Linear Aminopolyhydroxylated Structures Through Rapid Domino Assembly of a Highly Functionalized Heterotricyclic System and Its Selective Cleavage

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Dedicated to the memory of Professor Antonino Fava

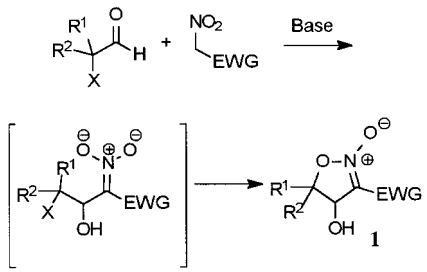
Abstract: This paper presents a new approach to linear aminopolyhydroxylated structures, based on the rapid assembly of a highly functionalized heterotricyclic system and its cleavage. The complex tricyclic structure is obtained by a sequence of two mild tandem reactions: the first involves a base-promoted nitroaldol-intramolecular cyclization between an activated primary nitroalkane and an aldehyde bearing a leaving group on the α-carbon atom to give 4-hydroxy-2-isoxazolines-2-oxides. In the second tandem process, the 4-hydroxy group was used as an anchor to link an olefinic residue (either an allyl group or a vinylsilane), which then gave rise to a spontaneous intramolecular cycloaddition with the nitrone moiety of the 2-isoxazoline-2-oxide to afford a complex tricyclic structure. These two tandem processes could be condensed into a single three-component domino reaction, which starting from the three acyclic substrates realizes a big jump in molecular complexity through the selective formation of five new bonds and four new chiral centers all concerted as a dynamic continuum in which every event depends on all the others. The second part of this project dealt with the cleavage of the tricyclic structure to unmask the target linear compounds. The richness of functionalities that were selectively installed on the tricyclic structures was screened for possible cleavages. Methods to reduce the exocyclic ester group, hydrogenolyse the bicyclic nitroso acetal, and hydroxydesylilate the cyclic silyl ether were found. In addition, during the early attempts of linearization of the tricyclic compounds, unexpected clean fragmentations of the products were observed, some of them affording synthetically useful new products. An array of interesting linear aminopolyhydroxylated structures was obtained by the combination of one or two cleavage steps from the tricycle, with overall very good acyclic selectivity, efficiency, and atom economy.

Keywords: amino alcohols · cycloadditions · domino reactions · heterocycles · tandem reactions

Introduction

For several years our group has been involved in the utilization of nitroalkanes[1] in the development of new methodologies for the preparation of aminopolyhydroxylated substrates, a biologically relevant class of compounds that often exhibit potent therapeutical properties. We are trying to design these syntheses keeping an eye on efficiency:[2] that is, obtaining the maximum needed molecular complexity in the smallest number of steps and under the mildest conditions possible.[3] The procedures are often divided into two distinct parts: a first part that sets up much of the elements of molecular complexity needed in the final products through the assembly of cyclic (or polycyclic) structures; and a second part that just unfolds these cyclic compounds into linear structures with no further addition in terms of complexity.

That was the case when we found that the base-promoted reaction of aldehydes bearing a leaving group on the α carbon with activated primary nitroalkanes results in the efficient formation of a 4-hydroxy-2-isoxazoline-2-oxide (**1**) through a tandem process[4] (Scheme 1). This turned out to be a general



Scheme 1. Tandem preparation of 4-hydroxy-2-isoxazolines (EWG = electron-withdrawing group).

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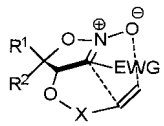


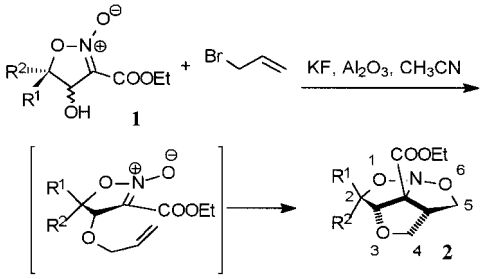
Figure 1. Hydroxyl-directed 1,3-dipolar cycloaddition of 4-hydroxy-2-isoxazolines-2-oxides (EWG = electron-withdrawing group).

process that works with different leaving groups and electrophiles.[5]

The well-known stereoselective, reductive ring cleavage by lithium aluminum hydride of 2-isoxazolines[6] allowed an effective unfolding of this heterocycle into linear aminohydroxylated compounds.[5b] More recently we thought that the molecular complexity of the 2-isoxazolines-2-oxide could be further increased by exploiting the nitrone moiety present on the system. Moreover the free hydroxyl of the isoxazoline ring could be used as an anchor to link an olefinic residue in the attempt to have a regio- and stereoselective intramolecular 1,3-dipolar cycloaddition (Figure 1).

Results and Discussion

The assembly of a highly functionalized heterotricyclic system: When we treated 2-isoxazoline-2-oxides **1** with allyl bromide in the presence of a very mild base, such as KF/Al_2O_3 at room temperature, a new tandem process took place (Scheme 2, Table 1). After the binding of the allyl group to the free hydroxyl of the isoxazoline, the intramolecular 1,3-dipolar cycloaddition occurs *spontaneously* under the very mild conditions required for hydroxyl derivatization. The process gives rise to a previously unknown type of heterotricycle **2**, featuring an uncommon nitroso acetal functionality.[7]



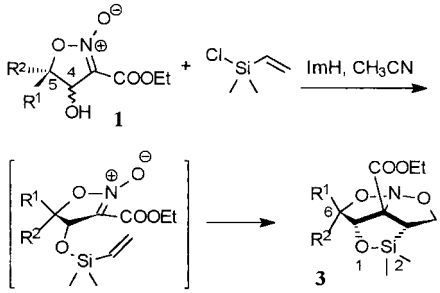
Scheme 2. Tandem intramolecular 1,3-dipolar cycloaddition of 4-hydroxy-2-isoxazolines-2-oxides with an allyl residue.

Table 1. Results of the reaction depicted in Scheme 2.

	R^1	R^2	Product stereochemistry	Yield [%]
a	H	*anti*-PhCH(OH)	2-*endo*	62
b	Ph	CH_3	2-*exo*	43
c[a]	$nC_{12}H_{25}$	H	2-*exo*:2-*endo* = 2:1	84
d	$(CH_2)_5$		n.a.	64
e	CH_3	CH_3	n.a.	91

[a] Reaction performed on a mixture of 4,5-*trans*- and 4,5-*cis*-2-isoxazoline-2-oxides in a ratio 2:1. n.a. = not applicable.

After these encouraging results we were attracted by the possibility to effect a silicon-tethered[9] 1,3-dipolar cycloaddition. The temporary silicon connection methodology, deeply investigated during the last years by the Stork[10] and Tamao[11] groups, achieves the regio- and stereoselective formation of new bonds by temporarily linking together the two reactants by means of an eventually removable[12] silicon atom. When we treated **1** with one equivalent of commercially available chlorodimethylvinylsilane in the presence of imidazole at room temperature (Scheme 3, Table 2), we observed, by tlc, a fast hydroxyl functionalization followed by a smooth conversion to the corresponding heterotricyclic compound **3**.[13] Again the intramolecular 1,3-dipolar cycloaddition occurs *spontaneously* under the very mild reaction conditions employed.[14] It should be noted that in the large majority of the cases the product is obtained in a rather pure form and needs no further purification.



Scheme 3. Tandem intramolecular silicon tethered cycloaddition of 4-hydroxy-2-isoxazolines-2-oxides.

Abstract in Italian: *Viene presentato un nuovo approccio alla sintesi di composti aminopoliossidrilati lineari, basato su un rapido assemblaggio di un sistema eterotriciclico polifunzionalizzato e la sua apertura selettiva. Il sistema triciclico è stato ottenuto attraverso una sequenza di due reazioni tandem. La prima di queste, una reazione nitroaldolica tra un nitroderivato alifatico ed una aldeide con un gruppo uscente in posizione α, è seguita da una ciclizzazione intramolecolare e porta alla formazione di 4-idrossi-2-isoxazoline-2-ossido. Nel secondo processo tandem, il gruppo ossidrilico in C^4 è stato utilizzato per l'ancoraggio di un residuo olefinico, premessa per una cicloaddizione intramolecolare spontanea con il nitrone del sistema 2-isoxazolinico-2-ossido. Queste due reazioni tandem sono state compattate in un unico processo domino a tre componenti che attua un grande salto in complessità molecolare con la formazione selettiva di cinque nuovi legami e quattro nuovi centri chirali, il tutto concertato secondo un continuum dinamico dove ogni evento dipende da tutti gli altri. La seconda parte di questo progetto riguarda l'apertura del sistema eterotriciclico per liberare le strutture aminopolioliche lineari. È stato possibile trovare metodi adeguati per ridurre il gruppo estereo esociclico, per idrogenolizzare il nitroso acetale biciclico, e per idrossidesililare il silil etere ciclico. Durante i primi tentativi di linearizzazione del sistema triciclico, sono state osservate anche delle interessanti frammentazioni, alcune delle quali sono state sfruttate sinteticamente ampliando la versatilità di utilizzazione dei tricicli studiati. Le trasformazioni chimiche effettuate tramite la manipolazione selettiva del sistema triciclico hanno permesso di ottenere un insieme di strutture aminopolioliche lineari. L'intero progetto è stato realizzato con particolare attenzione ai criteri di efficienza, selettività ed economia atomica.*

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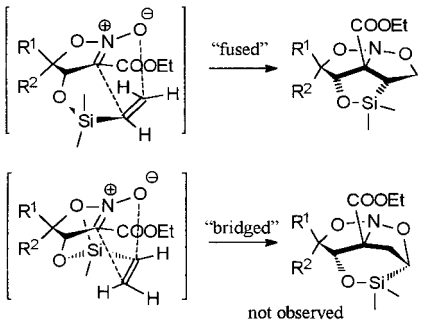
Table 2. Results of the reaction depicted in Scheme 3.

	R^1	R^2	Product stereochemistry	Yield [%]
a	H	*anti*-PhCH(OH)	6-*endo*	95
b	Ph	CH_3	6-*exo*	99
c[a,b]	$nC_{12}H_{25}$	H	6-*exo*:6-*endo* = 2:1	79
d	$(CH_2)_5$		n.a.	97
e	CH_3	CH_3	n.a.	96
f	*anti*-PhCH(OH)	H	6-*exo*	99
g	C_2H_5	C_2H_5	n.a.	95
h[a,c]	Bu	H	6-*exo*:6-*endo* = 5:1	97

[a] Reaction performed on a mixture of 4,5-*trans*- and 4,5-*cis*-2-isoxazoline-2-oxides. [b] In a ratio 2:1. [c] In a ratio 5:1. n.a. = not applicable.

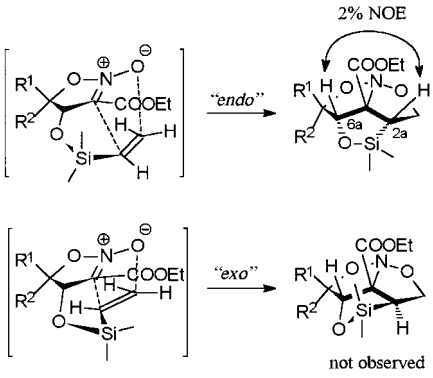
For the structural assignment of the products, we had to establish both the regio- and stereochemistry of the cycloaddition process. With regard to the regiochemistry of the cycloaddition there are two possibilities (Scheme 4): the olefin can react with the CH_2 binding to the oxygen of the dipole to give a fused tricyclic system, or it can react the other



Scheme 4. Fused and bridged modes of the intramolecular cycloaddition.

way around, with the CH binding to the oxygen, to give a bridged tricycle. From proton and carbon NMR spectroscopy we could easily establish that the cycloaddition proceeds regiospecifically to give only the fused product. In fact we always observed a downfield methylene and we never observed products with a downfield methyne, indicating that it is the methylene of the olefin that binds to the oxygen of the dipole and so ruling out the bridged product.

With respect to the stereochemistry of the cycloaddition, an *endo*- or an *exo*-cyclization is possible (Scheme 5), where the

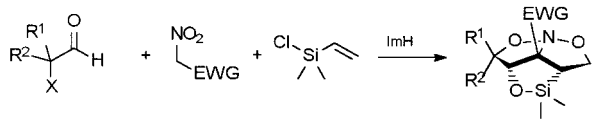


Scheme 5. *Exo* and *endo* modes of the intramolecular cycloaddition.

terms *endo* and *exo* refer to the position of the silicon with respect to the forming cycle. An *endo* cyclization, in which the silicon atom lies *endo* to the forming cycle, results in the formation of a fused tricyclic system with a *cis*,*cis* fusion, while an *exo*-cyclization leads to the *cis*,*trans* isomer. From MM2 calculations[15] we found that the first product is about 16 kcal mol^{-1} lower in energy than the second one. This high difference in energy can also be easily seen by trying to build Dreiding models of the two structures. Furthermore we could also measure a 2% NOE between the two protons at C^{2a} and at C^{6a}. Although not definitive proofs, these two observations allow us to establish that the cycloaddition proceeds stereospecifically with the formation of the fused product with the *cis*,*cis* stereochemistry.

Two factors seem to be crucial for the cycloaddition to occur: the length of the tether and the intramolecularity. In fact, when the tether was lengthened by one unit treating compound **1b**[16] with allylchlorodimethylsilane under the same conditions reported above, we observed a clean protection of the hydroxyl without any detectable tricyclization product, even after refluxing the resulting silyl ether in toluene for two days. Moreover, no appreciable amounts of intermolecular 1,3-dipolar cycloaddition products were observed when compound 4,5-*trans*-**1h**[16] was allowed to react with 1,3-divinyl-1,1,3,3-tetramethyldisiloxane for three days under the same reaction conditions. It is likely that entropic factors and the required length of the tether to achieve the appropriate geometries make the intramolecular 1,3-dipolar cycloaddition possible.

The procedure to form these tricyclic compounds is composed by two mild tandem processes in which materials keep adding up onto the starting primary nitroalkane, each step giving more complex structures. Since both of the tandem reactions are promoted by a base, we looked into the possibility to perform a domino multicomponent reaction, in which all the reagents are put in the reaction flask from the beginning. We found that even in domino conditions[17] the three starting materials spontaneously add up in the desired way to give the products in more than satisfactory yields,[18] especially considering that these are the isolated overall yields of four different reactions (Scheme 6, Table 3).



