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Synthetic studies on nucleoside-type muraymycins antibiotics based on the use of sulfur ylides. Synthesis of bioactive 5′-epimuraymycin analogues

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Abstract—A new synthetic approach to the 5-epimers of muraymycins, a family of complex nucleoside-type antibiotics, is reported based on the synthesis of epoxy amides obtained via the reaction of sulfur ylides with the uridyl aldehyde derivatives **16**, **29** and **30**, followed by a subsequent oxirane ring opening reaction with diamines. This new strategy offers an excellent opportunity for the preparation of muraymycin analogues of biological interest. In fact, biological studies have revealed these 5′-epimers to be as biologically potent as the natural antibiotics, aside of representing a convergent and flexible route towards the natural congeners.
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1. Introduction

The search and discovery of new antibiotics with novel mechanisms of action is of great importance in chemical, biological and clinical circles due to the growing appearance of drug resistant bacterial strains.[1] Among these new antibiotics, the group composed of the uridyl lipopeptide antibiotics,[2] that include mureidomycins,[3] pacidamycins,[4] napsamycins,[5] liposidomycins,[6] FR-900493[7] and caprazamycins,[8] are of special interest due to their intriguing mechanism of action, characterized by the inhibition of the phospho-*N*-acetyl-muramoyl-pentapeptide-transferase (MraY),[9] also known as translocase I, an enzyme responsible for the biosynthesis of the cell-wall of bacteria. Recently, the muraymycins,[10] another group of nucleoside-lipopeptide antibiotics, have been discovered, isolated and recognized as inhibitors of MraY, displaying in vitro and in vivo activities against Gram-positive bacteria comparable to liposidomycin C and mureidomycin A.[11] Coupled with their prominent biological properties, the muraymycins reveal an attractive molecular architecture, characterized by an unusual nucleotide disaccharide and an unprecedented peptidic chain. So far, 19 different members of the muraymycins have been isolated and identified, among which the selected compounds **1**–**5** are depicted in Figure 1.[12] The various muraymycin compounds differ in the amino sugar (group R^2) or in the lipidic side chain contained in one of the amino acid residues (group R^1).

Recent synthetic studies of the muraymycins have demonstrated that truncated derivatives, in which, the 5′-amino ribose sugar moiety and the lipophilic side chain were removed, and, in addition, the cyclic arginine amino acid residue was replaced by arginine, were as active as the natural congeners against Gram positive bacteria. Moreover, the authors demonstrated that the 5′-epimer derivatives **7**–**12** (Fig. 2) showed a biological activity comparable to the natural congeners.[13] In this synthetic study, the construction of the muraymycin structural core was efficiently accomplished by an aldolic reaction between the lithium enolate of dibenzylglycine *tert*-butyl ester and the uridyl-5′ aldehyde **16**.[14] Other synthetic contributions to this family of antibiotics include semisynthesis of analogues[15] and the preparation of the unusual cyclic guanidine amino acid residue,[16] named capreomycidine, which is present not only in the muraymycins, but also in other natural products such as the capreomycin-type antibiotics.[17]

Recently, we reported a stereoselective synthetic approach to liposidomycin antibiotics based on the use of sulfur ylides.[18] According to this methodology, epoxy amide **13** was efficiently prepared and transformed into the diazepanone derivative **14** through an indole epoxy amide intermediate, obtained by oxidation of the indoline ring with DDQ,[19] followed by treatment with diamines (strategy a). In contrast, the reaction of epoxy amide **13** with diamines would provide the corresponding amino alcohols **15** in

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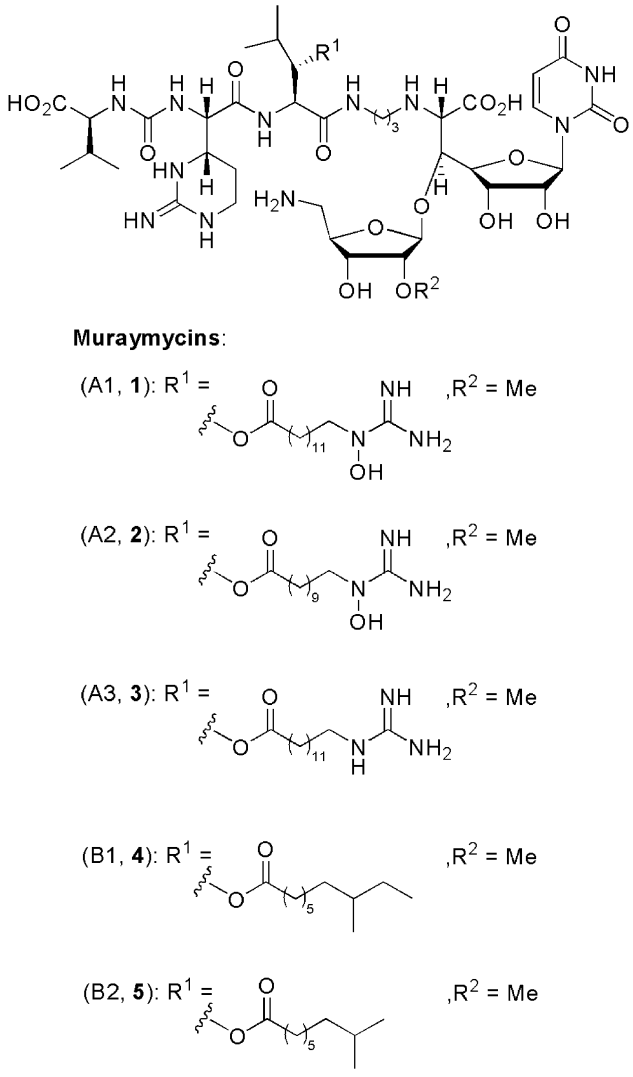
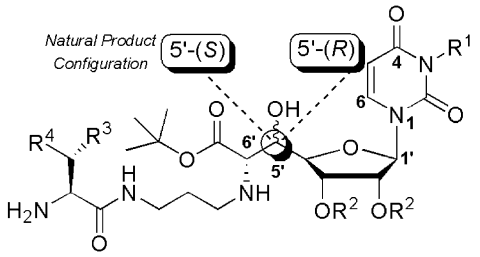


Figure 1. Molecular structures of muraymycins A1, A2, A3, B1 and B2.

a regioselective manner,[20] as a straightforward and convergent approach towards either the 5′-epimers of muraymycins or the natural members, requiring in this case, an epimerization process at this position (strategy b) (Scheme 1). Furthermore, this synthetic strategy has the potential of delivering further structural variations, allowing entry into a variety of muraymycin analogues via modifications of the amine nucleophile, which is introduced in the oxirane ring opening step.

2. Results and discussion

These synthetic studies were initiated with the reaction of epoxy amide **13** (Scheme 2), readily prepared by condensation of aldehyde **16** with the sulfur ylide, in situ generated from sulfonium salt **17**,[18] with different nitrogen nucleophiles including sodium azide, allylamine, and various diamines such as *N*-*Z*-1,3-propanediamine,[21] which furnished the corresponding oxirane ring opening products **15a–j** in good to excellent yields (62–96%) and complete regioselectivity, with the exception of reaction with *N*-methyl-1,3-propanodiamine, in which a 1:1 unseparable mixture of isomers **15f** and **15f′** was obtained in a combined

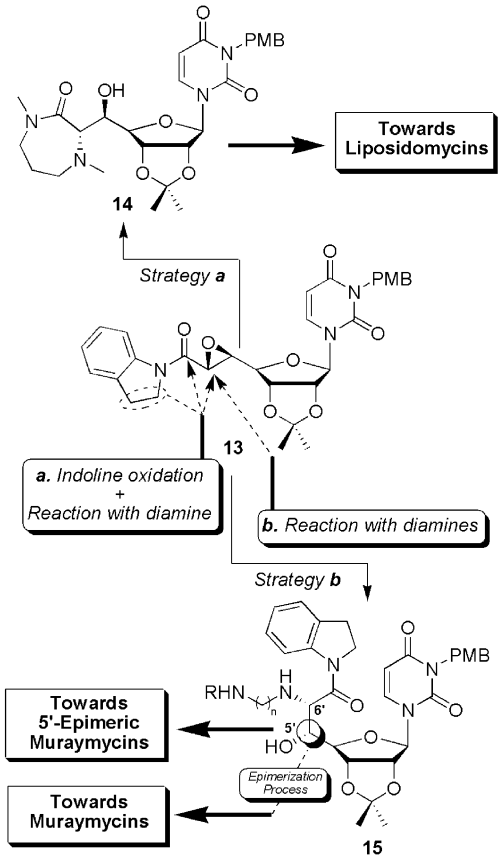


Muraymycin	R^1	R^2	R^3	R^4	IC_{50}[a]	MIC[b]
5'-(S) *Natural Product Configuration*						
A1 (**1**)					---	1-16
(**6**)	PMB	TBS	OH	Me	10.7	8-128
5'-(R) *5′-Epimer*						
(**7**)	PMB	TBS	OH	Me	32.0	4-8
(**8**)	PMB	TBS	OH	*i*-Pr	----	4-16
(**9**)	PMB	TBS	H	*i*-Pr	----	4-64
(**10**)	PMB	TBS	H	H	----	4-8
(**11**)	H	TBS	H	*i*-Pr	----	1-2
(**12**)	H	H	H	*i*-Pr	----	>128

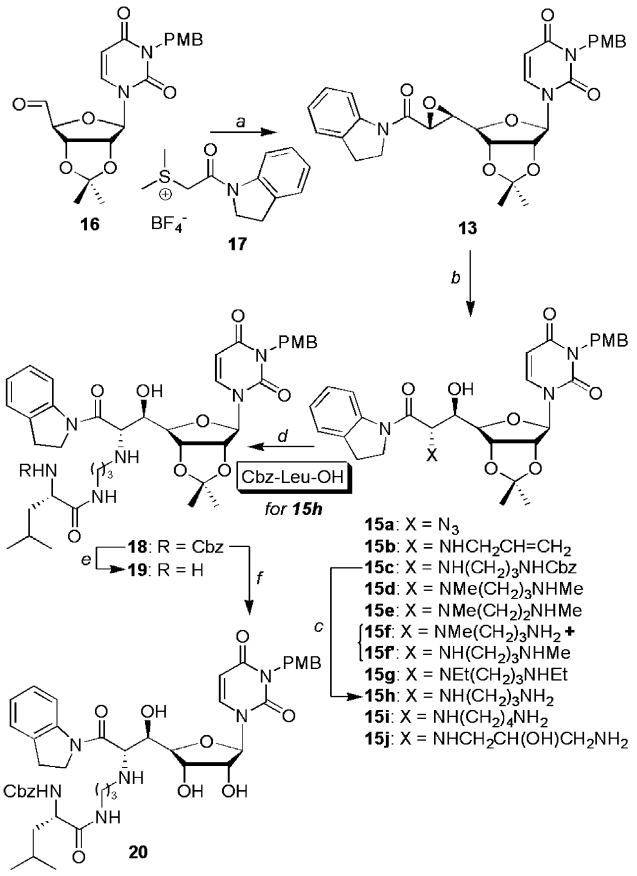
[a] IC_{50} values (μg/mL) in the soluble peptidoglycan assay (SPG).
[b] MIC (Minimal inhibitory concentration) (μg/mL): In vitro activity against various Gram-positive microorganisms.

Figure 2. Molecular structures of representative muraymycins analogues and antibiotics properties.

75% yield (see Table 1 for details). With the objective of designing a synthetic route capable of reaching so the natural muraymycins as the bioactive 5′-epimer derivatives, we proceeded with the construction of the peptidyl chain linkage. To this aim, we focused on the product **15h**, prepared directly by reaction of **13** with 1,3-propanediamine, or by the *Z*-cleavage[22] of the opening product **15c**, which contained the requisite diamine present in the natural muraymycins. Thus, the coupling of **15h** with the aminoacid derivative Cbz-Leu-OH[23] was accomplished by the action of the coupling reagent EDCI/HOBt[24] that afforded compound **18**. Having incorporated the L-leucine residue, the access to bioactive muraymycin analogues as depicted in Figure 2, required the transformation of the indoline amide to the corresponding ester, for which the oxidation to the indole derivative was attempted. Unfortunately, this oxidation did not yield the desired product, resulting in either decomposition products, when DDQ was used, or the recovery of starting material when milder oxidation conditions were used by the action of chloroanil[25] (Scheme 2). On the other hand, the cleavage of the Cbz group was efficiently accomplished, by the action of hydrogen, to obtain amine **19** in good yield (70%). In order to give access to unprotected derivatives, the PMB deprotection constituted a key step. Thus, treatment of amide **19** with CAN,[26] however, failed in the formation of the desired unprotected derivative. In contrast, the acetal cleavage mediated by the action of trifluoroacetic acid in



Scheme 1. Synthetic strategy towards the liposidomycin and the muraymycin antibiotics.



Scheme 2. Reagents and conditions: (a) 1.1 equiv **17**, 1.1 equiv 20% NaOH, CH_2Cl_2/H_2O, 0 °C, 2.5 h, 78%; (b) See Table 1 for conditions and yields; (c) 5.5 equiv $NH_4^+HCOO^-$, Pd–C, MeOH, reflux, 2 h, 65%; (d) 1.0 equiv **15h**, 1.2 equiv Cbz-Leu-OH, 1.2 equiv EDCI, 1.2 equiv HOBt, CH_2Cl_2, 25 °C, 2 h, 92%; (e) H_2, Pd–C, MeOH, 25 °C, 0.5 h, 70%; (f) TFA/H_2O, 0 °C, 1.5 h, 75%.

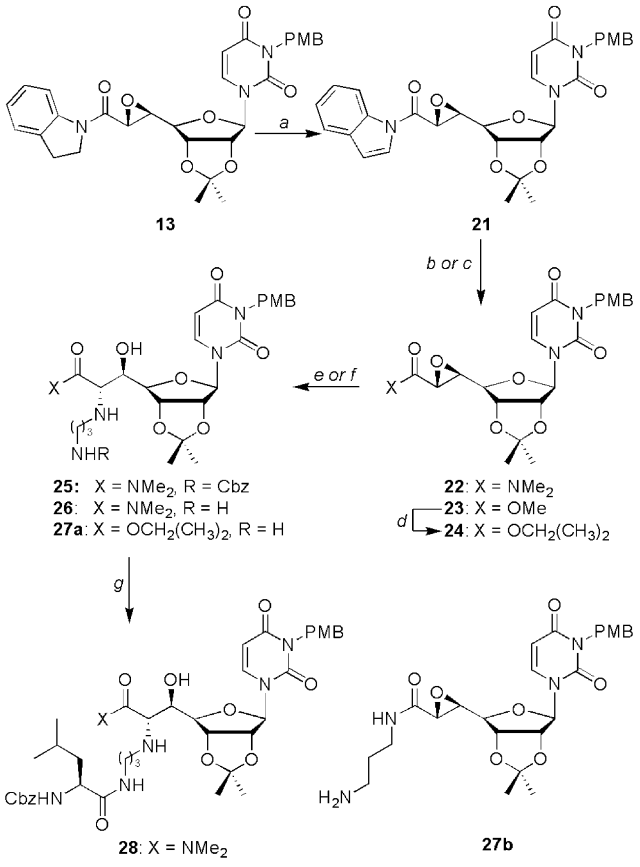
the presence of H_2O proved to be efficient to give triol derivative **20** in form of its ammonium salt.

