **16b,** 68 %, dr 97:3	 **21b,** /
 **7c,** 54 %, dr >99:1	 **12c,** 63 %, dr 98:2	 **16c,** 74 %, 96:4	 **21c,** /
 **7d,** 68 %, dr >99:1	 **12d,** 60 %, dr 77:23	 **16d,** 70 %, dr 98:2	 **21d,** 6 %, dr 70:30
 **7e,** 67 %, dr 98:2	 **12e,** 74 %, dr 96:4	 **16e,** 62 %, dr 93:7	 **21e,** 2 %, dr 77:23
 **7f,** 69 %, dr 95:5	 **12f,** 66 %, dr 95:5	 **16f,** 78 %, 97:3	 **21f,** /

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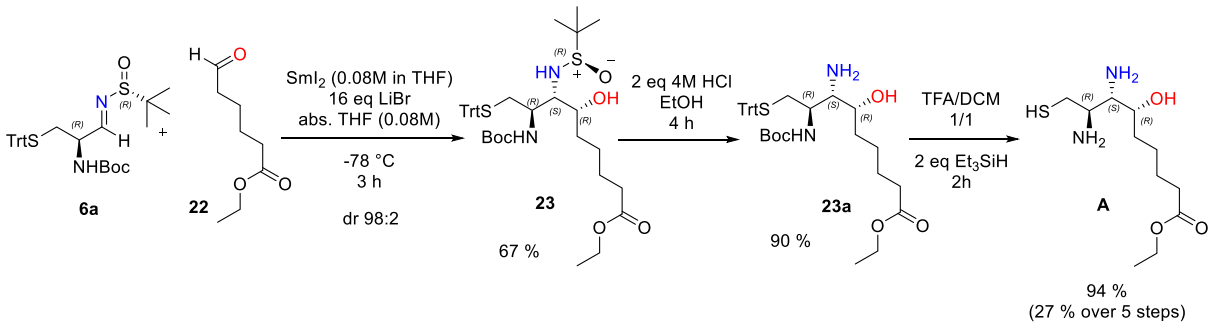

Scheme 4. Synthesis of biosynthesis intermediate **A**.

mediated cross-coupling reaction is predominantely determined by the sulfinylimine group. Thus the influence of the protected amino group in α-position to the sulfinyl moiety of the imine substrate on the selectivity of the coupling reaction via a matched/mismatched relation seems to be rather low. In literature it is assumed that the stereoselectivity of the SmI_2-LiBr-mediated cross-coupling reaction arises from a transition state which is avoiding an unfavourable gauche interaction of the residues originating from the imine and aldehyde substrate [38,71].

The removal of the chiral auxiliary of **23** under acidic condition with 4M HCl delivered compound **24** in 90% yield. Treatment with 50% trifluoroacetic acid in DCM in presence of 2.0 eq Et_3SiH led to the removal of the Boc and Trt protecting groups to furnish intermediate **A** in 94% isolated yield (27% overall yield after 5 reaction steps starting from commercially available Boc-Trt-L-cysteine).

3. Conclusion

In summary, we have presented an efficient stereoselective access to chiral 1,2-amino-alcohols containing thiol groups via the SmI_2-LiBr-mediated coupling of aldehydes with Ellman sulfinylimines. Key element is the use of suitable protecting groups for the thiol moiety which has to be protected either as *S*-trityl ether or phenylthiazolidine. The scope of the reaction has been established for 18 compounds (yields of 58−78%, dr up to 99:1). It shows broad tolerance to various alkyl aldimine substrates but is less suitable for aromatic aldimines. The presented methodology forms the 1,2-amino-alcohol moiety in *trans* fashion. Thus, our method appears to be complementary to a recently published photocatalytic method for the preparation of *syn*-1,2-amino-alcohols [72]. It might become a valuable tool for the synthesis of such highly functionalized thiol containing small molecule intermediates, as we could advantageously use it for the synthesis of intermediate **A**.

4. Experimental section

4.1. General information

Reactions carried out under inert conditions were performed with standard Schlenk techniques under exclusion of oxygen. The reaction vessel was evacuated, flame dried, and flushed with argon or nitrogen gas for three times. Solvents were dried and/or degassed with common methods and afterwards stored under inert gas atmosphere (argon or N_2) over molecular sieves (SI). The addition of chemicals was conducted under argon or nitrogen counter flow, which should exclude traces of moisture and oxygen. All reactions were stirred with Teflon-coated magnetic stirring bars unless otherwise stated. Oxidation sensitive reactions were accomplished under argon or nitrogen atmosphere and absolute degassed solvents were used. For degassing, the solvent or reaction mixture was first evacuated and then reflushed with protective gas. This process was repeated several times, dependent on the solvent volume. For work-up procedures with compounds sensitive to oxidation, the solvents were degassed for 15 min in an ultrasonic bath under nitrogen counter flow before use. In general, temperatures were measured externally if not otherwise stated. When working at a temperature of 0 °C, an ice-water bath served as the cooling medium. Lower temperatures were achieved by either using an acetone/dry ice cooling bath or a cryostatic temperature regulator. Reactions, which were carried out at higher temperatures than RT, were heated in a silicon oil bath on a heating plate (RCT basic IKAMAG® safety control, 0−1500 rpm) equipped with an external temperature controller. SmI_2- or $SmBr_2$-catalysed reactions were carried out under exclusion of light, and absolute THF free of any stabilizer was used. For hydrogenation reactions special safety conditions were necessary. During work-up the catalyst filtration was carried out via an inverse filter funnel through a pad of Celite under inert gas. After the product had been isolated, the catalyst pad was rinsed with water and the used catalyst was then stored under water. A description of the utilized analytical methods can be found in the Supporting Information.

4.2. SAA strategy

4.2.1. Ethyl (R,E)-4-((tert-butoxycarbonyl)amino)-5-(tritylthio) pent-2-enoate (*3*)

In an inert 100 mL round bottom flask 334 mg (0.75 mmol, 1.00 eq) **5** were dissolved in 7 mL ab. THF. 313 mg (0.90 mmol/1.2 eq) ethyl 2-(triphenyl-λ5-phosphaneylidene)acetate were added to this clear colorless solution. The resulting yellowish mixture was stirred at RT for 1 h. Complete conversion was indicated via TLC. For work-up the solvent was removed under reduced pressure. The crude product (yellowish oil) was purified via flash column chromatography [100 g silica, 16 × 4 cm, CH/EA = 9/1, fraction: 1−30, fraction size: 20 mL] to afford a clear colorless oil (246.1 mg, 0.48 mmol, 63%). HPLC-MS: t_R = 8.65 min (Na^+, H^+ adduct); TLC: R_f = 0.5 (CH/EA = 5/1); ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.57−7.17 (m, 15H), 6.72 (dd, $^3J_{HH}$ = 15.6 Hz, 4.8 Hz, 1H), 5.85 (d, $^3J_{HH}$ = 15.6 Hz, 1H,), 4.64 (s, 1H), 4.21 (q, $^3J_{HH}$ = 7.1 Hz, 2H), 2.48 (s, 2H), 1.47 (s, 9H), 1.31 (t, $^3J_{HH}$ = 7.1 Hz, 3H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 166.1, 154.9, 146.7, 144.5, 129. 7, 128.2, 127.0, 121.8, 80.0, 67.3, 60.6, 50.6, 36.4, 28.5, 14.4.

4.2.2. Ethyl-(4R)-2,4-bis((tert-butoxycarbonyl)amino)-3-hydroxy-5-(tritylthio)pentanoate (*4*)

In a 5 mL glass vial 47.2 mg (0.40 mmol, 3.08 eq) *tert*-butyl carbamate were dissolved in a mixture of 500 μL NaOH (0.4M) and 500 μL 1-propanol. 44.5 μL (0.39 mmol, 3 eq) freshly prepared *tert*-

BuOCl-solution (**108**) were added to this clear colorless solution and it was stirred at rt for 5 min. Then a solution of 67.7 mg (0.13 mmol, 1.00 eq) **19** and 6.6 mg (8.00 μmol, 5.80 mol%) $(DHQ)_2AQN$ in 1 mL 1-propanol were added to the reaction mixture giving a clear yellow solution. In a separate 2 mL glass vial 2.4 mg (0.006 mmol, 5 mol %) $K_2OsO_2(OH)_4$, were dissolved in 1 mL NaOH (0.4M). The clear purple catalyst-solution was then added to the reaction mixture giving a green-yellowish coloured mixture which was stirred at rt for at least 1 h. TLC and HPLC-MS indicated full conversion and for work-up 500 mg $NaHSO_3/Na_2S_2O_3$ (1/1) were added. The aqueous phase was extracted with EtOAc (3 × 5 mL) and the combined organic layers were dried over $MgSO_4$. The solvent was removed under reduced pressure resulting in an orange oil. The crude product was purified via flash chromatography [10 g silica, 7 × 1 cm; CH/EA = 5/1 (fraction 1–68), fraction size: 6 mL) to afford a clear oil (35.3 mg, 0.05 mmol, 41%). HPLC-MS: $t_R = 8.45$ min (Na^+, H^+ adduct); TLC: R_f = 0.11 (CH/EA = 5/1); ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.29 (m, 15H), 5.32 (s, 1H, NH), 4.71 (d, $^3J_{HH}$ = 8.3 Hz, 1H, OH), 4.27 (d,$^3J_{HH}$ = 7.7 Hz, 1H), 4.16 (dt, $^3J_{HH}$ = 19.6, 7.3 Hz, 2H), 3.90 (s, 1H), 3.42 (s, 1H), 2.56 (dd, $^3J_{HH}$ = 12.5, 4.2 Hz, 1H), 2.41 (dd, $^3J_{HH}$ = 12.5, 5.1 Hz, 1H), 1.42 (s, 18H), 1.25 (m, 3H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 170.9, 156.4, 144.5, 129.6, 128.0, 126.8, 79.7, 73.7, 67.1, 61. 7, 55.9, 52.3, 33.4, 28.3, 14.1.