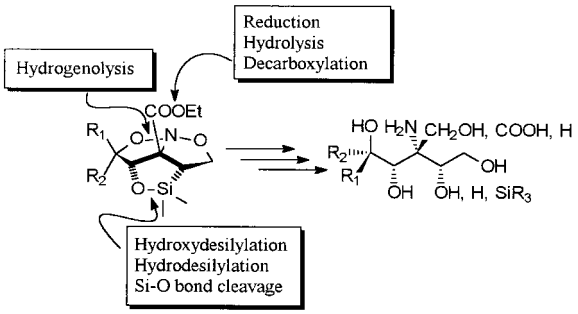
Scheme 6. Domino preparation of tricyclic compounds **3**.

Table 3. Results of the domino preparation of **3**.

R^1	R^2	X	EWG	Yield [%]	ratio
H	$nC_{12}H_{25}$	Br	COOEt	61	1.0
H	$nC_{12}H_{25}$	Br	SO_2Ph	57	1.0
H	CH_3	OTs	COOEt	60	1.1
H	CH_3	OTs	SO_2Ph	76	0.7
Ph	CH_3	Br	COOEt	72	0.0
H	$PhCH_2CH_2$	OTs	COOEt	89	1.3
H	$PhCH_2CH_2$	OTs	SO_2Ph	87	0.9

The process is rather stereoselective as the products are obtained in a mixture of only two diastereoisomers (6-*exo* and 6-*endo*) out of the possible eight (sixteen if the stereogenic nitrogen is also considered). The formation of the two diastereoisomers occurs during the very first step of the process, the nitroaldol step, while all the other chiral centers are formed during the closure of rings and are obtained in an absolute specific manner.

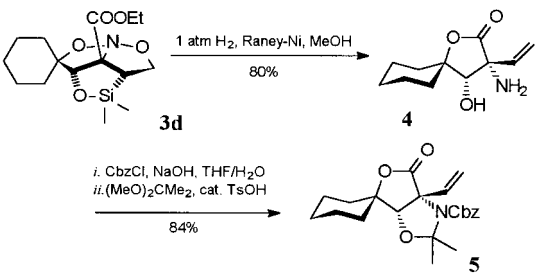
The unfolding of the highly functionalized heterotricyclic system: Having exploited any chance to increase the molecular complexity on our tricyclic systems we embarked in the second stage of our project. The tricyclic compounds contain a chain of five functionalized carbon atoms, four of them stereogenic. If this chain is completely unfolded it would be possible to obtain polyhydroxylated amino acid derivatives or aminopolyols. The silylated tricyclic compounds bearing the ester group as the electron-withdrawing group appeared to be particularly attractive in this sense, since in this case the unfolding might be achieved by cleaving the nitroso acetal and the silyl ether, and manipulating the ester function (Scheme 7).



Scheme 7. Possible sites of manipulation of **3**.

So it is possible to imagine that a sequence of synthetic operations on the three functionalities, in an order to be established, would allow the opening of the tricyclic compounds into linear structures. On the other hand it is also possible that the three functionalities, which lie so close in space on the tricyclic compounds, will interfere with one another making it difficult to treat one selectively with respect to the others.

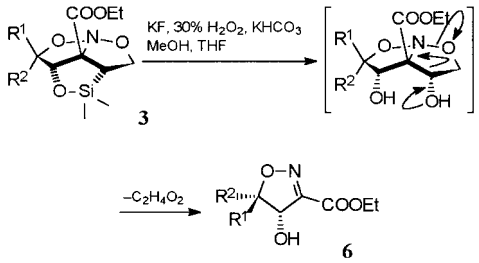
We found this latter situation to be the case during our very first attempt to disassemble the tricycle (Scheme 8). We performed the hydrogenolysis of the nitroso acetal **3d** and we ended up with a product (**4**) in which none of starting functionalities went untouched. The nitroso acetal, as expected, was no longer there, the ester was still there though under different clothes, the silyl ether was gone, and an oxygen atom had disappeared. The quick and easy transformation of the product into the corresponding cyclic-protected derivative **5** allowed us to chemically confirm the *cis* stereochemistry between the hydroxyl and the amino groups.



Scheme 8. The first attempt of unfolding.

To explain the formation of lactone **4** we have assumed that a cascade of five different steps takes place during the reaction, including, in addition to the two N–O bonds cleavages, a Peterson type olefination. Performing the reaction at 3 atm of hydrogen afforded the same product, but with the double bond hydrogenated. Though giving interesting *cis*-substituted aminohydroxylated lactones, which are known to be biologically active,[19] this reaction proceeded well only for a limited number of substrates.

So we decided to perform the hydrogenolysis of the nitroso acetal later and we started considering hydroxydesilylation as the first event of the unfolding stage. This reaction appeared to be particularly suited to our needs, since it consists of the cleavage of the cyclic silyl ether and replacement of the silicon atom with a hydroxyl group with retention of configuration.[20] When we performed the hydroxydesilylation on the tricyclic systems we found that, under the conditions developed by Tamao, a smooth fragmentation occurred, although the diol in most of the cases can be observed by NMR spectroscopy (Scheme 9, Table 4).



Scheme 9. Hydroxydesilylation-fragmentation of **3**.

Table 4. Results of the reaction depicted in Scheme 9.

Starting material[16]	Yield [%]
3d	> 95
3e	71
3g	83
6-*exo*-**3h**	64

The net result of this reaction was to remove the two carbon-atom fragment that was set up during the tricyclization step and to give back the starting isoxazoline with the *N*-oxide function reduced. In principle the fragmentation from either newly formed hydroxyl is possible, but in the majority of the cases we observed only the fragmentation depicted in Scheme 9, in which the primary alcolate serves as the leaving group. In a few cases, along with this major product, we were able to isolate also small amounts the product arising from the fragmentation beginning at the other hydroxyl group.

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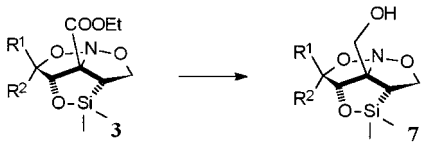
To avoid this unwanted fragmentation we thought of two strategies: a) to remove the possibility to form a product with conjugated double bonds by reducing the ester before attempting the oxidation, and b) to trap the intermediate diol immediately after the oxidation step. The ester reduction was easily performed in quantitative yields with either $LiAlH_4$ or $NaBH_4$ (Scheme 10, Table 5) affording the corresponding primary alcohols **7** in good yields.



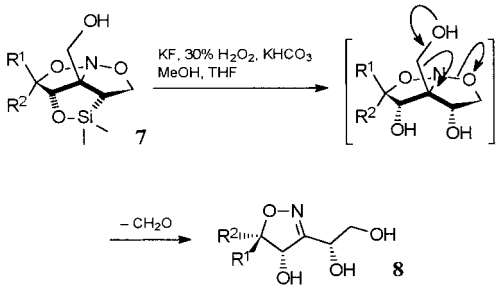
Scheme 10. Reduction of the ester function of **3**.

Table 5. Results of the reaction depicted in Scheme 10.

Starting material[16]	Method[a]	Yield [%]
3b	B	96
6-*endo*-**3c**	A	95
6-*exo*-**3c**	A	95
3d	A	86
3g	A, B	88, 96

[a] A. $NaBH_4$, MeOH, 0 °C; B. 1M $LiAlH_4$, Et_2O, −20 °C

Then we tried the oxidation of such reduced tricyclic compounds, only to see that a new, faster fragmentation takes place to give a new type of isoxazoline (**8**) in very good yields (Scheme 11, Table 6). This last fragmentation gives rise to a

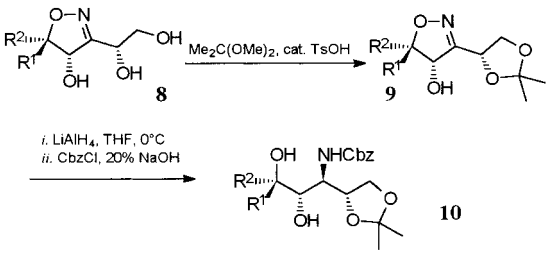


Scheme 11. Hydroxydesilylation-fragmentation of **7**.

Table 6. Results of the reaction depicted in Scheme 11.

Starting material[16]	Yield [%]
7b	90
6-*exo*-**7c**	95
7g	88

new isoxazoline with the loss of a one-carbon fragment, but with the main chain of carbon atoms preserved and with only one ring left to open. To completely unfold these substrates (Scheme 12, Table 7) we first performed a protection, which turned out to give selectively the 5-membered acetal, and then a 4-hydroxyl-directed stereoselective $LiAlH_4$ reduction of the 2-isoxazolines.[6] We obtained the corresponding aminopolyol that was protected at the nitrogen atom during the basic workup of the reduction.



Scheme 12. Linearization of 2-isoxazolines **8**.

Table 7. Results of the reaction depicted in Scheme 12.

Starting material[16]	Yield[a] [%]
8b	74
4,5-*trans*-**8c**	71
8g	72

[a] Overall yield of the protection-reduction steps.

The products so obtained closely resemble the ones found in the skeleton of a class of antibiotics of the anthracycline family with a prominent antitumoral activity. Indeed the compound depicted in Figure 2 was employed in a synthetic approach to CDEF Nogalamycin analogues.[21]

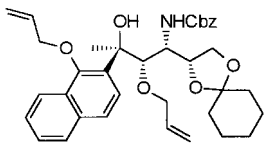
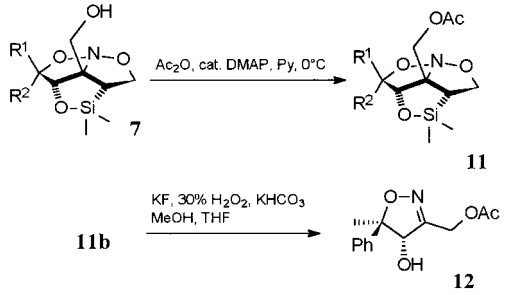


Figure 2. A precursor of Nogalamycin analogues.[21]

We also investigated the possibility to block the second type of fragmentation shown in Scheme 11, by protecting the primary hydroxy group as an acetate. This protection proved not to be useful, since during the following oxidation the first type of fragmentation again came into play, giving rise to the loss of the two-carbon-atom fragment and forming a 2-isoxazoline (**12**) with no conjugated double bonds (Scheme 13, Table 8). This last observation allowed us to establish that the formation of a 2-isoxazoline with conjugated double bonds is not the driving force of the fragmentation reported in Scheme 9.

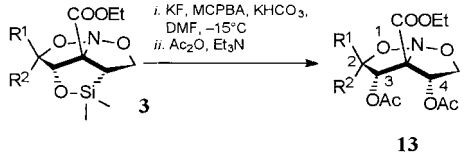


Scheme 13. Acetylation of **7**.

Table 8. Results of the reaction depicted in Scheme 13.

Starting material[16]	Yield [%]
7b	97
6-*endo*-**7c**	98
7d	99
7g	92

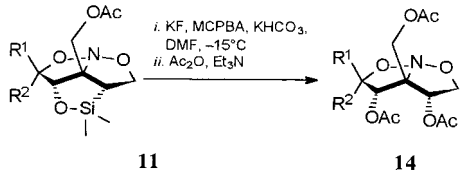
To avoid this latter fragmentation, observed during the hydroxydesilylation of the starting tricyclic compound, we tried to trap the intermediate diol. Direct acetylation of the reaction mixture after completion of the oxidation proved only partially satisfactory, so we performed the oxidation at $-15\,^{\circ}C$ by cooling with an external ice–salt bath. At this temperature hydrogen peroxide proved ineffective and was replaced by stronger oxidants such as 3-chloroperbenzoic acid (MCPBA) or magnesium monoperphthalate (MMPP) in DMF. Under these conditions the reaction is complete within few minutes and the quenching by the addition of acetic anhydride and triethylamine allowed us to cleanly trap the diols in more than 90% yield (Scheme 14).[22] It was also



3 13

Scheme 14. Hydroxydesilylation of **3**.

possible to reduce the reported needed amount of peracid from 3 equiv to 1.1 equiv, thus demonstrating a stronger migratory aptitude of the secondary carbon with respect to that of the methyls on the silicon atom, which under these conditions do not migrate. We found also that the same conditions are applicable to the products with the ethoxycarbonyl group reduced and protected (Scheme 15, Table 9).



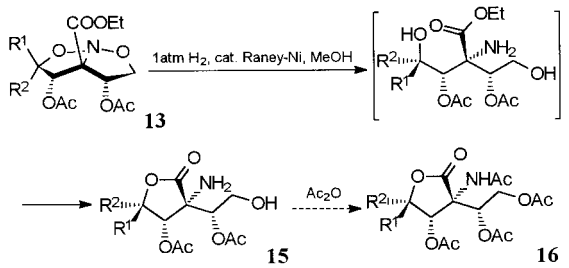
11 14

Scheme 15. Hydroxydesilylation of **11**.

Table 9. Results of the reaction depicted in Schemes 14 and 15.

Starting material[16]	Yield [%]
6-*endo*-**3c**	98
3d	97
3g	96
6-*exo*-**3h**	88
6-*endo*-**3h**	92
6-*endo*-**11c**	98
11g	95

Having secured the hydroxydesilylation, we were ready to try the hydrogenolysis of the O–N–O moiety. Nitroso acetals are known, mainly from the work of Seebach[23] and Denmark,[24] to undergo Raney-Ni-catalyzed hydrogenolysis. This time the reaction, performed with the products obtained from the hydroxydesilylation step (**13**), proceeded smoothly giving the hydrogenolized product (**15**) in less than one hour at room temperature under an atmospheric pressure of hydrogen (Scheme 16, Table 10). The products were obtained in the form of the corresponding lactone. Sometimes acetyl migration occurred during the reduction affording mixtures of products. In these cases an extra acetylation step gives back one single characterizable product.



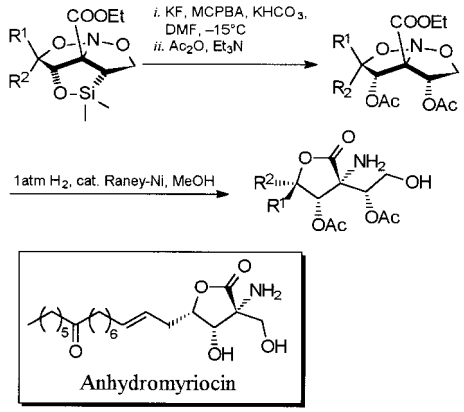
13 15 16

Scheme 16. Nickel-catalyzed hydrogenolysis of nitroso acetals **13**.

