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Enantioselective Total Synthesis of (-)-Denticulatins A and B Using a Novel Group-Selective Aldolization of a *meso* Dialdehyde as a Key Step

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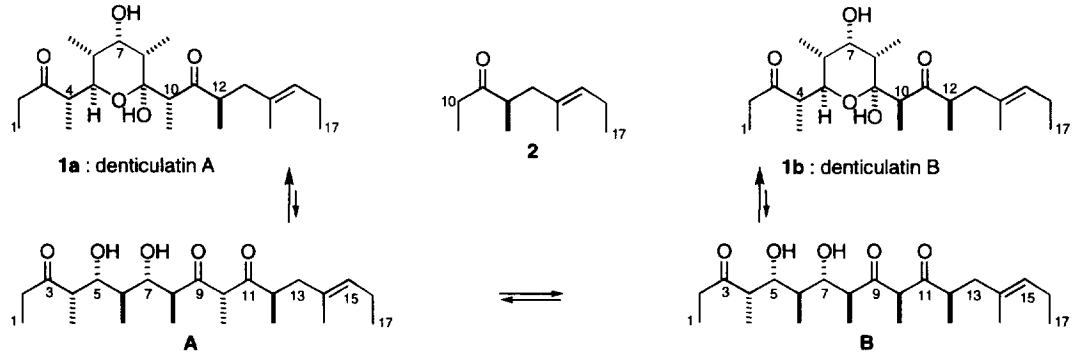
Abstract: The diastereoselective synthesis of (-)-denticulatin A (**1a**) was achieved for the first time in 9 steps (41% yield) based on a novel group-selective aldolization of a *meso* dialdehyde as a key step. The inherent chirality present in bornanesultam **4** was thus transmitted to the five stereocenters spanning C_4-C_8 in key intermediate **8**. In addition, denticulatin B (**1b**) was obtained from the common intermediate **8** *en route* to denticulatin A in 10 steps and 35% overall yield. © 1997 Elsevier Science Ltd.

The architectural complexity and beauty of compounds derived from marine animals makes them attractive targets for total synthetic approaches. Many of them are biosynthetically derived from a polyketide pathway through the assembly of acetate or propionate units followed by further structural modifications.[1] Among several approaches towards the synthesis of such compounds[2], the aldol reaction, and especially the stereocontrolled version of it, remains one of the most powerful methods for generating the contiguous stereogenic centers during the carbon-carbon bond forming steps.[3] In this context, we developed the asymmetric aldol addition of *N*-acetyl- and *N*-propionylsultams to aldehydes.[4]

The marine natural products denticulatins A (**1a**) and B (**1b**) provide an ideal platform to probe the viability and power of the auxiliary-based aldol approach as a promising tool in natural product synthesis. The denticulatins are marine polypropionates whose biological significance remains unclear - these compounds are ichtyotoxic and may be involved as antifeedants - and were isolated from the pulmonate mollusc *Siphonaria denticulata*.[5]



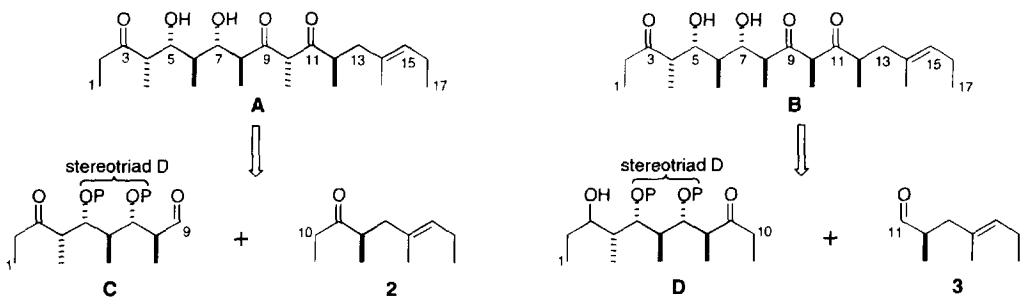
Scheme 1

† Deceased March 15, 1996.