4.3. Reductive cross coupling strategy

4.3.1. General procedure for the DIBAL-H reduction of protected amino acids

In an inert Schlenk flask 1.0 eq of the carboxylic acid substrate was dissolved in dry DCM (6.5 mL/mmol substrate). The resulting solution was cooled to 0 °C in an ice bath. 1.1 eq CDI were added and the Schlenk flask was equipped with a bubbler. The resulting solution was stirred for 1 h at 0 °C and was then further cooled down to −78 °C in an acetone/dry ice bath. At this temperature 2.1 eq DIBAL-H (1M in DCM) were added via syringe pump over 60 min. After complete addition the reaction mixture was stirred at −78 °C for further 30 min. Complete conversion was detected via TLC and HPLC-MS. For work-up the reaction mixture was quenched by the addition of EtOAc (7.5 mL/mmol substrate) and (25% w/w) tartaric acid (7.5 mL/mmol substrate). The aqueous phase was extracted with EtOAc (2 × 3.75 mL/mmol substrate). The combined organic layers were washed with 1M HCl (7.5 mL/mmol substrate), (10% w/w) $NaHCO_3$ (38.5 mL/mmol substrate), brine (38.5 mL/mmol substrate) and dried over $MgSO_4$. The solvent was removed under reduced pressure to afford the crude product. The reaction and the work-up were carried out under exclusion of light. In order to prevent oxidation of the product all solvents had to be degassed for 30 min in an ultrasonic bath prior use in the work-up procedure. The crude product was stored under inert conditions and exclusion of light.

4.3.2. tert-Butyl (R)-(1-oxo-3-(tritylthio)propane-2-yl)carbamate (**5**)

600.7 mg (1.3 mmol/1.0 eq) Boc-Trt-L-cysteine were converted following general procedure 4.3.1. As crude product a clear, sticky oil (534 mg, 1.19 mmol, 92%) could be obtained. It was used without further purification in the next reaction step. HPLC-MS: $t_R = 8.17$ min (Na^+, H^+ adduct); TLC: $R_f = 0.42$ (CH/EA = 5/1); ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 9.18 (s, 1H), 7.46-7.22 (m, 15 H), 5.13-4.97 (m, 1H), 2.71 (m, 2H), 1.43 (s, 9H); ^{13}C NMR (75,53 MHz, $CDCl_3$) δ 198.2, 155.4, 144.3, 129.6, 128.2, 127.1, 80.5, 77.0, 67.4, 31.5, 28.4.

4.3.3. (4R)-2-Phenylthiazolidine-4-carboxylic acid (**8**)

In a 100 mL round bottom flask 3.00 g L-cysteine (24.60 mmol, 1.00 eq) were dissolved in a mixture of 46 mL EtOH and 14 mL dist. H_2O (EtOH/dist. H_2O = 10/3). 2.5 mL (2.60 g, 24.5 mmol, 0.99 eq) benzaldehyde were added to the clear colorless solution, giving a cloudy suspension, which was stirred at rt overnight. Complete conversion was detected via TLC. For work-up the white precipitate was collected by filtration and washed with 40 mL ice cold Et_2O. The crude product was dried in high vacuum and used without further purification in the next reaction step. 4.96 g (23.6 mmol, 96%) crude product could be obtained in form of off-white crystals. TLC: $R_f = 0.42$ (MeOH/DCM = 3/1 + 1% NH_3); ^{1}H NMR (300.36 MHz, DMSO) δ 7.73–7.12 (m, H_{Ar}, 5H), 5.67 (s, 1H), 5.50 (s, 1H), 4.24 (dd, $^3J_{HH}$ = 6.8, 4.6 Hz, 1H), 3.96–3.84 (m, 1H), 3.36 (ddd, $^3J_{HH}$ = 23.5, 10.0, 7.2 Hz, 2H), 3.21–3.03 (m, 2H); ^{13}C NMR (75.53 MHz, DMSO) δ 173.0, 172.2, 141.2, 138.94, 128.5, 128.3, 128.2, 127.6, 127.3, 126.9, 71.8, 71.1, 65.4, 64.9, 38.4, 38.0.

4.3.4. (4R)-3-(tert-Butoxycarbonyl)-2-phenylthiazolidine-4-carboxylic acid (**9**)

In a 100 mL round bottom flask 1.65 g (7.88 mmol, 1.00 eq) **8** were dissolved in 33 mL of a dioxane water mixture (1,4-dioxane: dist. H_2O: 0.1 M NaOH = 2:1:1). The resulting off-white suspension was cooled to 0 °C in an ice bath. At this temperature 1.89 g (8.67 mmol, 1.10 eq) Boc-anhydride were added. The mixture was allowed to warm up to RT and stirred overnight. The reaction was monitored via TLC. For work-up the 1,4-dioxane was removed under reduced pressure. The remaining colorless suspension was diluted with 20 mL 10% $NaHSO_3$ solution and 20 mL EtOAc. The pH-value of this mixture was adjusted to 2 via the addition of additional 4 mL HCl (6M). The two phases were separated and the aqueous phase was extracted with EtOAc (5 × 20mL). The combined organic phases were dried over $MgSO_4$, filtrated in vacuum and the solvent was removed under reduced pressure, giving colorless crystals as crude product (2.39 g, 7.73 mmol, 98%). The product was used without further purification in the next reaction step. TLC: R_f = 0.42 (MeOH/DCM = 3/1 + 1% NH_3); m.p. = 174–176 °C; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.73–7.19 (m, 5H), 5.96 (s, 1H), 4.90 (s, 1H), 3.36 (dd, J = 23.5, 17.1 Hz, 2H), 1.45 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 173.4, 146.9, 128.5, 128.1, 126.7, 85.3, 66.9, 64.3, 28.1, 27.6.

4.3.5. tert-Butyl-(4R)-4-formyl-2-phenylthiazolidine-3-carboxylate (**10**)

2.09 g (6.76 mmol/1.0 eq) **9** were converted following general procedure 4.3.1. As crude product a yellowish oil (1.61 g, 5.47 mmol, 81%) could be obtained. It was used without further purification in the next reaction step. HPLC-MS: $t_R = 8.66$ min (Na^+, H^+ adduct); TLC: $R_f = 0.39$ (CH/EA = 5/1); ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 9.72 (s, 1H), 7.47–7.07 (m, 5H), 5.94 (s, 1H), 4.76 (s, 2H), 3.20 (m, 1H), 1.16 (m, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 198.8, 171.2, 140.7, 128.5, 128.3, 126.4, 82.0, 69.6, 66.3, 28.0, 21.0.

4.3.6. N-(tert-Butoxycarbonyl)-S-trityl-L-homocysteine (**13**)

In a 100 mL three necked round bottom flask equipped with Schlenk adapter and dry ice reflux condenser 3.00 g (12.00 mmol, 1.00 eq) L-Boc-methionine were dissolved in 25 mL liquid ammonia at −78 °C (dry ice/acetone cooling bath). 1.38 g (60.20 mmol, 5.00 eq) Na were added in portions to this clear colorless solution. The reaction mixture turned dark blue and was allowed to reflux at −40 °C for 1 h. The reaction was monitored via HPLC-MS. After complete conversion 2.51 g (46.9 mmol, 3.90 eq) NH_4Cl were added and the reaction mixture was allowed to warm up to rt overnight. The next day the white residue was suspended in 50 mL DCM and 3.66 g (14.10 mmol, 1.17 eq) triphenylmethanol and 2.5 mL (5% v/v) trifluoroacetic acid were added to the off-white suspension. The reaction mixture was stirred for 2 h at rt and reaction conversion

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was monitored via HPLC-MS. After complete conversion the reaction mixture was quenched by the addition of 25 mL dist. H_2O and the aqueous phase was extracted with DCM (3 × 25 mL). The combined organic phases were extracted with brine (1 × 20 mL) and dried over $MgSO_4$. After filtration the solvent was removed under reduced pressure giving a colorless solid. The product was purified via column chromatography [250 g silica gel, 13 × 3.5 cm, CH/EE/AcOH = 4/1/0.02, fraction 1–15, fraction size 150 mL] to afford a colorless solid (3.00 g, 6.28 mmol, 52%). HPLC-MS: t_R = 7.79 min (Na^+, K^+ adduct); TLC: R_f = 0.31 (CH/EA = 5/1); m.p. = 143–146 °C; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.57–7.17 (m, 15H), 4.68 (d, $^3J_{H,H}$ = 7.6 Hz, 1H), 2.48-2.21 (m, 2H), 1.99-1.54 (m, 2H), 1.49 (s, 9H); ^{13}C-APT-NMR (75,53 MHz, $CDCl_3$) δ 176.3, 155.5, 144.7, 129.6, 127.9, 126.8, 80.3, 67.2, 52.9, 31.9, 28.4, 20.7.

4.3.7. tert-Butyl (R)-(1-oxo-4-(tritylthio)butan-2-yl)carbamate (**14**)

1 g (2.09 mmol/1.0 eq) **13** were converted following general procedure 4.3.1. As crude product a clear, sticky oil (920 mg, 2.00 mmol, 95%) was obtained. It was used without further purification in the next reaction step. TLC: R_f = 0.47 (CH/EA = 4/1);^{1}H NMR (300.36 MHz, $CDCl_3$) δ 9.40 (s 1H), 7.53-7.15 (m, 15H), 4.87 (d, $^3J_{HH}$ = 11.6 Hz, NH, 1H), 4.13 (m, 1H), 2.46–2.17 (m, 2H), 1.89 (m, 1H), 1.55 (m, 1H), 1.42 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 199.0, 155.5, 144.7, 129.7, 128.1, 126.9, 80.2, 59.2, 28.6, 28.4, 27.8.

