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Synthesis of 5-deazathiogirollines: analogs of a natural antitumor agent

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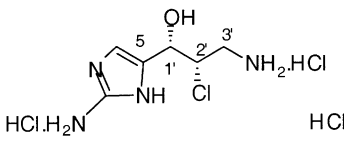
Abstract—2-Aminothiazole analogs of the natural antitumor agent, girolline, were prepared in natural stereochemistry series (*threo*) and in a non-natural series (*erythro*). The key-step involved a coupling reaction between 2,3-*O*-isopropylidene-D-glyceraldehyde and a properly protected 2-aminothiazole, via a dianion species. The biological activity of the prepared analogs was evaluated on human cancer cells to determine structure–activity relationship.

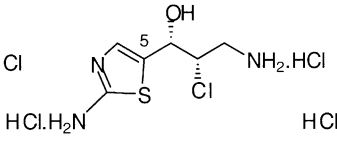
1. Introduction

Girolline **1** was extracted from a New Caledonian marine Sponge,[1] *Cymbastela cantharella*[2] (previously *Pseudaxinyssa cantharella*)[3] which has shown in vitro cytotoxicity and in vivo antitumor activity.[4] Because the phase I clinical trials with girolline have been discontinued due to undesired side-effects, the synthesis of analogs might allow for improvement of its biological profile.

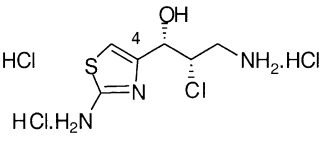
Our goal is to synthesize some analogs in which the side-chain of the natural product is preserved, while the 2-aminoimidazole ring is replaced by a 2-aminothiazole ring. This change results into two isomer analogs that we have called: 5-deazathiogirolline **2** and 4-deazathiogirolline **3**. In this paper, we disclose the synthesis of compound **2**.



Girolline **1**



5-deazathiogirolline **2**



4-deazathiogirolline **3**

2. Results and discussion

The key-step is the condensation of 2,3-*O*-isopropylidene-D-glyceraldehyde[5] with the dianion of a protected 2-aminothiazole.

After many trials, the acyl protecting group family proved to be most suitable for this task. After optimization, the pivaloyl protected 2-aminothiazole was prepared in 97% yield from **4**, in presence of triethylamine (TEA) and pivaloyl chloride to yield compound **5**. The triol **6** was prepared in 99% yield from **5** and 2,3-*O*-isopropylidene-D-glyceraldehyde, in the presence of an excess of lithium diisopropylamide (LDA) in THF at −78°C. Two diastereoisomers were formed (ratio 3:2) (Scheme 1).

The two isomers **6A/6B** proved to be very difficult to separate by flash chromatography. Eventually, a four-step sequence was proposed to access stereochemically pure alcohols **6A** and **6B** (Scheme 2).

At first, the mixture of alcohols **6A/6B** was oxidized into the single ketone **7** by treatment with manganese dioxide in dioxane (82% yield). The ketone **7**, whose structure was secured by X-Ray analysis[6] was then converted into the single diastereoisomer **6A** by use of the L-Selectride® in THF at −78°C. Thus, by this route, the pure compound **6A** was easily prepared in two steps (75% yield).

Keywords: aminothiazole; antitumor compounds; marine metabolite; structure–activity.

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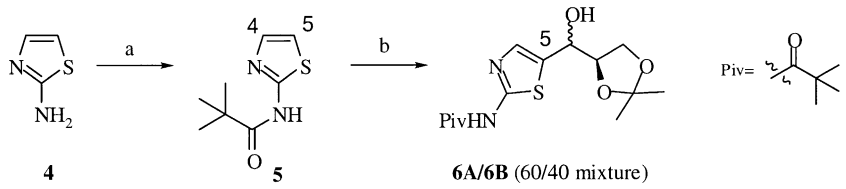
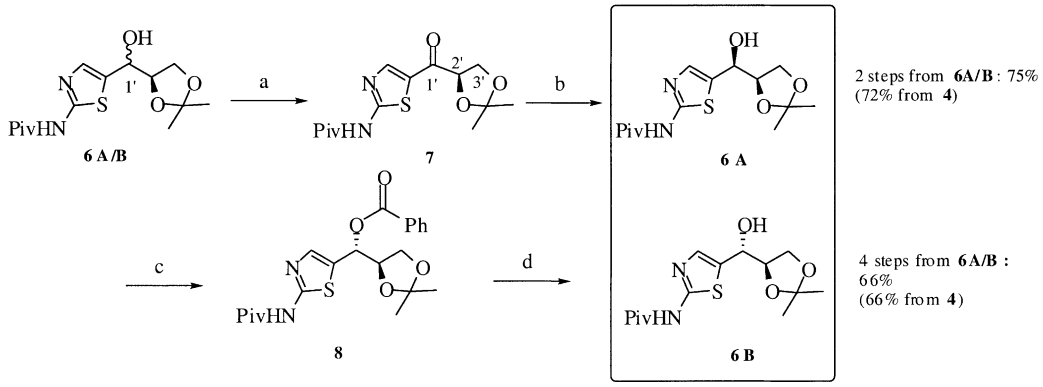
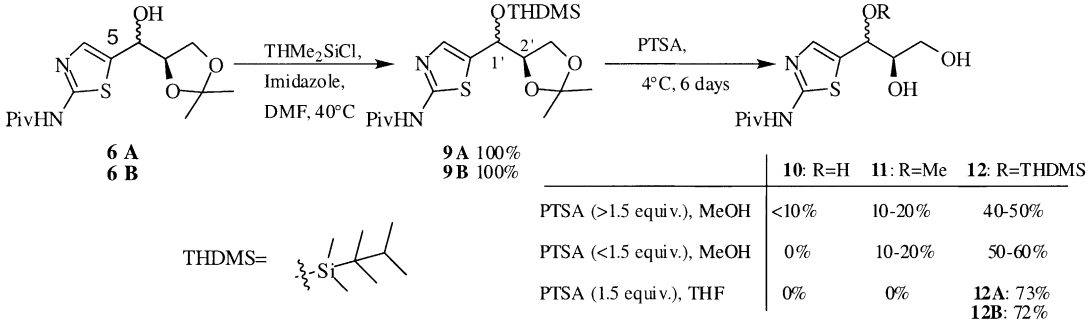


Scheme 1. (a) PivCl, TEA, CH_2Cl_2, 97%; (b) 2,3-*O*-isopropyliden-D-glyceraldehyde, LDA, THF, −78°C, 99%.



Scheme 2. (a) MnO_2, dioxane, rt,82%; (b) L-Selectride®,THF, rt, 91%; (c) PhCOOH, DEAD, PPh_3, THF, −78°C, 85%; (d) MeONa, THF, 100%.



	10: R=H	11: R=Me	12: R=THDMS
PTSA (>1.5 equiv.), MeOH	<10%	10-20%	40-50%
PTSA (<1.5 equiv.), MeOH	0%	10-20%	50-60%
PTSA (1.5 equiv.), THF	0%	0%	**12A**: 73% **12B**: 72%

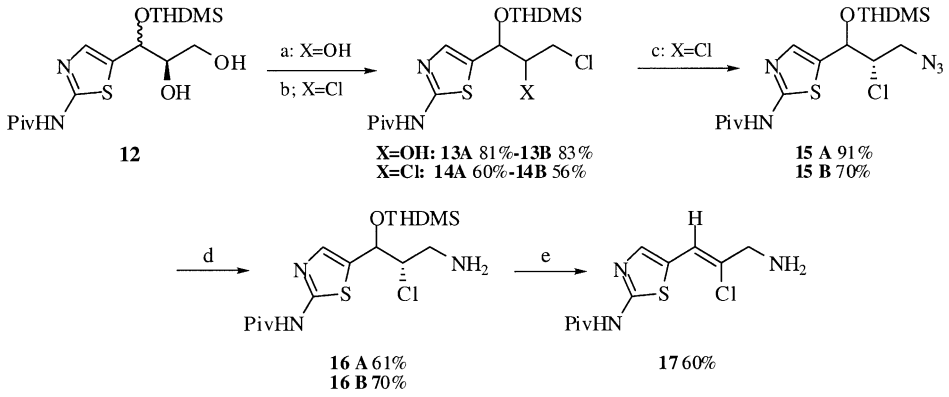
Scheme 3.

Alcohol **6B** was obtained by inverting the configuration of the free-alcohol **6A** by a Dodge esterification reaction.[7] A first attempt with the *para*-nitrobenzoic acid led to the ester in quantitative yield but with partial epimerization at C-1′. This result was probably due to the strong electron-withdrawing effect of the nitro group. The use of benzoic acid provided **8** in 89% yield without any epimerization. Methanolysis of ester **8** gave the diastereoisomer **6B** in 100% yield. Thus, pure compound **6B** could be easily prepared in four steps (66% yield).

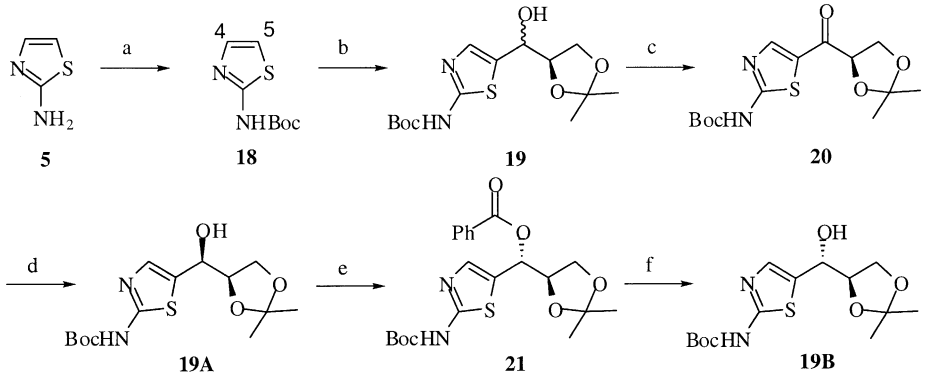
Functionalization of the side-chain could be easily effected on each diastereoisomer. Firstly, the hydroxyl group in position 1′ was protected as thexyldimethylsilylether **9**; this silyl group is known to be 2–3 times more stable than *t*-butyldimethylsilyl (TBDMS).[8] This protection was carried out in 100% yield on both **6A** and **6B** (Scheme 3).

The selective deprotection of the acetonide **9** was carried out in THF in the presence of *para*-toluenesulfonic acid (PTSA), at 4°C for 6 days. The corresponding diols **12A** and **12B** were isolated in 73 and 72% yield, respectively. The use of more than 1.5 equiv. of PTSA in methanol gave a mixture of the expected diols but also a small amount of the fully deprotected triols **10** and the unexpected methoxy 1′-substituted compound which was isolated as an unseparable 60/40 mixture of diastereoisomers **11**. Use of the non-nucleophilic solvent THF and a reduced amount of acid, allowed elimination of these side-reactions (Scheme 3).

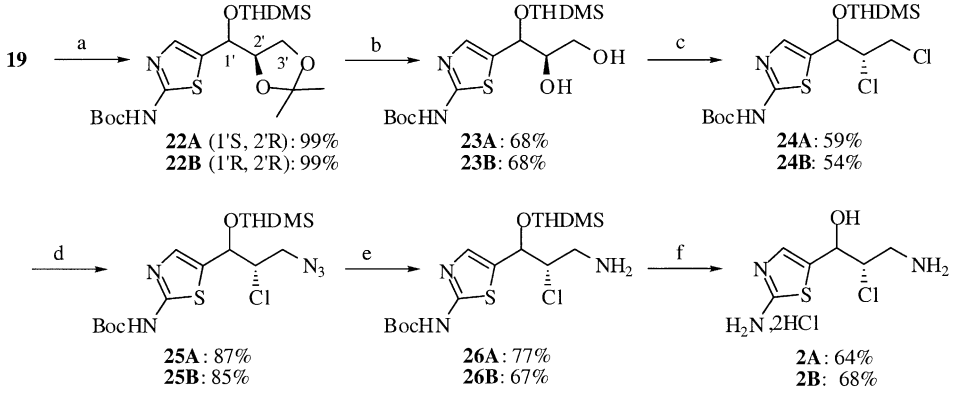
After several unsuccessful experiments to introduce an amino group at position 3′ followed by a chlorination at position 2′, the 2′,3′-bis-chlorination was preferred. It was performed on **12A** and **12B** using 2.5 equiv. of triphenylphosphine (PPh_3) and *N*-chloro-succinimide (NCS)[9] in 60 and 56% yield, respectively (Scheme 4); the concomitant inversion of the configuration at C-2′ gave the absolute configuration observed in the natural girolline. Substitution of the 3′-chloro by an azide (NaN_3, DMF)[10] and catalytic hydrogenation led to free amines **16A** and **16B** (Scheme 4). At this point, it was expected that deprotection of both 1′-hydroxyl and 2-amino groups would provide the 5-deazathiogirolline **2**. Unfortunately, various attempts only led to the degradation of the product, to unchanged starting material or to the formation of the dehydration compound **17**.



Scheme 4. (a) PPh_3 (2 equiv.), NCS (2 equiv.), THF, 60°C; (b) PPh_3 (2.5 equiv.), NCS (2.5 equiv.), THF, 60°C; (c) NaN_3, DMF, 80°C; (d) H_2, Pd 5%/C, ethanol; (e) 6N HCl, T>60°C.



Scheme 5. (a) Boc_2O, TEA, DMAP, CH_2Cl_2, 89%; (b) 2,3-*O*-isopropyliden-D-glyceraldehyde, LDA, THF, −78°C, 93%; (c) MnO_2, dioxane, 85%; (d) L-Selectride®, THF, 93%; (e) PhCOOH, DEAD, PPh_3, THF, −78°C, 90%; (f) MeONa, THF, 100%.



Scheme 6. (a) $ThMe_2SiCl$, imidazole; (b) PTSA, THF, 4°C, 6 days; (c) PPh_3, NCS; (d) NaN_3, DMF; (e) H_2, Pd 5%/C; (f) 6N HCl.

To overcome this difficulty, another protective group was chosen. 2-Aminothiazole **4** was protected as 2-*N*-*tert*-butoxycarbonylthiazole **18**. The previously described sequences were followed to yield diastereoisomers **19A** and **19B** in 65% (four steps) and 59% (six steps) yield, respectively (Scheme 5).

The acetonides **19** were converted into 5-deazathiogirollines **2A** and **2B** in six steps (Scheme 6, Fig. 1).[6,11]

Thus, the total synthesis of 5-deazathiogirolline **2B** could be carried out from 2-aminothiazole **4** in 12 steps in 8.3% overall yield while the synthesis of its isomer **2A** was completed in 10 steps in 11.3% total yield.

The final compounds as well as some intermediates were tested on human cancerous cells. The in vitro cytotoxic activities of the compounds were evaluated using KB cells, derived from an epidermoid carcinoma in the mouth of an adult Caucasian male in 1954.[12] We originally obtained this cell line from the American Type Culture Collection. Results are summarized in Table 1.