With respect to the indoline amide oxidation, these fruitless, although not surprising,[27] results forced us to adopt a second strategy, initiated with the DDQ oxidation of the indoline epoxy amide **13** that provided indole epoxy amide **21** in a 76% yield (Scheme 3).[18] Having secured the formation of the indole amide, we proceeded with the reaction of **21** with *N*,*N*-dimethyl amine providing the corresponding *N*,*N*-dimethyl amide **22** (66%) together with its *N*,*N*-dimethyl-amino oxirane ring opening product in a 19% yield. On the other hand, the preparation of bulky esters, such as the isopropyl ester **24**, was not possible in a straightforward manner from indole epoxy amide **21**, requiring an additional transesterification step, from its corresponding methyl ester **23** intermediate, by the catalytic action of di-*n*-butyltin oxide.[28] The oxirane ring opening process with *N*-*Z*-1,3-propanediamine of epoxy amide **22** afforded amino alcohol **25** albeit in a modest 33% yield after a long reaction time (8 days at reflux). Taking into account that steric hindrance of the *N*-*Z*-1,3-propanediamine could justify the required long reaction time for completion, which might promote secondary processes, we decided to carry out these reactions with 1,3-propanodiamine. In fact, compounds **22** and **24** smoothly reacted with this diamine in 48 h, although with different results for each case. Thus, for epoxy amide **22**, the desired product **26** was cleanly obtained, according to its ^1H NMR spectra, not requiring further purification, in contrast to the reaction of epoxy ester **24** that yielded a complex mixture of products, isolating a 1:1 unseparable mixture of compounds **27a**:**27b** among them. In the light of these results, we opted to continue with *N*,*N*-dimethyl amide **26**, which was coupled with the L-leucine aminoacid derivative, under similar conditions as described above for compound **18**, to obtain compound **28** in a modest yield (36% overall yield from **22**).

Table 1. Reaction of epoxy amide **13** with nitrogen nucleophiles

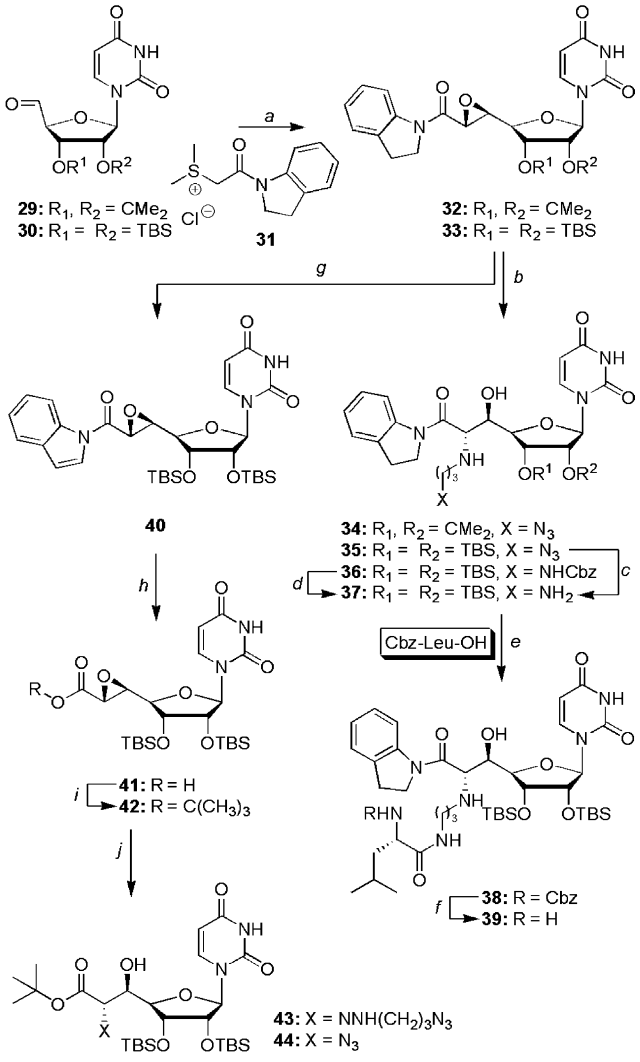
Entry	X	Conditions	Yield (%)
1	N_3	AcOH/DMF, 65 °C, 12 h	**15a** (65%)
2	$NHCH_2CH{=}CH_2$	MeOH, reflux, 12 h	**15b** (96%)
3	$NH(CH_2)_3NHCbz$	MeOH, reflux, 4 days	**15c** (83%)
4	$NMe(CH_2)_3NHMe$	MeOH, reflux, 24 h	**15d** (81%)
5	$NMe(CH_2)_2NHMe$	MeOH, reflux, 24 h	**15e** (79%)
6	$NMe(CH_2)_3NH_2$ + $NH(CH_2)_3NHMe$	MeOH, reflux, 24 h	**15f**+**15f'** (75%)
7	$NEt(CH_2)_3NHEt$	MeOH, reflux, 8 days	**15g** (66%)
8	$NH(CH_2)_3NH_2$	MeOH, reflux, 30 h	**15h** (73%)
9	$NH(CH_2)_4NH_2$	MeOH, reflux, 24 h	**15i** (62%)
10	$NHCH_2CH(OH)CH_2NH_2$	MeCN, reflux, 24 h	**15j** (69%)

In pursuit of circumventing all the synthetic obstacles associated with the presence of the PMB protecting group and the indoline-type amide and their subsequent cleavages, as it has been described above, we chose aldehydes **29**[29]



Scheme 3. Reagents and conditions: (a) 5.0 equiv DDQ, C_6H_6, reflux, 24 h, 76%; (b) 1.3 equiv Me_2NH, THF, 25 °C, 5 h, 66% of **22**, plus a 19% yield of the *N*,*N*-dimethylamino opening product; (c) 1.0 equiv Et_3N, MeOH, 25 °C, 0.5 h, 99% for **23**; (d) 0.1 equiv nBu_2SnO, *i*PrOH, reflux, 12 h, 67%; (e) 1.0 equiv **22**; 1.4 equiv $H_2N(CH_2)_3NHCbz$, MeOH, reflux, 8 days, 33% for **25**; (f) 2.0 equiv $H_2N(CH_2)_3NH_2$, MeOH, reflux, 48 h, no purification required for **26**, complex mixture for reaction of **24**, containing **27a** and **27b**; (g) 1.0 equiv **26**; 1.2 equiv Cbz-Leu-OH, 1.2 equiv EDCI, 1.2 equiv HOBt, CH_2Cl_2, 25 °C, 4 h, 36% from **22**.

and **30**[30] as starting points and 1-azido-3-propanoamine[31] as nucleophile in the subsequent oxirane ring opening reaction of the resulting epoxy amides (Scheme 4). Thus, aldehydes **29** and **30**, prepared from their corresponding alcohols by oxidation with DMP[32] and IBX,[33] respectively, were reacted with the sulfur ylide derived from the sulfonium salt **31**, to obtain epoxy amides **32** and **33** according to the one- and two-phases methodologies[34] in modest 43 and 61% yields, respectively, and high stereoselectivities. The installation of the 1,3-propanediamine linker, required for the construction of the peptidic chain, was undertaken through the reaction of epoxy amides **32** and **33** with 1-azido-3-propanoamine to obtain azido alcohols **34** and **35** in 48 and 83% yields, respectively. In a similar way, the reaction of **33** with *N*-*Z*-1,3-propanediamine afforded opening product **36** in a 83% yield. Either from **35** as from **36**, the amine **37** was obtained in very good yields, by treatments with triphenylphosphine or ammonium formate in the presence of palladium. The coupling with the L-leucine derivative produced amide **38**, without further difficulties, and was converted into amino alcohol **39** by *Z*-cleavage mediated by hydrogen. This product represents an interesting analogue related to the highly bioactive compound **11** (see Fig. 2). Having failed to oxidize indoline

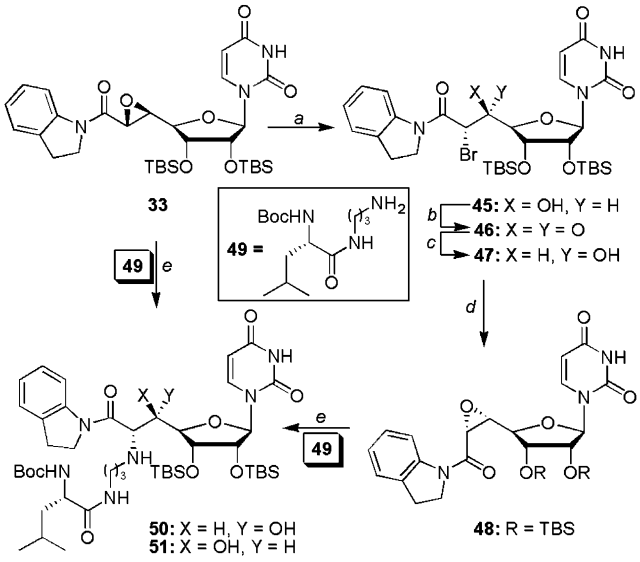


Scheme 4. Reagents and conditions: (a) (i) 1.03 equiv **31**, 3.2 equiv NaH, CH_3CN, 0 °C, 3 h, then addition over a solution of **29**, CH_2Cl_2, 0 °C, 2.5 h, 43% for **32**; (ii) 1.1 equiv **31**, 1.1 equiv 20% NaOH, 1.0 equiv **30**, CH_2Cl_2/H_2O, 0 °C, 1.5 h, 61% for **33**; (b) (i) 1.0 equiv **32** 1-azido-3-propanoamine, MeOH, 70 °C, 72 h, 48% for **34**; (ii) 1.0 equiv **33** 2.1 equiv 1-azido-3-propanoamine, MeOH, 70 °C, 48 h, 83% for **35**; (iii) 1.0 equiv **33** 2.0 equiv 1-*N*-*Z*-1,3-propanodiamine, MeOH, reflux, 48 h, 83% for **36**. (c) 4.0 equiv Ph_3P, THF, 25 °C, 1 h, then H_2O, 5 h, 75%; (d) Excess of $NH_4^+HCOO^-$, Pd–C, EtOH, 25 °C, 0.5 h, 72%; (e) 1.0 equiv **37**, 1.3 equiv Cbz-Leu-OH, 1.3 equiv EDCI, 1.3 equiv HOBt, CH_2Cl_2, 25 °C, 6 h, 74%; (f) H_2, Pd–C, MeOH, 25 °C, 0.5 h, 86%; (g) 1.0 equiv **33** 5.0 equiv DDQ, C_6H_6, 80 °C, 24 h, 86%; (h) 2.0 equiv LiOH, THF/H_2O, 0 °C, 20 min, 83%; (i) 2.0 equiv $Cl_3CC(=NH)OtBu$, CH_2Cl_2, 25 °C, 24 h, 98%; (j) (i) 1.5 equiv 1-azido-3-propanoamine, MeOH, 70 °C, 96 h, 20% for **43**; (ii) 2.0 equiv NaN_3, DMF, 65 °C, 3 h, 83% for **44**.

amides, containing *N*-*Z*-peptidic residues, to the corresponding indole amides, according to precedent results from our laboratories,[27] we then proceeded to investigate the possibility of fulfilling this oxidation from compounds **34** and **35**. However, the DDQ treatments of these indoline amides failed again to produce the desired indole amides, leading instead to a complex mixture of decomposition products. These discouraging results forced us to the accomplishment of such oxidation in earlier steps. Thus, epoxy amide **33** was transformed into the epoxy indole amide **40** by the action of DDQ, followed by basic hydrolysis with LiOH to obtain acid **41**. The formation of

the *tert*-butyl ester **42** was carried out by reaction of **41** with the corresponding *tert*-butyl trichloroacetimidate[35] to obtain the *tert*-butyl ester **42** in almost quantitative yield. With this ester in hand, we proceeded with the introduction of the diamine linker by reaction with 1-azido-3-aminopropane, expecting no interferences with the ester function, as it was observed for the isopropyl ester, described above. Unfortunately, this opening reaction proceeded in a low 20% yield in the formation of **43**, in contrast to the reaction of **42** with simple nucleophiles, such as sodium azide, which resulted in the formation of the 2-azido opening product **44** in a 83% yield (Scheme 4).

Despite that the 5′-epimers of truncated muraymycin analogues were as active as the derivatives with the right configuration at this position, we were strongly interested in the preparation of the 5′-(S) analogues in case of an eventual total synthesis of the natural congeners. From the *anti* amino alcohol derivative **15c**, we attempted the isomerization at C-5′ position by application of different methodologies described in the literature,[36] but, unfortunately, all these attempts failed. Finally, according to previous studies in our laboratories concerning with isomerization of *trans* epoxy amides,[37] we decided to undertake this epimerization from epoxy amide **33** by conversion to its corresponding cis isomer **48**, through bromohydrine intermediate. Thus, *anti* bromohydrine **45**, obtained by treatment of epoxy amide **33** with sodium bromide in the presence of amberlyst-15,[38] was subjected to the action of Dess–Martin periodinane to obtain ketone **46**, which was reduced with sodium borohydride to provide *syn* bromohydrine **47**. Finally, exposure of **47** to catalytic amounts of sodium methoxide in methanol afforded *cis* epoxy amide **48** in a 40% yield over four steps from **33**. With the requisite stereochemistry contained in the key precursor **48**, we devised the introduction of the peptidic chain in one step by reaction of epoxy amide **48** with amine **49**. Pleasingly, opening product **50** was obtained in excellent yield when **48** was treated with amine **49** in refluxing MeOH, despite the long time reaction that was required for almost completion (71% convesrion). In a similar way, *trans* epoxy amide **33** was treated with amine **49** to obtain **51** in a 99% yield (79% conversion) (Scheme 5).



Scheme 5. Reagents and conditions: (a) 4.0 equiv NaBr, Amberlyst-15, acetone, −20 °C, 12 h, 99%; (b) 2.0 equiv DMP, CH_2Cl_2, 0 °C, 8 h; (c) 1.0 equiv $NaBH_4$, EtOH, 0 °C, 1.25 h, 38% over two steps; (d) 3.0 equiv NaOMe, MeOH, 25 °C, 24 h, 99%; (e) 2.0–4.0 equiv **49**, MeOH, 70 °C, 4–14 days, 97% for **50** (71% conversion), 99% for **51** (79% conversion).

3. Conclusions

In conclusion, we have described a new and convergent synthetic approach towards the 5′-epimuraymycins, based on the use of epoxy amides, which are readily prepared by the reaction of aldehydes with stabilized sulfur ylides. An inspection of the structural features present in the muraymycins reveals the intriguing possibility of applying an oxirane ring opening reaction to construct modified 5′-epimuraymycins of biological interest. These preliminary synthetic results are of notable importance for the design of new muraymycin-type antibiotics and for the establishment of an efficient strategy for the eventual total synthesis of these natural complex nucleosides, that required the epimerization at C-5′ and the incorporation at this position of the 5′-aminoribose residue contained in these compounds by a glycosylation reaction. Whereas the epimerization at C-5 was successfully achieved via a *trans-cis* epoxy amide isomerization, the glycosylation reaction is divised as a much more difficult synthetic task,[39] in which we are currently devoting our synthetic efforts.

4. Experimental

4.1. General techniques

All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. Tetrahydrofuran (THF) and ethyl ether (ether) were distilled from sodium benzophenone, and methylene chloride (CH_2Cl_2), benzene (PhH), and toluene from calcium hydride. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. All solutions used in workup procedures were saturated unless otherwise noted. All reagents were purchased at highest commercial quality and used without further purification unless otherwise stated.

All reactions were monitored by thin-layer chromatography carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and 7% ethanolic phosphomolybdic acid or *p*-anisaldehyde solution and heat as developing agents. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography (PTLC) separations were carried out on 0.25, 0.50 or 1 mm E. Merck silica gel plates (60F-254).

NMR spectra were recorded on a Bruker Avance-400 instrument and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; band, several overlapping signals; b, broad. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter. High-resolution mass spectra

(HRMS) were recorded on a Kratos MS 80 RFA mass spectrometer under fast atom bombardment (FAB) conditions.