4.3.8. (4S)-5,5-Dimethyl-2-phenylthiazolidine-4-carboxylic acid (**17**)

In a 100 mL round bottom flask 2.00 g (13.40 mmol, 1.00 eq) D-penicillamine were dissolved in 40 mL H_2O:EtOH (10/3). 1.37 mL (1.42 g, 13.40 mmol, 1.00 eq) benzaldehyde were added to this clear colorless solution and the mixture was stirred at rt overnight. Full conversion was detected via TLC and the product was collected by filtration and washed with ice cold Et_2O (20 mL). The product was dried in vacuo, giving a white powder (2.63 g, 11.1 mmol, 83%) as crude product. The crude product was used without further purification in the next step. TLC: R_f = 0.28 (DCM/MeOH/NH_3 = 3/1/0.01); m.p. = 165 °C;

4.3.9. (4S)-3-(tert-Butoxycarbonyl)-5,5-dimethyl-2-phenylthiazolidine-4-carboxylic acid (**18**)

In a 100 mL round bottom flask 2.63 g (12.60 mmol, 1.00 eq) **17** were dissolved in 42 mL Et_2O/1M NaOH/H_2O (2/1/1). 3.02 g (13.9 mmol, 1.10 eq) Boc_2O were added to this two phase colorless solution and the reaction mixture was stirred at rt overnight. Full conversion was detected via TLC and HPLC-MS. For reaction work-up the reaction mixture was acidified to pH 2 with 1M HCl until a white precipitate formed. The aqueous layer was extracted with EtOAc (3 × 50 mL) and the combined organic layers were dried over $MgSO_4$. The drying reagent was filtered off and the solvent was removed via rotary evaporator. The crude product was purified via column chromatography [250 g SiO_2, 6.5 cmx15 cm, CH/EA/AcOH = 4/1/0.001, 160 mL fraction size, fraction 6 to 15] to afford **18** as colorless powder (1.93 g, 5.72 mmol, 46%). HPLC-MS: t_R = 6.69 min (Na^+, K^+ adduct); TLC: R_f = 0.25 (CH/EA/AcOH = 3/1/0.1%); m.p. = 215–217 °C; ^{1}H NMR (300.36 MHz, DMSO-d_6) δ 12.91 (s, 1H, OH), 7.74 (s, 2H), 7.30 (d, $^3J_{HH}$ = 7.1 Hz, 3H), 6.03 (d, $^3J_{HH}$ = 35.9 Hz, 1H), 4.32 (s, 1H), 1.57 (s, 3H), 1.32 (s, 4H), 1.30–1.15 (m, 3H), 1.04 (s, 5H); ^{13}C NMR (75.53 MHz, DMSO-d_6) δ 171.0, 152.7, 141.2, 127.8, 127.2, 80.1, 72.8, 65.0, 51.3, 30.8, 27.6, 24.4.

4.3.10. tert-Butyl (4S)-4-formyl-5,5-dimethyl-2-phenylthiazolidine-3-carboxylate (**19**)

1.00 g (2.97 mmol/1.0 eq) **18** were converted following general procedure 4.3.1. As crude product a colorless oil (930 mg, 2.89 mmol, 98%) could be obtained. It was used without further purification in the next reaction step. HPLC-MS: t_R = 7.49 min (Na^+, K^+ adduct); TLC: R_f = 0.65 (CH/EA/AcOH = 52/1/0.01).

4.3.11. General procedure for the synthesis of tert-butanesulfinyl imines

In a round bottom flask the respective aldehydes (1.00 eq) and the *(R)-tert*-butanesulfinamide or *(S)-tert*-butanesulfinamide (1.10 eq) were dissolved in abs. THF (0.5M) at rt. After the educts had dissolved completely, $Ti(OiPr)_4$ (1.50 eq) was added dropwise via septum to the reaction mixture upon which the reaction mixture turned bright yellow. This solution was stirred at rt for 3 h until complete conversion was detected via TLC and HPLC-MS. For reaction work-up the reaction mixture was filtrated through a pad of Celite, which later was washed with DCM (3 × 10 mL). The solvent of the filtrate was removed under reduced pressure giving the crude product as yellowish oil. The product was further purified via column chromatography.

4.3.12. tert-Butyl ((R,E)-1-(((R)-tert-butylsulfinyl)imino)-3-(tritylthio)propan-2-yl)carbamate (**6a**)

According to general procedure 4.3.11, 2.00 g (4.47 mmol, 1.00 eq) **5** and 596 mg (4.92 mmol, 1.10 eq) *(R)-tert*-butanesulfinamide were dissolved in 9 mL THF. 1.98 mL (1.91 g, 6.70 mmol, 1.50 eq) isopropyltitanate were added dropwise. Complete conversion was detected via HPLC-MS. Column Chromatography [250 g SiO_2, 6.5 cmx15 cm; CH/EA = 9/1; fraction size 166 mL; fraction 15 to 30] afforded **6a** as yellowish oil (2.22 g, 4.03 mmol, 90%). HPLC-MS: t_R = 8.56 min; TLC: R_f = 0.57 (CH/EA = 3/1); ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.82 (d, $^3J_{HH}$ = 23.6 Hz, 1H), 7.55-7.13 (m, 15H), 5.23-4.93 (m, 1H, NH), 4.56-4.18 (m, 1H), 2.55 (dd, $^2J_{HH}$ = 36.8, 11.8 Hz, 2H), 1.48 (s, 9H), 1.21 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 166.8, 155.5, 144.5, 144.4, 129.7, 129.6, 128.2, 128.2,127.1, 127.0, 80.2, 80.1, 67.1, 66.9, 57.7, 57.5, 55.6, 34.2, 28.4, 22.3.

4.3.13. tert-Butyl ((R,E)-1-(((S)-tert-butylsulfinyl)imino)-3-(tritylthio)propan-2-yl)carbamate (**6b**)

According to general procedure 4.3.11, 200 mg (0.447 mmol, 1.00 eq) **5** and 60 mg (0.492 mmol, 1.10 eq) *(S)-tert*-butanesulfinamide were dissolved in 1 mL THF. 198 μL (191 mg, 0.670 mmol, 1.50 eq) isopropyltitanate were added dropwise. Complete conversion was detected via HPLC-MS. Column chromatography [100 g SiO_2; 4 cmx12 cm; CH/EA = 9/1; fraction size 70 mL, fraction 6 to 12] gave **6b** as yellowish oil (208 mg, 0.376 mmol, 85%). HPLC-MS: t_R = 8.57 min (H^+-, Na^+- adduct); TLC: R_f = 0.57 (CH/EA = 3/1); ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.82 (d, $^3J_{HH}$ = 23.6 Hz, 1H), 7.60-6.91 (m, 15H), 5.26-5.00 (m, 1H, NH), 4.38 (dd, $^3J_{HH}$ = 22.9, 15.7 Hz, 1H), 2.82-2.48 (m, 2H), 1.48 (s, 9H), 1.23 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 166.8, 155.7, 144.4, 129.6, 128.2, 127.0, 80.7, 67.1, 57.7, 55.6, 28.5, 22. 7, 22.3.

4.3.14. tert-Butyl (4R)-4-((E)-(((S)-tert butylsulfinyl)imino) methyl)- 2-phenylthiazolidine-3-carboxylate (**11**)

According to general procedure 4.3.11, 902 mg (3.07 mmol, 1.00 eq) **10** and 410 mg (3.38 mmol, 1.10 eq) *(S)-tert*-butanesulfinamide were dissolved in 6.20 mL THF. 1.37 mL (1.31 g, 4.61 mmol, 1.50 eq) isopropyltitanate were added dropwise. Complete conversion was detected via HPLC-MS. Column Chromatography [125 g SiO_2, 4 cmx24 cm, CH/EA = 9/1; fraction size 80 mL; fraction 9 to 19] gave **11** as yellowish foam (310 mg, 0.78 mmol, 96%). HPLC-MS: t_R = 7.56 min (H^+-, Na^+- adduct); TLC: R_f = 0.23 (CH/EA = 5/1); ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.48–7.10 (m, 5 H), 5.92 (d, $^3J_{HH}$ = 45.6 Hz, 1H), 5.23 (s, 1H), 3.65 (s, 1H), 3.40-3.01 (m, 2H), 1.14 (s, 18H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 167.7, 153.6, 128.7, 128.5, 128.0, 126.5, 81.7, 66.8, 65.3, 57.5, 28.2, 22.6, 22.3.

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*4.3.15. tert-Butyl ((R,E)-1-(((S)-tert-butylsulfinyl)imino)-4-(tritylthio)butan-2-yl)carbamate (**15**)*

According to general procedure 4.3.11, 1.00 g (2.17 mmol, 1.00 eq) **14** and 289 mg (9.83 mmol, 1.10 eq) *(S)-tert*-butanesulfinamide were dissolved in 4.5 mL THF. 963 μL (924 mg, 3.25 mmol, 1.50 eq) isopropyltitanate were added dropwise. Complete conversion was detected via TLC. Column chromatography [125 g SiO_2; 4 cmx24 cm, CH/EE = 9/1, CH/EE = 4/1, fraction size 80 mL; fraction 12–24] gave **15** as a yellowish foam (585 mg, 1.04 mmol, 48%). TLC: R_f = 0.33 (CH/EA = 4/1); m.p. = 62–65 °C; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.83 (d, $^3J_{HH}$ = 2.9 Hz, 1H), 7.52–7.27 (m, 15H), 4.76 (s, 1H, NH), 4.42 (m, 1H), 2.45-2.23 (m, 2H), 1.82 (m, 1H), 1.50 (m, 1H), 1.46 (s, 9H), 1.20 (m, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) = 167.5, 155.1, 144.8, 129.7, 128.1, 126.9, 80.1, 67.14, 57.1, 54.4, 32.0, 28.4, 28.0, 22.5.