Table 10. Results of the reaction depicted in Scheme 16.

Starting material[16]	Product	Yield [%]
13d	**16d**	86
13g	**16g**	93
2-exo-**13h**	*trans*-**15h**	70
2-endo-**13h**	*cis*-**15h**	71

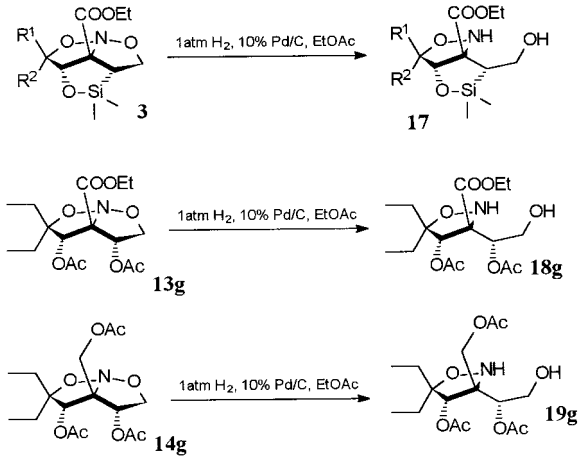
Scheme 17 illustrates very clearly how this two-step unfolding (silyl ether hydroxydesilylation/nitroso acetal hydrogenolysis) of the starting tricyclic compounds can be useful in the selective preparation of hydroxylated amino acid derivatives. For example, the lactones so obtained have the same



Scheme 17. Example of linearization of tricyclic compounds **3**.

core structure of myriocin (in the γ-lactone form, anhydromyriocin), a potent immunosuppressant.[25] The unexpectedly fast rate[26] of the Raney-Ni-catalyzed hydrogenolysis of the nitroso acetal prompted us to attempt the same reaction with palladium (Scheme 18, Table 11), which is known to be less effective in this type of reactions.[27] Indeed, in this case the reaction takes from 12 to 24 hours to complete and gives rise to the selective cleavage of the less hindered N–O bond. Moreover, in this case the reaction works equally well for the starting tricyclic compounds of type **3** and for the hydroxydesilylated compounds of type **13** and **14**, affording a new series of aminopolyhydroxilated structures amenable for further manipulations exploiting their residual functionalities.

  0947-6539/98/0412-2506 $ 17.50+.50/0 *Chem. Eur. J.* **1998**, *4*, No. 12



Scheme 18. Palladium-catalyzed hydrogenolyses.

Table 11. Results of the reactions depicted in Scheme 18.

Starting material[16]	Yield [%]
3d	88
3g	85
13g	90
14g	92

Conclusions

In this paper a new approach to linear aminopolyhydroxylated substrates has been reported. This approach is divided into two distinct parts: the folding and the unfolding of a heterotricyclic system. During this first part of our project a functionalized heterotricyclic system has been folded up from easily or commercially available linear starting materials with only one chiral center. During this synthetic operation all the elements of complexity needed in the final products (the central nitrogen, the main carbon-atom chain, the several adjacent chirality centers, etc.) are set up in a regiospecific and rather stereoselective fashion through the formation of five new bonds. Moreover, the process can be run in a single step under very mild conditions with good yields and with a minimum of trouble with respect to the workup, separation, and purification. The substantial increase in structural complexity on going from the reactants to the products ($\Delta C_T = +170$)[28] illustrates very nicely the great synthetic efficiency of such reaction.

The second part the procedure dealt with the unmasking of the target compounds preserving all the elements of molecular complexity that were set up during the assembling part. Different ways to unfold this class of tricyclic compounds have been found, allowing us to obtain interesting aminopolyhydroxylated structures in one or two steps. It is worthwhile to note that in spite of the many elements of complexity of the final products, the whole procedure takes only a few steps, achieving the assembly of many functionalities with a very good acyclic selectivity and with an overall good efficiency.

The potential usefulness of the target molecules, and the possibility to prepare them in the gram scale and in an optically active form[18] gives us good reason to hope that our procedure may be utilized, as an additional tool, for the synthesis of linear aminopolyols and hydroxylated amino acids.

Experimental Section

General: ^{1}H NMR spectra were recorded at 300.08 MHz at 20 °C with either tetramethylsilane ($\delta = 0.00$), chloroform ($\delta = 7.26$), CHD_2OD ($\delta = 3.30$), [D_5]dimethylsulfoxide ($\delta = 2.49$), or acetone ($\delta = 2.20$) as the internal standard; all coupling constants (J) refer to ^3J(H,H). ^{13}C NMR spectra were recorded at 75.46 MHz at 20 °C with either chloroform ($\delta = 77.0$), CD_3OD ($\delta = 49.0$), [D_6]dimethylsulfoxide ($\delta = 39.0$), or acetone ($\delta = 29.8$) as the internal standard; signal multiplicities were established by DEPT experiments. Flash chromatographic separations were performed over Merck Silica gel 60 (230–400 mesh ASTM). For TLC analyses, Merck precoated TLC plates (silica gel 60 GF_{254} 0.25 mm) were used throughout this work. Acetonitrile was freshly distilled before use from potassium carbonate; unless otherwise stated, all other solvents were reagent grade and used as received. Melting points are uncorrected. The preparations and physical data of compounds obtained through the domino procedure were described elsewhere.[18]

Preparation of tricyclic compounds of type 2: A flask equipped with a calcium chloride tube was charged with the starting material **1** (1.6 mmol) and acetonitrile (8 mL). 40 % Potassium fluoride over alumina (10 equiv) and allyl bromide (10 equiv) were added to the resulting solution. The mixture was stirred at room temperature and the course of the reaction was monitored by tlc (diethyl ether/petroleum ether = 2:1) until complete (48–96 h). The slurry was filtered over a Celite pad and the residue was thoroughly washed with dichloromethane. Evaporation of the solvent affords the crude material as an oil, which was purified by flash chromatography.

Compound **2a**: white solid; m.p. 167–170 °C; ^{1}H NMR ($CDCl_3$): $\delta = 7.50$–7.20 (m, 5H; aromatic), 4.97 (d, $J = 8.3$ Hz, 1H; $C^{2a}H$), 4.89 (dd, 1H; PhCH), 4.56 (dd, $J = 8.4$, 8.4 Hz, 1H; C^2H), 4.43 (br s, 1H; OH), 4.35 (dd, $J = 9.2$, 9.3 Hz, 1H; C^4H_A or C^5H_A), 4.28 (q, $J = 7.2$ Hz, 2H; CH_2), 4.16 (dd, $J = 9.3$ Hz, 1H; C^4H_B or C^5H_B), 4.08–4.00 (m, 2H; C^5H_2 or C^4H_2), 3.60–3.70 (m, 1H; $C^{4a}H$), 0.81 (t, $J = 7.2$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta =$ 169.0 (C), 141.4 (C), 128.5 (CH), 128.3 (CH), 128.2 (CH), 95.77 (C), 88.33 (CH), 81.59 (CH), 76.07 (CH), 71.66 (CH_2), 70.05 (CH_2), 62.96 (CH_2), 53.50 (CH), 13.95 (CH_3); MS (70 eV, EI): m/z : 321 [M^+], 276, 248; $C_{16}H_{19}NO_6$ (321.32): calcd C 59.81, H 5.96, N 4.36; found: C 59.98, H 5.91, N 4.46.

Compound **2b**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 7.58$–7.20 (m, 5H; aromatic), 4.97 (s, 1, CH), 4.55 (dd, $J = 8.2$, 8.1 Hz, 1H; C^5H_A), 4.38 (dd, $J = 9.3$, 8.2 Hz, 1H; C^5H_B), 4.14 (dd, $J = 9.3$, 1.2 Hz, 1H; C^4H_A), 4.03 (dd, $J = 9.3$, 1.2 Hz, 1H; C^4H_B), 3.89 (q, $J = 7.1$ Hz, 2H; CH_2), 3.49 (dddd, $J = 9.3$, 8.1, 4.5, 1.2 Hz, $C^{4a}H$), 1.56 (s, 3H; CH_3), 0.81 (t, $J = 7.1$ Hz, CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 169.5$ (C), 143.1 (C), 128.7 (CH), 127.9 (CH), 126.3 (CH), 94.62 (C), 86.15 (C), 75.59 (CH), 73.01 (CH_2), 71.74 (CH_2), 62.72 (CH_2), 55.28 (CH), 22.98 (CH_3), 14.17 (CH_3); $C_{16}H_{19}NO_5$ (305.33): calcd C 62.94, H 6.27, N 4.59; found C 62.81, H 6.12, N 4.79.

Compound 2-*exo*-**2c**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 4.76$ (m, 1H; $C^{2a}H$), 4.35 (q, $J = 7.2$ Hz, 2H; CH_2), 4.28–4.00 (m, 4H; C^4H_2 and C^5H_2), 3.85 (m, 1H; C^2H), 3.60–3.45 (m, 1H; $C^{4a}H$), 1.80–1.15 (m, 25H; $(CH_2)_{11}$ and CH_3), 0.88 (t, $J = 6.9$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 170.1$ (C), 94.85 (C), 93.10 (CH), 84.70 (CH), 73.37 (CH_2), 71.05 (CH_2), 63.00 (CH_2), 53.58 (CH), 32.35 (CH_2), 32.35 (CH_2), 31.70 (CH_2), 30.09 (CH_2), 29.92 (CH_2), 29.80 (CH_2), 25.99 (CH_2), 23.14 (CH_2), 14.56 (CH_3), 8.58 (CH_3); IR (film): $\tilde{\nu} =$ 2918, 2849, 1739, 1462 cm^{-1}; $C_{21}H_{37}NO_5$ (383.5): calcd C 65.77, H 9.72, N 3.65; found C 65.82, H 9.62, N 3.48.

Compound **2d**: white solid; m.p. 56–59 °C; ^{1}H NMR ($CDCl_3$): $\delta = 4.61$ (s, 1H; $C^{2a}H$), 4.48 (dd, $J = 8.5$, 8.3 Hz, 1H; C^5H_A), 4.31 (m, 3H; C^5H_B and CH_2), 4.04 (m, 2H; C^4H_2), 3.51 (dddd, $J = 8.5$, 8.3, 4.3, 2.6 Hz, 1H; $C^{4a}H$), 1.87–1.15 (m, 10H; $(CH_2)_5$), 1.32 (t, $J = 7.1$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 169.7$ (C), 95.48 (C), 91.59 (C), 83.83 (CH), 74.89 (CH_2), 71.75 (CH_2), 62.65 (CH_2), 54.44 (CH), 33.23 (CH_2), 29.34 (CH_2), 25.68 (CH_2), 23.19 (CH_2), 21.12 (CH_2), 14.29 (CH_3); IR (KBr): $\tilde{\nu} = 2924$, 1739, 1450 cm^{-1}; $C_{14}H_{21}NO_5$ (283.3): calcd C 59.35, H 7.47, N 4.94; found C 59.48, H 7.59, N 5.01.

Compound **2e**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 4.50$ (s, 1H; $C^{2a}H$), 4.49 (dd, $J =$ 8.2, 8.1 Hz, 1H; C^5H_A), 4.31 (q, $J = 7.3$ Hz, CH_2), 4.28 (dd, $J = 8.7$, 8.2 Hz, 1H; C^5H_B), 4.06 (m, 2H; C^4H_2), 3.53 (dddd, $J = 8.7$, 8.4, 4.5, 2.4 Hz, 1H; $C^{4a}H$), 1.34 (t, $J = 7.1$ Hz, 3H; CH_3), 1.33 (2s, 6H; $2CH_3$); ^{13}C NMR ($CDCl_3$): $\delta = 169.4$ (C), 95.63 (C), 93.05 (C), 81.84 (CH), 74.97 (CH_2), 71.69 (CH_2), 62.59 (CH_2), 54.27 (CH), 24.48 (CH_3), 19.97 (CH_3), 14.23 (CH_3); IR

(film): $\tilde{\nu}$ = 2980, 1729, 1463 cm^{-1}; $C_{11}H_{17}NO_5$ (243.24): calcd C 54.31, H 7.04, N 5.76; found C 54.48, H 7.02, N 5.75.

Preparation of tricyclic compounds 3: A mixture of the starting material **1** (4 mmol), chlorodimethylvinylsilane (5 mmol; 10 mmol for entries **3a** and **3f** in Table 2), and imidazole (5 mmol; 10 mmol for **3a** and **3f**), in acetonitrile (20 cm^3) was stirred at room temperature in a round-bottomed flask with a calcium chloride tube for 6–24 h. The mixture was diluted with water (50 cm^3) and extracted with diethyl ether (3 × 15 cm^3). The organic layer was washed with brine (5 cm^3), dried over sodium sulfate and evaporated under vacuum to afford the crude product, which can be used without further purification. Analytically pure samples were obtained by flash chromatography (diethyl ether/petroleum ether = 1:1).

Compound **3a**: white solid; m.p. 94–96 °C; ^{1}H NMR ($CDCl_3$): δ = 7.46–7.22 (m, 5H; arom), 5.03 (d, J = 3.4 Hz, 1H; $C^{6a}H$), 4.91 (dd, J = 7.7, 4.8 Hz, 1H; $C^{2a}H$), 4.50 (dd, J = 10.0, 8.2 Hz, 1H; C^3H_A), 4.44 (dd, J = 11.2, 8.2 Hz, 1H; C^3H_B), 4.24 (q, J = 7.1 Hz, 2H; CH_2), 4.04 (dd, J = 7.8, 3.5 Hz, 1H; C^6H), 3.19 (bd, J = 4.8 Hz, 1H; OH), 2.48 (dd, J = 11.2, 10.0 Hz, 1H; $C^{2a}H$), 1.30 (t, J = 7.1 Hz, 3H; CH_3), 0.40 (s, 3H; CH_3), 0.35 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 170.2 (C), 141.7 (C), 128.9 (CH), 128.5 (CH), 126.7 (CH), 95.70 (C), 86.15 (CH), 81.27 (CH), 74.87 (CH_2), 71.37 (CH), 63.02 (CH_2), 35.89 (CH), 14.51 (CH_3), 0.14 (CH_3), −2.66 (CH_3); IR (KBr): $\tilde{\nu}$ = 3481, 2962, 1729, 1453 cm^{-1}; $C_{17}H_{23}NO_6Si$ (365.5): calcd C 55.87, H 6.34, N 3.83, Si 7.69; found C 55.95, H 6.31, N 3.83.