Unfortunately, both compounds **2A** and **2B** were inactive;

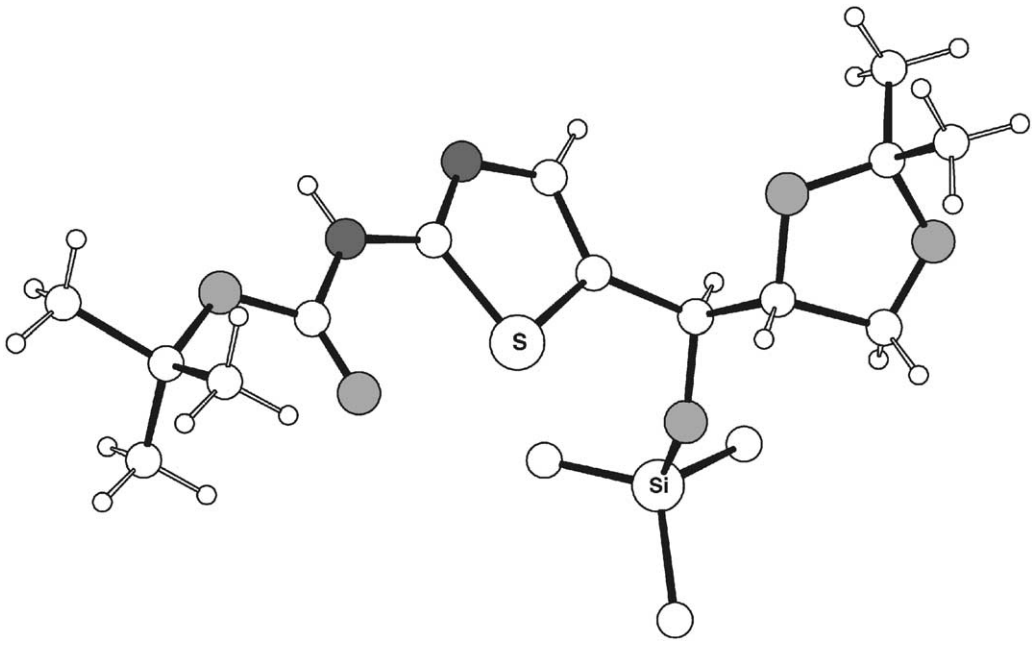
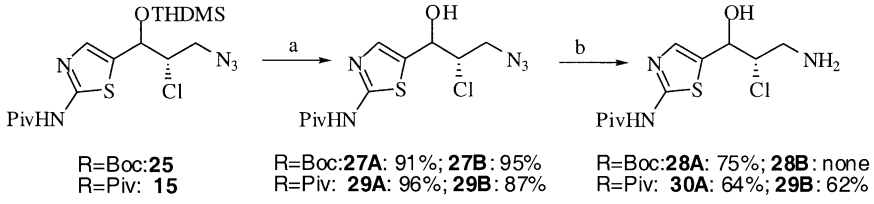
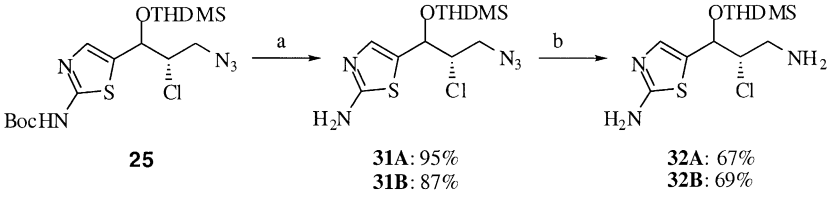


Figure 1. X-Ray structure of **22B** (the protective silyl group is only partially visible).



Scheme 7. (a) Bu_4NF, AcOH, THF; (b) H_2, Pd 5%/C, ethanol.



Scheme 8. (a) CF_3COOH, CH_2Cl_2; (b) H_2, Pd 5%/C, ethanol.

on the contrary, intermediates **15A**, **16A** and **26A** (still protected in positions 2 and 1′) have shown an interesting and unexpected in vitro activity: these three compounds have the opposite configuration of the girolline; so, LD_{50} is 3.4×10^{-6} M for **16A** while it is 2.8×10^{-7} M for the girolline **1**. Dilution experiments have shown that this activity decreased promptly with the concentration.

To improve the knowledge of the structure–activity relationships, other analogs were prepared: we decided to selectively deprotect each position of the bioactive molecules.

Table 1. Activity of products tested on cancerous cells (KB): killed-cells % at 5×10^{-6} M concentration

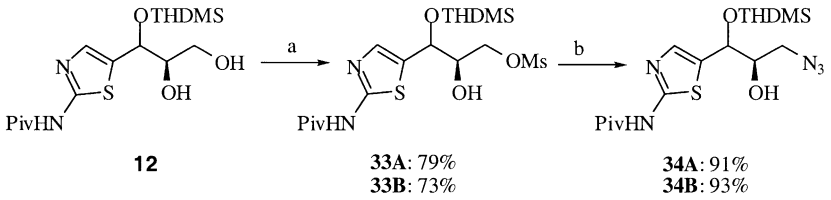
1	**12A**	**12B**	**23A**	**23B**	**15A**	**15B**	**25A**	**25B**	**2A**
100%	0%	17%	20%	33%	62%	35%	9%	16%	0%
	14A	**14B**	**25A**	**25B**	**16A**	**16B**	**26A**	**26B**	**2B**
	33%	29%	16%	18%	100%	0%	85%	42%	0%

The silyl group was selectively removed by treatment of azides **25** and **15** with tetrabutylammonium fluoride in the presence of acetic acid, in order to prevent the degradation of the starting material. Free hydroxyazides **27** and **29** were isolated in good yield (87–96%) in both series (*N*-Piv and *N*-Boc). The corresponding amines **28** and **30** were easily prepared (one exception **28B**) in 62–75% yields (Scheme 7).

Selective deprotection of the 2-amino group of the azides **25** was effected by treatment with trifluoroacetic acid (TFA) in CH_2Cl_2 (87–95%); catalytic hydrogenation provided diamines **32** (67–69%) (Scheme 8).

Hydroxy-azides **34** were prepared from diols **12** by monomesylation then displacement with azide (Scheme 9).

In vitro cytotoxicity on KB cells was also evaluated for all these analogs. None showed the activity of **16** and **26**.



Scheme 9. (a) MsCl, pyridine; (b) NaN_3, DMF.

From these results, it can be concluded that chlorine and nitrogen functional groups are necessary (amine better than azide) for the activity. Also the 1′-hydroxy group and 2-aminogroup must be protected. The effect of the position of the substituents and of the configuration of the carbons of the side-chain as well as the mechanism of cell toxicity are under investigation.

3. Experimental

3.1. General procedures

All reactions were carried out under an argon atmosphere, using freshly distilled solvents under anhydrous conditions unless otherwise stated. Methylene chloride was distilled from calcium hydride, tetrahydrofuran (THF) was distilled from sodium/benzophenone. Reaction temperatures were measured externally. Analytical TLC, for monitoring and measuring R_f values, was carried out on 0.25 mm E.Merck precoated silicagel plates (60F254), using UV light. Preparative flash chromatography was performed using silica Chromagel SDS 60 Å(40–60 μm). ^1H and ^{13}C NMR spectra are recorded on a Bruker AC250, AM300 or AM400 spectrometer and calibrated by using TMS as an internal reference. Chemical shifts (δ) were measured in parts per million, and coupling constants (J values) are in Hertz (Hz). IR spectra were taken with a Perkin–Elmer BX FT-IR spectrometer. $[\alpha]_D$ were measured using a Perkin–Elmer 241 MC polarimeter (589 nm, 20°C). Chemical ionization mass spectra were recorded on AEI MS-9 spectrophotometer with isobutane as carrier, electron impact spectra on AEI MS-50. UV spectra were taken with a Varian Cary 100 spectrometer, using EtOH solution. Melting points were determined using a Büchi BS540 and are uncorrected.

Biological procedure. The KB cells were serially cultured in MEM (minimum essential medium, with Earle's salt solution), purchased from Seromed, containing 10% fetal calf serum, 2 mM/L-glutamine, 60 μg/mL penicillin G and streptomycin sulfate and 40 μg/mL gentamycin. For the tests, KB cells were grown as monolayers in 24-well plastic plates (25000 cells seeded per well in 1 mL medium). Serial dilutions of the stock solutions of the compounds under test were made in the medium and added to the cultures under a volume of 10 μL per well, immediately after plating the cells. All cultures were incubated at 37°C in a 95% air-5% CO_2 humidified incubator. After 3 days incubation, cell viability was determined by further 8–16 h incubation following addition to each well of 100 μL of a 0.02% solution in medium of the vital dye neutral red, followed by washing the cell monolayers with phosphate-buffered saline, lysis of the cells with a 1% solution of sodium lauryl-dodecyl sulfate and photometric quantification of the extracted dye at 540 nm, using a ELX 800 microplate reader (BIO-TEK Instruments, Inc.) as originally described by Borenfreund and Puerner.[13]

3.2. Protection of the amino group of 2-aminothiazole

3.2.1. By pivaloyl group: 2,2-dimethyl-*N*-thiazol-2-yl-propionamide 5. 2-Aminothiazole **4** (100 g, 1 mol) was dissolved in dichloromethane (800 mL) and treated at −5°C (ice/salt) with triethylamine (280 mL, 2 equiv.) and pivaloyl chloride (1.77 mL, 1.2 equiv.). The solution was stirred at room temperature for 1 h. The mixture was diluted with dichloromethane (400 mL) and washed with 0.1N HCl, brine and water. The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure. Crystallization from heptane furnished compound **5** with 97% yield (179 g). $C_8H_{12}N_2OS$. White crystals. Mp=141°C (heptane). R_f: 0.8 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) m/z: 185 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3427 (NH), 2970–2870 (CH), 1680 (amide). UV (λ, nm [ϵ]): 266 (10500). ^1H NMR (300 MHz) δ (ppm): 9.65 (m, 1H, NH); 7.49 (d, J=5.5 Hz, 1H, H-4); 7.00 (d, J=5.5 Hz, 1H, H-5); 1.34 (s, 9H, $(CH_3)_3C$). ^{13}C NMR (75 MHz) δ (ppm): 176.00 (C=O); 158.45 (C-2); 137.45 (C-4); 113.85 (C-5); 39.25 ($C(CH_3)_3$); 27.35 ($C(CH_3)_3$). Calcd for $C_8H_{12}N_2OS$: C, 52.15; H, 6.56; N, 15.20; found: C, 52.21; H, 6.61; N, 15.36.

3.2.2. By *tert*-butoxycarbonyl group: 2-(*tert*-butoxycarbonylamino)-thiazole 18. 2-Aminothiazole (10 g, 0.1 mol) was dissolved in THF (50 mL); ditertbutyldicarbonate (24 g, 1.1 equiv.), triethylamine (17.8 mL, 1.2 equiv.) and dimethylaminopyridine (DMAP, 10 mg) were added. After stirring for 3 h at room temperature, the mixture was diluted with dichloromethane (150 mL) and washed with 0.1N HCl, brine then water and dried over $MgSO_4$. Solvent was removed under reduced pressure and the residue was crystallized from heptane to yield **18** (17.7 g, 89%). $C_8H_{12}N_2O_2S$. White crystals. Mp=183°C (heptane). R_f: 0.8 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C), m/z: 201 $(M+H)^+$; 101 $(Boc)^+$. IR (KBr, ν_{max}, cm^{-1}): 1722 (carbamate). UV (λ, nm [ϵ]): 257 (15400). ^1H NMR (250 MHz) δ (ppm): 11.82 (s large, 1H, NH); 7.38 (d, J=3.7 Hz, 1H, H-5); 6.88 (d, J=3.7 Hz, 1H, H-4); 1.57 (s, 9H, $(CH_3)_3C$. ^{13}C NMR (62.5 MHz) δ (ppm): 162.05 (C=O); 153.15 (C-2); 136.95 (C-4); 112.10 (C-5); 81.95 ($(C(CH_3)_3$); 28.45 ($C(CH_3)_3$). Calcd for $C_8H_{12}N_2O_2S$: C, 47.98; H, 6.04; N, 13.99; found: C, 47.81; H, 6.01; N, 13.87.

3.3. Condensation step of 2,3-*O*-isopropylidene-D-glyceraldehyde via a dianion species. Compounds 6A, 6B, 19A, 19B

Diisopropylamine (2.2 equiv.) was dissolved in THF (1.66 mL/mmol) and cooled to −78°C. The solution was treated dropwise with 1.6 M *n*-butyllithium in hexane (2.2 equiv.) and stirred for 30 min. The LDA solution was then added by cannulation to a solution of compound **5** (1 equiv.) in anhydrous THF (3.6 mL/mmol) at −78°C and stirred for 30 min. A solution of 2,3-*O*-isopropylidene-D-glyceraldehyde (1.5 equiv.) in THF (0.3 mL/mmol) was then added. The reaction was allowed to warm to room temperature and stirred overnight. The reaction was quenched by dropwise addition of water. The mixture was diluted with dichloromethane (four volumes), washed with water, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The resulting solid was purified by flash chromatography (dichloromethane/methanol: 99/1) to yield a white solid of both diastereoisomers.

The product **6** was isolated in 99% yield (3.35 g); both diastereoisomers were characterized separately after column chromatography on silica (dichloromethane/methanol: 99/1) of an aliquot, but most of the product was isolated as a mixture of diastereoisomers.

3.3.1. *N*-{5-[(2,2-Dimethyl-[1,3(*S*)]dioxolan-4-yl)-(*S*)-hydroxy-methyl]-thiazol-2-yl}-2,2-dimethyl-propionamide 6. Compound **6A**. $C_{14}H_{22}N_2O_4S$. White solid. Mp=143°C. R_f: 0.4 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C), *m/z*: 315 $(M+H)^+$; 297 $(M+H-H_2O)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3424 (NH), 3400–3200 (alcohol), 1682 (amide). UV (λ, nm [ϵ]): 271 (14600). $[\alpha]_D$=+7 (c=3.5; ethanol). ^{1}H NMR (250 MHz) δ (ppm): 9.65 (s large, 1H, NH); 7.36 (s, 1H, H-4); 4.82 (d, J=6.8 Hz, 1H, H-1′); 4.31 (m, 1H, H-2′); 3.96 (dd, J=6.6, 8.6 Hz, 1H, H-3′); 3.77 (dd, J=5.5, 8.6 Hz, 1H, H-3′); 3.49 (s large, 1H, OH); 1.49 (s, 3H, CCH_3); 1.39 (s, 3H, CCH_3); 1.31 (s, 9H, (CH_3)$_3$). ^{13}C NMR (62.5 MHz) δ (ppm): 176.45 (C=O); 159.50 (C-2); 134.65 (C-4); 131.40 (C-5); 110.25 (C(CH$_3$)$_2$); 79.35 (C-2′); 69.50 (C-1′); 65.90 (C-3′); 39.20 (C(CH$_3$)$_3$); 26.60 (CCH$_3$); 26.25 (C(CH_3)$_3$); 25.05 (CCH_3). Calcd for $C_{14}H_{22}N_2O_4S$: C, 53.48; H, 7.05; N, 8.91; found: C, 53.33; H, 7.05; N, 8.74.

Compound **6B**. $C_{14}H_{22}N_2O_4S$. White solid. R_f: 0.4 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) *m/z*: 315 $(M+H)^+$, 297 $(M+H-H_2O)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3425 (NH), 3400–3200 (alcohol), 1682 (amide). UV (λ, nm [ϵ]): 271 (14200). $[\alpha]_D$=−31 (c=2.0; ethanol). ^{1}H NMR (400 MHz) δ (ppm): 9.65 (s large, 1H, NH); 7.32 (s, 1H, H-4); 4.95 (d, J=5.5 Hz, 1H, H-1′); 4.28 (m, 1H, H-2′); 3.98 (ABX sys; J=5.7, 8.6 Hz, 1H, H-3′); 3.97 (sys ABX; J=6.6, 8.6 Hz, 1H, H-3′); 1.46 (s, 3H, CCH_3); 1.35 (s, 3H, CCH_3); 1.30 (s, 9H, (CH_3)$_3$C). ^{13}C NMR (62.5 MHz) δ (ppm): 176.75 (C=O); 159.50 (C-2); 134.80 (C-4); 132.45 (C-5); 110.40 (C(CH$_3$)$_2$)); 79.40 (C-2′); 69.00 (C-1′); 66.05 (C-3′); 39.50 (C(CH$_3$)$_3$); 27.00–27.55 (C(CH_3)$_2$); 25.45 (C(CH_3)$_3$). HRMS: *m/z* calcd for $C_{14}H_{23}N_2O_4S$: 315.1378; found: 315.1388.

The product **19** was isolated in 93% yield (15.3 g); both diastereoisomers were characterized separately after chromatography on a silica column (dichloromethane/methanol: 99/1) of an aliquot, but most of the product was isolated as a mixture of diastereoisomers.