*4.3.16. tert-Butyl (4S)-4-((E)-(((S)-tert- butylsulfinyl)imino) methyl)-5,5-dimethyl-2-phenylthiazolidine-3-carboxylate (**20**)*

According to general procedure 4.3.11 930 mg (2.89 mmol, 1.00 eq) **19** and 395 mg (3.26 mmol, 1.10 eq) *(S)-tert*-butanesulfinamide were dissolved in 5.93 mL THF. 1.31 mL (1.26 g, 4.45 mmol, 1.50 eq) isopropyltitanate were added dropwise. Complete conversion was detected via TLC. Column chromatography [125 g SiO_2, 5 cmx20 cm, CH/EA = 4/1, fraction size 80 mL, fraction 5 to 11] gave **20** as colorless oil (402 mg, 0.945 mmol, 32%). HPLC-MS: t_R = 7.91 min (Na^+-, K^+- adduct); TLC: R_f = 0.25 (CH/EA = 4/1); ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 8.23 (d, $^3J_{HH}$ = 4.3 Hz, 1H), 7.59 (m, 2H), 7.36–7.28 (m, 3H), 6.02 (s, 1H), 4.81 (s, 1H), 1.68 (s, 3H), 1.43 (s, 3H), 1.29 (s, 9H), 1.21 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 166.2, 153.6, 140.4, 128.3, 127.9, 127.2, 81.3, 74.0, 66.8, 57.4, 53.0, 30.9, 28.1, 24.1, 22.7.

4.3.17. General procedure for SmI_2-LiBr-catalysed reactions

A dark blue SmI_2-solution (2.00 eq, 0.04M in THF) in an inert Schlenk flask was slowly cooled down to −78 °C via an acetone/dry-ice cooling bath. In the meantime, in an inert Schlenk flask the respective imine (1.00 eq) was dissolved in abs. THF (0.16M) and in a second inert Schlenk flask the respective aldehyde was dissolved in abs. THF (0.16M). 16 eq LiBr were added in one portion at −78 °C to the SmI_2-solution and the reaction mixture was stirred for 15 min at this temperature. Then both educt-solutions were added simultaneously via syringe pump over a time period of 15 min to the $SmBr_2$-THF-solution at −78 °C. After the addition the reaction mixture was stirred under exclusion of light for 2 h. Complete conversion of the reaction was detected via TLC and HPLC-MS. For work-up the reaction mixture was quenched by the addition of sat. $NaHSO_3$-solution upon which the dark blue reaction mixture immediately turned yellow and the aqueous layer was extracted with EtOAc (3x). The combined organic phases were washed with brine and dried over $MgSO_4$. The solvent was removed under reduced pressure with a rotary evaporator. The crude product was purified via preparative HPLC.

*4.3.18. tert-Butyl ((2R,3S,4R)-3-(((S)-tert-butylsulfinyl)amino)-4-hydroxy-5,5-dimethyl-1-(tritylthio)hexan-2-yl)carbamate (**7a**)*

According to general procedure 4.3.16, 126 mg (1.45 mmol, 16.00 eq) LiBr were added to 4.50 mL (0.182 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.091 mmol, 1.00 eq) **6b** and 15 μL (0.136 mmol, 1.50 eq, 11.7 mg) pivaldehyde were dissolved in 567 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (38 μL/min). The crude product was purified via preparative HPLC [method A] to afford **7a** as clear, colorless oil (42.9 mg, 0.067 mmol, 74%). HPLC-MS: t_R = 8.97 min (Na^+-, K^+- adduct); TLC: R_f = 0.35 (CH/EA = 3/1); $[a]_D^{20}$ +23.1° [$CHCl_3$]; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.37 (m, 15H), 5.55 (d, $^3J_{HH}$ = 8.7 Hz, 1H, NH-2), 3.98 (dd, $^3J_{HH}$ = 16.6, 8.3 Hz, 1H), 3.89 (d, $^3J_{HH}$ = 10.6 Hz, 2H, NH, OH), 3.31 (d, $^3J_{HH}$ = 10.6 Hz, 1H), 3.15 (d, $^3J_{HH}$ = 10.6 Hz, 1H), 2.85 (dd, J = 12.0, 8.5 Hz, 1H), 2.48 (dd, J = 12.1, 7.5 Hz, 1H), 1.50 (s, 9H), 1.28 (s, 9H), 0.98 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 156.8, 144.8, 129.8, 128.1, 126.8, 83.6, 80.5, 67.3, 60.8, 56.4, 49.5, 36.2, 35.5, 28.5, 27.2, 22.7. HR-MS (ESI): MNa^+, found 661.3079. $C_{36}H_{50}N_2O_4S_2Na$ requires 661.3110.

*4.3.19. tert-Butyl ((2R,3S,4R)-3-(((S)-tert-butylsulfinyl)amino)-4-hydroxy-5-methyl-1-(tritylthio)hexan-2-yl)carbamate (**7b**)*

According to general procedure 4.3.16, 126 mg (1.45 mmol, 16.00 eq) LiBr were added to 4.50 mL (0.182 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.091 mmol, 1.00 eq) **6b** and 12 μL (0.136 mmol, 1.50 eq, 9.80 mg) isobutyraldehyde were dissolved in 567 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (38 μL/min). The crude product was purified via preparative HPLC [method A] to afford **7b** as clear, colorless oil (42.5 mg/0.068 mmol, 75%). HPLC-MS: t_R = 8.69 min (Na^+-, K^+- adduct); TLC: R_f = 0.31 (CH/EA = 3/1); $[a]_D^{20}$ -18.1° [$CHCl_3$]; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.37 (m, 15H), 5.08 (d, $^3J_{HH}$ = 8.7 Hz, 1H, NH-2), 3.76 (d, $^3J_{HH}$ = 10.5 Hz, 1H, NH), 3.49 (dd, $^3J_{HH}$ = 16.4, 8.7 Hz, 1H), 3.43 (d, $^3J_{HH}$ = 8.8 Hz, 1H, OH), 3.14 (dd, $^3J_{HH}$ = 10.5, 4.7 Hz, 1H), 3.00 (m, 1H), 2.73 (m, 2H), 1.82-1.65 (m, 1H), 1.48 (s, 9H), 1.29 (s, 9H), 1.00 (d, $^2J_{HH}$ = 6.6 Hz, 3H), 0.86 (d, $^2J_{HH}$ = 6.6 Hz, 3H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 157.0, 144.8, 129.8, 128.1, 126.9, 80.5, 79.2, 67.5, 60.6, 56.5, 49.3, 35.7, 30.2, 28.5, 22.7, 20.1, 17.9. HR-MS (ESI): MNa^+, found 647.2957. $C_{35}H_{48}N_2O_4S_2Na$ requires 647.2953.

*4.3.20. tert-Butyl ((2R,3S,4R)-3-(((S)-tert-butylsulfinyl)amino)-4-hydroxy-6-methyl-1-(tritylthio)heptan-2-yl)carbamate (**7c**)*

According to general procedure 4.3.16, 126 mg (1.45 mmol, 16.00 eq) LiBr were added to 4.50 mL (0.182 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.091 mmol, 1.00 eq) **6b** and 15 μL (0.136 mmol, 1.50 eq, 11.7 mg) isovaleraldehyde were dissolved in 567 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (38 μL/min). The crude product was purified via preparative HPLC [method A] to afford **7c** as clear, colorless oil (31.3 mg, 0.049 mmol, 54%). HPLC-MS: t_R = 8.69 min (Na^+-, K^+- adduct); TLC: R_f = 0.33 (CH/EA = 3/1); $[a]_D^{20}$ -23.4° [$CHCl_3$]; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.37 (m, 15H), 5.06 (d, $^3J_{HH}$ = 8.7 Hz, 1H, NH), 3.74 (d, $^3J_{HH}$ = 10.1 Hz, 1H, NH), 3.60-3.48 (m, 1H), 3.48-3.32 (3, 1H), 3.05-2.92 (m, 1H), 2.69 (m, 2H), 1.87 (m, 1H), 1.48 (s, 9H), 1.41-1.32 (m, 1H), 1.23 (s, 9H), 1.22-1.18 (m, 1H), 1.01 (d, $^3J_{HH}$ = 6.6 Hz, 3H), 0.91 (d, $^3J_{HH}$ = 6.6 Hz, 3H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 156.8, 144.7, 129.8, 128.1, 126.9, 80.5, 71.9, 67.5, 63.5, 56., 49.1, 43.2, 35.3, 28.4, 24.8, 23.8 (CH_3, C-7), 22.8, 21.9. HR-MS (ESI): MNa^+, found 647.3104. $C_{36}H_{50}N_2O_4S_2Na$ requires 661.3110.