The structures were unequivocally established by a single X-ray analysis. Treatment of the denticulatins with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) gave (*R*)-ketone **2** as a degradation product, thus assigning the absolute configuration of the denticulatins as shown. Furthermore, brief treatment of denticulatin A or B with DBU, resulted in their interconversion through retrohemiketalization via the β-diketone enolate.[6] Later, Paterson's group showed that the natural product may actually be one single C_{10}-epimer which isomerises upon chromatographic isolation.[7] Based on a configurational model which they recently proposed for siphonariid metabolites, this is likely to be denticulatin A.[8] In this paper, we present for the first time a short and highly stereoselective synthesis of denticulatin A (**1a**) avoiding epimerization at C_{10}. Furthermore, we report also a stereoselective synthesis of denticulatin B (**1b**) from a common precursor *en route* to denticulatin A.

Synthesis Plan

The denticulatins contain a hemiketal ring and are therefore formally derived from the dihydroxy triketones **A** or **B**. Ziegler's group[6] and later Paterson's group[7], demonstrated that protected open-chain triketones such as **A** or **B** underwent only one of the three possible modes of hemiketalization upon careful deprotection. Furthermore, Hoffmann's group showed that other possible hemiketals isomerize to the thermodynamically favored hemiketal present in the denticulatins.[9] Encouraged by these results, we planned to take an avenue which would lead us also to an acyclic triketone precursor such as **A** or **B**. A stereoselective synthesis of either denticulatin A (**1a**) *via* open chain triketone **A** or denticulatin B (**1b**) *via* triketone **B**, would rely on the ability to control the stereochemistry at C_{10}, without subsequent loss of the stereochemical information thus installed during the final deprotection/hemiketalization step.

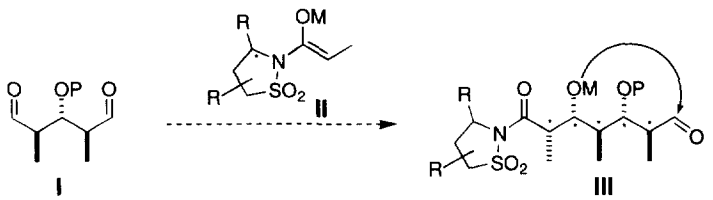


Scheme 2

Sectioning the triketone **A** at C_9-C_{10} by a retro-aldol disconnection conveniently divides the molecule in two fragments, stereopentad **C** and **2**. In the corresponding assemblage process, a substrate-controlled aldol coupling between a *Z(O)*-metal enolate derived from **2** and an aldehyde **C** was expected to give the desired stereochemistry for denticulatin A (**1a**) at C_{10}. Using a similar aldol bond construction, Hoffmann's group

obtained the desired stereochemistry for denticulatin A at C_{10}. However, the stereochemical integrity of this center was lost during the final steps of the synthesis.[9] Disconnection of the C_{10}-C_{11} bond in triketone **B** reveals the aldol retrons **D** and **3**. Substrate-controlled aldol coupling between these two fragments was now expected to establish the stereocenter with the opposite configuration at C_{10}, required for denticulatin B (**1b**). In fact, this strategy was applied by Paterson and Perkins to the first stereoselective synthesis of denticulatin B. Since denticulatin B was obtained after recrystallization, it is not clear weather some epimerization at C_{10} had occurred during the final deprotection step.[7]

Stereochemical examination of building blocks **C** and **D** reveals the presence of the same stereopentad, embedding the stereotriad *D* which is still not easily obtained. An efficient and rapid assembly of these fragments was therefore considered to be one of the major challenges towards a successful synthesis of the denticulatins. Because of its frequent occurrence in polyketide natural products a lot of synthetic efforts aimed at introducing the stereotriad *D* have been undertaken.[2b] Our approach is based on the attractive idea of an enantiotopic group desymmetrization of a *meso* dialdehyde which reflects the internal symmetry present in the stereotriad *D* (**Scheme 3**).