Compound **3b**: white solid. m.p. 73–75 °C; ^{1}H NMR ($CDCl_3$): δ = 7.49 (m, 2H; arom), 7.21 (m, 3H; arom), 5.06 (s, 1H; $C^{6a}H$), 4.42 (dd, J = 10.0, 8.1 Hz, 1H; C^3H_A), 4.37 (dd, J = 11.4, 8.1 Hz, 1H; C^3H_B), 3.89 (dd, J = 10.7, 7.0 Hz, 1H;CH_A), 3.77 (dd, J = 10.7, 7.0 Hz, 1H; CH_B), 2.30 (dd, J = 11.3, 10.0 Hz, 1H; C^3H_A), 1.38 (s, 3H; CH_3), 0.75 (t, J = 7.1 Hz, 3H; CH_3), 0.36 (s, 3H; CH_3), 0.31 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 170.6 (C), 143.9 (C), 128.3 (CH), 127.2 (CH), 126.0 (CH), 95.58 (C), 91.65 (CH), 85.53 (C), 73.81 (CH_2), 62.13 (CH_2), 37.57 (CH), 23.55 (CH_3), 13.79 (CH_3), 0.11 (CH_3), −2.63 (CH_3); IR (KBr): $\tilde{\nu}$ = 2974, 1742 cm^{-1}; $C_{17}H_{23}NO_5Si$ (349.5): calcd C 58.43, H 6.63, N 4.01, Si 8.04; found C 58.31, H 6.61, N 4.01.

Compound 6-*exo*-**3c**: oil; ^{1}H NMR ($CDCl_3$): δ = 4.78 (d, J = 3.5 Hz, 1H; $C^{6a}H$), 4.44–4.20 (m, 4H; C^3H_2 and CH_2), 4.12–4.02 (m, 1H; C^6H), 2.55 (dd, J = 10.0, 10.0 Hz, 1H; ^{2a}H), 1.90–1.20 (m, 25H; $(CH_2)_{11}$ and CH_3), 0.88 (t, J = 6.7 Hz, 3H; CH_3), 0.38 (s, 3H; CH_3), 0.32 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 170.8 (C), 93.61 (C), 90.19 (CH), 87.06 (CH), 72.79 (CH_2), 62.75 (CH_2), 36.90 (CH), 32.32 (CH_2), 32.01 (CH_2), 30.06 (CH_2), 29.88 (CH_2), 29.77 (CH_2), 25.97 (CH_2), 23.11 (CH_2), 14.52 (CH_3), 14.45 (CH_3), 0.40 (CH_3), −2.02 (CH_3); $C_{22}H_{41}NO_5Si$ (427.6): calcd C 61.79, H 9.66, N 3.28, Si 6.57; found C 61.92, H 9.68, N 3.27.

Compound 6-*endo*-**3c**: white solid; ,p. 72–74 °C; ^{1}H NMR ($CDCl_3$): δ = 4.75 (d, J = 3.4 Hz, 1H; $C^{6a}H$), 4.47 (dd, J = 10.0, 8.0 Hz, 1H; C^3H_A), 4.38 (dd, J = 11.1, 8.0 Hz, 1H; C^3H_B), 4.27 (q, J = 7.1 Hz, 2H; CH_2), 3.86 (dt, J_d = 3.4 Hz, J_t = 6.7 Hz, 1H; C^6H), 2.43 (dd, J = 11.1, 10.0 Hz, 1H; $C^{2a}H$), 1.70–1.58 (m, 2H; CH_2), 1.45–1.20 (m, 23H; $(CH_2)_{10}$ and CH_3), 0.90 (t, J = 7.1 Hz, 3H; CH_3), 0.37 (s, 3H; CH_3), 0.33 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 170.8 (C), 95.91 (C), 86.36 (CH), 79.05 (CH), 74.53 (CH_2), 62.75 (CH_2), 35.80 (CH), 32.38 (CH_2), 30.10 (CH_2), 29.91 (CH_2), 29.81 (CH_2), 26.75 (CH_2), 26.31 (CH_2), 23.14 (CH_2), 14.57 (CH_3), 0.22 (CH_3), −2.64 (CH_3); IR (KBr): $\tilde{\nu}$ = 2915, 1739, 1465 cm^{-1}; $C_{22}H_{41}NO_5Si$ (427.6): calcd C 61.79, H 9.66, N 3.28, Si 6.57; found C 61.71, H 9.69, N 3.28.

Compound **3d**: white solid; M.p. 68–69 °C; ^{1}H NMR ($CDCl_3$): δ = 4.69 (s, 1H; $C^{6a}H$), 4.43 (dd, J = 10.1, 8.1 Hz, 1H; C^3H_A), 4.38 (dd, J = 11.82, 8.1 Hz, 1H; C^3H_B), 4.31 (dd, J = 7.1, 4.7 Hz, 1H; H_A of ethyl CH_2), 4.25 (dd, J = 7.1, 4.7 Hz, 1H; H_B of ethyl CH_2), 2.33 (dd, J = 11.2, 10.1 Hz, 1H;^{2a}H), 1.93–1.38 (m, 10H; $(CH_2)_5$), 1.31 (t, J = 7.1 Hz, 3H; CH_3), 0.38 (s, 3H; CH_3), 0.35 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 171.4 (C), 95.61 (C), 89.75 (CH), 83.16 (C), 73.48 (CH_2), 62.60 (CH_2), 37.52 (CH), 33.59 (CH_2), 29.99 (CH_2), 25.99 (CH_2), 23.29 (CH_2), 22.84 (CH_2), 14.45 (CH_3), 0.44 (CH_3), −2.44 (CH_3); IR (KBr): $\tilde{\nu}$ = 2935, 1715 cm^{-1}; MS (70 eV, EI): *m/z*: 327 [M^+], 282, 254; $C_{15}H_{25}NO_5Si$ (327.4): calcd C 55.02, H 7.70, N 4.28, Si 8.58; found C 55.11, H 7.72, N 4.29.

Compound **3e**: white solid; m.p. = 62–64 °C; ^{1}H NMR ($CDCl_3$): δ = 4.61 (s, 1H; $C^{6a}H$), 4.49–4.18 (m, 4, C^3H_2 and CH_2), 2.35 (dd, J = 11.1, 9.9 Hz, 1H; ^{2a}H), 1.38 (s, 3H; CH_3), 1.32 (t, J = 7.1 Hz, 3H; CH_3), 1.21 (s, 3H; CH_3), 0.38 (s, 3H; CH_3), 0.34 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 171.5 (C), 95.78 (C), 91.12 (CH), 81.73 (C), 73.72 (CH_2), 62.77 (CH_2), 37.49 (CH), 25.17 (CH_3), 20.91 (CH_3), 14.61 (CH_3), 0.46 (CH_3), −2.38 (CH_3); IR (KBr): $\tilde{\nu}$ = 2984, 1746 cm^{-1}; $C_{12}H_{21}NO_5Si$ (287.4): calcd C 50.15, H 7.37, N 4.87, Si 9.77; found C 50.27, H 7.39, N 4.85.

Compound **3f**: white solid; m.p. = 118–120 °C; ^{1}H NMR ($CDCl_3$): δ = 7.40–7.20 (m, 5H; arom), 5.21 (d, J = 1.5 Hz, 1H; $C^{6a}H$), 5.03 (dd, 1H; PhCH), 4.45–4.20 (m, 5H; C^3H_2, C^6H and CH_2), 3.10 (bd, 1H; OH), 2.26 (dd, J = 10.1, 10.0 Hz, 1H; $C^{2a}H$), 1.32 (t, J = 7.1 Hz, 3H; CH_3), 0.30 (2s, 6H; 2 CH_3); ^{13}C NMR ($CDCl_3$): δ = 170.8 (C), 139.8 (C), 128.9 (CH), 128.2 (CH), 126.6 (CH), 94.91 (C), 90.44 (CH), 86.00 (CH), 74.18 (CH), 73.36 (CH_2), 62.77 (CH_2), 37.97 (CH), 14.58 (CH_3), 0.32 (CH_3), −2.29 (CH_3); IR (KBr): $\tilde{\nu}$ = 3536, 2881, 1717 cm^{-1}; $C_{17}H_{23}NO_5Si$ (349.5): calcd C 58.43, H 6.63, N 4.01, Si 8.04; found C 58.49, H 6.66, N 4.04.

Compound **3g**: white solid; m.p. = 40–42 °C; ^{1}H NMR ($CDCl_3$): δ = 4.61 (s, 1H; $C^{6a}H$), 4.46–4.22 (m, 4H; C^3H_2 and CH_2), 2.28 (dd, J = 11.3, 10.2 Hz, 2H; $C^{2a}H$), 1.85–1.35 (m, 4H; 2 CH_2), 1.33 (t, J = 7.1 Hz, 3H; CH_3), 0.94 (t, J = 6.9 Hz, 3H; CH_3), 0.88 (t, J = 6.7 Hz, 3H; CH_3), 0.38 (s, 3H; CH_3), 0.36 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 171.5 (C), 95.54 (C), 89.73 (CH), 86.70 (C), 73.42 (CH_2), 62.56 (CH_2), 38.00 (CH), 24.92 (CH_2), 21.87 (CH_2), 14.49 (CH_3), 8.52 (CH_3), 7.64 (CH_3), 0.43 (CH_3), −2.48 (CH_3); IR (KBr): $\tilde{\nu}$ = 2980, 1723, 1248, 1044, 867 cm^{-1}; $C_{14}H_{25}NO_5Si$ (315.4): calcd C 53.31, H 7.99, N 4.44, Si 8.90; found C 53.47, H 8.01, N 4.42.

Compound 6-*exo*-**3h**: oil; ^{1}H NMR ($CDCl_3$): δ = 4.76 (d, J = 3.4 Hz, 1H; $C^{6a}H$), 4.47 (dd, J = 10.0, 8.0 Hz, 1H; C^3H_A), 4.38 (dd, J = 11.1, 8.0 Hz, 1H; C^3H_B), 4.27 (q, J = 7.1 Hz, 2H; CH_2), 3.86 (dt, J_d = 3.4 Hz, J_t = 6.7 Hz, 1H; C^6H), 2.44 (dd, J = 11.1, 10.0 Hz, 1H; $C^{2a}H$), 1.70–1.55 (m, 2H; CH_2), 1.45–1.25 (m, 7H; $2CH_2$, CH_3), 0.90 (t, J = 7.1 Hz, 3H; CH_3), 0.38 (s, 3H; CH_3), 0.32 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 169.9 (C), 95.01 (C), 85.46 (CH), 78.15 (CH), 73.66 (CH_2), 61.84 (CH_2), 34.96 (CH), 27.59 (CH_2), 25.59 (CH_2), 22.32 (CH_2), 13.66 (CH_3), 13.49 (CH_3), 0.66 (CH_3), −3.54 (CH_3); $C_{14}H_{25}NO_5Si$ (315.4): calcd C 53.31, H 7.99, N 4.44, Si 8.90; found C 53.37, H 7.93, N 4.47.

Compound 6-*endo*-**3h**: oil; ^{1}H NMR ($CDCl_3$): δ = 4.79 (d, J = 3.5 Hz, 1H; $C^{6a}H$), 4.40 (dd, J = 9.3, 8.4 Hz, 1H; C^3H_A), 4.32 (dd, J = 10.8, 8.4 Hz, 1H; C^3H_B), 4.28 (q, J = 7.1 Hz, 2H; CH_2), 4.07 (ddd, J = 8.1, 5.6, 3.5 Hz, 1H; C^6H), 2.45 (dd, J = 11.0, 9.5 Hz, 1H; $C^{2a}H$), 1.80–1.20 (m, 9H; 3 CH_2 and CH_3), 0.90 (t, J = 7.1 Hz, 3H; CH_3), 0.38 (s, 3H; CH_3), 0.32 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 170.3 (C), 93.08 (C), 89.66 (CH), 86.54 (CH), 72.24 (CH_2), 62.24 (CH_2), 36.36 (CH), 31.16 (CH_2), 27.56 (CH_2), 22.32 (CH_2), 13.93 (CH_3), 13.80 (CH_3), 0.09 (CH_3), −2.53 (CH_3); $C_{14}H_{25}NO_5Si$ (315.4): calcd C 53.31, H 7.99, N 4.44, Si 8.90; found C 53.39, H 7.96, N 4.42.

(3,4-*cis*)-3-Amino-3-ethenyl-4-hydroxy-1-oxaspiro[4.5]decan-2-one (4): An hydrogenation flask was charged with methanol (50 mL) and a catalytic amount of a 50% slurry of W-2 Raney nickel in water. The suspension was stirred for about 1 min and the methanol was decanted off. The residue was washed four more times with methanol (50 mL) and finally added to a solution of the tricyclic compound **3d** (1.00 g, 3.06 mmol) in methanol (50 mL). The flask was connected to a gas burette filled with hydrogen through a three-way stopcock and purged three times. The mixture was stirred at room temperature, and the course of the reaction was monitored by tlc (petroleum ether/diethyl ether = 3:7). After 5 h the starting material was completely consumed and the reaction mixture was filtered over a Celite pad. The solids were thoroughly washed with methanol (150 mL) and the solution was concentrated in vacuo. The residue was purified by flash column chromatography (diethyl ether/methanol = 99:1) to obtain 0.520 g (80%) of lactone **4** as a white solid that can be crystallized from carbon tetrachloride/hexane; m.p. = 64–66 °C; ^{1}H NMR ([D_6]acetone): δ = 6.17 (dd, J = 17.5, 10.6 Hz, 1H; CH), 5.42 (d, J = 17.5 Hz, 1H; CH_A), 5.34 (d, J = 10.5 Hz, 1H; CH_B), 4.03 (s, 1H; C^4H), 2.92 (brs, 3H; OH and NH_2), 1.79–1.40 (m, 10H; $5CH_2$); ^{13}C NMR ([D_6]acetone): δ = 176.8 (C), 141.1 (CH), 116.5 (CH_2), 87.71 (C), 77.00 (CH), 64.17 (CH_2), 36.90 (CH_2), 32.47 (CH_2), 26.11 (CH_2), 23.64 (CH_2), 23.41 (CH_2); MS (70 eV, EI): *m/z* (%): 167 (9) [M^+ − 44], 150 (20), 100 (100), 85 (58), 56 (38); $C_{11}H_{17}NO_3$ (211.3): calcd C 62.54, H 8.11, N 6.63; found C 62.47, H 8.08, N 6.59.