4.2. Opening reactions of epoxy amide 13 with nucleophiles

4.2.1. Azido alcohol 15a. A solution of epoxy amide **13** (0.2 g, 0.356 mmol, 1.0 equiv) in DMF (5 mL) was treated with sodium azide (93 mg, 1.42 mmol, 4.0 equiv) and acetic acid (20 μL, 0.356 mmol, 1.0 equiv) and the mixture was heated at 65 °C. After stirring for 12 h, the solution was allowed to reach room temperature, diluted with Et_2O (5 mL) and washed with saturated aqueous NH_4Cl solution (5 mL). The aqueous solution was extracted with Et_2O (2× 2 mL) and the combined organic phase was washed with brine (4 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography (silica gel, 60% EtOAc in hexanes) to provide azido alcohol **15a** (0.14 g, 65%) as a white solid: R_f=0.42 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −14.3 (*c* 0.7, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J*= 8.6 Hz, 1H, Ar indoline), 7.55 (d, *J*=8.1 Hz, 1H, H_6), 7.41 (d, *J*=8.6 Hz, 2H, Ar PMB), 7.12–7.09 (m, 2H, Ar indoline), 7.04 (dd, *J*=7.5, 7.5 Hz, 1H, Ar indoline), 6.79 (d, *J*=8.6 Hz, 2H, Ar PMB), 5.94 (d, *J*=3.8 Hz, 1H, $H_{1'}$), 5.76 (d, *J*=8.1 Hz, 1H, H_5), 5.02 (dd, *J*=5.9, 2.7 Hz, 1H, $H_{3'}$), 4.99 (d, *J*=4.3 Hz, 2H, CH_2Ar), 4.83 (dd, *J*=5.9, 3.8 Hz, 1H, $H_{2'}$), 4.60 (bs, 1H, OH), 4.53 (bs, 1H, $H_{4'}$), 4.35 (d, *J*=9.1 Hz, 1H, $H_{5'}$), 4.12–4.06 and 4.02–3.95 (2m, 2H, CH_2CH_2N indoline), 3.89 (d, *J*=9.1 Hz, 1H, $H_{6'}$), 3.72 (s, 3H, CH_3O), 3.19–3.00 (m, 2H, CH_2CH_2N indoline), 1.60 and 1.35 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 162.2, 159.1, 151.2, 141.9, 139.5, 131.7, 130.9, 128.6, 127.5, 125.0, 124.8, 117.6, 114.7, 113.6, 102.8, 94.4, 84.1, 83.2, 80.9, 71.4, 60.4, 55.2, 48.1, 43.7, 27.8, 27.3, 25.3; FAB HRMS (NBA): *m/e* 604.2297, M^+ calcd for $C_{30}H_{32}N_6O_8$ 604.2281.

4.2.2. *N*-Allylamino alcohol 15b. To a solution of epoxy amide **13** (0.2 g, 0.356 mmol, 1.0 equiv) in MeOH (5 mL) was added allylamine (82 μL, 1.06 mmol, 3.0 equiv). After stirring for 12 h at 60°, the solution was allowed to warm to 25 °C, and the reaction mixture was diluted with toluene (1.5 mL) and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 70% EtOAc, 5% MeOH in hexanes) furnished amino alcohol **15b** (212 mg, 96%) as a white solid: R_f=0.66 (silica gel, 60% EtOAc, 5% MeOH in hexanes); $[\alpha]_D^{22}$ +1.8 (*c* 0.2, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J*=7.5 Hz, 1H, Ar indoline), 7.53 (d, *J*=8.1 Hz, 1H, H_6), 7.41 (d, *J*=9.1 Hz, 2H, Ar PMB), 7.15–7.11 (m, 2H, Ar indoline), 7.01 (dd, *J*= 7.0 Hz, 1H, Ar indoline), 6.79 (d, *J*=9.1 Hz, 2H, Ar PMB), 5.87 (d, *J*=3.8 Hz, 1H, $H_{1'}$), 5.82–5.75 (m, 1H, CH_2CH), 5.72 (d, *J*=8.1 Hz, 1H, H_5), 5.15–4.96 (m, 4H, CH_2Ar, CH_2CH), 4.92 (dd, *J*=6.4, 3.2 Hz, 1H, $H_{3'}$), 4.79 (dd, *J*= 6.4, 3.8 Hz, 1H, $H_{2'}$), 4.60 (d, *J*=1.6 Hz, 1H, $H_{4'}$), 4.02–3.97 (m, 2H, CH_2CH_2N indoline), 3.90 (dd, *J*=8.1, 1.6 Hz, 1H, $H_{5'}$), 3.73 (s, 3H, CH_3O), 3.62 (d, *J*=8.1 Hz, 1H, $H_{6'}$), 3.25 (dd, *J*=14.0, 5.9 Hz, 1H, CH_2NH), 3.11 (dd, *J*=14.0, 6.4 Hz, 1H, CH_2NH), 3.07–2.90 (m, 2H, CH_2CH_2N indoline), 1.57 and 1.33 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 162.3, 159.1, 151.0, 142.2, 139.5, 136.6, 131.7, 130.9, 128.7, 127.3, 124.7, 124.4, 117.3, 116.5, 114.4, 113.7, 102.5, 93.8, 84.9, 83.2, 81.3, 73.2, 60.5, 55.2, 50.4, 48.0, 43.6, 27.7, 27.3, 25.3; FAB HRMS (NBA): *m/e* 641.2584, $M+Na^+$ calcd for $C_{33}H_{38}N_4O_8$ 641.2587.

4.2.3. Amino alcohol 15c. A solution of *N*-*Z*-1,3-diaminopropane hydrochloride (0.16 g, 0.64 mmol, 1.2 equiv) in MeOH (2 mL) was treated with triethylamine (0.15 mL, 1.07 mmol, 2.0 equiv) for 30 min at room temperature. After this time, this solution was added to a solution of epoxy amide **13** (0.3 g, 0.53 mmol, 1.0 equiv) in MeOH (3 mL) and the mixture was heated at reflux for 4 days. Then, the mixture was allowed to reach room temperature and toluene (1.5 mL) was added. The solution was concentrated under reduced pressure and the crude product was purified by flash column chromatography (silica gel, 60% EtOAc, 5% MeOH in hexanes) to provide amino alcohol **15c** (0.34 g, 83%) as a white solid: R_f=0.42 (silica gel, 65% EtOAc, 5% MeOH in hexanes); $[\alpha]_D^{22}$ +36.0 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J*=8.1 Hz, 1H, Ar indoline), 7.40 (d, *J*=8.6 Hz, 2H, Ar PMB), 7.34–7.27 (m, 6H, aromatics Cbz, H_6), 7.14–7.10 (m, 2H, Ar indoline), 7.01 (dd, *J*=7.5, 7.5 Hz, 1H, Ar indoline), 6.78 (d, *J*=8.6 Hz, 2H, Ar PMB), 5.78 (d, *J*=3.2 Hz, 1H, $H_{1'}$), 5.69 (d, *J*=8.1 Hz, 1H, H_5), 5.36 (m, 1H, N*H*Cbz), 5.09–4.93 (m, 5H, $H_{3'}$, CH_2ArPMB, CH_2ArCbz), 4.83–4.80 (m, 1H, $H_{2'}$), 4.57 (bs, 1H, $H_{4'}$), 4.04–3.98 (m, 2H, CH_2CH_2N indoline), 3.88 (d, *J*=8.1 Hz, 1H, $H_{5'}$), 3.72 (s, 3H, CH_3O), 3.61 (d, *J*=8.1 Hz, 1H, $H_{6'}$), 3.32–3.18 (m, 2H, CH_2NHCO), 3.01–2.96 (m, 2H, CH_2CH_2N indoline), 2.72–2.66 and 2.47–2.41 (2m, 2H, CH_2NH), 1.60–1.58 (m, 2H, CH_2), 1.55 and 1.31 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 162.2, 159.0, 156.4, 151.0, 142.3, 139.8, 136.6, 131.9, 131.7, 130.8, 128.5, 128.4, 128.0, 127.3, 124.7, 124.4, 117.3, 114.3, 113.6, 102.4, 94.3, 85.1, 83.1, 81.1, 72.9, 66.4, 61.7, 55.1, 48.1, 45.3, 43.6, 39.1, 29.4, 27.7, 27.2, 25.3; FAB HRMS (NBA): *m/e* 792.3220, $M+Na^+$ calcd for $C_{41}H_{47}N_5O_{10}$ 792.3220.

4.2.4. Amino alcohols 15d–j. *General procedure*. A solution 0.04–0.07 M of epoxy amide **13** (1.0 equiv) in MeOH was treated with the corresponding diamine (1.7–3.0 equiv) with the exception of alcohol **15j**, in which the solvent used was CH_3CN. After stirring for 12–30 h at reflux, the reaction mixture was diluted with toluene and the solvent was concentrated under reduced pressure for obtaining **15d**, **15e**, **15h**, **15i**, **15j** and a mixture 1:1 of **15f** and **15f'**. Particularly complete formation of alcohol **15g** required 8 days.

4.2.4.1. Compound [15d]. Purification by flash column chromatography (silica gel, 60% EtOAc, 5% MeOH in hexanes) provided amino alcohol **15d** (81%) as a yellow oil: R_f=0.56 (silica gel, 70% EtOAc, 5% MeOH in hexanes); $[\alpha]_D^{22}$ +1.8 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J*=8.2 Hz, 1H, Ar indoline), 7.65 (d, *J*=8.2 Hz, 1H, H_6), 7.43 (d, *J*=8.8 Hz, 2H, Ar PMB), 7.16–6.99 (m, 3H, Ar indoline), 6.79 (d, *J*=8.8 Hz, 2H, Ar PMB), 6.04 (d, *J*=4.1 Hz, 1H, $H_{1'}$), 5.71 (d, *J*=8.2 Hz, 1H, H_5), 5.05–4.90 (m, 3H, $H_{3'}$, CH_2Ar), 4.69 (dd, *J*=5.3, 4.1 Hz, 1H, $H_{2'}$), 4.38 (bs, 1H, $H_{4'}$), 4.27 (m, 1H, N*H*CH_3), 4.14–4.06 (m, 1H, CH_2CH_2N indoline), 3.95–3.88 (m, 2H, $H_{5'}$, CH_2CH_2N indoline), 3.77–3.75 (m, 1H, CH_2), 3.74 (s, 3H, CH_3O), 3.52

(d, J=8.2 Hz, 1H, $H_{6'}$), 3.07–2.99 (m, 3H, CH_2CH_2N indoline, CH_2), 2.65–2.52 (m, 2H, CH_2), 2.40 (s, 3H, NCH_3), 2.35–2.30 (m, 1H, CH_2), 1.57 (s, 3H, $NHCH_3$), 1.59 and 1.34 (2s, 6H, $C(CH_3)_2$) 1.30–1.25 (m, 1H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 162.4, 159.1, 151.2, 142.5, 139.1, 131.6, 131.0, 128.9, 127.4, 124.7, 124.4, 117.4, 114.2, 113.6, 102.6, 92.6, 84.9, 83.6, 81.5, 69.9, 66.3, 55.2, 51.5, 48.2, 43.7, 39.1, 33.9, 30.9, 29.7, 28.0, 27.5, 25.4; FAB HRMS (NBA): *m/e* 686.3175, $M+Na^+$ calcd for $C_{35}H_{45}N_5O_8$ 686.3166.

4.2.4.2. Compound [15e]. Purification by flash column chromatography (silica gel, 60% EtOAc, 5% MeOH in hexanes) provided alcohol **15e** (79%) as a white solid: R_f=0.56 (silica gel, 60% EtOAc, 5% MeOH in hexanes); $[\alpha]_D^{22}$ −7.6 (*c* 0.2, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J=7.6 Hz, 1H, Ar indoline), 7.63 (d, J=8.2 Hz, 1H, H_6), 7.43 (d, J=8.8 Hz, 2H, Ar PMB), 7.16–6.94 (m, 3H, Ar indoline), 6.77 (d, J=8.8 Hz, 2H, Ar PMB), 5.97 (d, J=4.1 Hz, 1H, $H_{1'}$), 5.73 (d, J=8.2 Hz, 1H, H_5), 5.03 and 4.93 (2d, J=13.5 Hz, 2H, CH_2Ar), 4.90 (dd, J=5.9, 2.3 Hz, 1H, $H_{3'}$), 4.68 (dd, J=5.9, 4.7 Hz, 1H, $H_{2'}$), 4.42 (bs, 1H, $H_{4'}$), 4.34 (m, 1H, $NHCH_3$), 4.24–4.17 and 3.92–3.85 (2m, 2H, CH_2CH_2N indoline), 3.76–3.70 (m, 3H, CH_2, $H_{5'}$), 3.73 (s, 3H, CH_3O), 3.51 (d, J=8.8 Hz, 1H, $H_{6'}$), 2.97–2.82 (m, 3H, CH_2CH_2N indoline, CH_2), 2.70–2.65 (m, 1H, CH_2), 2.40 (s, 3H, NCH_3), 1.56 (s, 3H, $NHCH_3$), 1.55 and 1.33 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 162.4, 159.1, 151.3, 142.5, 139.1, 131.5, 131.0, 128.9, 127.4, 124.7, 124.4, 117.2, 114.2, 113.6, 102.7, 92.6, 84.7, 83.6, 81.5, 69.6, 66.7, 55.2, 52.9, 47.9, 43.7, 38.6, 29.7, 27.7, 27.4, 27.3, 25.4; FAB HRMS (NBA): *m/e* 672.3005, $M+Na^+$ calcd for $C_{34}H_{43}N_5O_8$ 672.3009.

4.2.4.3. Compounds [15f]+[15f′]. Purification by flash column chromatography (silica gel, 60% EtOAc, 5% MeOH in hexanes) provided an inseparable 1:1 mixture of alcohols **15f** and **15f′** (75%) as a colourless oil: R_f=0.36 (silica gel, 60% EtOAc, 5% MeOH in hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 and 8.14 (2d, J=7.0 Hz, 2H, Ar indoline), 7.68 (d, J=8.2 Hz, 2H, H_6), 7.42 and 7.39 (2d, J=8.2 Hz, 4H, Ar PMB), 7.19–7.12 (m, 4H, Ar indoline), 7.05–6.97 (m, 2H, Ar indoline), 6.77 (d, J=8.2 Hz, 4H, Ar PMB), 6.08 and 5.78 (2d, J=4.1 Hz, 2H, $H_{1'}$), 5.73 and 5.71 (2d, J=8.2 Hz, 2H, H_5), 5.06 and 4.87 (m, 6H, $H_{3'}$, CH_2Ar), 4.80 and 4.68 (2dd, J=6.4, 4.1 Hz, 2H, $H_{2'}$), 4.47 and 4.37 (2br s, 2H, $H_{4'}$), 4.34–3.84 (m, 6H, $H_{5'}$, CH_2CH_2N indoline), 3.74 and 3.73 (2s, 6H, CH_3O), 3.53 and 3.47 (2d, J=8.2 Hz, 2H, $H_{6'}$), 3.02–2.97 (m, 4H, CH_2CH_2N indoline), 3.10–3.04, 2.69–2.66, 2.60–2.54 and 2.35–2.26 (4m, 8H, CH_2), 2.42 (s, 3H, NCH_3), 1.75–1.60 (m, 4H, CH_2), 1.59, 1.54, 1.34, and 1.31 (4s, 2H, $C(CH_3)_2$), 1.23 (s, 3H, $NHCH_3$); FAB HRMS (NBA): *m/e* 672.3015, $M+Na^+$ calcd for $C_{34}H_{43}N_5O_8$ 672.3009.