3.3.2. {5-[(2,2-Dimethyl-[1,3]dioxolan-4-yl)-hydroxy-methyl]-thiazol-2-yl}-carbamic acid *tert*-butyl ester 19. Compound **19A**. $C_{14}H_{22}N_2O_5S$. White solid. R_f: 0.4 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) *m/z*: 387 $(M+57)^+$, 331 $(M+H)^+$, 313 $(M+H-H_2O)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1716 (carbamate). UV (λ, nm [ϵ]): 263 (11700). $[\alpha]_D$=+21 (c=0.19; ethanol). ^{1}H NMR (250 MHz) δ (ppm): 12.08 (s large, 1H, NH); 7.27 (s, 1H, H-4); 4.76 (d, J=6.7 Hz, 1H, H-1′); 4.32 (m, 1H, H-2′); 3.98 (dd, J=6.6, 8.7 Hz, 1H, H-3′); 3.77 (dd, J=5.7, 8.7 Hz, 1H, H-3′); 1.58 (s, 9H, (CH_3)$_3$C); 1.49 (s, 3H, CCH_3); 1.39 (s, 3H, CCH_3). ^{13}C NMR (62.5 MHz) δ (ppm): 162.70 (C=O); 152.70 (C-2); 134.45 (C-4); 129.80 (C-5); 110.30 (C(CH$_3$)$_2$); 82.00 (C(CH$_3$)$_3$); 79.25 (C-2′); 69.45 (C-1′); 66.00 (C-3′); 28.15 (C(CH$_3$)$_3$); 25.00–26.65 (C(CH$_3$)$_2$).

Compound **19B**. $C_{14}H_{22}N_2O_5S$. White solid. R_f: 0.4 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) *m/z*: 331 $(M+H)^+$, 313 $(M+H-H_2O)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1719 (carbamate). UV (λ, nm [ϵ]): 263 (11500). $[\alpha]_D$ = −23 (c=0.19; ethanol). ^{1}H NMR (250 MHz) δ (ppm): 11.85 (s large, 1H, NH); 7.28 (s, 1H, H-4); 4.97 (d, J=5.2 Hz, 1H, H-1′); 4.29 (m, 1H, H-2′); 4.04 (m, 2H, H-3′); 1.57 (s, 9H, (CH_3)$_3$C); 1.47 (s, 3H, CCH_3); 1.37 (s, 3H, CCH_3). ^{13}C NMR (62.5 MHz) δ (ppm): 162.00 (C=O); 152.90 (C-2); 134.35 (C-4); 130.40 (C-5); 110.10 (C(CH$_3$)$_2$); 82.25 (C(CH$_3$)$_3$); 79.10 (C-2′); 68.65 (C-1′); 65.60 (C-3′); 28.45 (C(CH$_3$)$_3$); 25.20–26.75 (C(CH$_3$)$_2$). HRMS: *m/z* calcd for $C_{14}H_{23}N_2O_5S$: 331.1327; found: 331.1316.

3.4. Oxidation of the mixture of alcohols in position 1′ to the single ketone. Compounds 7, 20

The mixture of alcohols (1 equiv.) was dissolved in dioxane (1.75 mL/mmol); the solution was then treated with manganese dioxide (15 equiv.) and stirred overnight at room temperature. The solution was treated with additional manganese dioxide (15 equiv.) and stirred overnight. Filtration through a Celite® pad, concentration under reduced pressure and flash chromatography (dichloromethane/methanol: 99/1) yielded the product as a white solid.

3.4.1. *N*-[5-(2,2-Dimethyl-[1,3(*S*)]dioxolane-4-carbonyl)-thiazol-2-yl]-2,2-dimethyl-propionamide 7. Yield: 82%, 889 mg. $C_{14}H_{20}N_2O_4S$. White crystals. Mp=125°C (ethanol). R_f: 0.8 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) *m/z*: 313 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3420 (NH), 1690 (amide), 1654 (ketone). UV (λ, nm [ϵ]): 226 (10500), 308 (30600). $[\alpha]_D$=−15 (c=2.30; ethanol). ^{1}H NMR (250 MHz) δ (ppm): 9.74 (s large, 1H, NH); 8.42 (s, 1H, H-4); 4.89 (t, J=6.4 Hz, 1H, H-2′); 4.28 (d, J=6.4 Hz, 2H, H-3′); 1.47 (s, 3H, CCH_3); 1.46 (s, 3H, CCH_3); 1.34 (s, 9H, (CH_3)$_3$C). ^{13}C NMR (75 MHz) δ (ppm): 191.75 (1′-C=O); 176.80 (C=O); 164.95 (C-2); 146.45 (C-4); 130.15 (C-5); 111.50 (C(CH$_3$)$_2$); 79.50 (C-2′); 66.80 (C-3′); 39.45 (C(CH$_3$)$_3$); 27.15 (C(CH$_3$)$_3$); 25.40–26.05 (C(CH$_3$)$_2$). HRMS: *m/z* calcd for $C_{14}H_{21}N_2O_4S$: 313.1221; found: 313.1221. Calcd for $C_{14}H_{20}N_2O_4S$: C, 53.83; H, 6.45; N, 8.97; found: C, 53.49; H, 6.39; N, 8.91.

3.4.2. [5-(2,2-Dimethyl-[1,3]dioxolane-4-carbonyl)-thiazol-2-yl]-carbamic acid *tert*-butyl ester 20. Yield 85%, 170 mg. $C_{14}H_{20}N_2O_5S$. White solid. R_f: 0.8 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) m/z: 329 $(M+H)^+$, 272 $(M+H-57)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1725 (carbamate), 1648 (ketone). UV (λ, nm [ϵ]): 218 (10600); 308 (25900). $[\alpha]_D$=−53 (c=1.4; chloroform). ^1H NMR (400 MHz) δ (ppm): 8.36 (s, 1H, H-4); 4.87 (dd, J=5.7, 7.3 Hz, 1H, H-2′); 4.32 (dd, J=5.4, 8.6 Hz, 1H, H-3′); 4.25 (dd, J=7.3, 8.6 Hz, 1H, H-3′); 1.57 (s, 9H, $(CH_3)_3C$); 1.41 (s, 6H, $(CH_3)_2C$). ^{13}C NMR (62.5 MHz) δ (ppm): 191.20 (1′-C=O); 177.65 (C=O); 167.55 (C-2); 146.40 (C-4); 129.60 (C-5); 111.35 ($C(CH_3)_2$); 83.25 ($C(CH_3)_3$); 79.30 (C-2′); 66.50 (C-3′); 28.15 ($C(CH_3)_3$); 25.35–25.95 ($C(CH_3)_2$).

3.5. Isolation of pure alcohol 6A or 19A by reduction of the ketone

The ketone (**7** or **20**) was dissolved in THF and treated at −78°C with 3 equiv. of L-Selectride®. After total disappearance of the starting material, the reaction was quenched by addition of methanol. The solution was then filtered through a Celite® pad and the solvent removed under reduced pressure. The residue was purified by flash chromatography (dichloromethane/methanol: 99/1) to yield alcohol **6A** or **19A**.

3.6. Dodge reaction: inversion of stereochemistry of alcohol in position 1′. Compounds 8, 21

The alcohol (1 equiv.) was dissolved in THF (0.045 mmol/mL) and treated with triphenylphosphine (4 equiv.) and benzoic acid (4 equiv.). The mixture was cooled to −78°C and treated with DEAD (4 equiv.). The mixture was allowed to warm to room temperature and stirred for 3 h. The mixture was then diluted with dichloromethane (four volumes), washed with water (four volumes), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by flash chromatography (heptane/ethyl acetate: 7/3).

3.6.1. Benzoic acid (2,2-dimethyl-[1,3]dioxolan-4-yl)-[2-(2,2-dimethyl-propionylamino)-thiazol-5-yl]-methyl ester 8. Yield: 85%, 79 mg. $C_{21}H_{26}N_2O_5S$. White solid. R_f: 0.9 (CH_2Cl_2/MeOH: 95/5). MS CI (T=160°C) m/z: 419 $(M+H)^+$, 297 $(M+H-PhCOOH)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1722 (ester), 1682 (amide). UV (λ, nm [ϵ]): 271 (13700), 231 (15300). $[\alpha]_D$=+26 (c=2.41; ethanol). ^1H NMR (250 MHz) δ (ppm): 9.54 (s large, 1H, NH); 8.04 (m, 2H, Ph); 7.4 to 7.6 (m, 3H, Ph); 7.44 (s, 1H, H-4); 6.31 (d, J=5.8 Hz, 1H, H-1′); 4.56 (m, 1H, H-2′); 4.18 (dd, J=6.4, 8.4 Hz, 1H, H-3′); 4.00 (dd, J=5.2, 8.4 Hz, 1H, H-3′); 1.44 (s, 3H, CCH_3); 1.37 (s, 3H, CCH_3); 1.30 (s, 9H, $(CH_3)_3C$). ^{13}C NMR (75 MHz) δ (ppm): 175.50 (C=O); 159.20 (C-2); 137.40 (C-4); 133.55 (Ph); 129.95 (C-5); 129.60 (Ph); 128.60 (Ph); 127.85 (Ph); 110.65 ($C(CH_3)_2$); 77.35 (C-2′); 70.25 (C-1′); 66.40 (C-3′); 39.20 ($C(CH_3)_3$); 27.30 ($C(CH_3)_3$); 25.25–26.70 ($C(CH_3)_2$). HRMS: m/z calcd for $C_{21}H_{27}N_2O_5S$: 419.1640; found: 419.1633.

3.6.2. Benzoic acid (2-*tert*-butoxycarbonylamino-thiazol-5-yl)-(2,2-dimethyl-[1,3]dioxolan-4-yl)-methyl ester 21. Yield 90%, 24 mg. $C_{21}H_{26}N_2O_6S$. White solid. R_f: 0.6 (CH_2Cl_2). MS CI (T=160°C) m/z: 313 (M+H–PhCOOH). IR ($CHCl_3$, ν_{max}, cm^{-1}): 1720. UV (λ, nm [ϵ]): 231 (11500); 263 (11000). $[\alpha]_D$=+14 (c=1.5; ethanol). ^1H NMR (250 MHz) δ (ppm): 10.28 (s large, 1H, NH); 8.04 (m, 2H, Ph); 7.4 to 7.6 (m, 3H, Ph); 7.27 (s, 1H, H-4); 6.28 (d, J=5.9 Hz, 1H, H-1′); 4.56 (m, 1H, H-2′); 4.18 (dd, J=6.5, 8.6 Hz, 1H, H-3′); 4.03 (dd, J=5.6, 8.6 Hz, 1H, H-3′); 1.55 (s, 9H, $(CH_3)_3C$); 1.43 (s, 3H, CCH_3); 1.37 (s, 3H, CCH_3). ^{13}C NMR (75 MHz) δ (ppm): 165.30 (C=O); 152.80 (C-2); 136.90 (C-4); 133.40 (Ph); 130.00 (C-5 or Ph); 129.60 (C-5 or Ph); 128.60 (Ph); 128.50 (Ph); 110.60 ($C(CH_3)_2$); 82.40 ($C(CH_3)_3$); 77.40 (C-2′); 70.30 (C-1′); 66.45 (C-3′); 29.80 ($C(CH_3)_3$); 25.25–26.70 ($C(CH_3)_2$).

3.7. Isolation of pure alcohol 6B or 19B by reduction of the ketone, esterification and methanolysis of ester

The phenylester (**8** or **21**) was dissolved in THF (10 mmol/mL) and treated at 0°C with a 1N solution of NaOMe (10 mmol/mL) and stirred at room temperature overnight. The alcohol was extracted with dichloromethane. The organic layer was dried over $MgSO_4$, filtered, concentrated under reduced pressure and purified by flash chromatography (dichloromethane/methanol: 99/1) to yield **6B** and **19B**.

3.8. Protection of 1′-hydroxyle by THDMS. Compounds 9A, 9B, 22A, 22B

The alcohol (1 equiv.) was dissolved in DMF (0.29 mmol/mL); imidazole (5 equiv.) and dimethylthexylsilyl chloride (2 equiv.) were added. After stirring for 24 h at 40°C the mixture was diluted with dichloromethane (four volumes) and washed with water. The organic layer was dried over $MgSO_4$, filtered, concentrated under reduced pressure and purified by flash chromatography (dichloromethane/methanol: 99/1).

3.8.1. *N*-(5-{(2,2-Dimethyl-[1,3]dioxolan-4-yl)-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-methyl}-thiazol-2-yl)-2,2-dimethyl-propionamide 9A. Quantitative yield, 7.9 g. $C_{22}H_{40}N_2O_4SSi$. Mp=159°C. R_f: 0.8 (CH_2Cl_2/MeOH: 95/5). MS CI (T=180°C) m/z: 457 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3429 (NH), 1682 (amide), 1214 (Si–O). UV (λ, nm [ϵ]): 271 (11900). $[\alpha]_D$=−38 (c=0.65; ethanol). ^1H NMR (250 MHz) δ (ppm): 9.80 (s large, 1H, NH); 7.31 (s, 1H, H-4); 4.93 (d, J=6 Hz, 1H, H-1′); 4.22 (m, 1H, H-2′); 3.84 (dd, J=6, 8 Hz, 1H, H-3′); 3.69 (dd, J=6, 8 Hz, 1H, H-3′); 1.62 (sept, J=7 Hz, 1H, $CH(CH_3)_2$); 1.35 (s, 3H, CCH_3); 1.33 (s, 3H, CCH_3); 1.29 (s, 9H, $(CH_3)_3C$); 0.87 (d, J=7 Hz, 6H, $CH(CH_3)_2$); 0.84 (s, 6H, CH_3 thexyl); 0.13 (s, 3H, CH_3–Si); 0.02 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz) δ (ppm): 176.30 (C=O); 159.40 (C-2); 134.20 (C-4); 132.50 (C-5); 110.00 ($C(CH_3)_2$)); 79.20 (C-2′); 70.55 (C-1′); 65.55 (C-3′); 39.15 ($C(CH_3)_3$); 34.15 ($CH(CH_3)_2$); 27.30 ($C(CH_3)_3$); 25.20–26.40 (CH_3 acetonide); 25.10 (Si–$C(CH_3)_2(C_3H_7)$); 18.60–18.70–20.20–20.31 (4 CH_3 thexyl); −2.70 (Si–CH_3); −2.90 (Si–CH_3). Calcd for $C_{22}H_{40}N_2O_4SSi$: 57.89; H, 8.71; N, 5.83; found: C, 57.86; H, 8.83; N, 6.13%.

3.8.2. *N*-(5-{(2,2-Dimethyl-[1,3]dioxolan-4-yl)-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-methyl}-thiazol-2-yl)-2,2-dimethyl-propionamide 9B. Quantitative yield, 73 mg.

$C_{22}H_{40}N_2O_4SSi$. White solid. R_f: 0.8 (CH_2Cl_2/MeOH: 95/5). MS CI (T=180°C) m/z: 457 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3426 (NH), 1681 (amide), 1220 (Si–O). UV (λ, nm [ϵ]): 273 (19900) $[\alpha]_D$=+38 (c=0.65; ethanol). ^1H NMR (300 MHz) δ (ppm): 9.47 (s large, 1H, NH); 7.29 (s, 1H, H-4); 4.80 (d, J=6.5 Hz, 1H, H-1′); 4.12 (m, 1H, H-2′); 4.06 (dd, J=5.8, 8.2 Hz, 1H, H-3′); 4.00 (dd, J=5.8, 8.2 Hz, 1H, H-3′); 1.62 (sept, J=6.9 Hz, 1H, CH(CH_3)$_2$); 1.44 (s, 3H, CCH_3); 1.31 (s, 12H, (CH_3)$_3$C+CCH_3); 0.88 (d, J=6.9 Hz, 3H, CHCH_3); 0.87 (d, J=6.9 Hz, 3H, CHCH_3); 0.85 (s, 3H, CH_3 thexyl); 0.84 (s, 3H, CH_3 thexyl); 0.16 (s, 3H, CH_3–Si); −0.05 (s, 3H, CH_3–Si). ^{13}C NMR (62.5 MHz) δ (ppm): 176.30 (C=O); 159.10 (C-2); 134.40 (C-4); 134.35 (C-5); 109.90 (C(CH_3)$_2$); 80.40 (C-2′); 70.20 (C-1′); 66.75 (C-3′); 39.20 (C(CH_3)$_3$); 34.20 (CH(CH_3)$_2$); 27.30 (C(CH$_3$)$_3$); 25.30–26.90 (C(CH$_3$)$_2$); 25.10 (Si–C(CH_3)$_2$(C_3H_7)); 18.75–20.30–20.35 (4CH$_3$ thexyl); 9.90–10.50 (Si–CH$_3$). HRMS: m/z calcd for $C_{22}H_{41}N_2O_4SSi$: 457.2554; found: 457.2556.