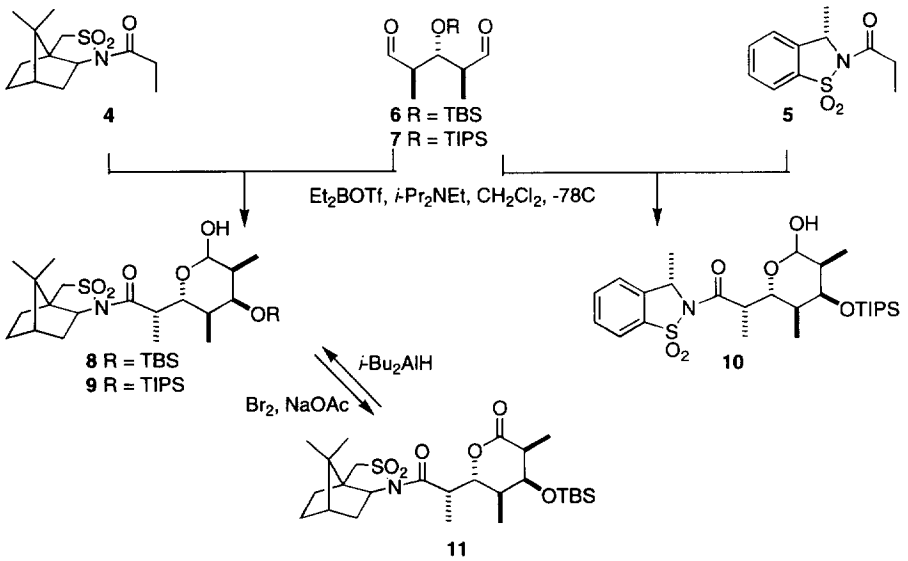
Scheme 3

The relative α,β-*syn*-β,γ-*anti* ("anti-Felkin) configuration would be patterned during an auxiliary controlled aldol reaction between a *Z(O)*-enolate derived from a homochiral *N*-propionylsultam and *meso* dialdehyde **I** in the key bond formation and desymmetrization step (**I + II → III**), thereby introducing the 5 contiguous stereogenic centers present in building blocks **C** or **D**. Solving most of the synthetic and stereochemical problems in one step, this approach would allow a very short access to the denticulatins.[10]

Group-Selective Aldolization of a *meso* Dialdehyde

Although no examples are known in the literature for desymmetrizations of *meso* dialdehydes during aldol additions[11], we were encouraged by the exceptional chiral efficiency and versatility of the sultam-based auxiliaries. The desymmetrization of *meso* dialdehydes such as **I** requires an enantiotopic group selection with an appropriate optically pure *N*-propionylsultam-derived enolate such as **II** and this operation has to be combined with diastereofacial selection at the chosen terminus.

In **Scheme 4** we present our results obtained from the desymmetrization of silyl-protected *meso* dialdehydes **6** and **7** with *N*-propionylsultams **4** and **5**. Thus, aldol reaction of the *Z(O)*-borylenolate derived from *N*-propionylbornane-10,2-sultam (**4**)[4a] with the *t*-butyldimethylsilyl-protected *meso* dialdehyde **6**[12] gave a mixture of anomeric lactols **8** in 75% yield. Careful inspection of the ^{1}H NMR spectrum of the crude mixture indicated the presence of less than 8% of other stereoisomers. The structure of the minor diastereomer (mixture of anomers) could not be determined however. Analogous condensation of the triisopropylsilyl-protected *meso* dialdehyde **7**[13] with the borylenolate derived from **4** provided a mixture of lactols **9** (95%) with a preference better then 20 to 1 (^{1}H NMR) for the α,β-*syn*-β,γ-*anti* ("anti-Felkin") configuration. Using the same protocol, lactol **10** was obtained from aldol-desymmetrization of *meso* dialdehyde **7** with *N*-propionyltoluene-1,2-sultam (**5**)[4b]. With the toluenesultam auxiliary however, the selectivity dropped to 10:1.



Scheme 4

It is remarkable to note that in none of these experiments the presence of double addition products could be observed. This is most likely due to the internal protection, as its lactol, of the second aldehyde moiety in the aldol product.

The absolute and relative configuration was unequivocally assigned from the X-ray diffraction study of lactone **11**.[10a] It is not surprising that the "anti-Felkin" products were obtained with the *Z(O)*-borylenolates derived from **4** or **5**. It is indeed well established that *Z(O)*-metal enolates belong to a special class of nucleophiles that exhibit selectivity for the anti-Felkin aldehyde diastereoface.[14] The discriminating capability excerted by the chiral sultam borylenolate forces the aldehyde to align itself to the less hindered face of the

enolate (**Figure 1**). Only the *pro-R* aldehyde moiety can do this in an anti-Felkin mode, giving rise to the α,β-*syn*-β,γ-*anti* or "anti-Felkin" product. The *pro-S* aldehyde moiety can align itself to the less hindered face of the enolate only in a Felkin mode, imposing severe gauche pentane interactions in the transition state.[14] The origin of the observed selectivity thus arises from the difference in energy of the two competing Felkin or anti-Felkin transition states, compatible with a *Re* π-facial bias of the aldehyde imposed by the very strong facial bias of the propionylsultam enolates.