*4.3.21. tert-Butyl ((2R,3S,4R)-3-(((S)-tert-butylsulfinyl)amino)-4-hydroxy-5-phenyl-1-(tritylthio)pentan-2-yl)carbamate (**7d**)*

According to general procedure 4.3.16, 126 mg (1.45 mmol, 16.00 eq) LiBr were added to 4.50 mL (0.182 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.091 mmol, 1.00 eq) **6b** and 16 μL (0.136 mmol, 1.50 eq, 16.4 mg) phenylacetaldehyde were dissolved in 567 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04 M) at −78 °C over a period of 15 min (38 μL/min). The crude product was purified via preparative HPLC [method A] to afford **7d** as clear, colorless oil (41.5 mg, 0.062 mmol, 68%). HPLC-MS: t_R = 8.69 min (Na^+-, K^+- adduct); TLC: R_f = 0.33 (CH/EA = 3/1); $[a]_D^{20}$ -7.0° [$CHCl_3$]; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.21 (ddt, $^3J_{HH}$ = 20.6, 18.8, 7.3 Hz, 20H), 4.87 (d, $^3J_{HH}$ = 8.1 Hz, 1H, NH-2), 3.65 (d, $^3J_{HH}$ = 9.9 Hz, 1H, NH), 3.58-3.35 (m, 2H, H-2), 2.97 (dd, $^3J_{HH}$ = 8.4, 5.2 Hz, 1H), 2.69 (t, $^3J_{HH}$ = 12.2 Hz,

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1H), 2.56 (m, 3H), 1.35 (s, 9H), 1.12 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 156.9, 144.7, 138.9, 129.8, 129.3, 128.5, 128.1, 126.9, 126.4, 80.6, 74.8, 67.5, 63.0, 56.6, 49.3, 40.4, 35.2, 28.4, 22.8. HR-MS (ESI): MNa^+, found 695.2957. $C_{39}H_{48}N_2O_4S_2Na$ requires 695.2953.

*4.3.22. tert-Butyl ((2R,3S,4R)-3-(((S)-tert-butylsulfinyl)amino)-4-hydroxy-6-phenyl-1-(tritylthio)hexan-2-yl)carbamate (**7e**)*

According to general procedure 4.3.16, 126 mg (1.45 mmol, 16.00 eq) LiBr were added to 4.50 mL (0.182 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.091 mmol, 1.00 eq) **6b** and 18 μL (0.136 mmol, 1.50 eq, 18.3 mg) phenylpropionaldehyde were dissolved in 567 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (38 μL/min). The crude product was purified via preparative HPLC [method A] to afford **7e** as clear, colorless oil (41.7 mg, 0.061 mmol, 67%). HPLC-MS: t_R = 8.86 min (Na^+-, K^+-adduct); TLC: R_f = 0.33 (CH/EA = 3/1); $[a]_D^{20}$ -6.7° [$CHCl_3$]; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.38 (ddd, $^3J_{HH}$ = 31.4, 23.9, 7.2 Hz, 20H), 4.95 (d, $^3J_{HH}$ = 8.2 Hz, 1H, NH), 3.65 (d, $^3J_{HH}$ = 8.2 Hz, 1H, NH), 3.61 (d, $^3J_{HH}$ = 9.9 Hz, 1H, OH), 3.49 (q, $^3J_{HH}$ = 8.2, 1H), 3.30 (m, 1H), 3.06 (dd, $^3J_{HH}$ = 8.2, 4.5 Hz, 1H), 2.98-2.86 (m, 1H), 2.83-2.61 (m, 3H), 1.86-1.64 (m, 2H), 1.50 (s, 9H), 1.27 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 156.9, 144.7, 142.2, 129.8, 128.7, 128.4, 128.1, 126.9, 125.9, 80.6, 72.6, 67.6, 63.1, 56.6, 49.3, 35.9, 35.1, 32.3, 28.4, 22.8. HR-MS (ESI): MNa^+, found 709.3141. $C_{40}H_{50}N_2O_4S_2Na$ requires 709.3110.

*4.3.23. tert-Butyl ((2R,3S,4R)-3-(((S)-tert-butylsulfinyl)amino)-4-hydroxy-1-(tritylthio)oct-7-en-2-yl)carbamate (**7f**)*

According to general procedure 4.3.16, 126 mg (1.45 mmol, 16.00 eq) LiBr were added to 4.50 mL (0.182 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.091 mmol, 1.00 eq) **6b** and 13 μL (0.136 mmol, 1.50 eq, 11.5 mg) 4-pentenal were dissolved in 567 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (38 μL/min). The crude product was purified via preparative HPLC [method A] to afford **7f** as colorless, clear oil (40 mg, 0.063 mmol, 69%). HPLC-MS: t_R = 8.66 min (Na^+-, K^+- adduct); TLC: R_f = 0.36 (CH/EA = 3/1); $[a]_D^{20}$ -17.4° [$CHCl_3$]; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.37 (m, 15H), 5.85 (m, 1H), 5.05 (m, 3H, NH), 3.69 (d, $^3J_{HH}$ = 10.2 Hz, 1H, NH), 3.61 (d, $^3J_{HH}$ = 8.7 Hz, 1H, OH), 3.48 (m, 1H), 3.33 (m, 1H), 3.05 (dd, $^3J_{HH}$ = 9.7, 4.6 Hz, 1H), 2.80 (dd, $^3J_{HH}$ = 13.2, 8.1 Hz, 1H), 2.64 (dd, $^3J_{HH}$ = 13.2, 7.4 Hz, 1H), 2.32 (m, 1H), 2.17 (m, 1H), 1.67-1.36 (m, 11H), 1.27 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 156.9, 144.7, 138.3, 129.8, 128.1, 126.9, 115.1, 80.6, 73.0, 67.6, 63.0, 56.6, 49.2, 35.2, 33.3, 30.3, 28.4, 22.8. HR-MS (ESI): MNa^+, found 659.2908. $C_{36}H_{48}N_2O_4S_2Na$ requires 659.2953.

*4.3.24. tert-Butyl (4S)-4-((1S,2R)-1-(((S)-tert-butylsulfinyl)amino)-2-hydroxy-3,3-dimethylbutyl)-2-phenylthiazolidine-3-carboxylate (**12a**)*

According to general procedure 4.3.16, 175 mg (2.02 mmol, 16.00 eq) LiBr were added to 6.30 mL (0.252 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.126 mmol, 1.00 eq) **11** and 21 μL (0.189 mmol, 1.50 eq, 16 mg) pivaldehyde were dissolved in 788 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (53 μL/min). The crude product was purified via preparative HPLC [method A] to afford **12a** as clear, colorless oil (39, 0.08 mmol, 63%). HPLC-MS: t_R = 7.99 min (Na^+-, K^+- adduct); TLC: R_f = 0.19 (CH/EA = 3/1); $[a]_D^{20}$ +72.7° [$CHCl_3$]; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.55 (d, $^3J_{HH}$ = 7.5 Hz, 2H), 7.45-7.30 (m, 3H), 6.10 (s, 1H), 5.09 (d, $^3J_{HH}$ = 3.0 Hz, 1H, NH), 5.00 (q, $^3J_{HH}$ = 9.0, 4.6 Hz, 1H), 4.15 (d, $^3J_{HH}$ = 5.0 Hz, 1H, OH), 3.80 (q, $^3J_{HH}$ = 8.2, 4.0 Hz, 1H), 3.59-3.47 (m, 1H), 3.46-3.32 (m, 2H), 1.28 (s, 9H), 1.12 (s, 9H), 1.09 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 156.7, 140.7, 128.6, 127.9, 126.4, 82.7, 82.3, 67.0, 62.5, 60.8, 56.3, 35.7, 35.5, 28.1, 27.4, 23.4. HR-MS (ESI): MNa^+, found 507.2314. $C_{24}H_{40}N_2O_4S_2Na$ requires 507.2327.

*4.3.25. tert-Butyl (4S)-4-((1S,2R)-1-(((S)-tert-butylsulfinyl)amino)-2-hydroxy-3-methylbutyl)-2-phenylthiazolidine-3-carboxylate (**12b**)*

According to general procedure 4.3.16, 175 mg (2.02 mmol, 16.00 eq) LiBr were added to 6.30 mL (0.252 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.126 mmol, 1.00 eq) **11** and 17 μL (0.189 mmol, 1.50 eq, 14 mg) isobutyraldehyde were dissolved in 788 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (53 μL/min). The crude product was purified via preparative HPLC [method A] to afford **12b** as clear, colorless oil (41 mg, 0.087 mmol, 69%). HPLC-MS: t_R = 7.84 min (Na^+-, K^+-adduct); TLC: R_f = 0.21 (CH/EA = 3/1); $[a]_D^{20}$ +77.3° [$CHCl_3$]; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.31-7.28 (m, 5H), 6.07 (s, 1H), 5.18 (s, 2H, NH, OH), 5.08 (d, $^3J_{HH}$ = 7.2 Hz, 1H), 3.49-3.30 (m, 4H), 2.13-2.02 (m, 1H), 1.24 (s, 9H), 1.12-1.00 (m, 12H), 0.94 (d, $^3J_{HH}$ = 6.7 Hz, 3H); ^{13}C NMR (75.53 MHz, $CDCl_3$) 156.6, 140.7, 128.7, 128.0, 125.4, 82.8, 76.0, 67.4, 62.5, 61.3, 56.3, 34.8, 28.0, 27.5, 23.3, 21.5, 14.7. HR-MS (ESI): MNa^+, found 493.2158. $C_{23}H_{38}N_2O_4S_2Na$ requires 493.2171.

*4.3.26. tert-Butyl (4S)-4-((1S,2R)-1-(((S)-tert-butylsulfinyl)amino)-2-hydroxy-4-methylpentyl)-2-phenylthiazolidine-3-carboxylate (**12c**)*

According to general procedure 4.3.16, 175 mg (2.02 mmol, 16.00 eq) LiBr were added to 6.30 mL (0.252 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.126 mmol, 1.00 eq) **11** and 20 μL (0.189 mmol, 1.50 eq, 16 mg) isovaleraldehyde were dissolved in 788 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (53 μL/min). The crude product was purified via preparative HPLC [method A] to afford **12c** as clear, colorless oil (38 mg, 0.078 mmol, 63%). HPLC-MS: t_R = 8.08 min (Na^+-, K^+-adduct); TLC: R_f = 0.19 (CH/EA = 3/1); $[a]_D^{20}$ +47.3° [$CHCl_3$]; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.39-7.28 (m, 5H), 6.10 (s, 1H), 5.27 (d, $^3J_{HH}$ = 3.0 Hz, 1H, NH), 5.09-4.99 (m, 1H), 4.79 (s, 1H, OH), 3.69 (s, 1H), 3.48-3.17 (m, 3H), 1.99-1.87 (m, 1H), 1.49-1.36 (m, 2H), 1.24 (s, 9H), 1.07 (s, 9H), 0.95 (d, $^3J_{HH}$ = 6.5 Hz, 3H), 0.89 (d, $^3J_{HH}$ = 6.5 Hz, 3H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 156.6, 140.6, 128.7, 128.0, 125.7, 82.8, 70.1, 66.9, 65.7, 61.1, 56.6, 41.5, 34.4, 28.0, 24.6, 24.3, 23.4, 21.4. HR-MS (ESI): MNa^+, found 507.2342. $C_{24}H_{40}N_2O_4S_2Na$ requires 507.2327.