3.8.3. (5-{(2,2-Dimethyl-[1,3]dioxolan-4-yl)-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-methyl}-thiazol-2-yl)-carbamic acid *tert*-butyl ester 22A. Yield: 99%, 102 mg. $C_{22}H_{40}N_2O_5SSi$. White solid. R_f: 0.9 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) m/z: 473 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1716 (carbamate). UV (λ, nm [ϵ]): 263 (13300). $[\alpha]_D$=+28 (c=1.6; ethanol). ^1H NMR (250 MHz, CD_3OD/$CDCl_3$: 9/1) δ (ppm): 7.16 (s large, 1H, H-4); 4.83 (d, J=6.3 Hz, 1H, H-1′); 4.11 (m, 1H, H-2′); 4.02 (dd, J=6.1, 8.1 Hz, 1H, H-3′); 3.93 (dd, J=6, 8.1 Hz, 1H, H-3′); 1.61 (sept, J=6.9 Hz, 1H, CH(CH_3)$_2$); 1.51 (s, 9H, (CH_3)$_3$C); 1.37 (s, 3H, CCH_3); 1.27 (s, 3H, CCH_3); 0.87 (d, J=6.9 Hz, 6H, CH(CH_3)$_2$); 0.84 (s, 3H, CH_3 thexyl); 0.83 (s, 3H, CH_3 thexyl); 0.14 (s, 3H, CH_3–Si); −0.06 (s, 3H, CH_3–Si). ^{13}C NMR (62.5 MHz, CD_3OD/$CDCl_3$: 9/1) δ (ppm): 162.30 (C=O); 154.20 (C-2); 135.80 (C-4); 135.50 (C-5); 110.80 (C(CH_3)$_2$); 82.90 (C(CH_3)$_3$); 81.35 (C-2′); 71.15 (C-1′); 67.45 (C-3′); 35.30 (CH(CH_3)$_2$); 28.50 (C(CH$_3$)$_3$); 25.40 (CCH$_3$); 25.95 (Si–C(CH_3)$_2$(C_3H_7)); 27.05 (CCH$_3$); 19.10–20.80 (4 CH$_3$ thexyl); −2.62 (CH$_3$–Si); −2.06 (CH$_3$–Si).

3.8.4. (5-{(2,2-Dimethyl-[1,3]dioxolan-4-yl)-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-methyl}-thiazol-2-yl)-carbamic acid *tert*-butyl ester 22B. Yield: 99%, 124 mg. $C_{22}H_{40}N_2O_5SSi$. White solid. R_f: 0.9 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) m/z: 473 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1716 (carbamate). UV (λ, nm [ϵ]): 263 (12900). $[\alpha]_D$=−28 (c=2.8; ethanol). ^1H NMR (250 MHz) δ (ppm): 7.20 (s large, 1H, H-4); 5.30 (d, J=6.1 Hz, 1H, H-1′); 4.25 (m, 1H, H-2′); 3.89 (dd, J=6.7, 8.6 Hz, 1H, H-3′); 3.74 (dd, J=6.4, 8.6 Hz, 1H, H-3′); 1.59 (sept, J=6.9 Hz, 1H, CH(CH_3)$_2$); 1.58 (s, 9H, (CH_3)$_3$C); 1.35 (s, 3H, CCH_3); 1.34 (s, 3H, CCH_3); 0.87 (d, J=6.9 Hz, 6H, CH(CH_3)$_2$); 0.86 (s, 3H, CH_3 thexyl); 0.84 (s, 3H, CH_3 thexyl); 0.15 (s, 3H, CH_3–Si); −0.03 (s, 3H, CH_3–Si). ^{13}C NMR (62.5 MHz) δ (ppm): 162.00 (C=O); 152.95 (C-2); 133.95 (C-4); 131.00 (C-5); 110.05 (C(CH_3)$_2$); 81.90 (C(CH_3)$_3$); 79.40 (C-2′); 70.75 (C-1′); 65.70 (C-3′); 34.20 (CH(CH_3)$_2$); 28.50 (C(CH$_3$)$_3$); 25.30–26.55 (C(CH$_3$)$_2$); 25.13 (Si–C(CH_3)$_2$(C_3H_7)); 18.60–18.65–20.25–20.35 (4CH$_3$ thexyl); 10.20–10.45 ((CH$_3$)$_2$–Si).

3.9. Selective deprotection of the 2′,3′-hydroxyles. Compounds 10A, 10B, 11, 12A, 12B, 23A, 23B

The acetonide (1 equiv.) was dissolved in THF (0.25 mmol/mL) and treated with PTSA (1.5 equiv.). After stirring for 6 days at 4°C, the mixture was neutralized by addition of a 32% ammonia solution. After filtration, solvent was removed under reduced pressure and the residue was purified by flash chromatography (dichloromethane/methanol: 99/1).

3.9.1. *N*-(5-{1-[Dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-2,3-dihydroxy-propyl}-thiazol-2-yl)-2,2-dimethyl-propionamide 12A. Yield: 73%, 3.4 g. $C_{19}H_{36}N_2O_4SSi$. White solid. R_f: 0.3 (CH_2Cl_2/MeOH: 95/5, revealed UV). MS CI (T=180°C) m/z: 473 $(M+57)^+$; 417 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3426 (NH), 3400–3200 (alcohol), 1683 (amide). UV (λ, nm [ϵ]): 272 (14000). $[\alpha]_D$=−37 (c=1.62; ethanol). ^1H NMR (250 MHz, $CDCl_3$+1 drop D_2O) δ (ppm): 7.30 (s, 1H, H-4); 4.98 (d, J=6.5 Hz, 1H, H-1′); 3.75 (ddd, J=3.6, 6.5, 11.6 Hz, 1H, H-2′); 3.67 (dd, J=3.6, 11.6 Hz, 1H, H-3′); 3.45 (dd, J=5.1, 11.6 Hz, 1H, H-3′); 1.63 (sept, J=6.8 Hz, 1H, CH(CH_3)$_2$); 1.32 (s, 9H, (CH_3)$_3$C); 0.89 (d, J=6.8 Hz, 3H, CHCH_3); 0.88 (d, J=6.8 Hz, 3H, CHCH_3); 0.86 (s, 3H, CH_3 thexyl); 0.84 (s, 3H, CH_3 thexyl); 0.16 (s, 3H, CH_3–Si); −0.05 (s, 3H, CH_3–Si). ^{13}C NMR (62.5 MHz) δ (ppm): 176.35 (C=O); 159.40 (C-2); 134.65 (C-4); 132.75 (C-5).; 76.25 (C-1′); 69.70 (C-2′); 62.35 (C-3′); 39.15 (C(CH_3)$_3$); 34.10 (CH(CH_3)$_2$); 27.20 (C(CH$_3$)$_3$); 25.05 (Si–C(CH_3)$_2$(C_3H_7)); 18.50–18.70–20.10–20.40 (4CH$_3$ thexyl); −2.40 (Si–CH$_3$).; −3.20 (Si–CH$_3$). HRMS: m/z calcd for $C_{19}H_{37}N_2O_4SSi$: 417.2243; found: 417.2224.

3.9.2. *N*-(5-{1-[Dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-2,3-dihydroxy-propyl}-thiazol-2-yl)-2,2-dimethyl-propionamide 12B. Yield: 72%, 2.3 g. $C_{19}H_{36}N_2O_4SSi$. White solid. Mp=77°C. R_f: 0.3 (CH_2Cl_2/MeOH: 95/5). MS CI (T=180°C) m/z: 473 $(M+57)^+$; 417 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3426 (NH), 3400–3200 (alcohol), 1683 (amide). UV (λ, nm [ϵ]): 271 (14200). $[\alpha]_D$=+47 (c=1.6; ethanol). ^1H NMR (400 MHz) δ (ppm): 9.27 (s large, 1H, NH); 7.26 (s, 1H, H-4); 4.93 (d, J=5.6 Hz, 1H, H-1′); 3.80 (m, 1H, H-2′); 3.69 (m, 2H, H-3′); 1.63 (sept, J=6.8 Hz, 1H, CH(CH_3)$_2$); 1.32 (s, 9H, (CH_3)$_3$C); 0.88 (d, J=6.8 Hz, 3H, CHCH_3); 0.87 (d, J=6.8 Hz, 3H, CHCH_3); 0.85 (s, 3H, CH_3 thexyl); 0.84 (s, 3H, CH_3 thexyl); 0.16 (s, 3H, CH_3–Si); −0.04 (s, 3H, CH_3–Si). ^{13}C NMR (62.5 MHz) δ (ppm): 176.15 (C=O); 159.10 (C-2); 134.90 (C-4); 133.20 (C-5); 75.80 (C-1′); 70.70 (C-2′); 63.05 (C-3′); 39.80 (C(CH_3)$_3$); 34.20 (CH(CH_3)$_2$); 27.30 (C(CH$_3$)$_3$); 25.10 (Si–C(CH_3)$_2$(C_3H_7)); 18.70–18.80–20.20–20.25 (4CH$_3$ thexyl); 10.00–10.70 (Si–(CH$_3$)$_2$). Calcd for $C_{19}H_{36}N_2O_4SSi$: C, 54.77; H, 8.71; N, 6.72. Found: C, 54.61; H, 8.52; N, 6.71%.

The product **10A** was isolated after chromatography with dichloromethane/methanol: 95/5, as secondary product from the formation of compound **12** when more than 1.5 equiv. of PTSA was used in methanol as solvent.

3.9.3. 2,2-Dimethyl-*N*-[5-(1,2,3-trihydroxy-propyl)-thiazol-2-yl]-propionamide 10A. $C_{11}H_{18}N_2O_4S$. R_f: 0.1

(CH_2Cl_2/MeOH: 90/10). MS CI (T=190°C) m/z: 275 $(M+H)^+$. IR (KBr, ν_{max}, cm^{-1}): 1654 (C=O). UV (λ, nm [ϵ]): 270 (17700). $[\alpha]_D$=−77 [c=0.09; $(NH_4)_6Mo_7O_{24}.4H_2O$]. ^{1}H NMR (250 MHz, CD_3OD) δ (ppm): 7.30 (s, 1H, H-4); 4.89 (d, J=4.7 Hz, 1H, H-1′); 3.7 (m, 1H, H-2′); 3.60 (dd, J=4.7, 11 Hz, 1H, H-3′); 3.45 (dd, J=6.1, 11 Hz, 1H, H-3′); 1.26 (s, 9H, $(CH_3)_3C$). ^{13}C NMR (62.5 MHz, CD_3OD) δ (ppm): 178.65 (C=O); 160.50 (C-2); 135.55 (C-4); 134.90 (C-5); 76.60 (C-2′); 69.30 (C-1′); 64.00 (C-3′); 40.10 ($C(CH_3)_3$); 27.30 ($C(CH_3)_3$). HRMS: m/z calcd for $C_{11}H_{19}N_2O_4S$: 275.1065; found: 275.1091.

The product **10B** was isolated after chromatography with dichloromethane/methanol: 95/5, as secondary product from the formation of compound **12** when more than 1.5 equiv. of PTSA was used in methanol.

3.9.4. 2,2-Dimethyl-*N*-[5-(1,2,3-trihydroxy-propyl)-thiazol-2-yl]-propionamide 10B. $C_{11}H_{18}N_2O_4S$. White solid. R_f: 0.1 (CH_2Cl_2/MeOH: 90/10). MS CI (T=200°C) m/z: 275 (M+H)+, 257 $(M-H_2O)^+$. IR (KBr, ν_{max}, cm^{-1}): 1654 (C=O). UV (λ, nm [ϵ]): 272 (19500). $[\alpha]_D$=+65 [c=0.08; $(NH_4)_6Mo_7O_{24}.4H_2O$]. ^{1}H NMR (250 MHz, pyridine-D_5) δ (ppm): 8.00 (s, 1H, H-4); 5.78 (d, J=6.1 Hz, 1H, H-1′); 4.72 (m, 1H, H-2′); 4.50 (m, 1H, H-3′); 1.48 (s, 9H, $(CH_3)_3C$). ^{13}C NMR (62.5 MHz, pyridine-D_5) δ (ppm): 177.05 (C=O); 159.90 (C-2); 135.80 (C-4); 135.50 (C-5); 76.80 (C-2′); 70.60 (C-1′); 64.90 (C-3′); 39.40 ($C(CH_3)_3$); 27.30 ($C(CH_3)_3$).

The mixture of inseparable products **11** was isolated after chromatography with dichloromethane/methanol: 98/2, as secondary product from the formation of compound **12** when more than 1.5 equiv. of PTSA was used in methanol.

3.9.5. *N*-[5-(2,3-Dihydroxy-1-methoxy-propyl)-thiazol-2-yl]-2,2-dimethyl-propionamide 11. $C_{12}H_{20}N_2O_4S$. White solid. R_f: 0.4 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) m/z: 289 $(M+H)^+$; 270 $(M-H_2O)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3424 (NH), 3400–3200 (OH), 1682 (amide). *Major compound*. ^{1}H NMR (250 MHz) δ (ppm): 9.57 (s large, 1H, NH); 7.31 (s, 1H, H-5); 4.45 (d, J=6 Hz, 1H, H-1′); 3.93 (m, 1H, H-2′); 3.71 (m, 1H, H-3′); 3.25 (s, 3H, CH_3O); 1.31 (s, 9H, $(CH_3)_3C$). ^{13}C NMR (75 MHz) δ (ppm): 176.90 (C=O); 160.45 (C-2); 137.15 (C-4); 129.90 (C-5); 79.14 (C-1′); 75.55 (C-2′); 63.70 (C-3′); 57.20 (CH_3–O); 39.60 ($C(CH_3)_3$); 27.55 ($C(CH_3)_3$). *Minor compound*. ^{1}H NMR (250 MHz) δ (ppm): 9.57 (s large, 1H, NH); 7.36 (s, 1H, H-5); 4.48 (d, J=8 Hz, 1H, H-1′); 3.84 (m, 1H, H-2′); 3.67 (m, 1H, H-3′); 3.28 (s, 3H, CH_3O); 1.31 (s, 9H, $(CH_3)_3C$). ^{13}C NMR (75 MHz) δ (ppm): 176.90 (C=O); 160.40 (C-2); 137.20 (C-4); 129.50 (C-5); 78.50 (C-1′); 74.55 (C-2′); 63.00 (C-3′); 57.00 (CH_3-O); 39.60 ($C(CH_3)_3$); 27.55 ($C(CH_3)_3$).

3.9.6. (5-{1-[Dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-2,3-dihydroxy-propyl}-thiazol-2-yl)-carbamic acid *tert*-butyl ester 23A. Yield: 68%, 6.8 g. $C_{19}H_{36}N_2O_5SSi$. White solid. R_f: 0.3 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) m/z: 489 $(M+57)^+$; 433 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1719 (carbamate). UV (λ, nm [ϵ]): 263 (10400). $[\alpha]_D$=−48 (c=1.02; ethanol). ^{1}H NMR (250 MHz) δ (ppm): 12.1 (s large, 1H, NH); 7.22 (s, 1H, H-4); 4.91 (d, J=6.6 Hz, 1H, H-1′); 3.73 (m, 1H, H-2′); 3.64 (dd, J=3.3, 11.6 Hz, 1H, H-3′); 3.44 (dd, J=5.1, 11.6 Hz, 1H, H-3′); 1.57 (sept, J=6.9 Hz, 1H, $CH(CH_3)_2$); 1.55 (s, 9H, $(CH_3)_3C$); 0.87 (d, J=6.9 Hz, 3H, $CHCH_3$); 0.86 (d, J=6.9 Hz, 3H, $CHCH_3$); 0.83 (s, 3H, CH_3 thexyl); 0.82 (s, 3H, CH_3 thexyl); 0.14 (s, 3H, CH_3–Si); −0.06 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz) δ (ppm): 162.45 (C=O); 152.05 (C-2); 134.90 (C-4); 131.40 (C-5); 82.35 ($C(CH_3)_3$); 76.50 (C-2′); 69.90 (C-1′); 62.60 (C-3′); 34.35 ($CH(CH_3)_2$); 28.60 ($C(CH_3)_3$); 25.30 (Si–$C(CH_3)_2(C_3H_7)$); 18.80–19.00–20.35–20.70 ($4CH_3$ thexyl); −2.05 (Si–CH_3); −2.90 (Si–CH_3). HRMS: m/z calcd for $C_{19}H_{37}N_2O_5SSi$: 433.2192; found: 433.2204.