4.2.4.4. Compounds [15g]. Purification by flash column chromatography (silica gel, 80% EtOAc in hexanes) provided alcohol **15g** (66%) as a white solid: R_f=0.65 (silica gel, 80% EtOAc in hexanes); $[\alpha]_D^{22}$ +11.6 (*c* 0.2, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J=8.2 Hz, 1H, Ar indoline), 7.76 (d, J=8.2 Hz, 1H, H_6), 7.42 (d, J=8.8 Hz, 2H, Ar PMB), 7.16–7.10 (m, 2H, Ar indoline), 7.00 (dd, J=7.6, 7.6 Hz, 1H, Ar indoline), 6.77 (d, J=8.8 Hz, 2H, Ar PMB), 6.11 (d, J=4.1 Hz, 1H, $H_{1'}$), 5.71 (d, J=8.2 Hz, 1H, H_5), 5.04 and 4.93 (2d, J=14.1 Hz, 2H, CH_2Ar), 4.89 (dd, J=5.9, 1.8 Hz, 1H, $H_{3'}$), 4.66 (dd, J=5.9, 4.1 Hz, 1H, $H_{2'}$), 4.42 (bs, 1H, $H_{4'}$), 4.25 (d, J=8.2 Hz, 1H, $H_{5'}$), 4.12–4.02 and 3.94–3.88 (2m, 2H, CH_2CH_2N indoline), 3.73 (s, 3H, CH_3O), 3.76–3.71 (m, 1H, CH_2), 3.63 (d, J=8.2 Hz, 1H, $H_{6'}$), 3.46–3.37 (m, 1H, CH_2), 3.12–2.92 (m, 2H, CH_2CH_2N indoline), 2.79–2.61 (m, 4H, CH_2CH_3), 1.92–1.64 (m, 2H, CH_2), 1.59 and 1.34 (2s, 6H, $C(CH_3)_2$), 1.55–1.46 and 1.14–1.03 (2m, 2H, CH_2), 1.31–1.23 (m, 3H, CH_2CH_3), 0.96 (t, J=7.0 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 162.5, 159.1, 151.2, 142.6, 138.8, 131.7, 131.0, 128.9, 127.4, 124.7, 124.3, 114.7, 114.1, 113.6, 102.6, 91.9, 84.7, 84.0, 81.6, 70.1, 64.3, 55.2, 49.2, 48.8, 48.2, 46.8, 43.7, 33.9, 28.5, 28.0, 27.5, 25.6, 25.4, 24.9; FAB HRMS (NBA): *m/e* 714.3485, $M+Na^+$ calcd for $C_{37}H_{49}N_5O_8$ 714.3479.

4.2.4.5. Compound [15h]. Purification by flash column chromatography (silica gel, 15% MeOH in CH_2Cl_2) provided alcohol **15h** (165 mg, 73%) as major product and epoxy amide opening product with NH_3 (45 mg, 22%) as minor product: [**15h**] white solid: R_f=0.71 (silica gel, 15% MeOH in CH_2Cl_2); $[\alpha]_D^{22}$ −9.4 (*c* 0.1, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, J=8.1 Hz, 1H, Ar indoline), 7.74 (d, J=8.1 Hz, 1H, H_6), 7.42 (d, J=8.6 Hz, 2H, Ar PMB), 7.14–7.11 (m, 2H, Ar indoline), 6.99 (dd, J=7.5, 7.5 Hz, 1H, Ar indoline), 6.78 (d, J=8.6 Hz, 2H, Ar PMB), 5.98 (d, J=3.8 Hz, 1H, $H_{1'}$), 5.74 (d, J=8.1 Hz, 1H, H_5), 4.98 (2d, J=13.4 Hz, 2H, CH_2Ar), 4.89–4.86 (m, 1H, $H_{3'}$), 4.74–4.70 (m, 1H, $H_{2'}$), 4.58 (bs, 1H, $H_{4'}$), 4.12–4.01 (m, 2H, CH_2CH_2N indoline), 3.83 (d, J=7.0 Hz, 1H, $H_{5'}$), 3.73 (s, 3H, CH_3O), 3.65 (d, J=7.0 Hz, 1H, $H_{6'}$), 3.07–2.99 (m, 2H, CH_2CH_2N indoline), 2.74–2.42 (m, 4H, CH_2), 1.56 and 1.31 (2s, 6H, $C(CH_3)_2$), 1.54–1.49 (m, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 162.5, 159.1, 151.1, 142.3, 139.6, 131.7, 130.1, 128.7, 127.4, 124.8, 124.6, 117.3, 114.3, 113.6, 102.4, 93.4, 85.0, 83.3, 81.5, 72.6, 61.8, 55.2, 48.2, 45.9, 43.7, 40.2, 31.5, 27.8, 27.3, 25.3; FAB HRMS (NBA): *m/e* 658.2854, $M+Na^+$ calcd for $C_{33}H_{41}N_5O_8$ 658.2853.

4.2.4.6. Compound [15i]. Purification by flash column chromatography (silica gel, 80% EtOAc, 10% MeOH in hexanes) provided alcohol **15i** (62%) as a colourless oil: R_f=0.64 (silica gel, 80% EtOAc, 10% MeOH in hexanes); $[\alpha]_D^{22}$ +5.7 (*c* 0.04, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J=8.2 Hz, 1H, Ar indoline), 7.49 (d, J=8.2 Hz, 1H, H_6), 7.39 (d, J=8.8 Hz, 2H, Ar PMB), 7.15–7.12 (m, 2H, Ar indoline), 7.00 (dd, J=7.0, 7.0 Hz, 1H, Ar indoline), 6.78 (d, J=8.2 Hz, 2H, Ar PMB), 5.83 (d, J=2.9 Hz, 1H, $H_{1'}$), 5.74 (d, J=8.2 Hz, 1H, H_5), 4.92–4.50 (m, 3H, $H_{3'}$, CH_2Ar), 4.82–4.79 (m, 1H, $H_{2'}$), 4.54 (bs, 1H, H_4), 4.07–3.97 (m, 3H, $H_{5'}$, CH_2CH_2N indoline), 3.74–3.72 (m, 1H, $H_{6'}$), 3.73 (s, 3H, CH_3O), 3.07–3.03 (m, 2H, CH_2CH_2N indoline), 2.64–2.37 (m, 4H, CH_2), 1.59–1.46 (m, 4H, CH_2), 1.55 and 1.31 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 159.1, 151.1, 142.3, 139.8, 131.6, 130.8, 128.6, 127.4, 124.7, 124.5, 117.4, 114.4, 113.7, 102.5, 94.4, 85.0, 82.9, 81.4, 72.7, 61.8, 55.2, 48.2, 47.5, 43.7, 33.9, 29.7, 27.9, 27.7, 27.3, 25.3; FAB HRMS (NBA): *m/e* 672.3015, $M+Na^+$ calcd for $C_{34}H_{43}N_5O_8$ 672.3009.

4.2.4.7. Compound [15j]. Purification by flash column chromatography (silica gel, 10% MeOH in CH_2Cl_2)

provided alcohol **15j** (69%) as a colourless oil: $R_f=0.43$ (silica gel, 10% MeOH in CH_2Cl_2); $[\alpha]_D^{22}$ −6.7 (*c* 0.1, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, $J=8.2$ Hz, 1H, Ar indoline), 7.77 and 7.72 (2d, $J=8.2$ Hz, 1H, H_6), 7.41 (d, $J=7.0$ Hz, 2H, Ar PMB), 7.14–7.10 (m, 2H, Ar indoline), 7.01–6.96 (m, 1H, Ar indoline), 6.78 (d, $J=$ 8.8 Hz, 2H, Ar PMB), 5.97 and 6.00 (2d, $J=3.5$ Hz, 1H, $H_{1'}$), 5.71 (d, $J=8.2$ Hz, 1H, H_5), 5.03–4.82 (m, 3H, $H_{3'}$, CH_2Ar), 4.74–4.70 (m, 1H, $H_{2'}$), 4.60–4.58 (m, 1H, $H_{4'}$), 4.15–3.96 (m, 2H, CH_2CH_2N indoline), 3.78–3.64 (m, 4H, $H_{5'}$, $H_{6'}$, CH_2), 3.71 (s, 3H, CH_3O), 3.09–2.99 (m, 2H, CH_2CH_2N indoline), 2.65–2.46 (m, 3H, CH, CH_2), 1.56 and 1.30 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 162.4, 159.0, 150.1, 142.2, 139.4, 131.8, 130.8, 128.5, 127.3, 124.8, 124.4, 117.1, 114.1, 113.6, 102.2, 92.7, 85.3, 83.7, 81.5, 72.8, 71.1, 62.3, 55.1, 51.2, 48.0, 45.1, 43.6, 33.8, 27.3, 25.3; FAB HRMS (NBA): *m/e* 674.2810, $M+Na^+$ calcd for $C_{33}H_{41}N_5O_9$ 674.2802.

4.3. Amino alcohol 15hReduction of N-Z-amino alcohol 15c

A solution of amino alcohol **15c** (116 mg, 0.15 mmol, 1.0 equiv) in MeOH (2.0 mL) was treated with 10% Pd–C (11 mg) and ammonium formate (52 mg, 0.82 mmol, 5.5. equiv) under an Ar atmosphere. The reaction mixture was refluxed for 2 h and, then, allowed to reach ambient temperature. The resulting suspension was filtered through a Celite pad, washed with MeOH (2×5 mL), and the organic clear solution was concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 15% MeOH in CH_2Cl_2) provided amino alcohol **15h** (62 mg, 65%).

4.4. Compound 18. Coupling between Cbz-Leu-OH and amino alcohol 15h

Cbz-Leu-OH (0.3 g, 1.13 mmol, 1.2 equiv) was dissolved in dry CH_2Cl_2 (4 mL) and treated with HOBt (0.16 g, 1.13 mmol, 1.2 equiv) at room temperature. After stirring for 5 min, EDCI (0.22 g, 1.13 mmol, 1.2 equiv) was added to the reaction mixture, which was stirred for 45 min, prior to the addition to a solution of **15h** (0.59 g, 0.94 mmol, 1.0 equiv) in CH_2Cl_2 (3 mL). The mixed system was stirred for an additional 1 h 15 min, after which, aqueous 15% NH_3 solution (0.2 mL) was added and the resulting mixture was diluted with Et_2O (5 mL) and washed with a saturated aqueous NH_4Cl soluton (5 mL). The layers were separated and the aqueous phase was extracted with Et_2O (2×5 mL). The combined organic solution was dried ($MgSO_4$), filtered and concentrated. Purification by flash column chromatography (silica gel, 10% MeOH in CH_2Cl_2) afforded peptidic derivative **18** (764 mg, 92%) as a white solid: $R_f=0.41$ (silica gel, 10% MeOH in CH_2Cl_2); $[\alpha]_D^{22}$ −1.6 (*c* 0.9, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, $J=8.1$ Hz, 1H, Ar indoline), 7.50 (d, $J=8.1$ Hz, 1H, H_6), 7.39 (d, $J=$ 8.6 Hz, 2H, Ar PMB), 7.32–7.27 (m, 5H, aromatics Cbz), 7.14–7.10 (m, 2H, Ar indoline), 7.00 (dd, $J=7.5$, 7.5 Hz, 1H, Ar indoline), 6.78 (d, $J=8.6$ Hz, 2H, Ar PMB), 5.85 (d, $J=3.2$ Hz, 1H, $H_{1'}$), 5.71 (d, $J=8.1$ Hz, 1H, H_5), 5.46 (bs, 1H, NHCbz), 5.09–4.95 (m, 4H, CH_2ArPMB, CH_2ArCbz), 4.91 (dd, $J=6.4$, 2.7 Hz, 1H, $H_{3'}$), 4.82 (d, $J=6.4$, 3.2 Hz, 1H, $H_{2'}$), 4.56 (bs, 1H, $H_{4'}$), 4.10–4.00 (m, 3H, CH_2CH_2N indoline, $CHCH_2CH(CH_3)_2$), 3.91 (d, $J=7.0$ Hz, 1H, $H_{5'}$), 3.73 (s, 3H, CH_3O), 3.59 (d, $J=7.0$ Hz, 1H, $H_{6'}$), 3.40–3.32 and 3.26–3.17 (2m, 2H, CH_2NHCO), 3.08–2.98 (m, 2H, CH_2CH_2N indoline), 2.67–2.57 and 2.46–2.40 (2m, 2H, CH_2NH), 1.63–1.50 (m, 5H, CH_2, $CHCH_2CH(CH_3)_2$, $CHCH_2CH(CH_3)_2$), 1.56 and 1.31 (2s, 6H, $C(CH_3)_2$), 0.87 and 0.85 (2s, 6H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 162.3, 159.1, 156.3, 151.1, 142.2, 139.9, 136.2, 131.6, 130.8, 128.6, 128.5, 128.2, 128.0, 127.5, 126.9, 124.7, 124.6, 117.4, 114.4, 113.6, 102.3, 94.6, 84.7, 82.7, 81.4, 72.6, 66.9, 62.0, 55.2, 53.7, 48.2, 45.0, 43.7, 41.1, 37.0, 28.9, 27.9, 27.3, 25.3, 24.7, 22.8, 22.0; FAB HRMS (NBA): *m/e* 905.4064, $M+Na^+$ calcd for $C_{47}H_{58}N_6O_{11}$ 905.4061.

4.5. Amino alcohol 19. Hydrogenation of compound 18

To a solution of compound **18** (0.12 g, 0.136 mmol, 1.0 equiv) in MeOH (4 mL) was added 10% Pd–C (120 mg). The reaction was allowed to proceed under an atmosphere of H_2 at 25 °C for 30 min. After this time, the mixture was filtered and the filtrate was washed with MeOH (2×5 mL). The combined organic solvents were removed by concentration under reduced pressure and the resulting residue was subjected to purification by flash column chromatography (silica gel, 15% MeOH in CH_2Cl_2) to afford amino alcohol **19** (71 mg, 70%) as a colourless oil: $R_f=0.56$ (silica gel, 10% MeOH in CH_2Cl_2); $[\alpha]_D^{22}$ +4.0 (*c* 0.1, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, $J=$ 7.6 Hz, 1H, Ar indoline), 7.72 (d, $J=8.1$ Hz, 1H, H_6), 7.40 (d, $J=9.1$ Hz, 2H, Ar PMB), 7.14–7.10 (m, 2H, Ar indoline), 7.00 (dd, $J=7.5$, 7.5 Hz, 1H, Ar indoline), 6.78 (d, $J=9.1$ Hz, 2H, Ar PMB), 5.95 (d, $J=3.8$ Hz, 1H, $H_{1'}$), 5.72 (d, $J=8.1$ Hz, 1H, H_5), 5.01–4.92 (m, 3H, $H_{3'}$, CH_2Ar), 4.75 (dd, $J=4.3$, 3.8 Hz, 1H, $H_{2'}$), 4.61 (bs, 1H, $H_{4'}$), 4.09–4.05 (m, 2H, CH_2CH_2N indoline), 3.94 (d, $J=7.5$ Hz, 1H, $H_{5'}$), 3.73 (s, 3H, CH_3O), 3.74–3.71 (m, 1H, $H_{6'}$), 3.55–3.48 (m, 1H, $CHCH_2CH(CH_3)_2$), 3.39–3.34 and 3.24–3.16 (2m, 2H, CH_2NHCO), 3.11–3.02 (m, 2H, CH_2CH_2N indoline), 2.72–2.67 and 2.55–2.49 (2m, 2H, CH_2NH), 1.67–1.60 (m, 5H, CH_2, $CHCH_2CH(CH_3)_2$, $CHCH_2CH(CH_3)_2$), 1.54 and 1.29 (2s, 6H, $C(CH_3)_2$), 0.90–0.86 (m, 6H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.4, 159.1, 151.1, 142.2, 139.6, 131.8, 130.8, 128.7, 127.3, 124.8, 124.5, 117.3, 114.2, 113.6, 102.4, 93.2, 84.8, 83.2, 81.6, 72.4, 62.0, 55.2, 53.2, 48.2, 45.6, 43.7, 43.0, 37.1, 29.3, 27.8, 27.3, 25.3, 24.7, 23.1, 21.6; FAB HRMS (NBA): *m/e* 771.3680, $M+Na^+$ calcd for $C_{39}H_{52}N_6O_9$ 771.3693.