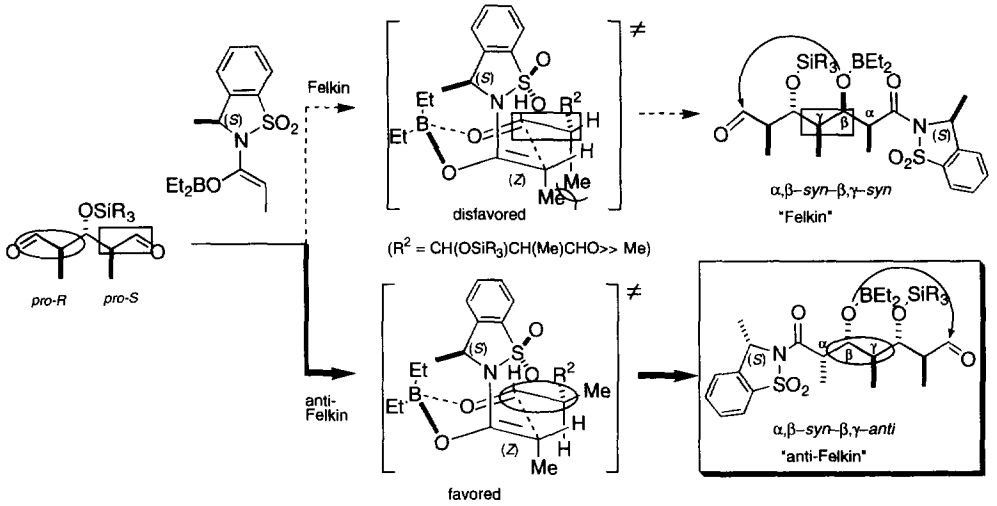


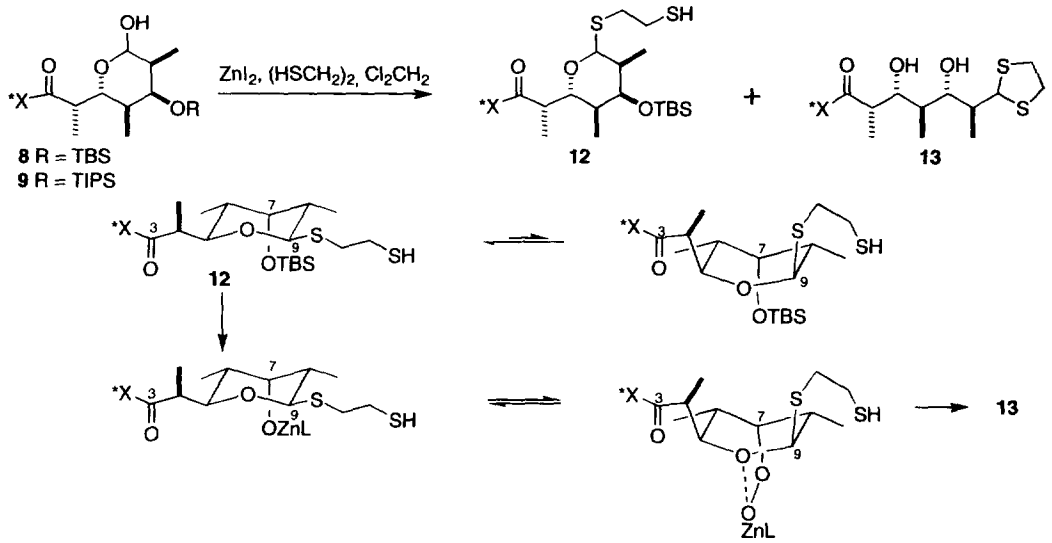
Figure 1

This study illustrates the synthetic utility of enantiotopic group differentiation of *meso* dialdehydes with the highly efficient and π-facial selective enolates derived from *N*-propionylsultams **4** and **5**.[15] Thus, in a one pot operation, the inherent bornanesultam chirality was transmitted to the five stereocenters within the key intermediates **C** and **D**.