3.9.7. (5-{1-[Dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-2,3-dihydroxy-propyl}-thiazol-2-yl)-carbamic acid *tert*-butyl ester 23B. Yield: 68%, 5.3 g. $C_{19}H_{36}N_2O_5SSi$. White solid. Mp=78°C. R_f: 0.3 (CH_2Cl_2/MeOH: 95/5). MS ESI (methanol) m/z: 455 $(M+Na)^+$; 433 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1719 (carbamate). UV (λ, nm [ϵ]): 263 (10600). $[\alpha]_D$=+59 (c=0.94; ethanol). ^{1}H NMR (250 MHz) δ (ppm): 11.90 (s large, 1H, NH); 7.19 (s, 1H, H-4); 4.88 (d, J=5.5 Hz, 1H, H-1′); 3.81 (m, 1H, H-2′); 3.68 (m, 2H, H-3′); 1.59 (sept, J=6.9 Hz, 1H, $CH(CH_3)_2$); 1.56 (s, 9H, $(CH_3)_3C$); 0.88 (d, J=6.9 Hz, 3H, $CHCH_3$); 0.87 (d, J=6.9 Hz, 3H, $CHCH_3$); 0.84 (s, 3H, CH_3 thexyl); 0.83 (s, 3H, CH_3 thexyl); 0.15 (s, 3H, CH_3–Si); −0.34 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz) δ (ppm): 162.40 (C=O); 152.80 (C-2); 134.70 (C-4); 131.40 (C-5); 82.15 ($C(CH_3)_3$); 75.70 (C-2′); 70.55 (C-1′); 63.00 (C-3′); 34.10 ($CH(CH_3)_2$); 28.40 ($C(CH_3)_3$); 25.05 (Si–$C(CH_3)_2(C_3H_7)$); 18.35–18.75–20.20–20.35 ($4CH_3$ thexyl); −2.35 (Si–CH_3); −3.10 (Si–CH_3). Calcd for $C_{19}H_{36}N_2O_5SSi$: C, 52.75; H, 8.39; N, 6.47; found: C, 52.61; H, 8.43; N, 6.16.

3.10. Dichlorination of 2′- and 3′-hydroxyles. Compounds 13A, 13B, 14A, 14B, 24A, 24B

The diol (1 equiv.) was dissolved in THF (0.2 mmol/mL) and treated with triphenylphosphine (2.5 equiv.) and *N*-chlorosuccinimide (2.5 equiv.). Mixture was refluxed for 12 h. Solvent was removed under reduced pressure and the residue purified by flash chromatography (dichloromethane/methanol: 98/2).

3.10.1. *N*-(5-{2,3-Dichloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-yl)-2,2-dimethyl-propionamide 14A. Yield: 60%, 834 mg. $C_{19}H_{34}Cl_2N_2O_2SSi$. White solid. R_f: 0.7 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) m/z: 453/455/457 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3424 (NH), 2965–2870 (CH), 1683 (amide), 1407–1289 (C–Cl). UV (λ, nm [ϵ]): 270 (10900). $[\alpha]_D$=−36 (c=1.09; ethanol). ^{1}H NMR (200 MHz) δ (ppm): 9.72 (s large, 1H, NH); 7.37 (s, 1H, H-4); 5.23 (d, J=6.1 Hz, 1H, H-1′); 4.19 (m, 1H, H-2′); 3.87 (dd, J=5, 11.7 Hz, 1H, H-3′); 3.72 (dd, J=5.3, 11.7 Hz, 1H, H-3′); 1.63 (sept, J=6.9 Hz, 1H, $CH(CH_3)_2$); 1.31 (s, 9H, $(CH_3)_3C$); 0.90 (d, J=6.9 Hz, 3H, $CHCH_3$); 0.89 (d, J=6.9 Hz, 3H, $CHCH_3$); 0.86 (s, 3H, CH_3 thexyl); 0.84 (s, 3H, CH_3 thexyl); 0.20 (s, 3H, CH_3–Si); −0.05 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz) δ (ppm): 176.60 (C=O); 159.55 (C-2); 135.95 (C-4); 132.15 (C-5); 70.00 (C-1′); 65.10 (C-2′); 45.85 (C-3′); 39.50 ($C(CH_3)_3$); 34.10 ($CH(CH_3)_2$); 27.70

($C(CH_3)_3$); 25.15 (Si–$C(CH_3)_2(C_3H_7)$); 18.95–19.05–20.50–20.70 ($4CH_3$ thexyl); −2.10 (CH_3–Si); −3.15 (CH_3–Si).

3.10.2. *N*-(5-{2,3-Dichloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-yl)-2,2-dimethyl-propionamide 14B. Yield: 56%, 1.15 g. $C_{19}H_{34}Cl_2N_2O_2SSi$. R_f: 0.7 (CH_2Cl_2/MeOH: 95/5). MS CI (T=180°C) *m/z*: 453/455/457 $(M+H)^+$, 383 $(M-2Cl)^+$, 369/371/373 $(M-Piv)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3424 (NH), 2965–2870 (CH), 1683 (amide), 1407–1289 (C–Cl). UV (λ, nm [ϵ]): 272 (15000). $[\alpha]_D$=+31 (c=1.02; ethanol). ^{1}H NMR (250 MHz) δ (ppm): 9.77 (s large, 1H, NH); 7.39 (s, 1H, H-4); 5.31 (d, J=3.9 Hz, 1H, H-1′); 4.08 (m, 1H, H-2′); 3.90 (dd, J=6.2, 11.5 Hz, 1H, H-3′); 3.53 (dd, J=5.9, 11.5 Hz, 1H, H-3′); 1.64 (sept, J=6.8 Hz, 1H, CH(CH_3)$_2$); 1.31 (s, 9H, (CH_3)$_3$C); 0.90 (d, J=6.8 Hz, 3H, CHCH_3); 0.89 (d, J=6.8 Hz, 3H, CHCH_3); 0.88 (s, 3H, CH_3 thexyl); 0.87 (s, 3H, CH_3 thexyl); 0.19 (s, 3H, CH_3–Si); −0.04 (s, 3H, CH_3–Si). ^{13}C NMR (62.5 MHz) δ (ppm): 159.50 (C-2); 136.45 (C-4); 132.00 (C-5); 69.45 (C-1′); 65.70 (C-2′); 46.80 (C-3′); 40.90 ($C(CH_3)_3$); 34.25 ($CH(CH_3)_2$); 27.45 (C(CH_3)$_3$); 27.30 (Si–$C(CH_3)_2(C_3H_7)$); 18.70–18.80–20.30–20.40 ($4CH_3$ thexyl); 10.10–10.70 (Si–(CH_3)$_2$).

The product **13A** of monochlorination was isolated with 81% yield (88 mg) when only 2 equiv. of NCS and PPh_3 were used.

3.10.3. *N*-(5-{3-Chloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-2-hydroxy-propyl}-thiazol-2-yl)-2,2-dimethyl-propionamide 13A. $C_{19}H_{35}ClN_2O_3SSi$. R_f: 0.4 (CH_2Cl_2/MeOH: 95/5). MS CI (T=180°C) *m/z*: 435/437 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3425 (NH), 3400–3200 (OH), 2965–2870 (CH_3), 1682 (amide), 1467–1289 (C-Cl). UV (λ, nm [ϵ]): 271 (8700). $[\alpha]_D$=−29 (c=2.33; ethanol). ^{1}H NMR (300 MHz) δ (ppm): 9.92 (s large, 1H, NH); 7.35 (s, 1H, H-5); 5.11 (d, J=4.7 Hz, 1H, H-1′); 3.85 (m, 1H, H-2′); 3.61 (dd, J=5.3, 11.3 Hz, 1H, H-3′); 3.40 (dd, J=5.5, 11.3 Hz, 1H, H-3′); 3.08 (s large, 1H, OH); 1.62 (sept, J=6.8 Hz, 1H, CH(CH_3)$_2$); 1.30 (s, 9H, (CH_3)$_3$C); 0.89 (d, J=6.8 Hz, 3H, CHCH_3); 0.88 (d, J=6.8 Hz, 3H, CHCH_3); 0.86 (s, 3H, CH_3 thexyl); 0.85 (s, 3H, CH_3 thexyl); 0.18 (s, 3H, CH_3–Si); −0.03 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz) δ (ppm): 176.40 (C=O); 159.70 (C-2); 134.95 (C-4); 132.35 (C-5); 75.70 (C-2′); 69.40 (C-1′); 44.90 (C-3′); 39.20 ($C(CH_3)_3$); 34.20 ($CH(CH_3)_2$); 27.25 (C(CH_3)$_3$); 25.15 (Si–$C(CH_3)_2(C_3H_7)$); 18.60–18.75–20.20–20.45 ($4CH_3$ thexyl); −2.40 (CH_3–Si); −3.10 (CH_3–Si). HRMS: *m/z* calcd for $C_{19}H_{36}ClN_2O_3SSi$: 435.1904 and 437.1874; found: 435.1887 and 437.1852.

The product **13B** of monochlorination was isolated with 83% yield (59 mg) when only 2 equiv. of NCS and PPh_3 were used.

3.10.4. *N*-(5-{3-Chloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-2-hydroxy-propyl}-thiazol-2-yl)-2,2-dimethyl-propionamide 13B. $C_{19}H_{35}ClN_2O_3SSi$. White solid. R_f: 0.4 (CH_2Cl_2/MeOH: 95/5). MS CI (T=180°C) *m/z*: 435/437 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3425 (NH), 3400–3200 (OH), 2965–2870 (CH), 1682 (amide), 1467–1289 (C–Cl). UV (λ, nm [ϵ]): 272 (7600). $[\alpha]_D$=+49 (c=3.04; ethanol). ^{1}H NMR (250 MHz) δ (ppm): 9.66 (s large, 1H, NH); 7.30 (s, 1H, H-5); 4.99 (d, J=5.8 Hz, 1H, H-1′); 3.96 (m, 1H, H-2′); 3.70 (dd, J=5.3, 11.2 Hz, 1H, H-3′); 3.54 (dd, J=4.8, 11.2 Hz, 1H, H-3′); 3.00 (s large, 1H, OH); 1.62 (sept, J=6.8 Hz, 1H, CH(CH_3)$_2$); 1.30 (s, 9H, (CH_3)$_3$C); 0.88 (d, J=6.8 Hz, 3H, CHCH_3); 0.87 (d, J=6.8 Hz, 3H, CHCH_3); 0.84 (s, 3H, CH_3 thexyl); 0.83 (s, 3H, CH_3 thexyl); 0.17 (s, 3H, CH_3–Si); −0.05 (s, 3H, CH_3–Si). ^{13}C NMR (62.5 MHz) δ (ppm): 176.30 (C=O); 159.60 (C-2); 135.40 (C-4); 132.20 (C-5); 75.25 (C-2′); 70.05 (C-1′); 45.65 (C-3′); 39.20 ($C(CH_3)_3$); 34.15 ($CH(CH_3)_2$); 27.25 (C(CH_3)$_3$); 25.10 (Si–$C(CH_3)_2(C_3H_7)$); 18.65–18.75–20.20–20.40 ($4CH_3$ thexyl); 9.94–10.67 (Si–(CH_3)$_2$).

3.10.5. (5-{2,3-Dichloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-yl)-carbamic acid *tert*-butyl ester 24A. Yield: 59%, 1.99 g. $C_{19}H_{34}Cl_2N_2O_3SSi$. White solid. R_f: 0.6 (CH_2Cl_2/MeOH: 95/5). MS CI (T=180°C) *m/z*: 469/471/473 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1718. UV (λ, nm [ϵ]): 263 (12400). $[\alpha]_D$=−30 (c=1.1; ethanol). ^{1}H NMR (250 MHz) δ (ppm): 12.38 (s large, 1H, NH); 7.28 (s, 1H, H-4); 5.19 (d, J=6.1 Hz, 1H, H-1′); 4.19 (m, 1H, H-2′); 3.95 (dd, J=4.7, 11.7 Hz, 1H, H-3′); 3.72 (dd, J=5.7, 11.7 Hz, 1H, H-3′); 1.60 (sept, J=6.9 Hz, 1H, CH(CH_3)$_2$); 1.59 (s, 9H, (CH_3)$_3$C); 0.88 (d, J=6.9 Hz, 6H, CH(CH_3)$_2$); 0.85 (s, 3H, CH_3 thexyl); 0.84 (s, 3H, CH_3 thexyl); 0.13 (s, 3H, CH_3–Si); −0.37 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz) δ (ppm): 162.60 (C=O); 153.00 (C-2); 135.55 (C-4); 130.40 (C-5); 82.20 ($C(CH_3)_3$); 70.00 (C-1′); 64.90 (C-2′); 45.80 (C-3′); 34.25 ($CH(CH_3)_2$); 28.50 (CH(CH_3)$_3$); 25.20 ($C(CH_3)_2$ (C_3H_7)); 18.70–18.85–20.45 (4 CH_3 thexyl); −2.40 (CH_3–Si); −3.10 (CH_3–Si).

3.10.6. (5-{2,3-Dichloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-yl)-carbamic acid *tert*-butyl ester 24B. Yield: 54%, 1.42 g. $C_{19}H_{34}Cl_2N_2O_3SSi$. White solid. R_f: 0.6 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) *m/z*: 469/471/473 $(M+H)^+$, 369/371/373 $(M+H\text{-Boc})^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1718 (carbamate). UV (λ, nm [ϵ]): 263 (7500). $[\alpha]_D$=+24 (c=1.2; ethanol). ^{1}H NMR (250 MHz) δ (ppm): 9.86 (s large, 1H, NH); 7.31 (s, 1H, H-4); 5.26 (d, J=4.3 Hz, 1H, H-1′); 4.10 (m, 1H, H-2′); 3.89 (dd, J=6, 13.6 Hz, 1H, H-3′); 3.58 (dd, J=5.7, 13.6 Hz, 1H, H-3′); 1.62 (sept, J=6.9 Hz, 1H, CH(CH_3)$_2$); 1.58 (s, 9H, (CH_3)$_3$C); 0.90 (d, J=6.9 Hz, 3H, CHCH_3); 0.89 (d, J=6.9 Hz, 3H, CHCH_3); 0.87 (s, 3H, CH_3 thexyl); 0.86 (s, 3H, CH_3 thexyl); 0.19 (s, 3H, CH_3–Si); −0.20 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz) δ (ppm): 162.30 (C=O); 152.75 (C-2); 134.90 (C-4); 130.10 (C-5); 82.05 ($C(CH_3)_3$); 69.50 (C-1′); 64.50 (C-2′); 45.20 (C-3′); 34.10 ($CH(CH_3)_2$); 28.30 ((CH_3)$_3$C); 25.10 ($C(CH_3)_2(C_3H_7)$); 20.25 ($CH(CH_3)_2$); 18.55–18.60–20.10 (4 CH_3 thexyl); −2.60 (CH_3–Si); −3.30 (CH_3–Si).

3.11. Substitution of the terminal chlorine by an azido group. Compounds 15A, 15B, 25A, 25B, 34A, 34B

The dichloro compound (1 equiv.) was dissolved in DMF (0.2 mmol/mL) and treated with sodium azide (1.5 equiv.). After heating at 80°C for 12 h, solvent was removed under reduced pressure and the residue was purified by flash chromatography (dichloromethane/methanol: 99/1).