4.6. Triol 20

Compound **19** (50 mg, 0.057 mmol, 1.0 equiv) was treated with a solution of TFA/H_2O 9:1 (1.7 mL) at 0 °C until the reaction was complete as judged by TLC (ca. 1.5 h). The crude mixture was then diluted with toluene and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 10% MeOH in CH_2Cl_2) provided triol **20** (36 mg, 75%) as a white solid: $R_f=0.40$ (silica gel, 10% MeOH in CH_2Cl_2); $[\alpha]_D^{22}$ +7.6 (*c* 0.3, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, $J=8.1$ Hz, 1H, H_6), 7.73 (d, $J=7.5$ Hz, 1H, Ar indoline), 7.37 (d, $J=$ 8.6 Hz, 2H, Ar PMB), 7.26–7.22 (m, 5H, aromatics Cbz), 7.13–7.06 (m, 2H, Ar indoline), 6.98 (dd, $J=7.5$, 7.5 Hz,

1H, Ar indoline), 6.75 (d, $J=8.6$ Hz, 2H, Ar PMB), 5.89 (bs, 1H, $H_{1'}$), 5.74 (bs, 1H, N*H*Cbz), 5.70 (d, $J=8.1$ Hz, 1H, H_5), 5.05–4.90 (m, 4H, CH_2ArPMB, CH_2ArCbz), 4.41 (bs, 1H, $H_{4'}$), 4.29–3.94 (m, 6H, $H_{2'}$, $H_{3'}$, $H_{5'}$, CH_2CH_2N indoline, $CHCH_2CH(CH_3)_2$), 3.73–3.70 (m, 1H, $H_{6'}$), 3.72 (s, 3H, CH_3O), 3.35–3.28 and 3.19–3.13 (2m, 2H, CH_2-NHCO), 3.05–3.01 (m, 2H, CH_2CH_2N indoline), 2.66–2.58 and 2.47–2.41 (2m, 2H, CH_2NH), 1.62–1.45 (m, 5H, CH_2, $CHCH_2CH(CH_3)_2$, $CHCH_2CH(CH_3)_2$), 0.89–0.82 (m, 6H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 162.5, 159.0, 156.5, 151.3, 142.1, 138.8, 136.0, 132.0, 130.7, 128.8, 128.5, 128.2, 127.8, 127.4, 124.9, 124.7, 117.3, 113.6, 102.0, 91.2, 84.2, 74.7, 72.2, 70.7, 67.0, 62.0, 55.2, 53.7, 48.2, 44.9, 43.6, 41.0, 37.1, 30.0, 27.8, 24.6, 22.8, 21.9; FAB HRMS (NBA): *m/e* 865.3752, $M+Na^+$ calcd for $C_{44}H_{54}N_6O_{11}$ 865.3748.

4.7. *N,N*-Dimethyl epoxy amide 22

A solution of epoxy-indole amide **21**[18] (89 mg, 0.159 mmol, 1.0 equiv) in THF (2 mL) was treated with dimethylamine (26 μL, 0.207 mmol, 1.3 equiv) and the mixture was stirred at room temperature for 5 h. After this time, the crude mixture was concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 70% EtOAc, 5% MeOH in hexanes) provided epoxy amide **22** (51 mg, 66%) as major product together with the *N,N*-dimethyl amino alcohol opening product (16 mg, 19%) as minor product.

*Compound [**22**]*. White solid; $R_f=0.40$ (silica gel, 100% EtOAc); $[\alpha]_D^{22}$ +18.9 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, $J=8.6$ Hz, 2H, Ar), 7.30 (d, $J=8.1$ Hz, 1H, H_6), 6.79 (d, $J=8.6$ Hz, 2H, Ar), 5.98 (d, $J=2.7$ Hz, 1H, $H_{1'}$), 5.76 (d, $J=8.1$ Hz, 1H, H_5), 5.04 and 4.95 (2d, $J=14.0$ Hz, 2H, CH_2Ar), 4.93 (dd, $J=5.9$, 3.8 Hz, 1H, $H_{3'}$), 4.75 (dd, $J=5.9$, 2.7 Hz, 1H, $H_{2'}$), 4.25 (dd, $J=3.8$, 3.8 Hz, 1H, $H_{4'}$), 3.75 (s, 3H, CH_3O), 3.67 (d, $J=2.1$ Hz, 1H, $H_{6'}$), 3.49 (dd, $J=3.8$, 2.1 Hz, 1H, $H_{5'}$), 3.09 and 2.96 (2s, 6H, $N(CH_3)_2$), 1.56 and 1.33 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 162.2, 159.1, 150.8, 138.4, 130.9, 128.7, 114.8, 113.6, 103.0, 92.4, 83.9, 83.2, 81.4, 57.2, 55.2, 50.4, 43.7, 36.4, 35.7, 27.2, 25.3; FAB HRMS (NBA): *m/e* 487.1945, M^+ calcd for $C_{24}H_{29}N_3O_8$ 487.1955.

4.8. Methyl epoxy ester 23

To a solution of epoxy-indole amide **21** (78 mg, 0.139 mmol, 1.0 equiv) in MeOH (2.5 mL) was added triethylamine (20 μL, 0.139 mmol, 1.0 equiv), and the reaction mixture was stirred for 30 min at 25 °C. After this time, the solvent was removed by concentration under reduced pressure and the crude product was purified by flash column chromatography (silica gel, 40% EtOAc, 5% MeOH in hexanes) to obtain epoxy ester **23** (66 mg, 99%) as a white solid: $R_f=0.43$ (silica gel, 40% EtOAc, 5% MeOH in hexanes); $[\alpha]_D^{22}$ +14.0 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, $J=8.6$ Hz, 2H, Ar), 7.20 (d, $J=8.1$ Hz, 1H, H_6), 6.80 (d, $J=8.6$ Hz, 2H, Ar), 5.82 (d, $J=2.7$ Hz, 1H, $H_{1'}$), 5.76 (d, $J=8.1$ Hz, 1H, H_5), 5.03 and 4.96 (2d, $J=14.0$ Hz, 2H, CH_2Ar), 4.95 (dd, $J=6.4$, 4.3 Hz, 1H, $H_{3'}$), 4.83 (dd, $J=6.4$, 2.7 Hz, 1H, $H_{2'}$), 4.12 (dd, $J=4.3$, 4.3 Hz, 1H, $H_{4'}$), 3.78 and 3.75 (2s, 6H, CH_3O), 3.55 (dd, $J=4.3$, 2.1 Hz, 1H, $H_{5'}$), 3.50 (d, $J=2.1$ Hz, 1H, $H_{6'}$), 1.54 and 1.33 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 162.2, 159.1, 139.0, 130.7, 114.8, 113.7, 102.9, 94.0, 84.8, 84.3, 81.6, 57.4, 55.2, 52.7, 50.2, 43.6, 27.1, 25.3; FAB HRMS (NBA): *m/e* 497.1532, $M+Na^+$ calcd for $C_{23}H_{26}N_2O_9$ 497.1536.

4.9. Isopropyl epoxy ester 24

To a stirred solution of methyl epoxy ester **23** (45 mg, 0.095 mmol, 1.0 equiv) in 2-methyl-2-propanol (2.5 mL) was added Bu_2SnO (2.4 mg, 9.5 μmol, 0.1 equiv). The reaction mixture was then heated at reflux with complete depletion of starting material after 12 h, according to TLC analysis. The crude mixture was allowed to warm to 25 °C, diluted with EtOAc (5 mL) and washed with saturated aqueous $NaHCO_3$ solution (5 mL). The aqueous solution was extracted with EtOAc (2×5 mL) and the combined organic layers were dried over $MgSO_4$, filtered through a pad of Celite and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 40% EtOAc, 5% MeOH in hexanes) furnished epoxy ester **24** (32 mg, 67%) as a white solid: $R_f=0.57$ (silica gel, 40% EtOAc, 5% MeOH in hexanes); $[\alpha]_D^{22}$ +8.0 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, $J=8.6$ Hz, 2H, Ar), 7.23 (d, $J=8.1$ Hz, 1H, H_6), 6.80 (d, $J=8.6$ Hz, 2H, Ar), 5.88 (d, $J=2.7$ Hz, 1H, $H_{1'}$), 5.77 (d, $J=8.1$ Hz, 1H, H_5), 5.12–4.93 (m, 4H, $H_{3'}$, CH_2Ar, $CH(CH_3)_2$), 7.81 (dd, $J=6.4$, 2.7 Hz, 1H, $H_{2'}$), 4.19 (dd, $J=3.8$, 3.8 Hz, 1H, $H_{4'}$), 3.75 (s, 3H, CH_3O), 3.53 (dd, $J=3.8$, 1.6 Hz, 1H, $H_{5'}$), 3.45 (d, $J=1.6$ Hz, 1H, $H_{6'}$), 1.55 and 1.33 (2s, 6H, $C(CH_3)_2$), 1.27 and 1.26 (2s, 6H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 162.2, 159.1, 150.8, 138.7, 130.7, 128.7, 114.8, 113.7, 102.9, 93.2, 84.2, 84.0, 81.5, 70.0, 57.3, 55.2, 50.5, 43.6, 27.1, 25.3, 21.7, 21.6; FAB HRMS (NBA): *m/e*=525.1852, $M+Na^+$ calcd for $C_{25}H_{30}N_2O_9$ 525.1849.

4.10. Amino alcohol 25

A solution of *N*-*Z*-1,3-diaminopropane hydrochloride (34.4 mg, 0.14 mmol, 1.4 equiv) in MeOH (2 mL) was treated with triethylamine (28 μL, 0.2 mmol, 2.0 equiv) for 30 min at room temperature. After this time, this solution was added to a solution of epoxy amide **22** (49 mg, 0.1 mmol, 1.0 equiv) in MeOH (2 mL) and the resulting reaction mixture was heated under reflux for 8 days. Then, the mixture was allowed to reach room temperature and toluene (1.0 mL) was added. The resulting azeotropic solution was concentrated under reduced pressure and the crude product was purified by flash column chromatography (silica gel, 75% EtOAc, 5% MeOH in hexanes) to furnish amino alcohol **25** (41 mg, 33%) as a white solid: $R_f=0.26$ (silica gel, 75% EtOAc, 5% MeOH in hexanes); $[\alpha]_D^{22}$ +22.9 (*c* 0.7, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, $J=8.6$ Hz, 2H, Ar PMB), 7.32–7.27 (m, 6H, aromatics Cbz, H_6), 6.77 (d, $J=8.6$ Hz, 2H, Ar PMB), 5.74–5.69 (m, 2H, $H_{1'}$, H_5), 5.38 (bs, N*H*Cbz), 5.10–4.98 (m, 4H, CH_2ArPMB, CH_2ArCbz) 4.91 (dd, $J=6.4$, 3.2 Hz, 1H, $H_{3'}$), 4.81–4.79 (m, 1H, $H_{2'}$), 4.47 (bs, 1H, $H_{4'}$), 3.80 (d, $J=8.1$ Hz, 1H, $H_{5'}$), 3.74 (bs, 4H, CH_3O, $H_{6'}$), 3.28–3.17 (m, 2H, CH_2NHCO), 2.91 (s, 6H, $N(CH_3)_2$), 2.64–2.58 and 2.42–2.36 (2m, 2H, CH_2NH), 1.60–1.55 (m, 2H, CH_2), 1.54 and 1.31 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 173.3, 162.3, 159.0, 156.5, 151.1, 140.0, 130.8, 128.7, 128.5, 128.0, 114.4, 113.6, 102.4, 94.6, 85.1, 83.0, 81.1, 72.4, 66.4, 58.8, 55.2, 45.3, 43.6, 39.1, 37.2, 35.8, 29.3, 27.3, 25.3; FAB HRMS (NBA): *m/e* 718.3071, $M+Na^+$ calcd for $C_{35}H_{45}N_5O_{10}$ 718.3064.

4.11. Amino alcohol 26

A solution of epoxy amide **22** (61 mg, 0.125 mmol, 1.0 equiv) in MeOH (2 mL) was treated with 1,3-diaminopropane (21 μL, 0.25 mmol, 2.0 equiv) for 48 h at 70 °C. After this time, the mixture was allowed to reach room temperature and toluene (1.0 mL) was added. Then, the solution was concentrated under reduced pressure and the crude product was used in the coupling step without purification.

4.12. Compound 28

Cbz-Leu-OH (40 mg, 0.15 mmol, 1.2 equiv) was dissolved in dry CH_2Cl_2 (2 mL) and treated with HOBt (21 mg, 0.15 mmol, 1.2 equiv) at room temperature. After stirring for 5 min, EDCI (29.4 mg, 0.15 mmol, 1.2 equiv) was added to the solution. The mixture was stirred for 45 min and then, the crude mixture was added to a solution of amino alcohol **26** (~0.125 mmol, 1.0 equiv) in CH_2Cl_2 (2 mL). The reaction mixture was then stirred for additional 3 h. After that time, a 15% aqueous NH_3 solution (0.5 mL) was added and the reaction mixture was diluted with Et_2O (10 mL) and washed with a saturated aqueous NH_4Cl solution (10 mL). The layers were separated and the aqueous phase was extracted with Et_2O (2×5 mL). The combined organic phase was dried ($MgSO_4$), filtered and concentrated. Purification by flash column chromatography (silica gel, 10% MeOH in EtOAc) afforded peptidic derivative **28** (36 mg, 36% over two steps from **22**) as a white solid: R_f=0.40 (silica gel, 10% MeOH in EtOAc); $[\alpha]_D^{22}$ +10.6 (*c* 0.8, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J*=8.1 Hz, 1H, H_6), 7.40 (d, *J*=8.6 Hz, 2H, Ar PMB), 7.32–7.29 (m, 5H, aromatics Cbz), 6.78 (d, *J*=8.6 Hz, 2H, Ar PMB), 5.87 (bs, 1H, $H_{1'}$), 5.74 (d, *J*=8.1 Hz, 1H, H_5), 5.63 (bs, 1H, N*H*Cbz), 5.09–4.96 (m, 4H, CH_2ArPMB, CH_2ArCbz), 4.89 (dd, *J*=6.4, 2.7 Hz, 1H, $H_{3'}$), 4.82–4.79 (m, 1H, $H_{2'}$), 4.44 (bs, 1H, $H_{4'}$), 4.10–4.04 (m, 1H, C*H*CH_2CH$(CH_3)_2$), 3.96–3.86 (m, 1H, $H_{5'}$), 3.78–3.73 (m, 1H, $H_{6'}$), 3.75 (s, 3H, CH_3O), 3.40–3.33 and 3.27–3.19 (2m, 2H, CH_2NHCO), 2.95–2.91 (m, 6H, N(CH_3)$_2$), 2.60–2.52 and 2.48–2.39 (2m, 2H, CH_2NH), 1.62–1.51 (m, 5H, CH_2, CHCH_2CH$(CH_3)_2$, CHCH_2C*H*$(CH_3)_2$), 1.56 and 1.31 (2s, 6H, C(CH_3)$_2$), 0.92–0.85 (m, 6H, CH(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 164.4, 159.1, 156.3, 151.1, 140.0, 136.3, 130.9, 130.7, 128.7, 128.5, 128.1, 128.0, 127.9, 114.5, 113.6, 102.6, 94.4, 84.8, 82.7, 81.3, 71.6, 66.9, 59.4, 55.2, 53.6, 44.9, 43.7, 43.6, 41.1, 37.3, 35.9, 29.6, 27.3, 25.3, 24.7, 22.7, 22.0; FAB HRMS (NBA): *m/e* 808.4001, $M+Na^+$ calcd for $C_{41}H_{56}N_6O_{11}$ 808.4007.