***N*-Benzyloxycarbonyl-*N,O*-isopropylidene-(3,4-*cis*)-3-amino-3-ethenyl-4-hydroxy-5,5-dimethyldihydrofuran-2(3*H*)-one (5)**: A solution of lactone **4** (0.27 g, 1.27 mmol) in dioxane (10 mL) was cooled to about 0 °C with a water–ice bath. 10% Na_2CO_3 (10 mL) and benzyl chloroformate (0.23 mL, 1.52 mmol, 1.2 equiv) was added to the solution. The mixture was stirred for two hours at 0 °C until the starting material was completely consumed (tlc: diethyl ether/petroleum ether = 1:1). The mixture was taken up with water (20 mL), transferred into a separating funnel, and extracted with ethyl acetate (4 × 10 mL). The reunited organic phase was washed with brine

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(5 mL), dried over sodium sulfate, and evaporated in vacuo to afford the crude product as an oil. The crude product was dissolved in 2,2-dimethoxypropane (5 mL) and a few crystals of 4-methylbenzensulfonic acid were added. The mixture was stirred at room temperature for three hours until the starting lactam was completely consumed (tlc: diethyl ether/petroleum ether = 1:1). The mixture was taken up with diethyl ether (15 mL) and washed with 10% $NaHCO_3$ (2 × 5 mL); the aqueous phase was back extracted with diethyl ether (2 × 5 mL). The organic phase was washed with brine (5 mL), dried over sodium sulfate, and concentrated in vacuo to afford the crude product as a solid, that was recrystallized from hexane (0.42 g, 84%). M.p. = 127–130 °C; ^{1}H NMR ($CDCl_3$, T = 50 °C): δ = 7.45–7.15 (m, 5H; arom), 5.94 (dd, J = 17.5 Hz, 1H; CH), 5.41 (d, J = 17.5 Hz, 1H; CH_A), 5.38 (d, J = 10.5 Hz, 1H; C^3H_B), 5.15 (s, 2H; $PhCH_2$), 4.30 (s, 1H; CH), 1.95–1.35 (m, 10H; $(CH_2)_5$); ^{13}C NMR ($CDCl_3$, T = 50 °C): δ = 172.4 (C), 152.5 (C), 136.5 (C), 134.8 (CH), 128.7 (CH), 128.4 (CH), 128.2 (C), 120.4 (CH2), 98.20 (C), 85.26 (C), 84.71 (CH), 72.28 (C), 67.57 (CH_2), 35.38 (CH_2), 31.66 (CH_2), 27.06 (CH_3), 25.63 (CH_3), 25.22 (CH_2), 22.67 (CH_2), 22.52 (CH_2); $C_{22}H_{27}NO_5$ (385.5): calcd C 68.55, H 7.06, N 3.63; found C 68.67, H 7.04, N 3.64.

Hydroxydesilylation-fragmentation of tricyclic compounds 3: A solution of the starting material **3** (2 mmol) in methanol/tetrahydrofuran = 1:1 (4 mL) was placed in a flask that was left open throughout the reaction course. Anhydrous potassium fluoride (2.8 mmol, 1.4 equiv), potassium bicarbonate (2 mmol, 1 equiv), and 30% hydrogen peroxide (0.70 mL, 3.3 equiv) were added to this solution, under stirring. After a while an exotherm was observed (up to 50 °C) and the mixture was stirred until consumption of the starting material (ca. 2 h; tlc: petroleum ether/ethyl acetate = 1:1). The reaction was quenched by the addition of a 50% solution of $Na_2S_2O_3 \cdot 5H_2O$ and stirring was continued until a negative starch–iodide test (ca. 30 min). A white precipitate was formed and the mixture was taken up with diethyl ether (5 mL) and filtered. The solids were washed with diethyl ether (20 mL), and the organic phase was washed with brine (5 mL), dried over sodium sulfate, and concentrated in vacuo. The crude residue was purified by flash chromatography (petroleum ether/diethyl ether = 1:1).

Compound **6d**: white solid; m.p. = 74–76 °C; ^{1}H NMR ($CDCl_3$): δ = 4.85 (d, J = 5.0 Hz, 1H; C^4H), 4.35 (q, J = 7.1 Hz, 2H; CH_2), 2.95 (d, J = 5.0 Hz, 1H; OH), 1.95–1.45 (m, 10H; $(CH_2)_5$), 1.35 (t, J = 7.1 Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 162.0 (C), 152.9 (C), 92.59 (C), 78.40 (CH), 62.67 (CH_2), 34.21 (CH_2), 28.57 (CH_2), 25.40 (CH_2), 23.69 (CH_2), 23.29 (CH_2), 14.58 (CH_3); $C_{11}H_{17}NO_4$ (227.3): calcd C 58.14, H 7.54, N 6.16; found C 58.02, H 7.56, N 6.19.

Compound **6e**: oil; ^{1}H NMR ($CDCl_3$): δ = 4.74 (d, J = 5.5 Hz, 1H; C^4H), 4.32 (q, J = 7.1 Hz, 2H; CH_2), 3.5 (d, J = 5.5 Hz, 1H; OH), 1.42 (s, 3H; CH_3), 1.32 (t, J = 7.1 Hz, 3H; CH_3), 1.28 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 161.3 (C), 152.5 (C), 90.58 (C), 79.04 (CH), 62.21 (CH_2), 25.04 (CH_3), 18.61 (CH_3), 14.07 (CH_3); $C_8H_{13}NO_4$ (187.2): calcd C 51.33, H 7.00, N 7.48; found C 51.44, H 6.97, N 7.43.

Compound **6g**: oil; ^{1}H NMR ($CDCl_3$): δ = 4.90 (d, J = 5.2 Hz, 1H; C^4H), 4.37 (q, J = 7.1 Hz, 2H; CH_2), 3.22 (d, J = 5.2 Hz, 1H; OH), 1.85 (m, 2H; CH_2), 1.65 (m, 2H; CH_2), 1.40 (t, J = 7.1 Hz, 3H; CH_3), 1.03 (t, J = 6.9 Hz, 3H; CH_3), 0.93 (t, J = 6.9 Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 161.4 (C), 152.4 (C), 95.52 (C), 77.99 (CH), 62.20 (CH_2), 27.29 (CH_2), 22.20 (CH_2), 14.10 (CH_3) 8.64 (CH_3), 7.59 (CH_3); $C_{10}H_{17}NO_4$ (215.2): calcd C 55.80, H 7.96, N 6.51; found C 55.85, H 7.99, N 6.59.

Compound 4,5-*trans*-**6h**: oil; ^{1}H NMR ($CDCl_3$): δ = 5.00 (s, 1H; C^4H), 4.60–4.50 (m, 1H; C^5H), 4.35 (q, J = 7.1 Hz, 2H; CH_2), 3.90 (brs, 1H; OH), 1.70–1.50 (m, 2H; CH_2), 1.50–1.30 (m, 7H; $(CH_2)_2$ and CH_3), 0.90 (t, J = 6.7 Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 160.0 (C), 152.4 (C), 90.94 (CH), 78.79 (CH), 62.26 (CH_2), 31.78 (CH_2), 26.99 (CH_2), 22.33 (CH_2), 14.03 (CH_3), 13.82 (CH_3); $C_{10}H_{17}NO_4$ (215.2): calcd C 55.80, H 7.96, N 6.51; found C 55.68, H 7.93, N 6.52.

Reduction of the ester function of tricyclic compounds 3.

Method A: A solution of the starting tricyclic compound **3** (4 mmol) in methanol (20 mL) was placed in a reaction flask equipped with a calcium chloride tube and cooled to 0 °C. Sodium borohydride (16 mmol) was added in four portions to the stirred solution. The mixture was stirred at room temperature until the starting material had completely disappeared (tlc: diethyl ether). The reaction was quenched by the careful addition of saturated NH_4Cl (25 mL), and the mixture was transferred into a separating funnel and repeatedly washed with diethyl ether (6 × 15 mL). The ethereal extracts were washed with brine (10 mL), dried over sodium sulfate, and concentrated in vacuo.

Method B: A solution of the starting tricyclic compound **3** (7.5 mmol) in anhydrous THF (25 mL), was placed under a positive pressure of nitrogen and cooled to −20 °C. $LiAlH_4$ in Et_2O (1M, 7.5 mL, 7.5 mmol) was added to this stirred solution by a syringe. The solution was stirred at −20 °C until the disappearance of the starting material was observed (tlc: petroleum ether/ethyl acetate = 3:7). The reaction was quenched by the careful addition of saturated NH_4Cl (25 mL). The aqueous layer was separated and washed with diethyl ether (5 × 15 mL). The combined organic layers were washed with brine (10 mL), dried over sodium sulfate, and concentrated in vacuo. When needed the crude product was purified by flash chromatography.

Compound **7b**: white solid; m.p. = 148–160 °C; ^{1}H NMR ($CDCl_3$): δ = 7.60–7.40 (m, 5H; arom), 4.85 (s, 1H; $C^{6a}H$), 4.45 (dd, J = 11.4, 8.4 Hz, 1H; C^3H_A), 4.40 (dd, J = 9.9, 8.4 Hz, 1H; C^3H_B), 3.35 (brs, 2H; CH_2), 1.80 (dd, J = 11.4, 9.9 Hz, 1H; $C^{2a}H$), 1.65 (brs, 1H; OH), 1.45 (s, 3H; CH_3), 0.40 (s, 3H; CH_3), 0.30 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 144.3 (C), 128.5 (CH), 127.3 (CH), 125.0 (CH), 95.50 (C), 89.92 (CH), 85.31 (C), 73.68 (CH_2), 65.39 (CH_2), 35.40 (CH), 23.86 (CH_3), 0.57 (CH_3), −2.44 (CH_3); IR (KBr): $\tilde{\nu}$ = 3390, 2940, 1500, 1450, 1260, 1050 cm^{-1}; $C_{15}H_{21}NO_4Si$ (307.4): calcd C 58.60, H 6.89, N 4.56, Si 9.14; found C 58.67, H 6.85, N 4.59.

Compound 6-*exo*-**7c**: oil; ^{1}H NMR ($CDCl_3$): δ = 4.39 (d, J = 4.6 Hz, 1H; $C^{6a}H$), 4.28 (d, J = 9.2 Hz, 2H; C^3H_2), 4.07 (m, 1H;C^6H), 3.75 (d, J = 3.6 Hz, 2H; CH_2), 2.80 (brs, 1H; OH), 1.95 (dd, J = 9.2, 9.1 Hz, 1H; $C^{2a}H$), 1.70–1.20 (m, 22H; $(CH_2)_{11}$), 0.90 (t, J = 7.1 Hz, 3H; CH_3), 0.85 (s, 3H; CH_3), 0.80 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 92.80 (C), 88.45 (CH), 87.64 (CH), 72.38 (CH_2), 65.15 (CH_2), 34.94 (CH), 32.44 (CH_2), 32.39 (CH_2), 30.12 (CH_2), 30.04 (CH_2), 29.94 (CH_2), 29.83 (CH_2), 26.07 (CH_2), 23.16 (CH_2), 14.59 (CH_3), 0.92 (CH_3), −1.59 (CH_3); $C_{20}H_{39}NO_4Si$ (385.6): calcd C 62.29, H 10.19, N 3.63, Si 7.28; found C 62.41, H 10.21, N 3.60.

Compound 6-*endo*-**7c**: white solid; m.p. = 74–76 °C; ^{1}H NMR ($CDCl_3$): δ = 4.31 (d, J = 3.7 Hz, 1H; $C^{6a}H$), 4.12 (dd, J = 9.0, 8.3 Hz, 1H; C^3H_A), 4.07 (dd, J = 9.2, 8.3 Hz, 1H; C^3H_B), 3.86 (m, 1H; C^6H), 3.55 (m, 2H; CH_2), 3.18 (brs, 1H; OH), 1.78 (dd, J = 9.2, 9.0 Hz, 1H; $C^{2a}H$), 1.50–1.20 (m, 22H; $(CH_2)_{11}$), 0.90 (t, J = 7.1 Hz, 3H; CH_3), 0.18 (s, 3H; CH_3), 0.14 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 94.99 (C), 83.73 (CH), 78.77 (CH), 73.61 (CH_2), 65.10 (CH_2), 34.22 (CH), 31.98 (CH_2), 29.74 (CH_2), 29.70 (CH_2), 29.67 (CH_2), 29.60 (CH_2), 29.51 (CH_2), 29.38 (CH_2), 26.46 (CH_2), 25.93 (CH_2), 22.71 (CH_2), 14.14 (CH_3), 0.09 (CH_3), −3.02 (CH_3); IR (KBr): $\tilde{\nu}$ = 3318, 2930, 2861, 1259, 1095 cm^{-1}; $C_{20}H_{39}NO_4Si$ (385.6): calcd C 62.29, H 10.19, N 3.63, Si 7.28; found C 62.31, H 10.15, N 3.57.

Compound **7d**: oil; ^{1}H NMR ($CDCl_3$): δ = 4.40 (s, 1H; $C^{6a}H$), 4.35 (m, 2H; C^3H_2), 3.73 (brs, 2H; CH_2), 3.29 (brs, 1H; OH), 1.84 (dd, J = 10.8, 10.2 Hz, 1H; $C^{2a}H$), 1.75–1.35 (m, 10H; $(CH_2)_5$), 0.35 (s, 3H; CH_3), 0.28 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 95.50 (C), 88.01 (CH), 82.95 (C), 73.02 (CH_2), 66.03 (CH_2), 35.23 (CH), 33.99 (CH_2), 30.47 (CH_2), 25.95 (CH_2), 23.30 (CH_2), 22.86 (CH_2), 0.84 (CH_3), −2.26 (CH_3); $C_{13}H_{23}NO_4Si$ (285.4): calcd C 54.71, H 8.12, N 4.91, Si 9.84. C 54.65, H 8.10, N 4.93.