*4.3.27. tert-Butyl (4S)-4-((1S,2R)-1-(((S)-tert-butylsulfinyl)amino)-2-hydroxy-3-phenylpropyl)-2-phenylthiazolidine-3-carboxylate (**12d**)*

According to general procedure 4.3.16, 175 mg (2.02 mmol, 16.00 eq) LiBr were added to 6.30 mL (0.252 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.126 mmol, 1.00 eq) **11** and 22 μL (0.189 mmol, 1.50 eq, 23 mg) phenylacetaldehyde were dissolved in 788 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (53 μL/min). The crude product was purified via preparative HPLC [method A] to afford **12d** as clear, colorless oil (39 mg, 0.075 mmol, 60%). HPLC-MS: t_R = 7.90 min (Na^+-, K^+-adduct); TLC: R_f = 0.28 (CH/EA = 3/1); $[a]_D^{20}$ +84.5° [$CHCl_3$]; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.54-7.29 (m, 10H), 6.15 (s, 1H), 5.44 (d, $^3J_{HH}$ = 3.6 Hz, 1H, NH), 5.18-5.05 (m, 1H), 4.82 (s, 1H, OH), 3.92 (s, 1H), 3.57-3.42 (m, 2H), 3.33 (d, $^3J_{HH}$ = 11.7 Hz, 1H), 3.21 (d, $^3J_{HH}$ = 14.0, 1H), 2.67 (dd, $^3J_{HH}$ = 14.0, 10.3 Hz, 1H), 1.23 (s, 9H), 1.17 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 156.7, 140.5, 139.9, 129.4, 128.8, 128.4, 128.11, 126.2, 125.7, 82.9, 73.7, 67.1, 65.5, 61.2, 56.6, 39.0, 34.6, 28.0, 23.4. HR-MS (ESI): MNa^+, found 541.2172.

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$C_{27}H_{38}N_2O_4S_2Na$ requires 541.2170.

*4.3.28. tert-Butyl (4S)-4-((1S,2R)-1-(((S)-tert-butylsulfinyl)amino)-2-hydroxy-4-phenylbutyl)-2-phenylthiazolidine-3-carboxylate (**12e**)*

According to general procedure 4.3.16, 175 mg (2.02 mmol, 16.00 eq) LiBr were added to 6.30 mL (0.252 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.126 mmol, 1.00 eq) **11** and 25 μL (0.189 mmol, 1.50 eq, 25 mg) phenylpropionaldehyde were dissolved in 788 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (53 μL/min). The crude product was purified via preparative HPLC [method A] to afford **12e** as clear, colorless oil (50 mg, 0.094 mmol, 74%). HPLC-MS: t_R = 8.17 min (Na^+-, K^+-adduct); TLC: R_f = 0.22 (CH/EA = 3/1); $[a]_D^{20}$ +39.6° [$CHCl_3$]; ^1H NMR (300.36 MHz, $CDCl_3$) δ 7.51-7.27 (m, 10H), 6.22 (s, 1H), 5.48 (s, 1H, OH), 5.36 (t, $^3J_{HH}$ = 6.8 Hz, 1H, NH), 5.25 (dd, $^3J_{HH}$ = 6.4, 3.1 Hz, 1H), 3.67 (d, $^3J_{HH}$ = 7.8 Hz, 1H), 3.61-3.34 (m, 3H), 3.14-2.94 (m, 2H), 2.29-2-22 (m, 1H), 1.99-1.180 (m, 1H), 1.37 (s, 9H), 1.17 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 156.4, 142.5, 140.5, 129.0, 128.6, 128.3, 127.9, 125.7, 125.2, 82.8, 69.9, 66.5, 65.3, 60.9, 56.6, 34., 33.4, 31.6, 28.0, 23.3. HR-MS (ESI): MNa^+, found 555.2344. $C_{28}H_{40}N_2O_4S_2Na$ requires 555.2327.

*4.3.29. tert-Butyl (4S)-4-((1S,2R)-1-(((S)-tertbutylsulfinyl)amino)-2-hydroxyhex-5-en-1-yl)-2-phenylthiazolidine-3-carboxylate (**12f**)*

According to general procedure 4.3.16, 175 mg (2.02 mmol, 16.00 eq) LiBr were added to 6.30 mL (0.252 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.126 mmol, 1.00 eq) **11** and 19 μL (0.189 mmol, 1.50 eq, 16 mg) 4-pentenal were dissolved in 788 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (53 μL/min). The crude product was purified via preparative HPLC [method A] to afford **12f** as clear, colorless oil (35 mg, 0.073 mmol, 66%). HPLC-MS: t_R = 7.83 min (Na^+-, K^+-adduct); TLC: R_f = 0.23 (CH/EA = 3/1); $[a]_D^{20}$ +45.5° [$CHCl_3$]; ^1H NMR (300.36 MHz, $CDCl_3$) δ 7.34-7.26 (m, 5H), 6.08 (s, 1H), 5.90-5.77 (m, 1H), 5.28 (d, $^3J_{HH}$ = 3.4 Hz, 1H, NH), 5.07-4.96 (m, 1H, OH), 3.65 (s, 1H), 3.48-3.20 (m, 3H), 2.44-2.12 (m, 2H), 1.92-1.75 (m, 1H), 1.59-1.40 (m, 1H), 1.24 (s, 9H), 1.07 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 156.8, 140.6, 138.8, 128.7, 128.1, 125.5, 114.8, 82.9, 71.0, 66.9, 65.3, 61.0, 56.5, 34.5, 31.4, 29.8, 28.0, 23.3. HR-MS (ESI): MNa^+, found 505.2127. $C_{24}H_{38}N_2O_4S_2Na$ requires 505.2171.

*4.3.30. tert-Butyl ((3S,4S,5R)-4-(((S)-tert-butylsulfinyl)amino)-5-hydroxy-6,6-dimethyl-1-(tritylthio)heptan-3-yl)carbamate (**16a**)*

According to general procedure 4.3.16, 123 mg (1.42 mmol, 16.00 eq) LiBr were added to 4.40 mL (0.177 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.089 mmol, 1.00 eq) **15** and 15 μL (0.133 mmol, 1.50 eq, 11.5 mg) pivaldehyde were dissolved in 553 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (37 μL/min). The crude product was purified via preparative HPLC [method A] to afford **16a** as clear, colorless oil (34 mg, 0.051 mmol, 58%). HPLC-MS: t_R = 9.12 min (Na^+-, K^+- adduct); TLC: R_f = 0.46 (CH/EA = 3/1); $[a]_D^{20}$ +1.7° [$CHCl_3$]; ^1H NMR (300.36 MHz, $CDCl_3$) δ 7.34 (m, 15H), 5.48 (d, $^3J_{HH}$ = 9.1 Hz, 1H, NH), 3.94 (m, 1 H, NH), 3.20 (bs, 1H), 3.16 (bs, 1H), 2.38-2.10 (m, 3H, H-1), 1.49 (s, 10H), 1.29 (s, 9H), 1.03 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 157.4, 145.0, 129.7, 128.0, 126.7, 83.5, 80.4, 66.8, 62.3, 56.4, 48.8, 35.5, 34.2, 28.8, 28.6, 27.4, 22.7. HR-MS (ESI): MNa^+, found 675.3297. $C_{37}H_{52}N_2O_4S_2Na$ requires 675.3266.

*4.3.31. tert-Butyl ((3S,4S,5R)-4-(((S)-tert-butylsulfinyl)amino)-5-hydroxy-6-methyl-1-(tritylthio)heptan-3-yl)carbamate (**16b**)*

According to 4.3.16, 123 mg (1.42 mmol, 16.00 eq) LiBr were added to 4.40 mL (0.177 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.089 mmol, 1.00 eq) **15** and 12 μL (0.133 mmol, 1.50 eq, 9.6 mg) isobutyraldehyde were dissolved in 553 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (37 μL/min). The crude product was purified via preparative HPLC [method A] to afford **16b** as clear, colorless oil (32 mg, 0.05 mmol, 68%). HPLC-MS: t_R = 8.78 min (Na^+-, K^+- adduct); TLC: R_f = 0.30 (CH/EA = 3/1); $[a]_D^{20}$ -5.4° [$CHCl_3$]; ^1H NMR (300.36 MHz, $CDCl_3$) δ 7.34 (m, 15H), 5.16 (d, $^3J_{HH}$ = 8.9 Hz, 1H, NH), 3.90 (m, 1H), 3.80 (d, $^3J_{HH}$ = 9.9 Hz, 1H, NH), 3.57 (d, $^3J_{HH}$ = 5.3 Hz, 1H, OH), 3.08 (m, 2H), 2.40-2.20 (m, 2H), 2.09 (m, 1H), 1.94 (dd, $^3J_{HH}$ = 12.9, 6.3 Hz, 1H), 1.59 (m, 1H), 1.49 (s, 9H), 1.28 (s, 9H), 1.05 (d, $^3J_{HH}$ = 6.3 Hz, 3H), 0.92 (d, $^3J_{HH}$ = 12.9 Hz, 3H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 157.5, 145.0, 129.7, 128.0, 126.7, 80.4, 79.0, 66.8, 62.1, 56.5, 48.7, 33.6, 30.5, 29.0, 28.5, 22.7, 20.0, 17.9. HR-MS (ESI): MNa^+, found 661.3113. $C_{36}H_{50}N_2O_4S_2Na$ requires 661.3110.