4.13. Epoxy amide 32

A solution of sulfonium salt **31** (93 mg, 0.361 mmol, 1.03 equiv) in CH_3CN (2.5 mL) was treated with NaH (45 mg, 1.13 mmol, 3.2 equiv). The reaction mixture was stirred at 25 °C for 3 h. After this time, *t*-butyl methyl ether (3 mL) was added and the combined organic solution was filtered, washed with *t*-butyl methyl ether and hexanes, and concentrated under reduced pressure. Thus, the resulting sulfur ylide was dissolved in CH_2Cl_2 (3 mL) and treated with crude aldehyde **29** (~0.352 mmol, 1.0 equiv), obtained by oxidation of its corresponding alcohol (0.1 g, 0.370 mmol) with DMP, at 0 °C. After 2.5 h, the crude mixture was concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 80% EtOAc in hexanes) afforded epoxy amide **32** (46 mg, 43% from precursor alcohol of aldehyde **29**) as a white solid: R_f=0.51 (silica gel, 100% EtOAc); $[\alpha]_D^{22}$ +24.0 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.70 (bs, 1H, N*H*), 8.13 (d, *J*=8.6 Hz, 1H, Ar), 7.34 (d, *J*=8.1 Hz, H_6), 7.17–7.13 (m, 2H, Ar), 7.01 (dd, *J*=7.0, 7.0 Hz, 1H, Ar), 5.89 (d, *J*=2.1 Hz, 1H, $H_{1'}$), 5.71 (dd, *J*=8.1, 1.6 Hz, 1H, H_5), 4.99 (dd, *J*=6.4, 3.8 Hz, 1H, $H_{3'}$), 4.84 (dd, *J*=6.4, 2.1 Hz, 1H, $H_{2'}$), 4.24–4.13 (m, 3H, $H_{4'}$, CH_2CH_2N indoline), 3.68 (d, *J*=2.1 Hz, 1H, $H_{6'}$), 3.63–3.62 (m, 1H, $H_{5'}$), 3.23–3.16 (m, 2H, CH_2CH_2N indoline), 1.55 and 1.33 (2s, 6H, C(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 163.1, 150.2, 142.3, 141.9, 131.7, 127.2, 124.9, 124.7, 117.4, 114.3, 102.5, 92.1, 84.7, 83.2, 81.9, 57.8, 50.5, 49.3, 48.7, 44.9, 30.0, 27.9, 27.5, 25.1; FAB HRMS (NBA): *m/e* 464.1429, $M+Na^+$ calcd for $C_{22}H_{23}N_3O_7$ 464.1434.

4.14. Epoxy amide 33

To a solution of crude aldehyde **30** (~0.9 g, 1.9 mmol, 1.0 equiv), prepared from its corresponding alcohol (0.93 g, 1.9 mmol) by oxidation with IBX, in CH_2Cl_2 (8 mL) was added at 0 °C, sulfonium salt **31** (0.56 g, 2.16 mmol, 1.1 equiv) and a 20% aqueous NaOH solution (0.43 mL, 2.16 mmol, 1.1 equiv). After stirring for 1.5 h, the crude mixture was diluted with H_2O (10 mL), the layers were separated and the aqueous phase was extracted with EtOAc (1×10 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 50% EtOAc in hexanes) gave epoxy amide **33** (0.76 g, 61% over two steps from its corresponding alcohol) as a white solid: R_f=0.45 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ +51.3 (*c* 1.4, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (bs, 1H, N*H*), 8.17 (d, *J*=8.1 Hz, 1H, H_6), 7.75 (d, *J*=8.1 Hz, 1H, Ar), 7.22–7.19 (m, 2H, Ar), 7.06 (dd, *J*=7.0, 7.0 Hz, 1H, Ar), 5.98 (d, *J*=4.8 Hz, 1H, $H_{1'}$), 5.76 (dd, *J*=8.1, 2.1 Hz, 1H, H_5), 4.35 (d, *J*=3.2 Hz, 1H, $H_{4'}$), 4.20–4.16 (m, 2H, CH_2CH_2N indoline), 4.11–4.09 (m, 2H, $H_{2'}$, $H_{3'}$), 3.78 (d, *J*=2.1 Hz, 1H, $H_{6'}$), 3.51 (d, *J*=2.1 Hz, 1H, $H_{5'}$), 3.28–3.24 (m, 2H, CH_2CH_2N indoline), 0.90 and 0.86 (2s, 18H, C(CH_3)$_3$), 0.12, 0.11, 0.05, and 0.03 (4s, 12H, Si(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 162.8, 150.4, 142.2, 139.5, 130.9, 127.7, 124.7, 124.6, 117.3, 103.0, 87.8, 79.2, 74.8, 73.6, 57.2, 50.6, 47.3, 28.1, 25.7, 25.6, 18.1, 17.9, −4.9, −4.8, −4.6, −4.5; FAB HRMS (NBA): *m/e* 652.2846, $M+Na^+$ calcd for $C_{31}H_{47}N_3O_7Si_2$ 652.2850.

4.15. Azido alcohol 34

A solution of epoxy amide **32** (46 mg, 0.104 mmol, 1.0 equiv) in MeOH (2 mL) was treated with a 6.4 M 1-azido-3-propanoamine solution in Et_2O (16 μL, 0.104 mmol, 1.0 equiv). After stirring at 70 °C for 72 h,

the crude mixture was diluted with toluene (0.5 mL) and concentrated in vacuo. Purification by flash column chromatography (silica gel, 100% EtOAc) provided compound **34** (27 mg, 48%) as a white solid: R_f=0.44 (silica gel, 100% EtOAc); $[\alpha]_D^{22}$ −7.2 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J*=7.5 Hz, 1H, Ar), 7.64 (d, *J*=8.1 Hz, 1H, H_6), 7.17–7.13 (m, 2H, Ar), 7.01 (dd, *J*=7.0, 7.0 Hz, 1H, Ar), 5.90 (d, *J*=3.4 Hz, 1H, $H_{1'}$), 5.67 (d, *J*=8.1 Hz, 1H, H_5), 4.91 (dd, *J*=5.9, 2.7 Hz, 1H, $H_{3'}$), 4.80 (dd, *J*=5.9, 3.4 Hz, 1H, $H_{2'}$), 4.59 (bs, 1H, $H_{4'}$), 4.16–4.04 (m, 2H, CH_2CH_2N indoline), 3.88 (d, *J*=8.6 Hz, 1H, $H_{5'}$), 3.68 (d, *J*=8.6 Hz, $H_{6'}$), 3.40–3.27 (m, 2H, CH_2N_3), 3.12–3.06 (m, 2H, CH_2CH_2N indoline), 2.75–2.64 and 2.55–2.49 (2m, 2H, CH_2NH), 1.72–1.65 (m, 2H, CH_2), 1.57 and 1.33 (2s, 6H, $C(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 163.2, 150.4, 142.1, 141.8, 131.8, 127.5, 124.8, 124.6, 117.4, 114.4, 102.8, 92.8, 84.9, 83.1, 81.4, 73.0, 61.6, 49.2, 48.2, 44.8, 29.4, 27.8, 27.3, 25.3; FAB HRMS (NBA): *m/e* 564.2288, $M+Na^+$ calcd for $C_{25}H_{31}N_7O_7$ 564.2183.

4.16. Azido alcohol 35

A solution of epoxy amide **33** (0.2 g, 0.318 mmol, 1.0 equiv) in MeOH (7 mL) was treated with a 6.4 M of 1-azido-3-propanoamine solution in Et_2O (0.1 mL, 0.68 mmol, 2.1 equiv). After stirring at 70 °C for 48 h, the crude mixture was then diluted with toluene (1.0 mL) and concentrated in vacuo. Purification by flash column chromatography (silica gel, 50% EtOAc in hexanes) provided compound **35** (193 mg, 83%) as a white solid: R_f=0.41 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −7.2 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (bs, 1H, N*H*), 8.22 (d, *J*=8.1 Hz, 1H, H_6), 7.68 (d, *J*=8.1 Hz, 1H, Ar), 7.19–7.17 (m, 2H, Ar), 7.03 (dd, *J*=7.0, 7.0 Hz, 1H, Ar), 5.68 (d, *J*=8.1 Hz, 1H, H_5), 5.62 (d, *J*=6.4 Hz, 1H, $H_{1'}$), 4.43 (dd, *J*=6.4, 4.8 Hz, 1H, $H_{2'}$), 4.39 (bs, 1H, $H_{4'}$), 4.20–4.09 (m, 3H, $H_{3'}$, CH_2CH_2N indoline), 3.80–3.71 (m, 2H, $H_{5'}$, $H_{6'}$), 3.41–3.28 (m, 2H, CH_2N_3), 3.16–3.12 (m, 2H, CH_2CH_2N indoline), 2.79–2.73 and 2.60–2.51 (2m, 2H, CH_2NH), 1.72–1.67 (m, 2H, CH_2), 0.88 and 0.82 (2s, 18H, $C(CH_3)_3$), 0.06, 0.003, and −0.05 (3s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 150.4, 142.4, 142.2, 131.7, 127.5, 124.7, 124.6, 117.5, 102.3, 91.8, 85.6, 73.5, 73.0, 72.0, 61.8, 49.1, 48.2, 44.8, 27.9, 25.8, 25.7, 18.0, 17.9, 2.2, 1.9, 1.7; FAB HRMS (NBA): *m/e* 752.3584, $M+Na^+$ calcd for $C_{34}H_{55}N_7O_7Si_2$ 752.3599.

4.17. Amino alcohol 36

A solution of *N*-*Z*-1,3-diaminopropane hydrochloride (0.16 g, 0.63 mmol, 2.0 equiv) in MeOH (2 mL) was treated with triethylamine (0.13 mL, 0.906 mmol, 2.9 equiv) for 30 min at room temperature. After this time, the resulting mixture was added to a solution of epoxy amide **33** (0.2 g, 0.318 mmol, 1.0 equiv) in MeOH (4 mL) and the reaction mixture was stirred under reflux for 48 h. Then, the mixture was allowed to reach room temperature and toluene (1.0 mL) was added. The solution was concentrated under reduced pressure and the crude product was purified by flash column chromatography (silica gel, 80% EtOAc in hexanes) to provide amino alcohol **36** (0.22 g, 83%) as a white solid: R_f=0.56 (silica gel, 80% EtOAc in hexanes); $[\alpha]_D^{22}$ −4.0 (*c* 0.4, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (bs, 1H, N*H*), 8.20 (d, *J*=8.1 Hz, 1H, Ar indoline), 7.34–7.26 (m, 6H, aromatics Cbz, H_6), 7.18–7.14 (m, 2H, Ar indoline), 7.02 (dd, *J*=7.5, 7.5 Hz, 1H, Ar indoline), 5.61 (d, *J*=8.1 Hz, 1H, H_5), 5.51 (d, *J*=5.4 Hz, 1H, $H_{1'}$), 5.27 (bs, 1H, N*H*Cbz), 5.04 (2d, *J*=12.4 Hz, 2H, CH_2Ar), 4.49–4.45 (m, 1H, $H_{2'}$), 4.33 (br s, 1H, $H_{4'}$), 4.17–4.10 (m, 3H, $H_{3'}$, CH_2CH_2N indoline), 3.96–3.81 (br s, 2H, $H_{5'}$, $H_{6'}$), 3.32–3.23 (m, 2H, CH_2NHCO), 3.17–3.13 (m, 2H, CH_2CH_2N indoline), 2.77 and 2.54 (2bs, 2H, CH_2NH), 1.66 (bs, 2H, CH_2), 0.86 and 0.81 (2s, 18H, $C(CH_3)_3$), 0.05, 0.04, −0.004 and −0.07 (4s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 156.6, 150.4, 142.7, 142.2, 136.6, 131.6, 128.5, 128.1, 128.0, 127.5, 124.7, 117.5, 102.4, 92.3, 86.1, 73.1, 73.0, 66.7, 62.2, 58.1, 48.2, 45.2, 38.6, 28.0, 25.7, 18.0, 17.9, −4.5, −4.6, −4.7, −5.0; FAB HRMS (NBA): *m/e* 860.4066, $M+Na^+$ calcd for $C_{42}H_{63}N_5O_9Si_2$ 860.4062.

4.18. Amino alcohol 37

Procedure A. A solution of azido alcohol **35** (19 mg, 0.028 mmol, 1.0 equiv) in THF (1.0 mL) was treated with Ph_3P (29 mg, 0.11 mmol, 4.0 equiv) at room temperature for 1 h. After this time, H_2O (1 mL) was added and the resulting mixture was vigorously stirred for additional 5 h. After this time, the crude mixture was diluted with Et_2O, the phases were separated and the aqueous phase was extracted with Et_2O (2×5 mL). The combined ethereal solution was washed with brine, dried ($MgSO_4$), filtered and concentrated to obtain a crude product, which was purified by flash column chromatography (silica gel, 10→15% MeOH in CH_2Cl_2) to provide amino alcohol **37** (15 mg, 75%) as a white solid. *Procedure B*. A solution of alcohol **36** (113 mg, 0.135 mmol, 1.0 equiv) in EtOH (10 mL) was treated with Pd–C 10% wt (0.15 g) and $HCOONH_4$ 25% w/v (1.7 mL) under Ar atmosphere. After stirring for 30 min at room temperature, the mixture was filtered through a pad of Celite, and the filtrates were washed with MeOH (2×5 mL) and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography (silica gel, 10→15% MeOH in CH_2Cl_2) to provide amino alcohol **37** (68 mg, 72%): R_f=0.32 (silica gel, 10% MeOH in CH_2Cl_2); $[\alpha]_D^{22}$ −5.1 (*c* 0.4, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J*=8.6 Hz, 1H, Ar), 8.02 (bs, 1H, H_6), 7.18–7.14 (m, 2H, Ar), 7.02 (dd, *J*=7.5 Hz, 1H, Ar) 6.03 (d, *J*=7.0 Hz, 1H, H_5), 5.65 (d, *J*=4.3 Hz, 1H, $H_{1'}$), 4.42–4.00 (m, 6H, $H_{2'}$, $H_{3'}$, $H_{5'}$, $H_{6'}$, CH_2CH_2N indoline) 4.12 (bs, 1H, $H_{4'}$), 3.39–3.14 (m, 4H, CH_2CH_2N indoline, CH_2NH), 3.10 and 2.66 (2bs, 2H, CH_2NH_2), 1.99 and 1.72 (2bs, 2H, CH_2), 0.80 and 0.70 (2s, 18H, $C(CH_3)_3$), −0.003, −0.02, −0.04, −0.1 (4s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 164.8, 153.8, 150.7, 142.5, 131.4, 127.4, 124.5, 124.3, 117.5, 102.7, 91.3, 85.5, 73.5, 68.4, 64.4, 48.2, 47.8, 41.2, 29.6, 28.3, 25.6, 24.3, 17.8, −4.5, −4.7, −4.9; FAB HRMS (NBA): *m/e* 726.3687, $M+Na^+$ calcd for $C_{34}H_{57}N_5O_7Si_2$ 726.3694.