Synthesis of the C_1-C_9 Fragment

Having satisfactorily set up the stereopentad spanning C_4-C_8, we had to proceed to the planned chain extensions at C_3 and C_9 with an ethyl group and C_{10}-C_{11} fragment **2** respectively. At first, we tried to elaborate lactone **11**, possessing already the correct oxidation state at C_3 and C_9, speculating that it should be possible to manipulate selectively either of both carbonyl functionality's by the appropriate choice of reagents. However, attempted additions of organomagnesium-, alkyl lithium reagents, lithium enolates and thiolates to either the C_3- or C_9-carbonyl group of lactone **11** failed, leading instead to slow elimination of the axially oriented silyloxy group.

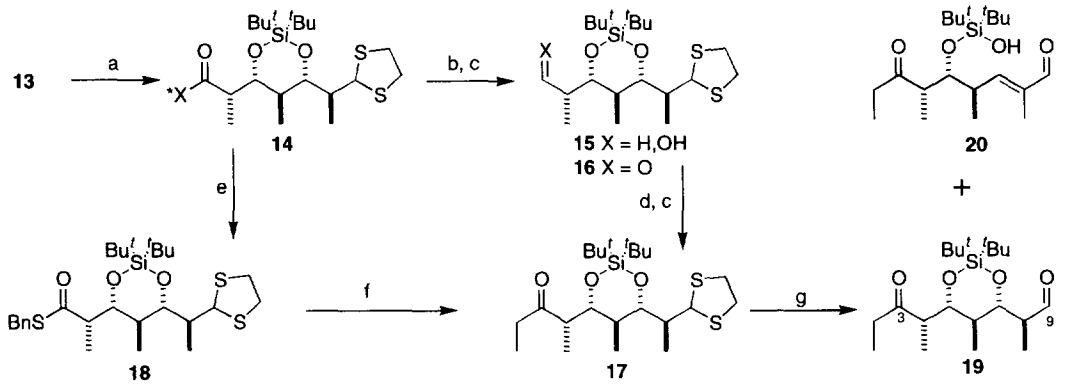
More gratifyingly, lactols **8** underwent smooth *O*-desilylation/ring opening when treated with ethanedithiol in the presence of ZnI_2 to give, after recrystallization, the pure dithiolane **13** in 92 % yield (**Scheme 5**). It turned out that *in situ* silyl ether cleavage was a prerequisite for dithiolane formation. This was based on the observation that by quenching the reaction before completion, only the dithiolane diol product **13** and the intermediate thiolactol **12**, containing the silyl protecting group, were present in the reaction mixture.[16] No sign of an intermediate thiolactol in which the silyl group was cleaved, or a dithiolane containing a silyl ether, could be observed. Apparently, the equatorial thiolactol intermediate **12** is easily formed but resists dithiolane formation in the presence of the axially oriented silyloxy group at C_7. Once the silyl ether is cleaved, the chair conformer can collapse into a boat conformer, which is stabilized as a chelate. Now, ring-opening occurs readily with concomitant formation of the dithiolane **13**. The silyl-protected intermediate **12** cannot easily adopt a boat conformation and as a consequence lacks intramolecular chelate-assisted ring opening (neighboring group participation of the C_7-hydroxyfunction).



Scheme 5

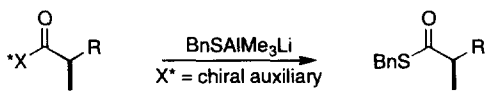
Further support for this hypothesis came from the observation that formation of dithiolane **13** from the triisopropylsilyl-protected lactol **9**, when subjected to identical reaction conditions, progressed much slower, providing product in only 60% yield. Longer reaction times resulted in cleavage of the chiral auxiliary and decomposition. Furthermore, the corresponding toluenesultam-derived lactol **10** underwent complete decomposition when subjected to the same reaction conditions. These observations all point to a rate-determining cleavage of the silyl protecting group, which is clearly more difficult to achieve in the case of a triisopropylsilyl ether.

After protection of the diol **13** as dioxasilinanyl derivative **14**, we had to proceed to the homologation of the acylsultam to an ethyl ketone and this proved not to be without difficulties (**Scheme 6**). Ethylmagnesium bromide failed to add to sultam **14**, even after many variations.[17] Reaction of **14** with the dilithio salt of ethyl phenyl sulfone, a method suitable for the transformation of *N*-acylsultams to methyl or ethyl ketones,[18] proved also unsuccessful. Obviously, the sultam was too sterically encumbered and even transformation to the corresponding carboxylic acid or Weinreb-amide[19] was impossible. On the basis of these non-encouraging results, the somewhat more tedious approach of reductively cleaving the sultam auxiliary was pursued. This reductive cleavage was best accomplished by lithium triethylborohydride, giving quantitatively the alcohol **15**, with recuperation of the chiral auxiliary.[20] Oxidation using the Swern conditions[21] followed by ethyl-Grignard addition to aldehyde **16** resulted in a 6.8:1 mixture of C_3-epimeric alcohols which were subjected to another Swern oxidation, affording the ethyl ketone **17** in 95% overall yield from **14**.