3.11.1. *N*-(5-{3-Azido-2-chloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-yl)-2,2-dimethyl-propionamide 15A. Yield: 91%, 548 mg. $C_{19}H_{34}ClN_5O_2SSi$. White solid. R_f: 0.4 (CH_2Cl_2/MeOH:

95/5). MS CI (T=180°C) m/z: 460/462 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 2966–2870 (CH), 2107 (azide), 1682 (amide). UV (λ, nm [ϵ]): 270 (13400). $[\alpha]_D$=−45 (c=0.68; ethanol). ^1H NMR (250 MHz) δ (ppm): 9.91 (s large,1H, NH); 7.35 (s, 1H, H-5); 5.08 (d, J=6.7 Hz, 1H, H-1′); 4.05 (ddd, J=3.9, 5.3, 6.7 Hz, 1H, H-2′); 3.74 (dd, J=5.3, 13 Hz, 1H, H-3′); 3.68 (dd, J=3.9, 13 Hz, 1H, H-3′); 1.62 (sept, J=6.8 Hz, 1H, CH(CH_3)$_2$); 1.30 (s, 9H, (CH_3)$_3$C); 0.89 (d, J=6.8 Hz, 3H, CHCH_3); 0.88 (d, J=6.8 Hz, 3H, CHCH_3); 0.85 (s, 3H, CH_3 thexyl); 0.84 (s, 3H, CH_3 thexyl); 0.19 (s, 3H, CH_3–Si); −0.06 (s, 3H, CH_3–Si). ^{13}C NMR (62.5 MHz) δ (ppm): 176.55 (C=O); 159.60 (C-2); 135.75 (C-4); 132.90 (C-5); 70.60 (C-1′); 64.90 (C-2′); 53.40 (C-3′); 39.25 (C(CH_3)$_3$); 34.10 (CH(CH_3)$_2$); 27.30 (C(CH$_3$)$_3$); 25.15 (Si–C(CH_3)$_2$(C_3H_7)); 18.70–18.75–20.20–20.40 (4 CH$_3$ thexyl); −2.40 (CH$_3$–Si); −3.15 (CH$_3$–Si). HRMS: m/z calcd for $C_{19}H_{35}ClN_5O_2SSi$: 460.1969 and 462.1939; found: 460.1981 and 462.1965.

3.11.2. *N*-(5-{3-Azido-2-chloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-yl)-2,2-dimethyl-propionamide 15B. Yield: 70%, 345 mg. $C_{19}H_{34}ClN_5O_2SSi$. White solid. R_f: 0.4 (CH_2Cl_2/MeOH: 95/5). MS CI (T=180°C) m/z: 460/462 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 2966–2869 (CH), 2107 (azide), 1682 (amide). UV (λ, nm [ϵ]): 271 (20900). $[\alpha]_D$=+13 (c=2.41; ethanol). ^1H NMR (250 MHz) δ (ppm): 10.00 (s large, 1H, NH); 7.37 (s, 1H, H-5); 5.13 (d, J=4.9 Hz, 1H, H-1′); 4.05 (ddd, J=4, 4.9, 7.4 Hz, 1H, H-2′); 3.70 (dd, J=4, 13 Hz, 1H, H-3′); 3.33 (dd, J=7.4, 13 Hz, 1H, H-3′); 1.63 (sept, J=6.8 Hz, 1H, CH(CH_3)$_2$); 1.31 (s, 9H, (CH_3)$_3$C); 0.89 (d, J=6.8 Hz, 6H, CH(CH_3)$_2$); 0.86 (s, 3H, CH_3 thexyl); 0.85 (s, 3H, CH_3 thexyl); 0.18 (s, 3H, CH_3–Si); −0.02 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz) δ (ppm): 176.65 (C=O); 159.75 (C-2); 135.60 (C-4); 131.55 (C-5); 70.75 (C-1′); 64.60 (C-2′); 53.65 (C-3′); 39.40 (C(CH_3)$_3$); 34.30 (CH(CH_3)$_2$); 27.40 (C(CH$_3$)$_3$); 25.30 (Si–C(CH_3)$_2$(C_3H_7)); 18.85–20.45 (4 CH$_3$ thexyl); −2.45 (CH$_3$–Si); −3.00 (CH$_3$–Si).

3.11.3. (5-{3-Azido, 2-dichloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-yl)-carbamic acid *tert*-butyl ester 25A. Yield: 87%, 500 mg. $C_{19}H_{34}Cl_2N_5O_3SSi$. White solid. R_f: 0.4 (CH_2Cl_2/MeOH: 95/5). MS CI (T=180°C) m/z: 476/478 $(M+H)^+$, 376/378 $(M+H\text{-Boc})^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 2107 (azide), 1717 (C=O). UV (λ, nm [ϵ]): 263 (12000). $[\alpha]_D$=−57 (c=5.38; ethanol). ^1H NMR (300 MHz) δ (ppm): 9.83 (s large, 1H, NH); 7.24 (s, 1H, H-4); 5.02 (d, J=6.8 Hz, 1H, H-1′); 4.04 (m, 1H, H-2′); 3.75 (sys ABX, J=4.7, 13 Hz, 1H, H-3′); 3.70 (sys ABX, J=3.3, 13 Hz, 1H, H-3′); 1.61 (sept, J=6.8 Hz, 1H, CH(CH_3)$_2$); 1.59 (s, 9H, (CH_3)$_3$C); 0.89 (d, J=6.8 Hz, 3H, CHCH_3); 0.88 (d, J=6.8 Hz, 3H, CHCH_3); 0.85 (s, 3H, CH_3 thexyl); 0.84 (s, 3H, CH_3 thexyl); 0.19 (s, 3H, CH_3–Si); −0.05 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz) δ (ppm): 162.10 (C=O); 152.65 (C-2); 135.05 (C-4); 130.95 (C-5); 81.90 (C(CH_3)$_3$); 70.35 (C-1′); 64.55 (C-2′); 53.25 (C-3′); 33.85 (CH(CH_3)$_2$); 28.20 (C(CH$_3$)$_3$); 24.90 (C(CH_3)$_2$(C_3H_7)); 18.40–18.50–19.90–20.10 (4 CH$_3$ thexyl); −2.65 (CH$_3$–Si); −3.40 (CH$_3$–Si).

3.11.4. 5-{3-Azido-2-dichloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-yl)-carbamic acid *tert*-butyl ester 25B. Yield: 85%, 805 mg. $C_{19}H_{34}Cl_2N_5O_3SSi$. R_f: 0.4 (CH_2Cl_2/MeOH: 95/5). MS CI (T=180°C) m/z: 476/478 $(M+H)^+$; 399; 376/378 $(M+H\text{-Boc})^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 2107 (azide), 1717 (C=O). UV (λ, nm [ϵ]): 263 (24300). $[\alpha]_D$=+13 (c=5.38, ethanol). ^1H NMR (250 MHz) δ (ppm): 11.97 (s, 1H, NH); 7.20 (s, 1H, H-4); 5.00 (d, J=5.2 Hz, 1H, H-1′); 4.04 (ddd, J=5.2, 3.9, 7.2 Hz, 1H, H-2′); 3.97 (dd, J=3.9, 13 Hz, 1H, H-3′); 3.62 (dd, J=7.2, 13 Hz, 1H, H-3′); 1.52 (sept, J=6.9 Hz, 1H, CH(CH_3)$_2$); 1.50 (s, 9H, (CH_3)$_3$C); 0.88 (d, J=6.9 Hz, 6H, CH(CH_3)$_2$); 0.85 (s, 3H, CH_3 thexyl); 0.84 (s, 3H, CH_3 thexyl); 0.09 (s, 3H, CH_3–Si); −0.9 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz) δ (ppm): 162.35 (C=O); 135.05 (C-4); 129.90 (C-5); 82.75 (C(CH_3)$_3$); 70.75 (C-1′); 64.60 (C-2′); 53.65 (C-3′); 34.20 (CH(CH_3)$_2$); 28.40 (C(CH$_3$)$_3$); 25.25 (C(CH_3)$_2$(C_3H_7)); 18.50–20.30–20.35 (4 CH$_3$ thexyl); −2.50 (CH$_3$–Si); −3.10 (CH$_3$–Si).

3.12. Hydrogenation of the terminal azido group. Compounds: 16A, 16B, 26A, 26B, 28A, 30A, 30B, 32A, 32B

After bubbling a stream of argon through a solution of azide (1 equiv.) in ethanol (0.7 mmol/mL), palladium on activated carbon, 5% Pd (0.1 equiv.) was added and the mixture was stirred under one atmosphere of H_2 for 12 h. The solution was then filtered through a Celite® pad to remove catalyst and the solvent removed under reduced pressure. The residue was purified by flash chromatography (dichloromethane/methanol: 98/2).

3.12.1. *N*-(5-{3-Amino-2-chloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-yl)-2,2-dimethyl-propionamide 16A. Yield: 61%, 19 mg. $C_{19}H_{36}ClN_3O_2SSi$. White solid. R_f: 0.2 (CH_2Cl_2/MeOH: 95/5). MS CI (T=180°C) m/z: 434/436 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3425 (NH), 2964–2870 (CH), 1683 (amide), 1410–1256 (C–Cl). UV (λ, nm [ϵ]): 270 (16100). $[\alpha]_D$=−32 (c=1.13; ethanol). ^1H NMR (250 MHz) δ (ppm): 7.31 (s, 1H, H-4); 5.05 (d, J=6.5 Hz, 1H, H-1′); 3.95 (m, 1H, H-2′); 3.20 (dd, J=3.2, 13.9 Hz, 1H, H-3′); 2.98 (dd, J=7.6, 13.9 Hz, 1H, H-3′); 1.63 (sept, J=6.8 Hz, 1H, CH(CH_3)$_2$); 1.30 (s, 9H, (CH_3)$_3$C); 0.89 (d, J=6.8 Hz, 3H, CHCH_3); 0.88 (d, J=6.8 Hz, 3H, CHCH_3); 0.85 (s, 3H, CH_3 thexyl); 0.84 (s, 3H, CH_3 thexyl); 0.17 (s, 3H, CH_3–Si); −0.06 (s, 3H, CH_3–Si). ^{13}C NMR (62.5 MHz) δ (ppm): 159.25 (C-2); 134.95 (C-4); 133.35 (C-5); 71.00 (C-1′); 69.75 (C-2′); 44.35 (C-3′); 39.00 (C(CH_3)$_3$); 33.85 (CH(CH_3)$_2$); 27.00 (C(CH$_3$)$_3$); 24.90 (Si–C(CH_3)$_2$(C_3H_7)); 18.45–18.50–20.00–20.10 (4 CH$_3$ thexyl); −2.60 (CH$_3$–Si); −3.30 (CH$_3$–Si). HRMS (CI): $C_{19}H_{37}ClN_3O_2SSi$: 434.2063 and 436.2034; found: 434.2058 and 436.2044.

3.12.2. *N*-(5-{3-Amino-2-chloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-yl)-2,2-dimethyl-propionamide 16B. Yield: 72%, 47 mg. $C_{19}H_{36}ClN_3O_2SSi$. White solid. R_f: 0.2 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) m/z: 434/436 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 3425 (NH), 2964–2870 (CH), 1683 (amide), 1410–1256 (C-Cl). UV (λ, nm [ϵ]): 272 (17000). $[\alpha]_D$=−30 (c=2.69; ethanol). ^1H NMR (250 MHz) δ (ppm): 7.34 (s, 1H, H-4); 5.11 (d, J=5.3 Hz, 1H, H-1′); 3.97 (ddd, J=3.4, 5.3, 8.3 Hz, 1H, H-2′); 3.08 (dd, J=3.4, 13.7 Hz, 1H, H-3′); 2.98 (dd, J=8.3, 13.7 Hz, 1H, H-3′);

1.63 (sept, J=6.9 Hz, 1H, CH(CH$_3$)$_2$); 1.32 (s, 9H, (CH_3)$_3$C); 0.89 (d, J=6.9 Hz, 6H, CH(CH_3)$_2$); 0.86 (s, 3H, CH_3 thexyl); 0.85 (s, 3H, CH_3 thexyl); 0.17 (s, 3H, CH_3–Si); −0.02 (s, 3H, CH_3–Si). ^{13}C NMR (62.5 MHz) δ (ppm): 176.30 (C=O); 159.15 (C-2); 135.05 (C-4); 132.40 (C-5); 71.40 (C-1′); 69.70 (C-2′); 44.60 (C-3′); 39.25 (C(CH$_3$)$_3$); 34.25 (CH(CH$_3$)$_2$); 27.30 (C(CH$_3$)$_3$); 25.15 (Si–C(CH$_3$)$_2$(C$_3$H$_7$)); 18.70–20.35 (4 CH$_3$ thexyl); −2.50 (CH$_3$–Si); −3.00 (CH$_3$–Si).

3.12.3. (5-{3-Amino-2-chloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-yl)-carbamic acid *tert*-butyl ester 26A. Yield: 77%, 238 mg. $C_{19}H_{36}ClN_3O_2SSi$. R_f: 0.2 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) m/z: 506/508 $(M+57)^+$; 450/452 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1717 (carbamate). UV (λ, nm [ϵ]): 263 (15300). $[\alpha]_D$=−39 (c=1.56; ethanol). ^{1}H NMR (200 MHz) δ (ppm): 7.22 (s, 1H, H-4); 4.99 (d, J=6.6 Hz, 1H, H-1′); 3.95 (m, 1H, H-2′); 3.22 (dd, J=3.1, 13.9 Hz, 1H, H-3′); 2.99 (dd, J=7.5, 13.9 Hz, 1H, H-3′); 1.63 (sept, J=7 Hz, 1H, CH(CH$_3$)$_2$); 1.58 (s, 9H, (CH_3)$_3$C); 0.88 (d, J=7 Hz, 3H, CHCH_3); 0.87 (d, J=7 Hz, 3H, CHCH_3); 0.85 (s, 3H, CH_3 thexyl); 0.84 (s, 3H, CH_3 thexyl); 0.17 (s, 3H, CH_3–Si); −0.05 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz) δ (ppm): 161.80 (C=O); 152.80 (C-2); 134.90 (C-4); 132.15 (C-5); 82.00 (C(CH$_3$)$_3$); 71.25 (C-1′); 70.00 (C-2′); 44.70 (C-3′); 34.00 (CH(CH$_3$)$_2$); 28.40 (C(CH$_3$)$_3$); 25.10 (Si–C(CH$_3$)$_2$(C$_3$H$_7$)); 18.60–18.70–20.15–20.30 (4 CH$_3$ thexyl); −2.40 (Si–CH$_3$); −3.10 (Si–CH$_3$). HRMS: m/z calcd for $C_{19}H_{37}ClN_3O_2SSi$: 452.1984 and 450.2013; found: 452.2006 and 450.2018.

3.12.4. 5-{3-Amino-2-chloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-yl)-carbamic acid *tert*-butyl ester 26B. Yield: 67%, 228 mg. $C_{19}H_{36}ClN_3O_2SSi$. White solid. R_f: 0.2 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) m/z: 506/508 $(M+57)^+$; 450/452 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1717 (carbamate). UV (λ, nm [ϵ]): 263 (14700). $[\alpha]_D$=+29 (c=1.17; ethanol). ^{1}H NMR (200 MHz) δ (ppm): 7.25 (s, 1H, H-4); 5.05 (d, J=5.5 Hz, 1H, H-1′); 3.97 (m, 1H, H-2′); 3.08 (dd, J=3.3, 13.7 Hz, 1H, H-3′); 2.75 (dd, J=8.4, 13.7 Hz, 1H, H-3′); 1.60 (sept, J=7 Hz, 1H, CH(CH$_3$)$_2$); 1.57 (s, 9H, (CH_3)$_3$C); 0.88 (d, J=7 Hz, 6H, CH(CH_3)$_2$); 0.86 (s, 3H, CH_3 thexyl); 0.85 (s, 3H, CH_3 thexyl); 0.16 (s, 3H, CH_3–Si); −0.18 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz) δ (ppm): 162.00 (C=O); 152.80 (C-2); 134.50 (C-4); 130.60 (C-5); 81.95 (C(CH$_3$)$_3$); 71.35 (C-1′); 69.60 (C-2′); 44.50 (C-3′); 34.00 (CH(CH$_3$)$_2$); 28.30 (C(CH$_3$)$_3$); 25.05 (Si–C(CH$_3$)$_2$(C$_3$H$_7$)); 18.60–20.20 (4 CH$_3$ thexyl); −2.70 (Si–CH$_3$); −3.20 (Si–CH$_3$).