4.19. Peptidic derivative 38

Z-Leu-OH (29.4 mg, 0.11 mmol, 1.3 equiv) was dissolved in dry CH_2Cl_2 (1 mL) and treated with HOBt (15.3 mg, 0.11 mmol, 1.3 equiv) at room temperature. After stirring

for 5 min, EDCI (21.7 mg, 0.11 mmol, 1.3 equiv) was added to the solution and the resulting mixture was stirred for 45 min and added to a solution of **37** (60 mg, 0.085 mmol, 1.0 equiv) in CH_2Cl_2 (1.5 mL). The reaction mixture was then stirred for additional 6 h. After that time, a 15% aqueous NH_3 solution (0.2 mL) was added and the crude mixture was diluted with Et_2O (4 mL) and washed with NH_4Cl (4 mL). The layers were separated and the aqueous phase was extracted with Et_2O (2×4 mL). The combined organic phase was dried over $MgSO_4$, filtered and concentrated. Purification by flash column chromatography (silica gel, 5% MeOH in CH_2Cl_2) afforded peptidic derivative **38** (60 mg, 74%) as a white solid: R_f=0.58 (silica gel, 10% MeOH in CH_2Cl_2); $[\alpha]_D^{22}$ −10.8 (*c* 1.5, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (d, J=7.5 Hz, 1H, Ar indoline), 7.50 (bs, 1H, H_6), 7.34–7.25 (m, 4H, aromatics Cbz), 7.17–7.12 (m, 2H, Ar indoline), 7.01 (dd, J=7.5, 7.5 Hz, 1H, Ar indoline) 5.65 (d, J=7.5 Hz, 1H, H_5), 5.53 (bs, 1H, $H_{1'}$), 5.07 (2d, J=12.4 Hz, 2H, CH_2Ar), 4.57 (bs, 1H, $H_{2'}$) 4.30 (bs, 1H, $H_{4'}$), 4.27–4.07 (m, 4H, CH_2CH_2N indoline, $H_{3'}$, $CHCH_2CH(CH_3)_2$), 3.83 (bs, 1H, $H_{5'}$), 3.70 (bs, 1H, $H_{6'}$), 3.36–3.24 (m, 2H, CH_2NHCO), 3.17–3.11 (m, 2H, CH_2CH_2N indoline), 2.78–2.70 and 2.57–2.51 (2m, 2H, CH_2NH), 1.67–1.41 (m, 5H, CH_2, $CHCH_2CH(CH_3)_2$, $CHCH_2CH(CH_3)_2$), 0.87–0.82 (m, 24H, $CH(CH_3)_2$, $C(CH_3)_3$), 0.03, 0.02, −0.01, −0.07 (4s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 169.3, 162.8, 156.3, 150.6, 143.3, 142.4, 142.3, 136.2, 131.4, 128.5, 128.1, 128.0, 127.5, 124.7, 124.5, 117.5, 102.4, 93.5, 86.8, 74.0, 73.5, 67.0, 66.9, 62.8, 53.4, 48.1, 41.5, 37.9, 28.0, 25.7, 24.6, 23.0, 22.8, 21.9, 18.0, 17.8, −4.5, −4.6, −4.7, −5.1; FAB HRMS (NBA): *m/e* 973.4905, $M+Na^+$ calcd for $C_{48}H_{74}N_6O_{10}Si_2$ 973.4903.

4.20. Amine alcohol 39

Compound **38** (31 mg, 0.033 mmol, 1.0 equiv) was dissolved in MeOH (3 mL) and purged with Ar. Then, 10% Pd–C (30 mg) was added and the reaction mixture was exposed to a H_2 atmosphere for 30 min. After this time, the mixture was filtered and the filtrate was washed with MeOH (2×3 mL). The combined organic solution was concentrated under reduced pressure and the resulting crude product was purified by flash column chromatography (silica gel, 10% MeOH in CH_2Cl_2) to obtain amine **39** (23 mg, 86%) as a white solid: R_f=0.39 (silica gel, 10% MeOH in CH_2Cl_2); $[\alpha]_D^{22}$ −11.3 (*c* 0.2, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J=8.1 Hz, 1H, Ar), 7.64 (d, J=8.1 Hz, 1H, H_6), 7.50 (bs, 1H, N*H*), 7.17–7.12 (m, 2H, Ar), 7.01 (dd, J=7.5, 7.5 Hz, 1H, Ar) 5.67 (d, J=8.1 Hz, 1H, H_5), 5.61 (d, J=6.4 Hz, 1H, $H_{1'}$), 4.44 (dd, J=6.4, 5.4 Hz, 1H, $H_{2'}$) 4.31 (bs, 1H, $H_{4'}$), 4.14–4.08 (m, 3H, $H_{3'}$, CH_2CH_2N indoline), 3.84 (d, J=6.4 Hz, 1H, $H_{5'}$), 3.72 (d, J=6.4 Hz, 1H, $H_{6'}$), 3.43–3.21 (m, 3H, CH_2NHCO, $CHCH_2CH(CH_3)_2$), 3.18–3.12 (m, 2H, CH_2CH_2N indoline), 2.72–2.68 and 2.53–2.43 (2m, 2H, CH_2NH), 1.63–1.61 (m, 4H, CH_2, $CHCH_2CH(CH_3)_2$, $CHCH_2CH(CH_3)_2$), 1.32–1.25 (m, 1H, $CHCH_2CH(CH_3)_2$), 0.89–0.81 (m, 24H, $CH(CH_3)_2$, $C(CH_3)_3$), 0.04, 0.02, −0.01, −0.06 (4s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 169.5, 163.1, 150.5, 142.8, 142.3, 131.5, 127.5, 124.7, 124.5, 117.5, 102.4, 91.2, 86.1, 73.4, 71.4, 62.4, 53.4, 48.1, 45.2, 43.8, 36.9, 30.9, 29.6, 28.0, 25.8, 25.7, 24.8, 23.2, 21.4, 18.0, 17.9, −4.5, −4.6, −4.7, −5.0; FAB HRMS (NBA): *m/e* 817.4718, $M+Na^+$ calcd for $C_{40}H_{68}N_6O_8Si_2$ 817.4715.

4.21. Epoxy indole amide 40

A solution of epoxy amide **33** (0.47 g, 0.75 mmol, 1.0 equiv) in C_6H_6 (8 mL) was treated with DDQ (0.89 g, 3.73 mmol, 5.0 equiv) for 24 h at 80 °C. After this time, the reaction mixture was allowed to reach room temperature and diluted with $CHCl_3$ (10 mL) and washed sequentially with a saturated aqueous $NaHCO_3$ solution (3×10 mL) and brine (5 mL). The combined organic solution was concentrated under reduced pressure and the crude product was purified by flash column chromatography (silica gel, 40% EtOAc in hexanes) to afford epoxy amide **40** (0.40 g, 86%) as a white solid: R_f=0.73 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ +44.0 (*c* 0.3, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (bs, 1H, N*H*), 8.39 (d, J=6.4 Hz, 1H, Ar), 7.73 (d, J=8.6 Hz, 1H, H_6), 7.58–7.56 and 7.39–7.29 (2m, 4H, CHC*H*N indoline, Ar), 6.73 (d, J=3.8 Hz, 1H, C*H*CHN indoline), 5.98 (d, J=4.8 Hz, 1H, $H_{1'}$), 5.79 (dd, J=8.6, 2.1 Hz, 1H, H_5), 4.43 (d, J=4.3 Hz, 1H, $H_{4'}$), 4.29 (d, J=1.6 Hz, 1H, $H_{5'}$), 4.30 (dd, J=4.3, 4.3 Hz, 1H, $H_{3'}$), 4.12 (dd, J=4.8, 4.3 Hz, 1H, $H_{2'}$), 3.61 (d, J=1.6 Hz, 1H, $H_{6'}$), 0.91 and 0.88 (2s, 18H, $C(CH_3)_3$), 0.13, 0.12, 0.07 and 0.05 (4s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 163.1, 150.4, 139.2, 135.5, 130.2, 125.7, 124.6, 123.3, 121.1, 116.4, 111.1, 103.0, 88.2, 78.7, 74.9, 73.3, 57.7, 51.0, 25.7, 25.6, 18.0, 17.9, −4.4, −4.7, −4.9; FAB HRMS (NBA): *m/e* 650.2692, $M+Na^+$ calcd for $C_{31}H_{45}N_3O_7Si_2$ 650.2694.

4.22. Epoxy acid 41. Reaction of epoxy amide 40 with lithium hydroxide

To a solution of epoxy amide **40** (57 mg, 0.091 mmol, 1.0 equiv) in THF (3 mL) was added a 0.1 M aqueous LiOH solution (1.82 mL, 0.182 mmol, 2.0 equiv) dropwise during 15 min at 0 °C. After 5 min, the reaction mixture was diluted with EtOAc (3 mL) and both phases were separated. The aqueous layer was washed with EtOAc (2×3 mL) and acidified with Amberlyst-15 until pH 5. Then, the solution was extracted with EtOAc (3×3 mL) and the combined organic extracts were concentrated in vacuo to obtain crude epoxy acid **41** (40 mg, 83%), which did not require further purification and was used in the next step: R_f=0.1 (silica gel, 50% AcOEt in hexanes); $[\alpha]_D^{22}$ +74.9 (*c* 0.3, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.33 (bs, 1H, N*H*), 7.68 (d, J=8.1 Hz, 1H, H_6), 5.88 (d, J=4.8 Hz, 1H, $H_{1'}$), 5.78 (d, J=8.1 Hz, 1H, H_5), 4.33 (d, J=4.3 Hz, 1H, $H_{4'}$) 4.13–4.09 (m, 1H, $H_{2'}$), 4.05 (dd, J=4.3, 4.3 Hz, 1H, $H_{3'}$), 3.64 (d, J=1.6 Hz, 1H, $H_{6'}$), 3.46 (bs, 1H, $H_{5'}$), 0.91 and 0.86 (2s, 18H, $C(CH_3)_3$), 0.11, 0.10, 0.04, 0.03 (4s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.4, 172.0, 163.7, 139.8, 102.7, 88.3, 78.8, 75.0, 73.3, 57.2, 50.0, 25.8, 25.7, 18.1, 17.9, −4.4, −4.7, −4.9; FAB HRMS (NBA): *m/e* 551.2223, $M+Na^+$ calcd for $C_{23}H_{40}N_2O_8Si_2$ 551.2221.

4.23. *t*-Butyl epoxy ester 42

To a stirred solution of epoxy acid **41** (35 mg, 0.066 mmol, 1.0 equiv) in CH_2Cl_2 (3 mL) was added *t*-Butyl 2,2,2-trichloroacetimidate 1 M in cyclohexane (0.132 mL,

0.132 mmol, 2.0 equiv). After being stirred for 24 h at 25 °C, the reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 35% EtOAc in hexanes) afforded *t*-butyl epoxy ester **42** (38 mg, 98%) as a pale yellow solid impurified with 2,2,2-trichloroacetamide: R_f=0.33 (silica gel, 30% EtOAc in hexanes); $[\alpha]_D^{22}$ +16.1 (*c* 0.6, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.39 (bs, 1H, N*H*), 7.66 (d, *J*=8.1 Hz, 1H, H_6), 5.85 (d, *J*=4.3 Hz, 1H, $H_{1'}$), 5.76 (dd, *J*=8.1, 1.6 Hz, 1H, H_5), 4.30 (dd, *J*=4.3, 1.1 Hz, 1H, $H_{4'}$) 4.11–4.08 (m, 1H, $H_{3'}$), 4.04 (dd, *J*=8.6, 4.3 Hz, 1H, $H_{2'}$), 3.48 (d, *J*=2.1 Hz, 1H, $H_{6'}$), 3.34 (dd, *J*=2.1, 1.1 Hz, 1H, $H_{5'}$), 1.47 (s, 9H, $OC(CH_3)_3$), 0.89 and 0.84 (2s, 18H, $C(CH_3)_3$), 0.1, 0.09, 0.03, 0.02 (4s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 150.1, 139.5, 139.4, 102.8, 88.0, 83.3, 78.9, 74.9, 73.5, 56.8, 50.1, 27.9, 25.8, 25.6, 18.1, 17.9, −4.4, −4.7, −4.8, −4.9; FAB HRMS (NBA): *m/e* 607.2845, $M+Na^+$ calcd for $C_{27}H_{48}N_2O_8Si_2$ 607.2847.

4.24. Azido alcohol 43

A solution of epoxy ester **42** (95 mg, 0.16 mmol, 1.0 equiv) in MeOH (3 mL) was treated with a 1.68 M of 1-azido-3-propanoamine solution in Et_2O (0.15 mL, 0.24 mmol, 1.5 equiv). After stirring at 70 °C for 4 days, the crude mixture was then diluted with toluene (1.0 mL) and concentrated in vacuo. Purification by flash column chromatography (silica gel, 40% EtOAc in hexanes) provided compound **43** (22 mg, 20%) as a white solid: R_f=0.47 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ +26.2 (*c* 0.4, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J*=8.1 Hz, 1H, H_6), 5.71 (d, *J*=8.1 Hz, 1H, H_5), 5.56 (d, *J*=4.3 Hz, 1H, $H_{1'}$), 4.28 (dd, *J*=4.3, 4.3 Hz, 1H, $H_{2'}$), 4.15–4.02 (m, 4H, $H_{3'}$, $H_{4'}$, $H_{5'}$, $H_{6'}$), 3.87 (bs, 1H, OH), 3.37 (m, 2H, CH_2N_3), 2.91–2.81 and 2.64–2.58 (2m, 2H, CH_2NH), 1.77–1.71 (m, 2H, CH_2), 1.47 (s, 9H, $OC(CH_3)_3$), 0.89 and 0.84 (2s, 18H, $C(CH_3)_3$), 0.09, 0.06, 0.04 and 0.03 (4s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.8, 150.0, 141.7, 141.6, 102.1, 92.1, 84.2, 74.0, 71.9, 68.7, 64.2, 57.2, 49.4, 45.9, 29.7, 28.0, 25.8, 25.7, 18.0, 17.9, −4.3, −4.7, −4.8, −4.9; FAB HRMS (NBA): *m/e* 707.3602, $M+Na^+$ calcd for $C_{30}H_{56}N_6O_8Si_2$ 707.3596.

4.25. Azido alcohol 44

A solution of epoxy ester **42** (53 mg, 0.091 mmol, 1.0 equiv) in DMF (2 mL) was treated with sodium azide (11.8 mg, 0.181 mmol, 2.0 equiv) and the mixture was heated until 65°. After stirring for 3 h, the solution was allowed to reach room temperature, diluted with Et_2O (5 mL) and washed with saturated aqueous NH_4Cl solution (5 mL). The aqueous solution was extracted with Et_2O (2×2 mL) and the combined organic phase was washed with brine (4 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude mixture was purified by flash column chromatography (silica gel, 40% EtOAc in hexanes) to provide azido alcohol **44** (47 mg, 83%) as a white solid: R_f=0.72 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ +10.1 (*c* 0.8, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (bs, 1H, N*H*), 7.64 (d, *J*=8.1 Hz, 1H, H_6), 5.74 (d, *J*=8.1, 2.1 Hz, 1H, H_5), 5.57 (d, *J*=5.9 Hz, 1H, $H_{1'}$), 4.45 (dd, *J*=5.9, 4.8 Hz, 1H, $H_{2'}$), 4.26 (d, *J*=6.4 Hz, 1H, OH), 4.20 (bs, 1H, $H_{4'}$), 4.14 (dd, *J*=4.8, 2.7 Hz, 1H, $H_{3'}$), 3.88–3.78 (m, 2H, $H_{5'}$, $H_{6'}$), 1.52 (s, 9H, $OC(CH_3)_3$), 0.89 and 0.84 (2s, 18H, $C(CH_3)_3$), 0.07, 0.02, and −0.03 (3s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 162.9, 150.4, 142.7, 102.5, 92.6, 84.4, 84.3, 73.4, 72.6, 70.1, 62.3, 28.0, 25.8, 25.7, 18.0, 17.9, −4.5, −4.6, −4.7, −5.0; FAB HRMS (NBA): *m/e* 650.3019, $M+Na^+$ calcd for $C_{27}H_{49}N_5O_8Si_2$ 650.3017.