Scheme 6: (a) *t*-$Bu_2(OTf)_2$, 2,6-lutidine, CH_2Cl_2, room temperature; (b) $LiEt_3BH$, THF, -78 → -40°C; (c) $(COCl)_2$, DMSO, NEt_3, -78°C; (d) EtMgBr, Et_2O, -78°C; (e) $BnSAlMe_3Li$, $PhCH_3$, 0°C; (f) EtMgBr, $Fe(acac)_3$, THF, -25°C; (g) $Hg(OClO_3)_2$, THF/pH 7.4 buffer, room temperature.

Despite the efficiency of this four step sequence, we were convinced that a more elegant and shorter method for accessing ketones from *N*-acylbornanesultams could be devised. With respect to this, a recent paper from the Naito group, which deals with the displacement of bornanesultam- or oxazolidinone-based chiral auxiliaries with the "ate-complex" derived from trimethylaluminum and lithium benzylthiolate, attracted our attention (**Scheme 7**).[22] The corresponding benzyl thioesters were obtained without concomitant epimerization at the α-chiral center.



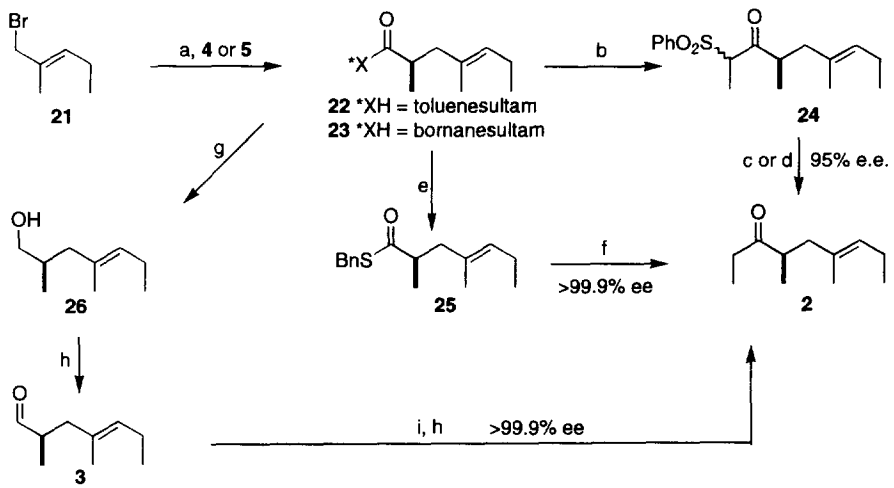
Scheme 7

Accordingly, replacement of the bornanesultam moiety in **14** *via* thiolysis with Naito's "ate-complex"[22], afforded the benzyl thioester **18** in 93% yield. Furthermore, treatment of benzyl thioester **18** with ethylmagnesium bromide in the presence of $Fe(acac)_3$ (10 mol%), based on a protocol developed by Marchese for the related coupling with phenyl thioesters[23], provided ethyl ketone **17** in 85%. Note that no epimerization had occurred during this two step sequence.[24]

Finally, the dithiolane protecting group had to be removed under mild conditions to avoid epimerization at the labile C_8-stereocenter. Considerable experimentation was required to define a satisfactory set of conditions. A modification of the procedure reported by Bernardi *et al.* proved to be suitable for this purpose,[25] involving treatment of the dithiolane **17** with mercury(II) trifluoroacetate or mercury(II) perchlorate in a buffered (pH 7) aqueous biphasic THF solution. Aldehyde **19** was thus obtained in 80-85% yield. In contrast, running this reaction in the presence of $CaCO_3$ to neutralize the acid formed,[25] elimination of the β-silyloxy group was operating in tandem, leading to the α,β-unsaturated aldehyde **20** instead.