3.12.5. [5-(3-Amino-2-chloro-1-hydroxy-propyl)-thiazol-2-yl]-carbamic acid *tert*-butyl ester 28A. Yield: 75%, 20 mg. $C_{11}H_{18}ClN_3O_3S$. White solid. R_f: 0.3 (CH_2Cl_2/MeOH: 95/5). MS ESI (methanol) m/z: 308/310 $(M+H)^+$. UV (λ, nm [ϵ]): 263 (8700). $[\alpha]_D$=−12 (c=1.3; ethanol). ^{1}H NMR (250 MHz, CD$_3$OD) δ (ppm): 7.17 (d, J=0.6 Hz, 1H, H-4); 5.04 (dd, J=0.6, 4.3 Hz, 1H, H-1′); 4.05 (m, 1H, H-2′); 2.99 (dd, J=4.3, 13.8 Hz, 1H, H-3′); 2.80 (dd, J=8.3, 13.8 Hz, 1H, H-3′); 1.44 (s, 9H, (CH_3)$_3$C). ^{13}C NMR (62.5 MHz, CD$_3$OD) δ (ppm): 162.40 (C=O); 136.10 (C-4); 133.15 (C-5); 82.95 (C(CH$_3$)$_3$); 70.55 (C-1′); 69.05 (C-2′); 45.90 (C-3′); 28.45 (C(CH$_3$)$_3$).

3.12.6. *N*-[5-(3-Amino-2-chloro-1-hydroxy-propyl)-thiazol-2-yl]-2,2-dimethyl-propionamide 30A. Yield: 64%, 23 mg. $C_{11}H_{18}ClN_3O_3S$. White solid. R_f: 0.1 (CH_2Cl_2/MeOH: 85/15). MS CI (T=170°C) m/z: 292/294 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1680 (amide). UV (λ, nm [ϵ]): 271 (11100). $[\alpha]_D$=+12 (c=1.9; ethanol). ^{1}H NMR (300 MHz, CD$_3$OD) δ (ppm): 7.30 (s, 1H, H-4); 4.97 (d, J=6.5 Hz, 1H, H-1′); 4.06 (m, 1H, H-2′); 3.06 (dd, J=3.8, 13.9 Hz, 1H, H-3′); 2.82 (dd, J=7.8, 13.9 Hz, 1H, H-3′); 1.21 (s, 9H, (CH_3)$_3$C). ^{13}C NMR (75 MHz, CD$_3$OD) δ (ppm): 178.80 (C=O); 160.55 (C-2); 136.55 (C-4); 134.25 (C-5); 71.30 (C-1′); 68.85 (C-2′); 45.80 (C-3′); 40.15 (C(CH$_3$)$_3$); 27.30 (C(CH$_3$)$_3$). HRMS: m/z calcd for $C_{11}H_{18}ClN_3O_2S$: 292.0886 and 294.0856; found: 292.0881 and 294.0849.

3.12.7. *N*-[5-(3-Amino-2-chloro-1-hydroxy-propyl)-thiazol-2-yl]-2,2-dimethyl-propionamide 30B. Yield: 62%, 33 mg. $C_{11}H_{18}ClN_3O_2S$. White solid. R_f: 0.1 (CH_2Cl_2/MeOH: 85/15). MS CI (T=180°C) m/z: 292/294 $(M+H)^+$; 256 $(M-Cl)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1683 (amide). UV (λ, nm [ϵ]): 272 (12700). $[\alpha]_D$=−16 (c=1.3; ethanol). ^{1}H NMR (300 MHz, CD$_3$OD) δ (ppm): 7.40 (d, J=0.6 Hz, 1H, H-4); 5.31 (dd, J=0.6, 3.9 Hz, 1H, H-1′); 4.16 (m, 1H, H-2′); 3.32 (dd, J=5.0, 13.5 Hz, 1H, H-3′); 3.18 (dd, J=4.7, 13.5 Hz, 1H, H-3′); 1.32 (s, 9H, (CH_3)$_3$C). ^{13}C NMR (75 MHz, CD$_3$OD) δ (ppm): 178.75 (C=O); 160.50 (C-2); 135.95 (C-4); 134.00 (C-5); 70.55 (C-1′); 69.65 (C-2′); 46.00 (C-3′); 40.15 (C(CH$_3$)$_3$); 27.30 (C(CH$_3$)$_3$). HRMS (CI): calcd for $C_{11}H_{19}ClN_3O_2S$: 294.0857 and 293.0886; found: 294.0859 and 292.0893.

3.12.8. 5-{3-Amino-2-chloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-ylamine 32A. Yield 67%, 10 mg. $C_{14}H_{28}ClN_3OSSi$. White solid. R_f: 0.1 (CH_2Cl_2/MeOH: 90/10). MS CI (T=180°C) m/z: 350/352 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1602. UV (λ, nm [ϵ]): 264 (7600). $[\alpha]_D$=−48 (c=0.07; ethanol). ^{1}H NMR (250 MHz, CD$_3$OD) δ (ppm): 6.80 (s, 1H, H-4); 4.93 (d, J=5.8 Hz, 1H, H-1′); 3.93 (m, 1H, H-2′); 3.10 (dd, J=3.4, 13.9 Hz, 1H, H-3′); 2.82 (dd, J=8.6, 13.9 Hz, 1H, H-3′); 1.58 (sept, J=6.9 Hz, 1H, CH(CH$_3$)$_2$); 0.85 (d, J=6.9 Hz, 3H, CHCH_3); 0.84 (d, J=6.9 Hz, 3H, CHCH_3); 0.80 (s, 3H, CH_3 thexyl); 0.79 (s, 3H, CH_3 thexyl); 0.18 (s, 3H, CH_3–Si); 0.00 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz, CD$_3$OD) δ (ppm): 172.20 (C-2); 137.20 (C-4); 128.10 (C-5); 70.65 (C-1′); 72.90 (C-2′); 45.65 (C-3′); 35.50 (CH(CH$_3$)$_2$); 26.10 (Si–C(CH$_3$)$_2$(C$_3$H$_7$)); 19.10–19.15–20.70–20.80 (4CH$_3$ thexyl); −2.45 (CH$_3$–Si); −2.90 (CH$_3$–Si). HRMS (CI): $C_{14}H_{29}ClN_3OSSi$: 350.1489 and 352.1459; found: 350.1470 and 352.1475.

3.12.9. 5-{3-Amino-2-chloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-ylamine 32B. Yield 69%, 18 mg. $C_{14}H_{28}ClN_3OSSi$. White solid. R_f: 0.1 (CH_2Cl_2/MeOH: 90/10). MS CI (T=180°C) m/z: 350/352 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1603. UV (λ, nm [ϵ]): 264 (11400). $[\alpha]_D$=+48 (c=0.09; ethanol). ^{1}H NMR (250 MHz, CD$_3$OD) δ (ppm): 6.85 (s, 1H, H-4); 4.97 (d, J=5.6 Hz, 1H, H-1′); 3.93 (m, 1H, H-2′); 2.93 (dd, J=3.6, 13.7 Hz, 1H, H-3′); 2.71 (dd, J=8.8, 13.7 Hz, 1H, H-3′); 1.63 (sept, J=6.9 Hz, 1H, CH(CH$_3$)$_2$); 0.87 (d, J=6.9 Hz, 6H, CH(CH_3)$_2$); 0.83 (s, 3H, CH_3 thexyl); 0.81 (s, 3H, CH_3 thexyl); 0.14 (s, 3H, CH_3–Si); −0.05 (s, 3H, CH_3–Si). ^{13}C

NMR (62.5 MHz, CD_3OD) δ (ppm): 172.45 (C-2); 136.95 (C-4); 127.50 (C-5); 72.60 (C-1′); 70.55 (C-2′); 45.70 (C-3′); 35.50 ($CH(CH_3)_2$); 26.10 (Si–$C(CH_3)_2(C_3H_7)$); 19.15–20.80 ($4CH_3$ thexyl); −2.50 (CH_3–Si); −2.90 (CH_3–Si).

3.13. Deprotection of 2-aminothiazole and hydroxyle in position 1′. Compounds 17, 2A, 2B

The amine **16A** (1 equiv.) was dissolved in a 6N HCl solution (0.04 mmol/mL) and heated at 80°C for 12 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (ethyl acetate/butanone/water/formic acid: 5/3/0.5/0.5=CTZZ), followed by a filtration through a Sephadex® LH20 column, eluting with methanol to yield a brown solid (86 mg, 60%).

3.13.1. 5-(3-Amino-2-chloro-propenyl)-thiazol-2-ylamine 17. $C_6H_8ClN_3S$,2HCl. Light brown solid. R_f: 0.1 (CH_2Cl_2/MeOH: 80/20). MS FAB: 190/192 $(M+H)^+$. IR (KBr, ν_{max}, cm^{-1}): 1635. UV (λ, nm [ϵ]): 307 (24200). ^1H NMR (300 MHz, CD_3OD) δ (ppm): 7.34 (s, 1H, H-4); 7.00 (s, 1H, H-1′); 3.98 (s, 2H, H-3′). ^{13}C NMR (75 MHz, CD_3OD) δ (ppm): 130.70 (C-4); 126.25 (C-2′ or C-5); 122.85 (C-1′); 120.40 (C-2′ or C-5); 47.45 (C-3′).

The amine **26A** (1 equiv.) was dissolved in 6N HCl (0.04 mmol/mL) and stirred at room temperature for 24 h. The solvent was removed under reduced pressure and the residue was filtered through a Sephadex® LH20 column, eluting with methanol, to give **2A** with 64% yield (70 mg).

3.13.2. 3-Amino-1-(2-amino-thiazol-5-yl)-2-chloro-propan-1-ol 2A. $C_6H_{10}ClN_3OS$, 2HCl. Brown solid. R_f: 0.3 (CTZZ). MS FAB, *m/z*: 208/210 $(M+H)^+$. IR (ethanol, ν_{max}, cm^{-1}): no characteristic wave (HATR). UV (λ, nm [ϵ]): 263 (7200). $[\alpha]_D$=+6 (*c*=0.10; ethanol). ^1H NMR (250 MHz, CD_3OD) δ (ppm): 7.22 (s, 1H, H-4); 4.98 (d, *J*=6.9 Hz, 1H, H-1′); 4.30 (ddd, *J*=3.5, 6.3, 9 Hz, 1H, H-2′); 3.51 (dd, *J*=3.5, 13.7 Hz, 1H, H-3′); 3.18 (dd, *J*=9, 13.7 Hz, 1H, H-3′). ^{13}C NMR (62.5 MHz, CD_3OD) δ (ppm): 177.90 (C-2); 127.55 (C-5); 125.05 (C-4); 70.50 (C-1′); 61.60 (C-2′); 43.60 (C-3′).

The same work-up as above afforded **2B** (68%, 75 mg).

3.13.3. 3-Amino-1-(2-amino-thiazol-5-yl)-2-chloro-propan-1-ol 2B. $C_6H_{10}ClN_3OS$, 2HCl. Brown solid. R_f: 0.3 (CTZZ). MS FAB, *m/z*: 208/210 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): no characteristic wave (HATR method). UV (λ, nm [ϵ]): 263 (10400). $[\alpha]_D$=−8 (*c*=0.16; ethanol). ^1H NMR (250 MHz, CD_3OD) δ (ppm): 7.05 (s, 1H, H-4); 5.10 (d, *J*=3 Hz, 1H, H-1′); 4.33 (dt, *J*=3, 9 Hz, 1H, H-2′); 3.40 (dd, *J*=3.5, 13.7 Hz, 1H, H-3′); 3.20 (dd, *J*=9, 13.7 Hz, 1H, H-3′). ^{13}C NMR (62.5 MHz, CD_3OD) δ (ppm): 172.05 (C-2); 128.45 (C-5); 127.30 (C-4); 65.60 (C-1′); 63.10 (C-2′); 44.30 (C-3′).

3.14. Selective desilylation in position 1′. Compounds: 27A, 27B, 29A, 29B

The azido compound (1 equiv.) was dissolved in anhydrous THF (0.04 mmol/mL) and treated with acetic acid (3 equiv.), then by Bu_4NF (3 equiv.) slowly added. After 3 h at room temperature, an additional equivalent of Bu_4NF was added. After 1 h at room temperature, the solvent was removed under reduced pressure. The residue was purified by flash chromatography (dichloromethane/methanol: 99/1).

3.14.1. [5-(3-Azido-2-chloro-1-hydroxy-propyl)-thiazol-2-yl]-carbamic acid *tert*-butyl ester 27A. Yield 91%, 38 mg. $C_{11}H_{16}ClN_5O_3S$. White solid. R_f: 0.3 (CH_2Cl_2/MeOH: 95/5). MS CI (*T*=170°C) *m/z*: 334/336 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 2109 (azide); 1718 (carbamate). UV (λ, nm [ϵ]): 263 (15400). $[\alpha]_D$=+31 (*c*=1; ethanol). ^1H NMR (250 MHz) δ (ppm): 11.6 (s large, 1H, NH); 7.32 (s, 1H, H-4); 5.19 (d, *J*=6.3 Hz, 1H, H-1′); 4.26 (m, 1H, H-2′); 3.83 (dd, *J*=6, 13.2 Hz, 1H, H-3′); 3.68 (dd, *J*=4.4, 13.2 Hz, 1H, H-3′); 1.63 (s, 9H, $(CH_3)_3C$). ^{13}C NMR (62.5 MHz) δ (ppm): 162.50 (C=O); 152.90 (C-2); 135.30 (C-4); 129.90 (C-5); 82.70 ($C(CH_3)_3$); 69.70 (C-1′); 63.65 (C-2′); 53.60 (C-3′); 28.40 ($C(CH_3)_3$).

3.14.2. [5-(3-Azido-2-chloro-1-hydroxy-propyl)-thiazol-2-yl]-carbamic acid *tert*-butyl ester 27B. Yield 95%, 39 mg. $C_{11}H_{16}ClN_5O_3S$. White solid. R_f: 0.3 (CH_2Cl_2/MeOH: 95/5). MS CI (*T*=170°C) *m/z*: 334/336 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 2109 (azide); 1718 (carbamate). UV (λ, nm [ϵ]): 263 (8800). $[\alpha]_D$=−3 (*c*=1.25; ethanol). ^1H NMR (250 MHz) δ (ppm): 7.32 (s, 1H, H-4); 5.16 (d, *J*=5.2 Hz, 1H, H-1′); 4.19 (m, 1H, H-2′); 3.73 (dd, *J*=5.2, 13.1 Hz, 1H, H-3′); 3.55 (dd, *J*=6, 13.1 Hz, 1H, H-3′); 1.59 (s, 9H, $(CH_3)_3C$). ^{13}C NMR (62.5 MHz) δ (ppm): 162.45 (C=O); 152.85 (C-2); 135.25 (C-4); 129.25 (C-5); 82.60 ($C(CH_3)_3$); 69.10 (C-1′); 64.90 (C-2′); 53.85 (C-3′); 28.35 ($C(CH_3)_3$). HRMS: *m/z* calcd for $C_{11}H_{17}ClN_5O_3S$: 334.0740 and 336.0711; found: 334.0733 and 336.0751.

3.14.3. *N*-[5-(3-Azido-2-chloro-1-hydroxy-propyl)-thiazol-2-yl]-2,2-dimethyl-propionamide 29A. Yield 96%, 38 mg. $C_{11}H_{16}ClN_5O_2S$. White solid. R_f: 0.4 (CH_2Cl_2/MeOH: 95/5). MS CI (*T*=170°C) *m/z*: 318/320 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 2109 (azide), 1683 (amide). UV (λ, nm [ϵ]): 272 (13800). $[\alpha]_D$=+27 (*c*=0.18; ethanol). ^1H NMR (250 MHz) δ (ppm): 9.35 (s large, 1H, NH); 7.39 (s, 1H, H-4); 5.19 (d, *J*=6.2 Hz, 1H, H-1′); 4.23 (ddd, *J*=6.2, 6.2, 4.5 Hz, 1H, H-2′); 3.77 (dd, *J*=6.2, 13.2 Hz, 1H, H-3′); 3.63 (dd, *J*=4.5, 13.2 Hz, 1H, H-3′); 1.33 (s, 9H, $(CH_3)_3C$). ^{13}C NMR (62.5 MHz) δ (ppm): 176.40 (C=O); 159.25 (C-2); 136.00 (C-4); 131.10 (C-5); 69.85 (C-1′); 63.80 (C-2′); 53.55 (C-3′); 39.25 ($C(CH_3)_3$); 27.25 ($C(CH_3)_3$).