4.26. Bromohydrine 45

A solution of epoxy amide **33** (0.19 g, 0.302 mmol, 1.0 equiv) in dry and freshly distilled acetone was cooled to −20 °C and treated with NaBr (0.127 g, 1.2 mmol, 4.0 equiv) and Amberlyst 15 (99 mg, 0.45 mmol, 1.5 equiv). The mixture was kept at −20 °C and vigorously stirred for 12 h. After that time, the mixture was filtered through a pad of Celite and washed with acetone (2×5 mL). The filtrates were concentrated under reduced pressure and the crude product was purified by flash column chromatography (silica gel, 50% EtOAc in hexanes) to provide bromohydrine **45** (0.214 g, 99%) as a white solid: R_f=0.40 (silica gel, 40% EtOAc in hexanes); $[\alpha]_D^{22}$ −76.0 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.25 (bs, 1H, N*H*), 8.22 (d, *J*=8.1 Hz, 1H, Ar), 7.86 (d, *J*=8.1 Hz, 1H, H_6), 7.22–7.18 (m, 2H, Ar), 7.07 (dd, *J*=7.0, 7.0 Hz, 1H, Ar), 5.85 (dd, *J*=5.4 Hz, 1H, $H_{1'}$), 5.70 (d, *J*=8.1 Hz, 1H, H_5), 4.55 (d, *J*=3.2 Hz, 1H, $H_{4'}$), 4.48 (d, *J*=9.7 Hz, 1H, $H_{5'}$), 4.39 (d, *J*=9.7 Hz, 1H, $H_{6'}$), 4.34–4.27 (m, 2H, $H_{2'}$, CH_2CH_2N indoline), 4.18 (dd, *J*=3.8, 3.8 Hz, 1H, $H_{3'}$), 4.09–4.01 (m, 1H, CH_2CH_2N indoline), 3.22–3.16 (m, 2H, CH_2CH_2N indoline), 0.91 and 0.85 (2s, 18H, $C(CH_3)_3$), 0.11, 0.09, 0.03 and −0.004 (4s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 163.3, 150.4, 142.2, 141.3, 131.7, 127.6, 125.1, 124.8, 117.7, 102.4, 89.7, 83.6, 74.7, 72.7, 71.2, 48.0, 43.3, 27.9, 25.8, 25.7, 18.0, 17.9, −4.9, −4.7, −4.6, −4.9; FAB HRMS (NBA): *m/e* 732.2117, $M+Na^+$ calcd for $C_{31}H_{48}BrN_3O_7Si_2$ 732.2112.

4.27. Bromohydrine 47. Oxidation of bromohydrine 45 with DMP and reduction of ketone 46 with $NaBH_4$

To a stirred solution of bromohydrine **45** (0.184 g, 0.259 mmol, 1.0 equiv) in CH_2Cl_2 (3 mL) was added DMP (0.226 g, 0.518 mmol, 2.0 equiv) at 0 °C. The reaction mixture was then stirred for 8 h with complete depletion of starting material according to TLC chromatography. The crude mixture was diluted with CH_2Cl_2 (10 mL) and washed with saturated aqueous $NaHCO_3$ solution (10 mL). The aqueous solution was extracted with CH_2Cl_2 (2×10 mL) and the combined organic phase was washed with brine (10 mL), dried over $MgSO_4$ and concentrated under reduced pressure to obtain ketone **46**, which was used in the next step without purification.

To a solution of the obtained ketone **46** (0.151 g, 0.213 mmol, 1.0 equiv) in EtOH (3 mL) was slowly added $NaBH_4$ (8.39 mg, 0.213 mmol, 1.0 equiv) at 0 °C. After stirring for 1 h 15 min, the reaction mixture was diluted with EtOAc (5 mL) and washed with H_2O (5 mL) and brine (5 mL). The combined organic phases were dried over $MgSO_4$ and concentrated in vacuo. Purification by flash column chromatography (silica gel, 30→50% EtOAc in

hexanes) provided pure *syn* bromohydrine **47** (56.7 mg 38%), *anti* bromohydrine **45** (7.8 mg, 5%), and a more polar fraction of unknown products (58.5 mg).

*Compound [**47**]*: White solid: R_f=0.51 (silica gel, 40% EtOAc in hexanes); $[\alpha]_D^{22}$ −75.5 (*c* 1.2, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (bs, 1H, N*H*), 8.17 (d, *J*=8.1 Hz, 1H, Ar), 7.22–7.18 (m, 2H, Ar), 7.15 (d, *J*=8.1 Hz, 1H, H_6), 7.07 (dd, *J*=7.0, 7.0 Hz, 1H, Ar), 5.66 (dd, *J*=8.1, 2.2 Hz, 1H, H_5), 5.27 (d, *J*=8.1 Hz, 1H, $H_{1'}$), 5.08 (bs, 1H, OH), 4.83 (dd, *J*=8.1, 4.3 Hz, 1H, $H_{2'}$), 4.78 (bs, 1H, $H_{4'}$), 4.35 (d, *J*=4.3 Hz, 1H, $H_{3'}$), 4.29–4.23 (m, 1H, CH_2CH_2N indoline), 4.12–4.01 (m, 2H, $H_{5'}$, CH_2CH_2N indoline), 3.93 (d, *J*=9.1 Hz, 1H, $H_{6'}$), 3.23–3.19 (m, 2H, CH_2CH_2N indoline), 0.92 and 0.81 (2s, 18H, $C(CH_3)_3$), 0.16, 0.12, 0.01 and −0.10 (4s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 163.1, 149.7, 144.9, 141.9, 131.9, 127.6, 124.7, 125.0, 117.8, 102.0, 96.0, 86.2, 73.3, 70.7, 70.2, 48.0, 46.2, 27.9, 25.8, 25.7, 18.0, 17.9, −4.5, −4.6, −4.8, −5.3; FAB HRMS (NBA): *m/e* 732.2117, $M+Na^+$ calcd for $C_{31}H_{48}BrN_3O_7Si_2$ 732.2112.

4.28. Epoxy amide 48

Syn bromohydrine **47** (43 mg, 0.06 mmol, 1.0 equiv) was treated with a 0.1 M NaOMe solution in MeOH (1.8 mL, 0.18 mmol, 3.0 equiv) at room temperature and the mixture was stirred for 24 h. After that, the solvent was concentrated under reduced pressure and the crude product was purified by flash column chromatography (silica gel, 50% EtOAc in hexanes) to obtain *cis* epoxy amide **48** (38 mg, 99%) as a white solid: R_f=0.30 (silica gel, 40% EtOAc in hexanes); $[\alpha]_D^{22}$ +8.9 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (bs, 1H, N*H*), 8.16 (d, *J*=8.1 Hz, 1H, Ar), 7.13 (d, *J*=8.1 Hz, 1H, H_6), 7.20–7.16 (m, 2H, Ar), 7.03 (dd, *J*=7.0, 7.0 Hz, 1H, Ar), 5.65 (dd, *J*=8.1, 2.2 Hz, 1H, H_5), 5.30 (d, *J*=7.5 Hz, 1H, $H_{1'}$), 4.95 (dd, *J*=7.5, 4.3 Hz, 1H, $H_{2'}$), 4.28 (d, *J*=4.3 Hz, 1H, $H_{3'}$), 4.17–4.07 (m, 2H, CH_2CH_2N indoline), 3.86 (d, *J*=8.1 Hz, 1H, $H_{4'}$), 3.79 (d, *J*=4.3 Hz, 1H, $H_{6'}$), 3.62 (dd, *J*=8.1, 4.3 Hz, 1H, $H_{5'}$), 3.17–3.13 (m, 2H, CH_2CH_2N indoline), 0.86 and 0.82 (2s, 18H, $C(CH_3)_3$), 0.1, 0.08, 0.03 and −0.05 (4s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9, 149.7, 144.0, 142.3, 130.9, 127.5, 124.5, 124.3, 117.1, 102.2, 95.1, 83.1, 74.2, 71.3, 55.4, 54.4, 46.5, 28.2, 25.6, 25.5, 17.9, 17.8, −4.6, −4.8, −4.9, −5.2; FAB HRMS (NBA): *m/e* 652.2847, $M+Na^+$ calcd for $C_{31}H_{47}N_3O_7Si_2$ 652.2850.

4.29. Amine 49

To a solution of Boc-Leu-OH (0.11 g, 0.48 mmol, 1.2 equiv) in CH_2Cl_2 (3 mL) was added HOBt (66 mg, 0.48 mmol, 1.2 equiv) and the mixture was stirred for 5 min. After that time, EDCI (94 mg, 0.48 mmol, 1.2 equiv) was added and the reaction mixture was stirred for 45 min at room temperature. The resulting mixture was added to a solution of *N*-*Z*-1,3-diaminopropane hydrochloride (0.1 g, 0.4 mmol, 1.0 equiv) in MeOH (2 mL), which was previously treated with triethylamine (0.22 mL, 1.6 mmol, 4.0 equiv) for 30 min at room temperature. The reaction mixture was stirred at room temperature for 1 h 10 min, and then, a 15% aqueous NH_3 solution (0.5 mL) was added. The mixture was diluted with ether (10 mL) and washed with a saturated aqueous NH_4Cl solution (2×10 mL). The combined organic phases were dried over $MgSO_4$ and concentrated in vacuo. Purification by flash column chromatography (silica gel, 60% EtOAc in hexanes) afforded the corresponding coupling product (0.157 g, 91%) as a white solid: R_f=0.45 (silica gel, 60% EtOAc in hexanes); $[\alpha]_D^{22}$ −20.6 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.29 (m, 5H, aromatics Cbz), 6.78 (bs, 1H, N*H*), 5.50 (br s, 1H, N*H*Cbz), 5.06 (bs, 2H, CH_2Ar), 5.00 (bs, 1H, NHBoc), −4.06 (bs, 1H, $CHCH_2CH(CH_3)_2$), 3.27–3.25 and 3.19–3.16 (2m, 4H, $CH_2NHC(O)O$, CH_2NHCO), 1.63–1.57 (m, 5H, CH_2, $CHCH_2CH(CH_3)_2$, $CHCH_2CH(CH_3)_2$), 1.40 (s, 9H, $C(CH_3)_3$), 0.91–0.88 (m, 6H, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 156.8, 155.8, 136.5, 128.4, 127.9, 80.1, 66.5, 53.2, 41.3, 37.3, 35.8, 29.8, 28.2, 24.7, 22.8, 21.9.

A solution of coupling product (0.113 g, 0.268 mmol, 1.0 equiv) in MeOH (3 mL) was purged with Ar. Then, a 10% Pd–C (113 mg) was added, and the mixture was allowed to be exposed to a H_2 atmosphere and stirred for 40 min. After this time, the mixture was filtered and the filtrate was washed with MeOH (2×5 mL). The combined organic solution was dried ($MgSO_4$), and concentrated under reduced pressure to obtain the corresponding free amine **49** (69 mg, 90%), which was used in the next step without purification.

4.30. Amino alcohol 50

Epoxy amide **48** (34 mg, 0.054 mmol, 1.0 equiv) was dissolved in MeOH (1.5 mL) and amine **49** (62 mg, 0.216 mmol, 4.0 equiv) was added. After stirring at 70 °C for 14 days, the solvent was concentrated under reduced pressure and the crude product was purified by flash column chromatography (silica gel, 75% EtOAc in hexanes) to give amino alcohol **50** (34 mg, 97%) and 10 mg of starting material [**50**]: white solid: R_f=0.29 (silica gel, 70% EtOAc in hexanes); $[\alpha]_D^{22}$ +4.5 (*c* 0.2, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J*=8.1 Hz, 1H, Ar), 7.38 (d, *J*=7.5 Hz, 1H, H_6), 7.16–7.12 (m, 2H, Ar), 7.01 (dd, *J*=7.5, 7.5 Hz, 1H, Ar), 6.85 (bs, 1H, N*H*CO), 5.73 (d, *J*=6.4 Hz, 1H, $H_{1'}$), 5.52 (d, *J*=7.5 Hz, 1H, H_5), 5.00 (bs, 1H, N*H*Boc), 4.37–4.27 (m, 3H, $H_{3'}$, $H_{4'}$, CH_2CH_2N indoline), 4.23 (br s, 1H, $H_{2'}$), 4.06–3.95 (m, 3H, $H_{5'}$, CH_2CH_2N indoline, $CHCH_2CH(CH_3)_2$), 3.87 (bs, 1H, $H_{6'}$), 3.54 (bs, 1H, N*H*), 3.40 and 3.25 (2bs, 2H, CH_2NHCO), 3.13 (bs, 2H, CH_2CH_2N indoline), 2.79 and 2.50 (2bs, 2H, CH_2NH), 1.71–1.53 (m, 4H, CH_2, $CHCH_2CH(CH_3)_2$, $CHCH_2CH(CH_3)_2$), 1.44–1.41 (m, 1H, $CHCH_2CH(CH_3)_2$), 1.41 (s, 9H, $OC(CH_3)_3$), 0.90 and 0.77 (2s, 18H, $C(CH_3)_3$), 0.89–0.83 (m, 6H, $CH(CH_3)_2$), 0.12, −0.08, −0.002 and −0.07 (4s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 172.0, 162.8, 155.9, 150.2, 142.0, 141.6, 131.7, 127.4, 124.7, 124.6, 117.7, 102.3, 89.3, 86.2, 80.1, 73.4, 72.5, 71.3, 62.3, 53.0, 48.2, 45.3, 40.8, 37.3, 29.7, 28.3, 25.8, 25.6, 24.6, 22.8, 18.1, 17.8, −4.5, −4.7, −4.8; FAB HRMS (NBA): *m/e* 939.5065, $M+Na^+$ calcd for $C_{45}H_{76}N_6O_{10}Si_2$ 939.5059.

4.31. Amino alcohol 51

Epoxy amide **33** (52 mg, 0.083 mmol, 1.0 equiv) was dissolved in MeOH (2 mL) and amine **49** (53 mg, 0.183 mmol, 2.2 equiv) was added. The mixture was heated

until 70 °C and stirred for 4 days. After this time, the solvent was concentrated under reduced pressure and the crude product was purified by flash column chromatography (silica gel, 50% EtOAc in hexanes →10% MeOH in CH_2Cl_2) to give amino alcohol **51** (59.1 mg, 99%) together with unreacted starting material (11 mg [**51**]): pale yellow: R_f=0.48 (silica gel, 10% MeOH in CH_2Cl_2); $[\alpha]_D^{22}$ –17.3 (*c* 0.4 CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.40 (br s, 1H, N*H*), 8.21 (d, *J*=8.6 Hz, 1H, Ar), 7.56 (d, *J*=8.1 Hz, 1H, H_6), 7.17–7.14 (m, 2H, Ar), 7.01 (dd, *J*=7.0, 7.0 Hz, 1H, Ar), 6.69 (bs, 1H, N*H*CO), 5.66 (d, *J*=8.1 Hz, 1H, H_5), 5.53 (d, *J*=5.9 Hz, 1H, $H_{1'}$), 4.99 (bs, 1H, N*H*Boc), 4.54 (bs, 1H, $H_{2'}$), 4.30 (bs, 1H, $H_{4'}$), 4.15–4.06 (m, 4H, $H_{3'}$, CH_2CH_2N indoline, C*H*$CH_2CH(CH_3)_2$), 3.82 (d, *J*=6.4 Hz, 1H, $H_{5'}$), 3.73–3.69 (m, 1H, $H_{6'}$), 3.38–3.23 (m, 2H, CH_2NHCO), 3.19–3.13 (m, 2H, CH_2CH_2N indoline), 2.80–2.71 and 2.43–2.33 (2m, 2H, CH_2NH), 1.67–1.51 (m, 4H, CH_2, $CHCH_2CH(CH_3)_2$, $CHCH_2CH(CH_3)_2$), 1.42–1.38 (m, 1H, $CHCH_2CH(CH_3)_2$), 1.40 (s, 9H, $OC(CH_3)_3$), 0.91–0.81 (m, 24H, $CH(CH_3)_2$, $C(CH_3)_3$), 0.03, −0.005, −0.013 and −0.08 (4s, 12H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 171.9, 162.7, 155.9, 150.6, 143.4, 142.3, 131.4, 127.5, 124.7, 124.5, 117.5, 102.4, 93.8, 86.9, 80.1, 77.2, 73.6, 72.4, 63.0, 52.8, 48.1, 45.7, 41.4, 37.9, 29.7, 28.3, 28.0, 25.7, 25.6, 24.7, 22.9, 21.9, 18.0, 17.9, −4.6, −4.7, −5.1; FAB HRMS (NBA): *m/e* 939.5072, $M+Na^+$ calcd for $C_{45}H_{76}N_6O_{10}Si_2$ 939.5059.

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