Compound **7g**: oil; ^{1}H NMR ($CDCl_3$): δ = 4.36 (m, 3H; $C^{6a}H$ and C^3H_2), 3.81 (d, J = 11.6 Hz, 1H; CH_A), 3.76 (d, J = 11.6 Hz, 1H; CH_B), 3.05 (brs, 1H; OH), 1.89 (t, J = 10.4 Hz, 1H; $C^{2a}H$), 1.80–1.40 (m, 4H; 2 CH_2), 0.91 (t, J = 7.1 Hz, 3H; CH_3), 0.87 (t, J = 7.1 Hz, 3H; CH_3), 0.35 (s, 3H; CH_3), 0.28 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ = 95.04 (C), 87.71 (CH), 86.18 (C), 72.65 (CH_2), 65.85 (CH_2), 34.87 (CH), 24.87 (CH_2), 21.93 (CH_2), 8.13 (CH_3), 7.37 (CH_3), 0.47 (CH_3), −2.69 (CH_3); $C_{12}H_{23}NO_4Si$ (273.4): calcd C 52.72, H 8.48, N 5.12, Si 10.27; found C 52.81, H 8.51, N 5.11.

Hydroxydesilylation-fragmentation of tricyclic compounds 7 (Scheme 11): The procedure was the same as reported above for the hydroxydesilylation of tricyclic compounds **3**.

Compound **8b**: oil; ^{1}H NMR (CD_3OD): δ = 7.50–7.20 (m, 5H; arom), 4.95 (s, 1H; C^4H), 4.55 (t, 1H; $C^{1'}H$), 3.75 (d, 2H; $C^{2'}H_2$), 1.75 (s, 3H; CH_3); ^{13}C NMR (CD_3OD): δ = 162.4 (C), 145.8 (C), 129.8 (CH), 128.7 (CH), 126.2 (CH), 91.50 (C), 83.53 (CH), 70.06 (CH), 66.10 (CH_2), 21.36 (CH_3); $C_{12}H_{15}NO_4$ (237.3): calcd C 60.75, H 6.37, N 5.90; found C 60.72, H 6.33, N 5.94.

Compound 4,5-*trans*-**8c**: oil; ^{1}H NMR ([D_6]acetone): δ = 5.65 (brs, 1H; OH), 5.20 (d, 1H; OH), 4.80 (m, 2H; C^4H and OH), 4.60 (dt, 1H; $C^{1'}H$), 4.20 (m, 1H; C^5H), 3.20 (m, 2H; $C^{2'}H_2$), 1.50–1.20 (m, 22H; $(CH_2)_{11}$), 0.90 (t, J = 7.1 Hz, 3H; CH_3); ^{13}C NMR ([D_6]acetone): δ = 161.5 (C), 88.29 (CH), 80.54 (CH), 69.13 (CH), 65.67 (CH_2), 32.64 (CH_2), 32.21 (CH_2), 30.41

(CH_2), 30.31 (CH_2), 30.22 (CH_2), 30.08 (CH_2), 29.97 (CH_2), 26.17 (CH_2), 23.36 (CH_2), 14.59 (CH_3); $C_{17}H_{33}NO_4$ (315.4): calcd C 64.73, H 10.54, N 4.44; found C 64.88, H 10.59, N 4.47.

Compound **8g**: oil; ^{1}H NMR ([D$_6$]acetone): $\delta = 5.10$ (d, $J = 5.8$ Hz, 1H; OH), 4.74 (d, $J = 5.4$ Hz, 1H; C^{4}H), 4.64 (t, $J = 4.6$ Hz, 3H; C$^{1'}$H), 3.78 (m, 2H; C$^{2'}$H$_2$), 3.42 (br s, 2H; 2 OH), 1.73 (m, 2H; CH_2), 1.50 (m, 2H; CH_2), 0.95 (t, $J = 7.1$ Hz, 3H; CH_3), 0.86 (t, $J = 7.1$ Hz, 3H; CH_3); ^{13}C NMR ([D$_6$]acetone): $\delta = 161.3$ (C), 91.26 (C), 79.25 (CH), 69.37 (CH), 65.56 (CH_2), 27.37 (CH_2), 22.76 (CH_2), 9.14 (CH_3), 8.08 (CH_3); $C_9H_{17}NO_4$ (203.2): calcd C 53.19, H 8.43, N 6.89; found calcd C 53.08, H 8.41, N 6.92.

Protection of 2-isoxazolines 8: A solution of **8** (2 mmol) in 2,2-dimethoxypropane (10 mL), with a few crystals of 4-methylbenzenesulfonic acid, was stirred at room temperature overnight. The reaction mixture was taken up with diethyl ether (15 mL) and washed with saturated sodium hydrogen carbonate (3×10 mL). The combined aqueous phase was back-extracted with diethyl ether (10 mL). The combined organic phase was washed with brine (10 mL), dried over sodium sulfate, and concentrated in vacuo. The residue was purified by silica-gel flash column chromatography (petroleum ether/diethyl ether = 1:1).

Compound **9b**: white solid; m.p. = 123 – 124 °C; ^{1}H NMR ($CDCl_3$): $\delta = 7.45$ (m, 5H; arom), 5.00 (d, $J = 5.0$ Hz, 1H; C^{4}H), 4.90 (t, $J = 6.3$ Hz, 1H; CH), 4.28 (dd, $J = 8.5$, 5.8 Hz, 1H; CH$_A$), 4.18 (dd, $J = 8.5$, 6.9 Hz, 1H; CH$_B$), 3.20 (d, $J = 5.0$ Hz, 1H; OH), 1.70 (s, 3H; CH_3), 1.45 (s, 3H; CH_3), 1.35 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 158.2$ (C), 143.8 (C), 129.0 (CH), 128.1 (CH), 124.9 (CH), 110.2 (C), 91.1 (C), 83.4 (CH), 71.9 (CH), 67.8 (CH_2), 26.6 (CH_3), 25.6 (CH_3), 20.9 (CH_3); IR (KBr): $\tilde{\nu} = 3330$, 2995, 1620, 1445, 1370, 1230 cm^{-1}. $C_{15}H_{19}NO_4$ (277.3): calcd C 64.97, H 6.91, N 5.05; found C 65.07, H 6.93, N 5.04.

Compound 4,5-*trans*-**9c**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 5.00$ (t, $J = 6.3$ Hz, C$^{1'}$H), 4.85 (dd, $J = 4.4$, 4.2 Hz, 1H; C^{4}H), 4.35 (m, 1H; C^{5}H), 4.25 (d, $J = 6.3$ Hz, 1H; C$^{2'}$H$_2$), 3.20 (d, $J = 4.2$ Hz, 1H; OH), 1.65 – 1.20 (m, 22H; $(CH_2)_{11}$), 1.50 (s, 3H; CH_3), 1.40 (s, 3H; CH_3), 0.90 (t, $J = 6.9$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 157.4$ (C), 110.4 (C), 88.22 (CH), 80.89 (CH), 71.23 (CH), 67.23 (CH_2), 32.39 (CH_2), 31.94 (CH_2), 29.66 (CH_2), 29.57 (CH_2), 29.47 (CH_2), 29.38 (CH_3), 26.24 (CH_3), 25.20 (CH_2), 25.15 (CH_2), 22.71 (CH_2), 14.14 (CH_3); IR (film): $\tilde{\nu} = 3346$, 2924, 2852, 1619, 1467, 1369 cm^{-1}. $C_{20}H_{37}NO_4$ (355.5): calcd C 67.57, H 10.49, N 3.94; found C 67.50, H 10.51, N 3.97.

Compound **9g**: white solid; m.p. = 69 – 70 °C; ^{1}H NMR ($CDCl_3$): $\delta = 4.92$ (t, $J = 6.4$ Hz, 1H; C$^{1'}$H), 4.63 (d, $J = 6.2$ Hz, 1H; C^{4}H), 4.21 (dd, $J = 8.05$, 6.2 Hz, 1H; C$^{2'}$H$_A$), 4.16 (dd, $J = 8.05$, 6.5 Hz, 1H; C$^{2'}$H$_B$), 3.15 (d, $J = 6.2$ Hz, 1H; OH), 1.75 (m, 2H; CH_2), 1.55 (m, 2H; CH_2), 1.44 (s, 3H; CH_3), 1.36 (s, 3H; CH_3), 0.93 (t, $J = 7.1$ Hz, 3H; CH_3), 0.84 (t, $J = 7.1$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 158.2$ (C), 110.6 (C), 92.13 (C), 79.86 (CH), 71.89 (CH), 67.64 (CH_2), 27.27 (CH_2), 26.61 (CH_3), 25.59 (CH_3), 22.48 (CH_2), 9.13 (CH_3), 8.12 (CH_3); IR (KBr): $\tilde{\nu} = 3306$, 2983, 2879, 1453 cm^{-1}. $C_{12}H_{21}NO_4$ (243.3): calcd C 59.24, H 8.70, N 5.76; found C 59.29, H 8.73, N 5.72.

Reduction of 2-isoxazolines 9: A two-necked flask was charged with a solution of the starting material **9** (1 mmol) in anhydrous THF (2 mL). The solution was stirred under a positive pressure of nitrogen and cooled to 0 °C. A solution of $LiAlH_4$ in Et_2O (1M, 4 mL, 4 mmol) was added dropwise to the reaction mixture through a septum by a syringe. The course of the reaction was monitored by tlc (dichloromethane/methanol = 9:1) and after one hour the disappearance of the starting material was observed. The reaction was quenched by the careful addition of 20% NaOH (0.22 mL) and benzyl chloroformate (0.2 mL, ca. 1.4 mmol). The mixture was stirred for another hour at 0 °C, then it was diluted with diethyl ether (30 mL) and transferred into a separating funnel partitioning with 20% NaOH (15 mL). The aqueous layer was extracted with diethyl ether (3×15 mL), and the combined organic phase was washed with brine (5 mL), dried over sodium sulfate, and concentrated in vacuo. The residue was purified by silica-gel flash column chromatography (petroleum ether/diethyl ether/methanol = 7:3:0.1).

Compound **10b**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 7.45 - 7.20$ (m, 10H; aromatic), 5.36 (d, $J = 9.4$ Hz, 1H; NH, disappears after D_2O exchange in about 14 days), 5.10 (d, $J = 12.2$ Hz, 1H; PhCH$_A$), 5.00 (d, $J = 12.2$ Hz, 1H; PhCH$_B$), 4.64 (br s, 1H; OH), 4.20 – 4.06 (m, 2H; CH_2), 3.98 (dd, $J = 8.7$, 6.3 Hz, 1H; CH), 3.70 (m, 2H), 3.26 (d, $J = 8.8$ Hz, 1H; OH), 1.50 (s, 3H; CH_3), 1.30 (s, 3H; CH_3), 1.00 (s, 3H; CH_3);^{13}C NMR ($CDCl_3$): $\delta = 156.4$ (C), 145.6 (C), 136.6 (C), 129.0 (CH), 128.7 (CH), 128.5 (CH), 127.4 (CH), 124.9 (CH), 110.9 (C), 79.13 (CH), 75.93 (C), 73.01 (CH), 68.33 (CH_2), 67.50 (CH_2), 54.89 (CH), 30.51 (CH_3), 26.25 (CH_3), 25.86 (CH_3); $C_{23}H_{29}NO_6$ (415.5): calcd C 66.49, H 7.04, N 3.37; found C 66.38, H 7.00, N 3.40.

Compound **10c**: white solid; m.p. = 61 – 63 °C; ^{1}H NMR ($CDCl_3$): $\delta = 7.35$ (m, 5H; arom), 5.65 (bd, 1H; NH), 5.10 (br s, 2H; PhCH$_2$), 4.25 (m, 1H; CH), 4.10 – 3.85 (m, 3H), 3.68 (m, 2H), 3.38 (m, 2H), 1.65 – 1.15 (m, 22H; $(CH_2)_{11}$), 1.45 (s, 3H; CH_3), 1.35 (s, 3H; CH_3), 0.90 (t, $J = 7.1$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 156.8$ (C), 136.7 (C), 129.0 (CH), 128.7 (CH), 128.6 (CH), 110.6 (C), 76.21 (CH), 74.13 (CH), 73.23 (CH), 68.19 (CH_2), 67.55 (CH_2), 54.66 (CH), 33.62 (CH_2), 32.40 (CH_2), 30.16 (CH_2), 29.84 (CH_2), 26.71 (CH_3), 26.10 (CH_3), 26.46 (CH_2), 23.18 (CH_2), 14.63 (CH_3); IR (KBr): $\tilde{\nu} = 3354$, 2918, 2850, 1691, 1670, 1266 cm^{-1}. $C_{28}H_{47}NO_6$ (493.7): calcd C 68.12, H 9.60, N 2.84; found 68.20, H 9.64, N 2.81.

Compound **10g**: white solid; m.p. = 103 – 104 °C; ^{1}H NMR (10% [D$_6$]DMSO in [D$_6$]acetone): $\delta = 7.45 - 7.20$ (m, 5H; arom), 6.65 (bd, $J = 9.4$ Hz, 1H; NH), 5.10 (m, 2H; PhCH$_2$), 4.56 (m, 1H), 4.10 (m, 1H), 3.96 (m, 2H), 3.58 (m, 3H), 1.55 – 1.45 (m, 4H), 1.30 (s, 3H; CH_3), 1.25 (s, 3H; CH_3), 0.84 (t, $J = 7.1$ Hz, 3H; CH_3), 0.81 (t, $J = 7.1$ Hz, 3H; CH_3); ^{13}C NMR (10% [D$_6$]DMSO in [D$_6$]acetone): $\delta = 156.9$ (C), 138.2 (C), 128.9 (CH), 128.4 (CH), 128.4 (CH), 110.4 (C), 76.07 (CH), 75.97 (C), 75.56 (CH), 66.50 (CH_2), 66.29 (CH_2), 53.93 (CH), 27.97 (CH_2), 26.98 (CH_2), 26.52 (CH_3), 25.83 (CH_3), 8.14 (CH_3), 7.98 (CH_3); IR (KBr): $\tilde{\nu} = 3371$, 2977, 1686, 1543, 1385, 1275 cm^{-1}. $C_{20}H_{31}NO_6$ (381.5): calcd C 62.97, H 8.19, N 3.67; found C 63.08, H 8.21, N 3.67.