*4.3.32. tert-Butyl ((3S,4S,5R)-4-(((S)-tert-butylsulfinyl)amino)-5-hydroxy-7-methyl-1-(tritylthio)octan-3-yl)carbamate (**16c**)*

According to general procedure 4.3.16, 123 mg (1.42 mmol, 16.00 eq) LiBr were added to 4.40 mL (0.177 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.089 mmol, 1.00 eq) **15** and 14 μL (0.133 mmol, 1.50 eq, 11.4 mg) isovaleraldehyde were dissolved in 553 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (37 μL/min). The crude product was purified via preparative HPLC [method A] to afford **16c** as clear, colorless oil (43 mg, 0.066 mmol, 74%). HPLC-MS: t_R = 8.93 min (Na^+-, K^+- adduct); TLC: R_f = 0.26 (CH/EA = 3/1); $[a]_D^{20}$ -7.8° [$CHCl_3$]; ^1H NMR (300.36 MHz, $CDCl_3$) δ 7.51-7.31 (m, 15H), 5.12 (d, $^3J_{HH}$ = 8.8 Hz, 1H, NH), 3.93 (m, 1H), 3.75 (d, $^3J_{HH}$ = 10.1 Hz, 2H, NH, OH), 3.46 (m, 1H), 2.83 (dd, $^3J_{HH}$ = 10.1, 4.9 Hz, 1H), 2.40-2.19 (m, 2H), 2.05-1.83 (m, 2H), 1.69-1.56 (m, 1H), 1.51 (s, 9H), 1.31 (s, 11H), 1.02 (d, $^3J_{HH}$ = 6.6 Hz, 3H), 0.97 (d, $^3J_{HH}$ = 6.4 Hz, 3H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 157.4, 145.0, 129.7, 128.0, 126.7, 80.5, 71.9, 66.8, 64.9, 56.6, 48.7, 43.4, 33.3, 28.9, 28.5, 24.9, 23.7, 22.8, 22.0. HR-MS (ESI): MNa^+, found 675.3273. $C_{37}H_{52}N_2O_4S_2Na$ requires 675.3266.

*4.3.33. tert-Butyl ((3S,4S,5R)-4-(((S)-tert-butylsulfinyl)amino)-5-hydroxy-6-phenyl-1-(tritylthio)hexan-3-yl)carbamate (**16d**)*

According to general procedure 4.3.16, 123 mg (1.42 mmol, 16.00 eq) LiBr were added to 4.40 mL (0.177 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.089 mmol, 1.00 eq) **15** and 15 μL (0.133 mmol, 1.50 eq, 16 mg) isovaleraldehyde were dissolved in 553 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (37 μL/min). The crude product was purified via preparative HPLC [method A] to afford **16d** as clear, colorless oil (43 mg, 0.063 mmol, 70%). HPLC-MS: t_R = 8.75 min (Na^+-, K^+- adduct); TLC: R_f = 0.22 (CH/EA = 3/1); $[a]_D^{20}$ -4.0° [$CHCl_3$]; ^1H NMR (300.36 MHz, $CDCl_3$) δ 7.49-7.28 (m, 20H), 5.00 (d, $^3J_{HH}$ = 8.4 Hz, 1H, NH), 4.02 (m, 1H), 3.87 (dd, $^3J_{HH}$ = 20.2, 9.2 Hz, 2H, OH,NH), 3.65 (m, 1H), 3.06-2.75 (m, 3H), 2.41-2.14 (m, 2H), 2.00 (m, 1H), 1.60 (m, 1H), 1.43 (s, 9H), 1.29 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 157.5, 145.0, 138.7, 129.7, 129.4, 128.6, 128.0, 126.7, 126.5, 80.6, 74.8, 66.8, 64.1, 56.7, 48.9, 40.5, 33.0, 28.9, 28.5, 22.9. HR-MS (ESI): MNa^+, found 709.3146. $C_{40}H_{50}N_2O_4S_2Na$ requires 709.3110.

*4.3.34. tert-Butyl ((3S,4S,5R)-4-(((S)-tert-butylsulfinyl)amino)-5-hydroxy-7-phenyl-1-(tritylthio)heptan-3-yl)carbamate (**16e**)*

According to general procedure 4.3.16, 123 mg (1.42 mmol, 16.00

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eq) LiBr were added to 4.40 mL (0.177 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.089 mmol, 1.00 eq) **15** and 18 μL (0.133 mmol, 1.50 eq, 18 mg) phenylpropionaldehyde were dissolved in 553 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (37 μL/min). The crude product was purified via preparative HPLC [method A] to afford **16e** as clear colorless oil (39 mg, 0.056 mmol, 62%). HPLC-MS: t_R = 8.89 min (Na^+-, K^+-adduct); TLC: R_f = 0.23 (CH/EA = 3/1); $[a]_D^{20}$ -10.4° [$CHCl_3$]; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.50-7.28 (m, 15H), 4.99 (d, $^3J_{HH}$ = 8.6 Hz, 1H, NH), 4.15 (d, $^3J_{HH}$ = 7.7 Hz, 1H, OH), 3.98 (m, 1H), 3.58 (d, $^3J_{HH}$ = 10.2 Hz, 1H, NH), 3.34 (m, 1H), 3.03-2.66 (m, 3H), 2.42-2.18 (m, 2H), 2.03-1.77 (m, 3H), 1.62 (m, 1H), 1.50 (s, 9H), 1.27 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 157.5, 144.9, 142.1, 129.7, 128.7, 128.5, 128.0, 126.7, 125.9, 80.6, 72.3, 66.8, 64.8, 56.7, 49.0, 35.9, 33.0, 32.3, 28.9, 28.5, 22.8. HR-MS (ESI): MNa^+, found 723.3251. $C_{41}H_{52}N_2O_4S_2Na$ requires 723.3266.

4.3.35. *tert-Butyl ((3S,4S,5R)-4-(((S)-tert-butylsulfinyl)amino)-5-hydroxy-1-(tritylthio)non-8-en-3-yl)carbamate (**16f**)*

According to general procedure 4.3.16, 123 mg (1.42 mmol, 16.00 eq) LiBr were added to 4.40 mL (0.177 mmol, 2.00 eq) SmI_2-solution at −78 °C. 50 mg (0.089 mmol, 1.00 eq) **15** and 13 μL (0.133 mmol, 1.50 eq, 11 mg) 4-pentenal were dissolved in 553 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (37 μL/min). The crude product was purified via preparative HPLC [method A] to afford **16f** as clear, colorless oil (45 mg, 0.069 mmol, 78%). HPLC-MS: t_R = 8.73 min (Na^+-, K^+- adduct); TLC: R_f = 0.21 (CH/EA = 3/1); $[a]_D^{20}$ -4.7° [$CHCl_3$]; ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 7.37 (m, 15H), 5.95-5.82 (m, 1H), 4.21–4.98 (m, 3H, NH), 3.96 (d, $^3J_{HH}$ = 6.6 Hz, 2H, OH), 3.68 (d, $^3J_{HH}$ = 10.3 Hz, NH), 3.39 (s, 1H), 2.88 (dd, $^3J_{HH}$ = 9.9, 6.6 Hz, 1H), 2.36-2.22 (m, 4H), 1.97 (m, 1H), 1.78-1.58 (m, 3H), 1.50 (s, 9H), 1.30 (s, 9H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 157.4, 144.9, 138.3, 129.7, 128.0, 126.7, 115.1, 80.5, 72.6, 66.7, 64.7, 56.7, 48.9, 33.3, 33.0, 30.2, 28.9, 28.4, 22.8. HR-MS (ESI): MNa^+, found 673.3142. $C_{37}H_{50}N_2O_4S_2Na$ requires 673.3110.

4.3.36. *tert-Butyl (4S)-4-((1S)-1-(((S)-tert-butylsulfinyl)amino)-2-hydroxy-3-phenylpropyl)-5,5-dimethyl-2-phenylthiazolidine-3-carboxylate (**21d**)*

According to general procedure 4.3.16, 147 mg (1.70 mmol, 16.00 eq) LiBr were added to 5.30 mL (0.212 mmol, 2.00 eq) SmI_2-solution at −78 °C. 45 mg (0.106 mmol, 1.00 eq) **20** and 19 μL (0.159 mmol, 1.50 eq, 19 mg) phenylacetaldehyde were dissolved in 660 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (44 μL/min). The crude product was purified via preparative HPLC [method A] to afford **21d** as clear, colorless oil (3.2 mg, 0.006 mmol, 6%). HPLC-MS: t_R = 8.68 min (Na^+-, K^+- adduct); TLC: R_f = 0.15 (CH/EA = 4/1); ^{1}H NMR-major diastereomer (499.98 MHz, CDCl3) δ 7.51-7.26 (m, 10H), 5.99 (s, 1H), 4.80 (d, $^3J_{HH}$ = 10.0 Hz, 1H, OH), 4.57 (s, 1H, NH), 4.24 (d, $^3J_{HH}$ = 7.3 Hz, 1H), 4.02 (t, $^3J_{HH}$ = 9.5 Hz, 1H), 3.92-3.85 (m, 1H), 3.12 (s, 1H), 2.89 (s, 1H), 1.49 (s, 3H), 1.46 (s, 3H), 1.37 (s, 9H), 1.11 (s, 9H); ^{1}H NMR-minor diastereomer (499.98 MHz, CDCl3) δ 7.51-7.26 (m, 10H), 5.99 (s, 1H), 5.04 (d, $^3J_{HH}$ = 8.4 Hz, 1H, OH), 3.71 (d, $^3J_{HH}$ = 10.3 Hz, 1H, NH), 3.53 (d, $^3J_{HH}$ = 8.3 Hz, 1H), 3.41 (s, 1H), 2.98 (d, $^3J_{HH}$ = 7.3 Hz, 1H), 2.73-2.60 (m, 2H), 1.64 (s, 9H), 1.49 (s, 3H), 1.25 (s, 9H), 0.98 (s, 3H), 0.89 (s, 3H). HR-MS (ESI): MNa^+, found 569.2485. $C_{29}H_{42}N_2O_4S_2Na$ requires 569.2484.