3.14.4. *N*-[5-(3-Azido-2-chloro-1-hydroxy-propyl)-thiazol-2-yl]-2,2-dimethyl-propionamide 29B. Yield 87%, 39 mg. $C_{11}H_{16}ClN_5O_2S$. White solid. R_f: 0.4 (CH_2Cl_2/MeOH: 95/5). MS CI (*T*=170°C) *m/z*: 318/320 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 2108 (azide), 1683 (amide). UV (λ, nm [ϵ]): 271 (11400). $[\alpha]_D$=−24 (*c*=0.21; ethanol). ^1H NMR (250 MHz) δ (ppm): 9.22 (s large, 1H, NH); 7.38 (s, 1H, H-4); 5.20 (d, *J*=4.9 Hz, 1H, H-1′); 4.20 (m, 1H, H-2′); 3.73 (dd, *J*=5.4, 13 Hz, 1H, H-3′); 3.56 (dd, *J*=6, 13 Hz, 1H, H-3′); 1.33 (s, 9H, $(CH_3)_3C$). ^{13}C NMR (62.5 MHz). δ (ppm): 176.40 (C=O); 159.10 (C-2); 135.80 (C-4); 131.00 (C-5); 69.10 (C-1′); 65.00 (C-2′); 53.40 (C-3′); 39.30 ($C(CH_3)_3$); 27.30 ($C(CH_3)_3$). HRMS: *m/z* calcd for $C_{11}H_{17}ClN_5O_2S$: 318.0791 and 320.0761; found: 318.0807 and 320.0778.

3.15. Selective elimination of the Boc group. Compounds 31A, 31B

The *N*-protected compound **25** was dissolved in dichloromethane and treated with trifluoroacetic acid (one volume). After 12 h at room temperature, the solvent was removed under reduced pressure. Purification of the crude medium was made by preparative TLC. (dichloromethane/methanol: 99/1).

3.15.1. 5-{3-Azido-2-chloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-ylamine 31A. Yield 95%, 12.4 mg. $C_{14}H_{26}ClN_5OSSi$. White solid. R_f: 0.2 (CH_2Cl_2/MeOH: 95/5). MS CI (T=180°C) *m/z*: 432/434 $(M+57)^+$; 376/378 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 2107 (azide). UV (λ, nm [ϵ]): 264 (7100). $[\alpha]_D$=−16 (c=1.24; ethanol). ^{1}H NMR (250 MHz) δ (ppm): 6.95 (s, 1H, H-4); 5.04 (s large, 2H, NH_2); 4.94 (d, J=6.5 Hz, 1H, H-1′); 3.98 (m, 1H, H-2′); 3.67 (m, 2H, H-3′); 1.61 (sept, J=6.8 Hz, 1H, C*H*$(CH_3)_2$); 0.88 (d, J=6.8 Hz, 3H, CHC*H*$_3$); 0.87 (d, J=6.8 Hz, 3H, CHC*H*$_3$); 0.85 (s, 3H, C*H*$_3$ thexyl); 0.84 (s, 3H, C*H*$_3$ thexyl); 0.16 (s, 3H, C*H*$_3$–Si); −0.35 (s, 3H, C*H*$_3$–Si). ^{13}C NMR (62.5 MHz) δ (ppm): 168.25 (C-2); 137.35 (C-4); 128.65 (C-5); 70.80 (C-1′); 64.90 (C-2′); 53.55 (C-3′); 34.15 (*C*H$(CH_3)_2$); 25.20 (Si–*C*$(CH_3)_2$ (C_3H_7)); 18.65–18.75–20.00–20.20 (4 C*H*$_3$ thexyl); 10.15–10.75 (Si–(C*H*$_3)_2$). HRMS (CI): $C_{14}H_{27}ClN_5OSSi$: 376.1393 and 378.1364; found: 376.1377 and 378.1359.

3.15.2. 5-{3-Azido-2-chloro-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-propyl}-thiazol-2-ylamine 31B. Yield 87%, 35 mg. $C_{14}H_{26}ClN_5OSSi$. White solid. R_f: 0.2 (CH_2Cl_2/MeOH: 95/5). MS CI (T=150°C) *m/z*: 432/434 $(M+57)^+$; 376/378 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 2107 (azide). UV (λ, nm [ϵ]): 266 (9400). $[\alpha]_D$=+24 (c=1.10; ethanol). ^{1}H NMR (250 MHz) δ (ppm): 6.97 (s, 1H, H-4); 5.00 (s large, 2H, NH_2); 4.99 (d, J=5.2 Hz, 1H, H-1′); 3.99 (m, 1H, H-2′); 3.65 (dd, J=4.4, 13 Hz, 1H, H-3′); 3.41 (dd, J=7, 13 Hz, 1H, H-3′); 1.63 (sept, J=6.8 Hz, 1H, C*H*$(CH_3)_2$); 0.89 (d, J=6.8 Hz, 6H, CH(C*H*$_3)_2$); 0.85 (s, 3H, C*H*$_3$ thexyl); 0.84 (s, 3H, C*H*$_3$ thexyl); 0.18 (s, 3H, C*H*$_3$–Si); −0.01 (s, 3H, C*H*$_3$–Si). ^{13}C NMR (62.5 MHz) δ (ppm): 168.65 (C-2); 136.85 (C-4); 127.30 (C-5); 70.55 (C-1′); 64.85 (C-2′); 53.75 (C-3′); 34.25 (*C*H$(CH_3)_2$); 25.20 (Si–*C*$(CH_3)_2(C_3H_7)$); 18.50–18.70–20.20–20.30 (4 *C*H$_3$ thexyl); −2.65 (*C*H$_3$–Si); −3.10 (*C*H$_3$–Si).

3.16. Monomesylation of the diol 22. Compounds 33A, 33B

The diol **22** (1 equiv.) was dissolved in freshly distilled pyridine (0.05 mmol/mL). At 0°C, the solution was treated with mesyl chloride (1 equiv.) and stirred for 12 h at room temperature. Then, the solvent was removed under reduced pressure. The residue was purified by flash chromatography (dichloromethane/methanol: 99/1).

3.16.1. Methanesulfonic acid 3-[2-(2,2-dimethyl-propionylamino)-thiazol-5-yl]-3-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-2-hydroxy-propyl ester 33A. Yield 79%, 93 mg. $C_{20}H_{38}N_2O_6S_2Si$. R_f: 0.5 (CH_2Cl_2/MeOH: 95/5). MS CI (T=180°C) *m/z*: 495 $(M+H)^+$; 399 $(M-Ms)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1683 (amide), 1364–1176 (SO_2). UV (λ, nm [ϵ]): 271 (10000). $[\alpha]_D$=−18 (c=1.28; ethanol). ^{1}H NMR (300 MHz) δ (ppm): 10.00 (s large, 1H, NH); 7.32 (s, 1H, H-5); 4.98 (d, J=5 Hz, 1H, H-1′); 4.33 (dd, J=3.7, 11 Hz, 1H, H-3′); 4.11 (dd, J=6, 11 Hz, 1H, H-3′); 3.94 (m, 1H, H-2′); 3.15 (s large, 1H, OH); 3.05 (s, 3H, C*H*$_3SO_2$); 1.60 (sept., J=6.9 Hz, 1H, C*H*$(CH_3)_2$); 1.29 (s, 9H, $(CH_3)_3$C); 0.90 (d, J=6.9 Hz, 3H, CHC*H*$_3$); 0.88 (d, J=6.9 Hz, 3H, CHC*H*$_3$); 0.86 (s, 3H, C*H*$_3$ thexyl); 0.85 (s, 3H, C*H*$_3$ thexyl); 0.13 (s, 3H, C*H*$_3$–Si); −0,05 (s, 3H, C*H*$_3$–Si). ^{13}C NMR (75 MHz) δ (ppm): 176.55 (C=O); 159.80 (C-2); 135.00 (C-4); 131.50 (C-5); 73.70 (C-2′); 70.05 (C-3′); 69.35 (C-1′); 39.10 (*C*$(CH_3)_3$); 37.60 (C*H*$_3SO_2$); 34.05 (*C*H$(CH_3)_2$); 27.10 (C(*C*H$_3)_3$); 25.05 (Si–*C*$(CH_3)_2(C_3H_7)$); 18.50–18.60–20.10–20.30 (4 *C*H$_3$ thexyl); −2.65 (*C*H$_3$–Si); −3.45 (*C*H$_3$–Si).

3.16.2. Methanesulfonic acid 3-[2-(2,2-dimethyl-propionylamino)-thiazol-5-yl-3-dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-2-hydroxy-propyl ester 33B. Yield 73%, 86 mg. $C_{20}H_{38}N_2O_6SSi$. White solid. Mp=69°C. R_f: 0.5 (CH_2Cl_2/MeOH: 95/5). MS ESI (methanol), *m/z*: 533 $(M+K)^+$; 517 $(M+Na)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 1684 (amide), 1363–1175 (SO_2). UV (λ, nm [ϵ]): 271 (11700). $[\alpha]_D$=+48 (c=0.75; ethanol). ^{1}H NMR (250 MHz) δ (ppm): 9.55 (s large, 1H, NH); 7.28 (s, 1H, H-5); 4.91 (d, J=5.9 Hz, 1H, H-1′); 4.31 (dd, J=3.7, 10.8 Hz, 1H, H-3′); 4.24 (dd, J=5.9, 10.8 Hz, 1H, H-3′); 4.02 (m, 1H, H-2′); 3.05 (s, 3H, C*H*$_3SO_2$); 1.61 (sept., J=6.9 Hz, 1H, C*H*$(CH_3)_2$); 1.32 (s, 9H, $(CH_3)_3$C); 0.88 (d, J=6.9 Hz, 3H, CHC*H*$_3$); 0.87 (d, J=6.9 Hz, 3H, CHC*H*$_3$); 0.85 (s, 3H, C*H*$_3$ thexyl); 0.83 (s, 3H, C*H*$_3$ thexyl); 0.16 (s, 3H, C*H*$_3$–Si); −0.06 (s, 3H, C*H*$_3$–Si). ^{13}C NMR (62.5 MHz) δ (ppm): 176.30 (C=O); 159.50 (C-2); 135.50 (C-4); 132.05 (C-5); 73.85 (C-2′); 70.25 (C-3′); 69.60 (C-1′); 39.25 (*C*$(CH_3)_3$); 37.55 (*C*H$_3SO_2$); 34.20 (*C*H$(CH_3)_2$); 27.30 (C(*C*H$_3)_3$); 25.10 (Si–*C*$(CH_3)_2(C_3H_7)$); 18.65–18.75–20.20–20.40 (4*C*H$_3$ thexyl); −2.40 (*C*H$_3$–Si); −3.15 (*C*H$_3$–Si). Calcd for $C_{20}H_{38}N_2S_2O_6$: C, 48.56; H, 7.77; N, 5.66; found: C, 48.26; H, 7.53; N, 5.46

3.17. Substitution of mesylate function by an azido function. Compounds 34A, 34B

The monomesylated compound **33** (1 equiv.) was dissolved in DMF (0.026 mmol/mL) and treated with sodium azide (1.6 equiv.) and heated at 80°C overnight. The mixture was diluted with dichloromethane, washed with water and dried over $MgSO_4$. After filtration, solvent was removed under reduced pressure and the residue purified by flash chromatography (heptane/ethyl acetate: 6/4).

3.17.1. *N*-(5-{3-Azido-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-2-hydroxy-propyl}-thiazol-2-yl)-2,2-dimethyl-propionamide 34A. Yield 93%, 53 mg. $C_{19}H_{35}N_5O_3SSi$. White solid. R_f: 0.5 (CH_2Cl_2/MeOH: 95/5). MS CI (T=170°C) *m/z*: 442 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 2965, 2107 (azide), 1682 (amide). UV (λ, nm [ϵ]): 273 (18600). $[\alpha]_D$=−5 (c=3.6; ethanol). ^{1}H NMR (300 MHz) δ (ppm): 9.64 (s large, 1H, NH); 7.31 (s, 1H, H-4); 4.93 (d, J=6 Hz, 1H, H-1′); 3.82 (m, 1H, H-2′); 3.38 (dd, J=3.8, 12.7 Hz, 1H, H-3′); 3.14 (dd, J=5.9, 12.7 Hz, 1H, H-3′); 1.63 (sept, J=6.8 Hz, 1H, C*H*$(CH_3)_2$); 1.31 (s, 9H,

(CH_3)$_3$C); 0.90 (d, J=6.8 Hz, 3H, CHCH_3); 0.88 (d, J=6.8 Hz, 3H, CHCH_3); 0.86 (s, 3H, CH_3 thexyl); 0.85 (s, 3H, CH_3 thexyl); 0.18 (s, 3H, CH_3–Si); −0.05 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz) δ (ppm): 176.10 (C=O); 159.10 (C-2); 135.00 (C-4); 132.20 (C-5); 75.30 (C-2′); 69.90 (C-1′); 52.20 (C-3′); 39.10 (C(CH_3)$_3$); 34.00 (CH(CH_3)$_2$); 27.10 (C(CH$_3$)$_3$); 25.00 (Si–C(CH_3)$_2$(C_3H_7)); 18.40–18.65–20.00–20.30 (4 CH$_3$thexyl); −2.50 (Si–(CH$_3$)$_2$). HRMS: m/z calcd for $C_{19}H_{36}N_5O_3SSi$: 442.2308; found: 442.2288.

3.17.2. *N*-(5-{3-Azido-1-[dimethyl-(1,1,2-trimethyl-propyl)-silanyloxy]-2-hydroxy-propyl}-thiazol-2-yl)-2,2-dimethyl-propionamide 34B. Yield 93%, 69 mg. $C_{19}H_{35}N_5O_3SSi$. White solid. R_f: 0.5 (CH_2Cl_2/MeOH: 95/5). MS CI (T=190°C) m/z: 442 $(M+H)^+$. IR ($CHCl_3$, ν_{max}, cm^{-1}): 2107 (azide), 1684 (amide). UV (λ, nm [ϵ]): 273 (9900). $[\alpha]_D$=+23 (c=1.3; ethanol). ^{1}H NMR (300 MHz) δ (ppm): 9.30 (s large, 1H, NH); 7.28 (s, 1H, H-4); 4.87 (d, J=5.8 Hz, 1H, H-1′); 3.89 (m, 1H, H-2′); 3.37 (sys ABX J_{AX}=4.3 Hz; J_{BX}=6.1 Hz; J_{AB}=12.6 Hz, 2H, H-3′); 1.61 (sept, J=6.8 Hz, 1H, CH(CH_3)$_2$); 1.32 (s, 9H, (CH_3)$_3$C); 0.88 (d, J=6.8 Hz, 3H, CHCH_3); 0.87 (d, J=6.8 Hz, 3H, CHCH_3); 0.84 (s, 3H, CH_3 thexyl); 0.83 (s, 3H, CH_3 thexyl); 0.16 (s, 3H, CH_3–Si); −0.05 (s, 3H, CH_3–Si). ^{13}C NMR (75 MHz δ, (ppm): 176.15 (C=O); 159.40 (C-2); 135.40 (C-4); 132.35 (C-5); 74.85 (C-2′′); 70.35 (C-1′); 52.70 (C-3′); 39.25 (C(CH_3)$_3$); 34.20 (CH(CH_3)$_2$); 27.30 (C(CH$_3$)$_3$); 25.10 (Si–C(CH_3)$_2$(C_3H_7)); 18.65–18.75–20.20–20.40 (4CH$_3$ thexyl); −2.40 (CH$_3$–Si); −3.15 (CH$_3$–Si).

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