Acetylation of tricyclic compounds 7: A solution of the starting material **7** (1.4 mmol) in pyridine (3 mL) was placed in a flask fitted with a calcium chloride tube. The stirred solution was cooled to 0 °C, and acetic anhydride (0.13 mL, 1.4 mmol) and a catalytic amount of 4-dimethylaminopyridine were added. The mixture was stirred at room temperature until the starting material was completely consumed (tlc: petroleum ether/ethyl acetate = 7:3). The mixture was diluted with diethyl ether (10 mL) and carefully transferred into a separating funnel containing an ice-cold 10% solution of HCl (25 mL). The aqueous layer was back-extracted with diethyl ether (3×10 mL) and the combined organic phase was washed with NaOH (2.5M, 10 mL) and brine (10 mL). After drying over sodium sulfate and concentrating in vacuo, the residue was purified by silica-gel flash column chromatography only when needed.

Compound **11b**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 7.59 - 7.23$ (m, 5H; arom), 4.90 (s, 1H; C^{6a}H), 4.51 (dd, $J = 11.5$, 8.3 Hz, 1H; C^{3}H$_A$), 4.46 (dd, $J = 9.9$, 8.3 Hz, 1H; C^{3}H$_B$), 3.94 (d, $J = 11.6$ Hz, 1H; CH$_A$OAc), 3.84 (d, $J = 11.6$ Hz, 1H; CH$_B$OAc), 1.75 (dd, $J = 11.5$, 9.9 Hz, 1H; C^{2a}H), 1.63 (s, 3H; CH_3), 1.44 (s, 3H; CH_3), 0.43 (s, 3H; CH_3), 0.34 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 170.7$ (C), 144.5 (C), 128.4 (CH), 127.2 (CH), 125.9 (CH), 93.32 (C), 90.03 (CH), 85.18 (C), 73.28 (CH_2), 65.75 (CH_2), 36.24 (CH), 23.97 (CH_3), 20.54 (CH_3), 0.558 (CH_3), – 2.43 (CH_3); $C_{17}H_{23}NO_5Si$ (349.5): calcd C 58.43, H 6.63, N 4.01, Si 8.04; found C 58.35, H 6.60, N 4.02.

Compound 6-*endo*-**11c**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 4.47$ (d, $J = 3.5$ Hz, 1H; C^{3}H$_A$), 4.40 (d, $J = 10.4$ Hz, 1H; C^{3}H$_B$), 4.26 (d, $J = 11.4$ Hz, 1H; CH$_A$OAc), 4.15 (d, $J = 11.4$ Hz, 1H; CH$_B$OAc), 3.75 (dt, $J_d = 3.4$ Hz, $J_t = 6.7$ Hz, 1H; C^{6}H), 2.10 (s, 3H; CH_3), 1.77 (t, $J = 10.5$ Hz, 1H; C^{2a}H), 1.63 (m, 2H), 1.30 (m, 20H), 0.90 (t, $J = 6.7$ Hz, 3H; CH_3), 0.38 (s, 3H; CH_3), 0.30 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 170.4$ (C), 92.49 (C), 84.08 (CH), 78.17 (CH), 73.60 (CH_2), 65.91 (CH_2), 35.06 (CH), 31.92 (CH_2), 29.67 (CH_2), 29.56 (CH_2), 29.47 (CH_2), 29.35 (CH_2), 26.36 (CH_2), 25.88 (CH_2), 22.69 (CH_2), 20.76 (CH_3), 14.12 (CH_3), – 0.013 (CH_3), – 3.01 (CH_3); $C_{22}H_{41}NO_5Si$ (427.7): calcd C 61.79, H 9.66, N 3.28, Si 6.57; found C 61.91, H 9.69, N 3.25.

Compound **11d**: white solid; m.p. = 88 – 89 °C; ^{1}H NMR ($CDCl_3$): $\delta = 4.38$ (dd, $J = 11.3$, 8.3 Hz, 1H; C^{3}H$_A$), 4.32 (s, 1H; C^{6a}H), 4.29 (dd, $J = 9.9$, 8.3 Hz, 1H; C^{3}H$_B$), 4.19 (d, $J = 11.5$ Hz, 1H; CH$_A$OAc), 4.14 (d, $J = 11.5$ Hz, 1H; CH$_B$OAc), 2.05 (s, 3H; CH_3), 1.72 (dd, $J = 11.3$, 9.9 Hz, 1H; C^{2a}H), 1.87 – 1.28 (m, 10H), 0.29 (s, 3H; CH_3), 0.25 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 170.9$ (C), 93.07 (C), 88.04 (CH), 82.80 (C), 73.05 (CH_2), 67.09 (CH_2), 36.22 (CH), 33.77 (CH_2), 30.32 (CH_2), 25.92 (CH_2), 23.26 (CH_2), 22.86 (CH_2), 21.22 (CH_3), 0.76 (CH_3), – 2.27 (CH_3); $C_{15}H_{25}NO_5Si$ (327.4): calcd C 55.02, H 7.70, N 4.28, Si 8.58; found C 55.12, H 7.72, N 4.31.

Compound **11g**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 4.41$ (dd, $J = 13.7$, 8.2 Hz, 1H; C^{3}H$_A$), 4.37 (dd, $J = 12.5$, 8.2 Hz, 1H; C^{3}H$_B$), 4.32 (s, 1H; C^{6a}H), 4.29 (d, $J = 11.5$ Hz, 1H; CH$_A$OAc), 4.19 (d, $J = 11.5$ Hz, 1H; C^{3}H$_B$OAc), 2.1 (s, 3H; CH_3), 1.90 – 1.70 (m, 3H), 1.65 – 1.45 (m, 2H), 0.93 (t, $J = 7.1$ Hz, 3H; CH_3), 0.87 (t, $J = 7.1$ Hz, 3H; CH_3), 0.36 (s, 3H; CH_3), 0.30 (s, 3H; CH_3);

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^{13}C NMR ($CDCl_3$): $\delta = 170.4$ (C), 92.48 (C), 87.64 (CH), 85.78 (C), 72.40 (CH_2), 66.64 (CH_2), 35.71 (CH), 24.35 (CH_2), 21.50 (CH_2), 20.58 (CH_3), 7.82 (CH_3), 7.08 (CH_3), 0.12 (CH_3), −2.93 (CH_3); $C_{14}H_{25}NO_5Si$ (315.4): calcd C 53.31, H 7.99, N 4.44, Si 8.90; found C 53.39, H 8.02, N 4.41.

Hydroxydesilylation-fragmentation of 11b: The procedure was the same as reported above for the hydroxydesilylation of tricyclic compounds of type **3** and **7**.

(4,5-trans)-3-Acetoxymethyl-4-hydroxy-5-methyl-5-phenyl-2-isoxazoline (**12**): M.p. = 73–75 °C; ^{1}H NMR ($CDCl_3$): $\delta = 7.34$ (m, 5H; arom), 4.97 (d, $J = 13.7$ Hz, 1H; CH_AOAc), 4.87 (d, $J = 7.6$ Hz, 1H; C^4H), 4.85 (d, $J = 13.7$ Hz, 1H; CH_BOAc), 3.90 (d, $J = 7.6$ Hz, 1H; OH), 2.05 (s, 3H; CH_3), 1.70 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 171.8$ (C), 156.2 (C), 143.8 (C), 129.0 (CH), 128.0 (CH), 125.0 (CH), 91.04 (C), 83.39 (CH), 58.05 (CH_2), 21.02 (CH_3), 20.98 (CH_3); $C_{13}H_{15}NO_4$ (249.3): calcd C 62.64, H 6.07, N 5.62; found C 62.72, H 6.10, N 5.62.

Hydroxydesilylation trapping of tricyclic compounds 3 and 11: A solution of the starting material **3** or **11** (2.5 mmol) in DMF (5 mL) was cooled to −15 °C with an ice–salt bath (3:1). Anhydrous potassium fluoride (0.16 g, 2.75 mmol) and potassium hydrogen carbonate (0.276 g, 2.75 mmol) were added to the stirred solution. *m*-Chloroperbenzoic acid (50%, 0.95 g, 2.75 mmol) was added to the reaction mixture in portions so as to keep the internal temperature below −10 °C. After another 30 min of stirring at −15 °C the disappearance of the starting material was observed (tlc: petroleum ether/ethyl acetate = 3:1). The reaction was quenched by the sequential addition of triethylamine (2.78 mL, 20 mmol, 4 equiv), 4-dimethylaminopyridine (0.12 g, 1 mmol, 0.4 equiv), and acetic anhydride (1.88 mL, 20 mmol, 4 equiv). The mixture was stirred at −15 °C for 2 h and then overnight at room temperature. After that it was taken up with diethyl ether (20 mL), transferred into a separating funnel, and was washed with 20% $Na_2S_2O_3$ (20 mL). The aqueous layer was back extracted with diethyl ether (2 × 20 mL) and the combined organic phases were subsequently washed with saturated ice-cold 5% HCl (10 mL), sodium carbonate (2 × 15 mL), and brine (10 mL). The organic solution was dried over magnesium sulfate, and concentrated in vacuo to afford the crude product containing only small amounts silylated impurities, which could be removed by a filtration over a silica-gel pad (petroleum ether/ethyl acetate = 3 :2).

Compound 2-*endo*-**13c**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 6.12$ (d, $J = 4.6$ Hz, 1H; C^3H), 5.92 (t, $J = 7.4$ Hz, 1H; C^4H), 4.32 (m, 5H; $C^{2'H}$; C^5H_2, and CH_2), 2.14 (s, 3H; CH_3), 2.05 (s, 3H; CH_3), 1.75 (m, 1H), 1.60 (m, 1H), 1.34 (t, $J = 7.1$ Hz, 3H; CH_3), 1.25 (m, 20H; $(CH_2)_{10}$), 0.88 (t, $J = 6.7$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 169.9$ (2C), 167.1 (C), 83.96 (C), 82.15 (CH), 75.87 (CH), 75.45 (CH), 72.06 (CH_2), 63.06 (CH_2), 31.92 (CH_2), 29.65 (CH_2), 29.51 (CH_2), 29.40 (CH_2), 29.35 (CH_2), 27.49 (CH_2), 26.01 (CH_2), 20.79 (CH_3), 20.43 (CH_3), 14.12 (CH_3), 13.91 (CH_3); $C_{24}H_{41}NO_8$ (471.6): calcd C 61.13, H 8.76, N 2.97; found C 61.01, H 8.74, N 2.99.

Compound **13d**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 6.18$ (dd, $J = 7.4$, 4.5 Hz, 1H; C^4H), 5.89 (s, 1H C^3H), 5.54 (dd, $J = 8.6$, 7.5 Hz, 1H; C^5H_A), 4.34 (dd, $J = 8.5$, 4.6 Hz, 1H; C^5H_B), 4.30 (q, $J = 7.1$ Hz, 2H; CH_2), 2.11 (s, 3H; CH_3), 2.10 (s, 3H; CH_3), 2.00–1.40 (m, 10H), 1.33 (t, $J = 7.1$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 170.3$ (C), 170.2 (C), 167.6 (C), 86.40 (C), 85.85 (C), 81.81 (CH), 75.52 (CH), 75.20 (CH_2), 63.44 (CH_2), 36.23 (CH_2), 31.06 (CH_2), 25.47 (CH_2), 23.09 ($2CH_2$), 21.33 (CH_3), 21.04 (CH_3), 14.30 (CH_3); $C_{17}H_{25}NO_8$ (371.4): calcd C 54.98, H 6.79, N 3.77; found C 55.08, H 6.82, N 3.73.

Compound **13g**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 6.16$ (dd, $J = 7.5$, 4.7 Hz, 1H; C^4H), 5.97 (s, 1H; C^3H), 4.50 (dd, $J = 8.5$, 7.8 Hz, 1H; C^5H_A), 4.31 (q, $J = 7.1$ Hz, 2H; CH_2), 4.30 (dd, $J = 8.5$, 4.9 Hz, 1H; C^5H_B), 2.10 (s, 3H; CH_3), 2.08 (s, 3H; CH_3), 1.90 (m, 2H), 1.70 (m, 2H), 1.35 (t, $J = 7.1$ Hz, 3H; CH_3), 0.92 (t, $J = 7.1$ Hz, 3H; CH_3), 0.89 (t, $J = 7.1$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 169.8$ (C), 169.7 (C), 167.2 (C), 90.14 (C), 85.48 (C), 80.48 (CH), 75.23 (CH), 74.33 (CH_2), 63.03 (CH_2), 27.90 (CH_2), 23.08 (CH_2), 20.87 (CH_3), 20.65 (CH_3), 13.88 (CH_3), 8.161 (CH_3), 7.775 (CH_3); $C_{16}H_{25}NO_8$ (359.4): calcd C 53.47, H 7.01, N 3.90; found C 53.54, H 7.02, N 3.91.

Compound 2-*exo*-**13h**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 6.21$ (dd, $J = 6.3$, 4.0 Hz, 1H; C^4H), 5.73 (d, $J = 6.7$ Hz, 1H; C^3H), 4.57 (dt, $J_d = 6.7$ Hz, $J_t = 6.7$ Hz, 1H; C^2H), 4.36 (dd, $J = 9.1$, 6.2 Hz, 1H; C^5H_A), 4.31 (q, $J = 7.1$ Hz, 2H; CH_2), 4.24 (dd, $J = 9.1$, 4.0 Hz, 1H; C^5H_B), 2.11 (s, 3H; CH_3), 2.07 (s, 3H; CH_3), 1.75 (m, 2H), 1.50–1.25 (m, 4H), 1.35 (t, $J = 7.1$ Hz, 3H; CH_3), 0.91 (t, $J = 7.1$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 170.1$ (2C), 167.2 (C), 84.87 (CH), 83.72 (C), 79.68 (CH), 75.46 (CH), 73.53 (CH_2), 63.43 (CH_2), 32.29 (CH_2), 28.11 (CH_2), 22.87 (CH_2), 21.23 (CH_3), 20.94 (CH_3), 14.25 ($2CH_3$); IR (film): $\tilde{\nu} = 2950$, 1752, 1363, 1232 cm^{-1}. MS (70 eV, EI): *m/z* : 359 [M^+] (0.91), 299 (7.2), 197 (32.5), 169 (11.0), 167 (7.0), 151 (6.8), 141 (6.7), 43 (100); $C_{16}H_{25}NO_8$ (359.3): calcd C 53.47, H 7.01, N 3.90; found C 53.40, H 7.04, N 3.93.