4.3.37. *tert-Butyl (4S)-4-((1S)-1-(((S)-tert-butylsulfinyl)amino)-2-hydroxy-4-phenylbutyl)-5,5-dimethyl-2-phenylthiazolidine-3-carboxylate (**21e**)*

According to general procedure 4.3.16, 147 mg (1.70 mmol, 16.00 eq) LiBr were added to 5.30 mL (0.212 mmol, 2.00 eq) SmI_2-solution at −78 °C. 45 mg (0.106 mmol, 1.00 eq) **20** and 21 μL (0.159 mmol, 1.50 eq, 21 mg) phenylpropionaldehyde were dissolved in 660 μL ab. THF each. The educt-solutions were added via syringe pump to the SmI_2-LiBr-solution in THF (0.04M) at −78 °C over a period of 15 min (44 μL/min). The crude product was purified via preparative HPLC [method A] to afford **21e** as clear, colorless oil (1.3 mg, 0.002 mmol, 2%). HPLC-MS: t_R = 8.42 min (Na^+-, K^+-adduct); TLC: R_f = 0.13 (CH/EA = 4/1); ^{1}H NMR (499.98 MHz, $CDCl_3$) δ 7.35-7.15 (m, 10H), 6.28 (s, 1H, OH), 5.83 (s, 1H), 4.48 (s, 1H), 3.92 (d, $^3J_{HH}$ = 8.3 Hz, 1H), 3.72 (t, $^3J_{HH}$ = 8.2 Hz, 1H), 2.97-2.78 (m, 2H), 2.23 (d, $^3J_{HH}$ = 21.7 Hz, 1H), 1.87 (q, $^3J_{HH}$ = 13.7, 5.1 Hz, 1H), 1.68 (s, 3H), 1.65 (s, 3H), 1.27 (s, 9H), 1.04 (s, 9 H). HR-MS (ESI): MNa^+, found 583.2134. $C_{30}H_{44}N_2O_4S_2Na$ requires 583.2640.

4.3.38. *Ethyl 6-oxohexanoate (**22**)*

In a 50 mL round bottom flask 2 mL (12.2 mmol, 1 eq) ethyl 6-hydroxyhexanoate were dissolved in 12.5 mL DCM. 195.5 mg (1.25 mmol, 10 mol%) TEMPO and 4.44 g (13.8 mmol, 1.1 eq) iodobenzenediacetate were added. The resulting orange solution was stirred at rt overnight. Complete conversion was detected via TLC. The reaction mixture was quenched by the addition of DCM (50 mL) and $Na_2S_2O_3$ (75 mL). The aqueous phase was extracted with DCM (3 × 25 mL). The organic layers were washed with saturated $NaHCO_3$ solution (75 mL) and brine (75 mL). The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product, an orange liquid, was purified via flash chromatography (200 g silica, 50 × 5 cm; CH/EA = 6/1 (fraction 1–9), fraction size: 125 mL) to afford **22** as colorless liquid (1.68 g, 10.6 mmol, 88%). GC-MS: t_r = 4.43 min, m/z = 130.0 (11%) [$M^+ - C_2H_5$], 113.0 (55%) [$M^+ - C_2H_5O$], 101.0 (55%) [$M^+ - C_3H_5O$], 87.0 (32%) [M^+-C_4H_7O], 73 (100%) [$C_3H_5O_2^+$], 57.0 (63%) [$C_3H_5O^+$]; TLC: R_f = 0.28 (CH/EA = 5/1); ^{1}H NMR (300.36 MHz, $CDCl_3$) δ 9.73 (s, 1H), 4.09 (q, $^3J_{HH}$ = 7.1 Hz, 2H), 2.43 (m, 2H), 2.29 (m, 2H), 1.68-1.60 (m, 4H), 1.22 (t, $^3J_{HH}$ = 7.1 Hz, 3H); ^{13}C NMR (75.53 MHz, $CDCl_3$) δ 202.1, 173.3, 60.4, 43. 6, 34.4, 24. 5, 21.6, 14.3.

4.3.39. *(7S,8R)-8-((tert-Butoxycarbonyl)amino)-7-(((R)-tert-butylsulfinyl)amino)-6-hydroxy-9-(tritylthio)nonanoate (**23**)*

According to general procedure 4.3.16, 2.20 g (4.00 mmol, 1.00 eq) **6a**, 948 mg (6.00 mmol, 1.50 eq) **22** and 750 μL (592 mg, 7.99 mmol, 2.00 eq) *t*-BuOH were dissolved in 50 mL ab. THF. The educt-solution was added dropwise to 100 mL SmI_2-solution in THF (0.08M) at −78 °C. The crude product was purified via flash chromatography [400 g SiO_2; 21 cmx6 cm; CH/EE = 3/1; fraction size: 250 mL; fraction: 12–34] to afford **23** as yellowish oil (1.02 g, 1.43 mmol, 86%). HPLC-MS-major diastereomer: t_R = 8.32 min (Na^+-, H^+- adduct); HPLC-MS-minor diastereomer: t_R = 8.48 min (Na^+-, H^+- adduct); TLC: R_f = 0.23 (CH/EA = 3/1); ^{1}H-NMR-major diastereomer (300.36 MHz, $CDCl_3$) δ 7.49-7.04 (m, 15H), 5.90 (dd, $^3J_{HH}$ = 8.40 Hz, 1H, NH), 4.06 (q, $^3J_{HH}$ = 14.1, 7.1 Hz, 3H), 3.09 (m, 2H), 2.51 (dd, $^3J_{HH}$ = 13.1, 4.5 Hz, 1H), 2.31 (dd, $^3J_{HH}$ = 13.1, 6.8 Hz, 1H), 2.23 (dd, $^3J_{HH}$ = 14.8, 7.3 Hz, 2H), 1.68-1.45 (m, 6H), 1.41 (s, 9H), 1.19 (t, $^3J_{HH}$ = 6.6 Hz, 3H), 1.12 (s, 9H); ^{13}C-NMR-major diastereomer (75.53 MHz, $CDCl_3$) δ 173.8, 156.0, 144.6, 129.8, 128.1, 126.9, 79.6, 72.7, 67.2, 66.0, 60.4, 56.4, 49.9, 34.3, 32.5, 28.6, 25.4, 25.1, 24.9, 23.1, 14.4.

4.3.40. *(7S,8R)-7,8-Diamino-6-hydroxy-9-mercaptononanoate (intermediate **A**)*

In a 1.50 mL glass vial 70 mg (0.10 mmol, 1.00 eq) **23** were

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dissolved in 490 μL EtOH (clear yellowish solution). 49 μL 4M HCl-solution were added to the reaction mixture at rt. After 10 h complete conversion was detected via HPLC-MS and the solvent was removed under reduced pressure. The residue was dissolved in 1.50 mL DCM (clear yellowish solution) and 34 mg (0.29 mmol, 2.00 eq) triethylsilane were added. 1.50 mL trifluoroacetic acid were added dropwise to this mixture giving an intense yellow solution which turned slightly yellowish again after 5 min. This reaction mixture was stirred for 2 h at rt. After complete conversion (indicated via HPLC-MS) the solvent was removed under reduced pressure in high vacuum with a cooling trap. The product was purified via reversed phase column chromatography [10 g C18 silica gel, 100% dist H_2O with 0.01% HCOOH, fraction size: 100 mL; fraction 9–15] to afford **A** as clear, colorless oil (23 mg, 0.09 mmol, 88%). HPLC-MS-major diastereomer: t_R = 2.47 min (Na^+-, H^+-, K^+-adduct); HPLC-MS-minor diastereomer: t_R = 2.61 min (Na^+-, H^+-, K^+- adduct); ^{1}H-NMR-diastereomeric mixture (300.36 MHz, D_2O) δ 4.07 (dd, $^3J_{HH}$ = 14.3, 7.1 Hz, 4H), 4.03-3.95 (m, 1H), 3.88 (m, 1H), 3.83-3.67 (m, 3H), 3.60 (t, $^3J_{HH}$ = 4.8 Hz, 1H), 3.15 (dd, $^3J_{HH}$ = 15.1, 3.9 Hz, 1H), 2.95 (dd, $^3J_{HH}$ = 14.6, 6.2 Hz, 2H), 2.76 (dd, $^3J_{HH}$ = 15.1, 8.6 Hz, 1H), 2.33 (t, $^3J_{HH}$ = 7.1 Hz, 4H), 1.64-1.39 (m, 10H), 1.32 (s, 2H), 1.16 (t, $^3J_{HH}$ = 7.1 Hz, 6H); ^{13}C-NMR-diastereomeric mixture (75.53 MHz, D_2O) δ 177.0, 70.1, 69.5, 61.7, 55.0, 53.3, 52.8, 33.8, 33.7, 32.6, 32.1, 24.4, 23.9, 23.4, 23.0, 13.3.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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