Synthesis of Ethyl Ketone 2 and Aldehyde 3

Ethyl ketone **2** was previously obtained by Ziegler and Becker in 89% ee *via* alkylation of the RAMP-hydrazone of 3-pentanone with the bromide **21**.[6] Hoffmann's group reported a reagent-controlled synthesis of ketone **2**, albeit with a lower optical purity of 70-85%, starting from kinetically resolved (*R*)-2-methyl-1-penten-3-ol.[9] Our approach towards the synthesis of the ethyl ketone **2** exploited a previously developed protocol for the face-selective alkylation of homochiral *N*-alkanoylsultams (**Scheme 8**).[26]



Scheme 8: (a) **4** or **5**, $NaN(TMS)_2$, THF, -78°C; **21**, HMPA, THF, -78°C; (b) $EtSO_2Ph$, *n*-BuLi, TMEDA, -78°C; (c) Al(Hg), THF/H_2O, reflux; (d) SmI_2, THF, -78°C; (e) $BnSAlMe_3Li$, $PhCH_3$, 0°C; (f) EtMgBr, $Fe(acac)_3$, THF, -35°C; (g) $LiEt_3BH$, THF, -78°C → room temperature; (h) PCC, CH_2Cl_2, room temperature; (i) EtMgBr, Et_2O, -78°C → room temperature.

Thus, alkylation of the sodium enolate of (*S*)-*N*-propionyltoluenesultam **5** with the known bromide **21**[6] yielded diastereomerically pure sultam **22** (71%). Alternatively, the sodium enolate derived from *N*-propionylbornanesultam **4** was alkylated with allyl bromide **21** to give essentially diastereomerically pure crystalline sultam **23** (69% yield after 3 recrystallizations). In a first attempt, acylsultam **22** was converted to an epimeric mixture of sulfones **24** using the dilithio salt of ethyl phenyl sulfone in 78% yield, followed by subsequent reduction to the ethyl ketone **2** (Al(Hg), THF-H_2O (72%) or SmI_2, THF (89%)).[18] Chiral phase GC analysis indicated an enantiomeric excess of 95% ee (*Lipodex E*). Considering the fact that some racemization was observed during this transformation, the possibility was explored of producing ethyl ketone **2** *via* the iron(III)-mediated coupling reaction of a benzyl thioester with ethylmagnesium bromide. We observed that this was a reliable way of transforming sultam **14** into ethyl ketone **17** avoiding epimerization at the α-stereogenic center (*vide supra*).[24] Indeed, treatment of bornanesultam derivative **23** with Naito's "ate-complex"[22] furnished thioester **25** (89%) which was subsequently coupled with ethylmagnesium bromide in the presence of $Fe(acac)_3$. Ethyl ketone **2** was now obtained in 99% yield and >99.8% enantiomeric excess (chiral phase GC, *Lipodex E*).

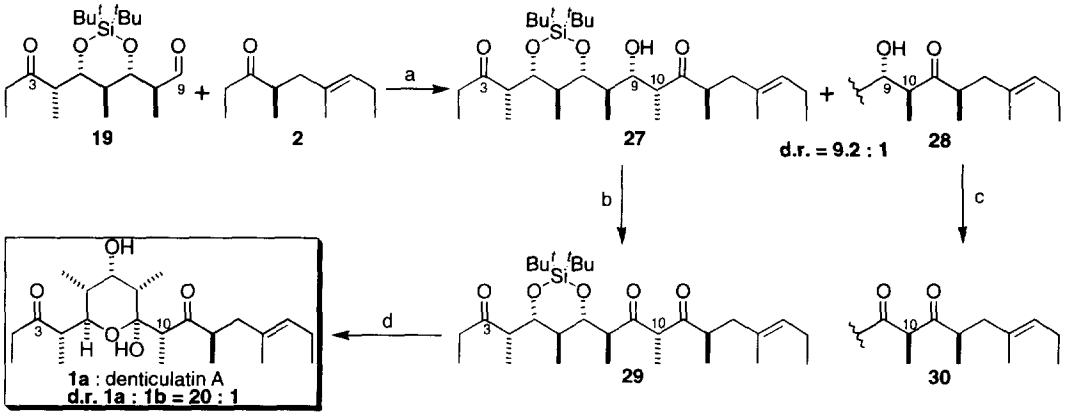
Aldehyde **3**, projected aldol coupling partner and intermediate in the synthesis of denticulatin B, can be obtained from the common intermediate **23** *via* reduction with lithium triethylborohydride (93%), followed by oxidation of alcohol **26** with PCC (88%).[27] The enantiomeric excess of aldehyde **3** was determined by transformation into ethyl ketone **2** (i. EtMgBr, Et_2O; ii. PCC, CH_2Cl_2) which was analyzed by chiral phase GC (*Lipodex E*, >99.8% ee).