Compound 2-*endo*-**13h**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 6.13$ (d, $J = 4.6$ Hz, 1H; C^3H), 5.93 (t, $J = 7.4$ Hz, 1H; C^4H), 4.45–4.15 (m, 5H; $C^{2'H}$; $C^{5'H}$; and CH_2), 2.10 (s, 3H; CH_3), 2.00 (s, 3H; CH_3), 1.80–1.10 (m, 6H), 1.35 (t, $J = 7.1$ Hz, 3H; CH_3), 0.82 (t, $J = 7.1$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 170.2$ (2C), 167.6 (C), 84.37 (C), 82.54 (CH), 76.28 (CH), 75.85 (CH), 72.49 (CH_2), 63.47 (CH_2), 28.52 (CH_2), 27.55 (CH_2), 22.96 (CH_2), 21.18 (CH_3), 20.84 (CH_3), 14.27 ($2CH_3$); $C_{16}H_{25}NO_8$ (359.3): calcd C 53.47, H 7.01, N 3.90; found C 53.44, H 7.03, N 3.93.

Compound 2-*endo*-**14c**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 5.65$ (d, $J = 4.9$ Hz, 1H; C^4H), 5.55 (d, $J = 4.5$ Hz, 1H; C^3H), 4.35–4.15 (m, 5H), 2.09 (s, 3H; CH_3), 2.04 (s, 3H; CH_3), 2.02 (s, 3H; CH_3), 1.80–1.10 (m, 22H), 0.85 (t, $J = 7.1$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 170.5$(C), 170.2 (C), 170.1 (C), 81.41 (CH), 81.09 (C), 75.66 (CH), 74.65 (CH), 72.16 (CH_2), 63.98 (CH_2), 32.36 (CH_2), 30.07 (CH_2), 29.96 (CH_2), 29.81 (CH_2), 29.77 (CH_2), 28.27 (CH_2), 26.49 (CH_2), 23.12 (CH_2), 21.21 (2 CH_3), 21.09 (CH_3), 14.56 (CH_3); $C_{24}H_{41}NO_8$ (471.6): calcd C 61.13, H 8.76, N 2.97; found C 60.98, H 8.72, N 3.01.

Compound **14g**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 5.64$ (dd, $J = 7.7$, 4.9 Hz, 1H; C^4H), 5.59 (s, 1H; C^3H), 4.44 (dd, $J = 8.6$, 7.7 Hz, 1H; C^5H_A), 4.29 (dd, $J = 8.6$, 5.0 Hz, 1H; C^5H_B), 4.18 (d, $J = 11.9$ Hz, 1H; CH_AOAc), 4.08 (d, $J = 11.9$ Hz, 1H; CH_BOAc), 2.10 (s, 3H; CH_3), 2.06 (s, 3H; CH_3), 2.04 (s, 3H; CH_3), 2.0–1.4 (m, 4H), 0.95 (t, $J = 7.1$ Hz, 3H; CH_3), 0.85 (t, $J = 7.1$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 170.6$ (C), 170.4 (C), 169.8 (C), 87.46 (C), 81.92 (C), 79.90 (CH), 74.74 (CH_2), 63.66 (CH_2), 29.37 (CH_2), 23.29 (CH_2), 21.57 (CH_3), 21.07 (2 CH_3), 8.55 (CH_3), 8.05 (CH_3); $C_{16}H_{25}NO_8$ (359.4): calcd C 53.47, H 7.01, N 3.90; found C 53.55, H 7.01, N 3.92.

Raney-nickel catalyzed hydrogenolysis of compounds 13: A catalytic amount of Raney nickel (50% slurry in water, active catalyst) was suspended in methanol (25 mL). The suspension was stirred for 1 min and then the solids were decanted and the methanol was removed. This operation was repeated four more times. After that the methanol was replaced with a solution of the starting material **13** (4 mmol) in methanol (25 mL) and the reaction flask was connected by three-way stopcock to gas burette filled with hydrogen. Hydrogen was flushed into the flask in four portions (50 mL each). The reaction mixture was then kept under an hydrogen atmosphere at room temperature until disappearance of the starting material was observed (tlc petroleum ether/ethyl acetate = 1:1). The mixture was carefully filtered over a Celite pad and the solids were thoroughly washed with methanol. The filtered solution was concentrated in vacuo to afford the crude material that needed no further purification. When NMR analysis showed that acetyl migration occurred during the reaction, the crude product was dissolved in pyridine (10 mL) and 4-dimethylaminopyridine (0.8 mmol) and acetic anhydride (12 mmol) were added. The mixture was stirred overnight at room temperature and after the standard workup, described above for the acetylation of compounds **7**, a single characterizable product was obtained.

Compound **16d**: white solid; m.p. 174–176 °C; ^{1}H NMR ($CDCl_3$): $\delta = 6.65$ (s, 1H; NH), 5.25 (dd, $J = 6.6$, 2.6 Hz, 1H; $C^{1'}H$), 4.95 (s, 1H; C^4H), 4.50 (dd, $J = 12.8$, 2.6 Hz, 1H; $C^{2'}H_A$), 4.25 (dd, $J = 12.8$, 6.6 Hz, 1H; $C^{2'}H_B$), 2.05 (s, 3H; CH_3), 1.97 (s, 3H; CH_3), 1.95 (s, 6H; 2 CH_3), 1.75–1.10 (m, 10H); ^{13}C NMR ($CDCl_3$): $\delta = 171.4$ (C), 170.9 (C), 170.4 (C), 169.9 (C), 169.7 (C), 86.30 (C), 74.94 (CH), 72.20 (CH), 64.53 (C), 63.07 (CH_2), 38.26 (CH_2), 30.85 (CH_2), 25.20 (CH_2), 22.63 (CH_2), 22.53 (CH_3 and CH_2), 21.07 (2 CH_3), 20.93 (CH_3); $C_{19}H_{27}NO_9$ (413.4): calcd C 55.20, H 6.58, N 3.39; found C 55.33, H 6.62, N 3.39.

Compound **16g**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 6.52$ (s, 1H; NH), 5.28 (dd, $J = 8.0$, 4.0 Hz, 1H), 5.15 (s, 1H), 4.54 (dd, $J = 12.6$, 3.9 Hz, 1H), 4.24 (dd, $J = 12.6$, 8.8 Hz, 1H), 2.12 (s, 3H; CH_3), 2.05 (s, 3H; CH_3), 2.03 (s, 3H; CH_3), 2.00 (s, 3H; CH_3), 2.00–1.50 (m, 4H), 0.91 (t, $J = 7.1$ Hz, 3H; CH_3), 0.89 (t, $J = 7.1$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 171.3$ (C), 170.6 (C), 170.3 (C), 169.9 (C), 169.6 (C), 89.80 (C), 73.72 (CH), 72.05 (CH), 64.79 (C), 63.04 (CH_2), 30.17 (CH_2), 23.58 (CH_2), 22.56 (CH_3), 21.25 (2 CH_3), 20.95 (CH_3), 8.08 (CH_3), 7.69 (CH_3); $C_{18}H_{27}NO_9$ (401.4): calcd C 53.86, H 6.78, N 3.49; found C 54.00, H 6.81, N 3.44.

Compound 4,5-*trans*-**15h**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 4.80$ (br s, 2H), 4.50–4.00 (m, 5H), 3.10 (br s, 1H), 2.10 (s, 3H; CH_3), 2.05 (s, 3H; CH_3), 1.90–1.60 (m, 2H), 1.55–1.30 (m, 4H), 0.95 (t, $J = 7.1$ Hz, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 174.4$ (C), 173.5 (C), 172.3 (C), 85.99 (CH), 73.41 (CH), 71.18

(CH), 65.48 (CH_2), 65.07 (CH_2), 33.44 (CH_2), 27.84 (CH_2), 22.86 (CH_2), 22.81 (CH_3), 21.29 (CH_3), 14.31 (CH_3); $C_{14}H_{23}NO_7$ (317.3): calcd C 52.99, H 7.31, N 4.41; found calcd C 52.90, H 7.29, N 4.42.

Compound 4,5-*cis*-**15h**: oil; ^{1}H NMR (CD_3OD): $\delta = 4.80-4.60$ (m, 5H), 4.40 (m, 1H), 4.15–4.00 (m, 2H), 3.85 (m, 2H), 2.05 (s, 3H; CH_3), 2.03 (s, 3H; CH_3), 1.80 (m, 2H), 1.45 (m, 4H), 1.15 (t, $J = 7.1$ Hz, 3H; CH_3); ^{13}C NMR (CD_3OD): $\delta = 176.5$ (C), 175.7 (C), 173.1 (C), 84.78 (CH), 74.64 (CH), 71.55 (CH), 70.46 (C), 66.60 (CH_2), 29.82 (CH_2), 29.00 (CH_2), 24.02 (CH_2), 22.86 (CH_3), 21.29 (CH_3), 14.78 (CH_3); $C_{14}H_{23}NO_7$ (317.3): calcd C 52.99, H 7.31, N 4.41; found calcd C 52.88, H 7.28, N 4.45.

Palladium-catalyzed hydrogenolysis: A solution of the starting nitroso acetal (2 mmol) in ethyl acetate (15 mL) was added with a catalytic amount of palladium (10% over carbon). The stirred solution was connected by a three-way stopcock to a gas burette filled with hydrogen. Hydrogen was flushed into the flask in four portions (50 mL each). The reaction mixture was then kept under an hydrogen atmosphere at room temperature until disappearance of the starting material was observed (tlc). The mixture was carefully filtered over a Celite pad and the solids were thoroughly washed with methanol. The filtered solution was concentrated in vacuo to afford the crude material that needed no further purification.

Compound **17d**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 6.50$ (brs, 1H; NH), 4.48 (s, 1H), 4.20 (q, $J = 7.1$ Hz, 2H; CH_2), 3.89 (dd, $J = 11.7$, 8.9 Hz, 1H), 3.71 (dd, $J = 11.7$, 4.0 Hz, 1H), 3.20 (s, 1H; OH), 1.93 (dd, $J = 8.9$, 4.0 Hz, 1H), 1.65–1.15 (m ,10H), 1.23 (t, $J = 7.1$ Hz, 3H; CH_3), 0.26 (s, 6H; 2 CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 174.5$ (C), 92.99 (CH), 87.39 (C), 78.27 (C), 62.33 (CH_2), 59.47 (CH_2), 37.63 (CH), 30.83 (CH_2), 29.78 (CH_2), 25.52 (CH_2), 22.99 (CH_2), 22.64 (CH_2), 14.08 (CH_3), −0.08 (CH_3), −1.16 (CH_3); $C_{15}H_{27}NO_5Si$ (329.5): calcd C 54.68, H 8.26, N 4.25, Si 8.52; found C 54.68, H 8.26, N 4.25.

Compound **17g**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 6.4$ (brs, 1H; NH), 4.52 (s, 1H), 4.28 (q, $J = 7.1$ Hz, 1H; CH_A), 4.26 (q, $J = 7.1$ Hz, 1H; CH_B), 3.96 (dd, $J = 11.6$, 8.4 Hz, 1H; CH_AOH), 3.78 (dd, $J = 11.6$, 3.9 Hz, 1H; CH_BOH), 3.54 (brs, 1H; OH), 1.98 (dd, $J = 8.4$, 3.9 Hz, 1H; CHSi), 1.62 (q, $J = 7.3$ Hz, 2H; CH_2), 1.39 (q, $J = 7.3$ Hz, 2H; CH_2), 1.32 (t, $J = 7.1$ Hz, 3H; CH_3), 0.90 (m, 6H), 0.36 (s, 3H; CH_3), 0.34 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): $\delta = 174.6$ (C), 92.98 (CH), 91.30 (C), 78.50 (C), 63.33 (CH_2), 59.47 (CH_2), 37.94 (CH), 22.31 (CH_2), 21.83 (CH_2), 14.10 (CH_3), 8.74 (CH_3), 7.25 (CH_3), −0.03 (CH_3), −1.08 (CH_3); $C_{14}H_{27}NO_5Si$ (317.5): calcd C 52.97, H 8.57, N 4.41, Si 8.85; found C 52.97, H 8.57, N 4.41.

Compound **18g**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 6.35$ (brs, 1H; NH), 5.61 (s, 1H), 5.35 (dd, $J = 4.7$, 4.5 Hz, 1H; CH_A), 4.40–4.20 (m, 2H), 3.79 (dd, $J = 12.3$, 4.2 Hz, 1H; CH_AOH), 3.70 (dd, $J = 12.3$, 4.9 Hz, 1H; CH_BOH), 3.30 (brs, 1H; OH), 2.16 (s, 3H; CH_3), 2.10 (s, 3H; CH_3), 1.80–1.30 (m, 4H), 1.30 (t, $J = 7.1$ Hz, 3H; CH_3), 0.90 (m, 6H); ^{13}C NMR (CDCl3): $\delta = 170.3$ (C), 170.2 (C), 168.4 (C), 89.56 (C), 82.98 (CH), 74.54 (C), 72.27 (CH), 63.27 (CH_2), 62.52 (CH_2), 25.62 (CH_2), 21.99 (CH_2), 21.16 (CH_3), 20.57 (CH_3), 13.88 (CH_3), 7.79 (CH_3), 7.44 (CH_3); $C_{16}H_{27}NO_8$ (361.4): calcd C 53.18, H 7.53, N 3.88; found C 53.31, H 7.57, N 3.80.

Compound **19g**: oil; ^{1}H NMR ($CDCl_3$): $\delta = 5.34$ (s, 1H), 5.11 (dd, $J = 4.8$, 3.7 Hz, 1H), 4.36 (d, $J = 12.0$ Hz, 1H; CH_AOAc), 4.12 (d, $J = 12.0$ Hz, 1H; CH_BOAc), 3.86 (dd, $J = 12.7$, 3.4 Hz, 1H; CH_AOH), 3.80 (dd, $J = 12.7$, 4.9 Hz, 1H; CH_BOH), 2.16 (s, 3H; CH_3), 2.12 (s, 3H; CH_3), 2.05 (s, 3H; CH_3), 1.85–1.40 (m, 4H), 1.0–0.80 (m, 6H); ^{13}C NMR ($CDCl_3$): $\delta = 170.5$ (C), 170.0 (C), 169.6 (C), 89.70 (C), 82.25 (CH), 72.10 (CH), 70.26 (C), 64.15 (CH_2), 61.90 (CH_2), 26.45 (CH_2), 21.10 (CH_3), 21.00 (CH_2), 20.77 (CH_3), 20.73 (CH_3), 8.12 (CH_3), 6.89 (CH_3); $C_{16}H_{27}NO_8$ (361.4): calcd C 53.18, H 7.53, N 3.88; found C 53.02, H 7.60, N 3.86.

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