Synthesis of Denticulatin A *via* C_9-C_{10} Aldol Bond Construction

The final challenges in the synthesis of denticulatin A (**1a**) involved (i) a stereoselective aldol coupling between the two fragments, stereopentad **19** and ethyl ketone **2**, generating the required stereochemistry at C_{10}, and (ii) avoiding epimerization at this center during the subsequent oxidation and final deprotection steps.

Aldol reaction of the *Z(O)*-titanium enolate[28] generated from ethyl ketone **2** [**2** (1.2 eq.), $TiCl_4$ (1.3 eq., neat), *i*-Pr_2NEt (1.4 eq.), CH_2Cl_2, -78°C, 1 h; then **19** (1 eq.), -78°C, 2 h followed by work up which involves $NaHCO_3$ washing], with aldehyde **19** gave a 9:1 mixture of two aldol products **27** and **28** in 61% yield together with 33% of the α,β-unsaturated aldehyde **20**. Carefully redefined conditions involving formation of the *Z(O)*-titanium enolate from **2** with a freshly prepared 1M solution of $TiCl_4$ in CH_2Cl_2 [**2** (1.5 eq.), $TiCl_4$ (1.6 eq.), CH_2Cl_2, -78°C, 15 min, *i*-Pr_2EtN (1.55 eq.), -78°C, 1 h] followed by addition of a pre-cooled (-78°C) solution of aldehyde **19** (1 eq.) in CH_2Cl_2 allowed, after pH 7 buffer work up, to obtain a 9.2:1 mixture of *syn* aldol **27** and *anti* aldol **28** in 89% combined yield (isomers separated by simple FC). Under these conditions the formation of the α,β-unsaturated aldehyde **20** was avoided. The major *syn* isomer **27** (diagnostic coupling constant: $J_{9,10}$ = 1.5 Hz)[9,29] was taken on to give denticulatin A (**1a**). The stereochemistry at C_{10} of the minor

anti isomer **28** (diagnostic coupling constant: $J_{9,10}$ = 9.9 Hz)[9,29] could be correlated to the one present in denticulatin B (**1b**) (*vide infra*).



Scheme 9: (a) **2**, $TiCl_4$, *i*-Pr_2NEt, CH_2Cl_2, -78°C; **19**, CH_2Cl_2, -78°C; (b) $(COCl)_2$, DMSO, NEt_3, CH_2Cl_2, -78°C; (c) Dess-Martin periodinane[34], CH_2Cl_2, room temperature; (d) HF.pyridine, pyridine, THF, room temperature.

It was somewhat surprising that such a good level of diastereoselection was obtained for this double-diastereodifferentiating aldol reaction. This aldol reaction reveals a level of complexity which is not covered in recent analyses of double-stereodifferentiating aldol processes and is clearly dependent on the configuration of all the stereogenic centers and protecting groups of both the aldehyde and enolate constituents.[30] Previous investigations have documented that titanium enolates derived from ethyl ketones undergo diastereoselective *syn* aldol reactions.[28] Furthermore, the prediction of the facial bias for a stereochemically complex aldehyde is very difficult and strongly correlates with enolate geometry in ethyl ketone aldol reactions. Simple α-substituted aldehydes tend to react via an anti-Felkin pathway with *Z(O)*-enolates, thus avoiding gauche pentane repulsion in the cyclic Zimmermann-Traxler transition state.[14] Evans *and coworkers* found that also β stereoinduction can play a significant role in dictating the facial bias of β-alkoxy substituted aldehydes, favoring a 1,3-*anti* diol relationship in the product.[31]

The stereochemical outcome from the aldol reaction between ethyl ketone **2** and aldehyde **19** indicates that the α-chiral center in the aldehyde partner is the major stereochemical determinant imposing an anti-Felkin bias with the *Z(O)*-enolate with only a minor influence from the residual β-silyloxy bearing stereocenter on the facial bias of aldehyde **19**.[32]

Having access to diastereochemically pure aldol product **27**, it was of primary importance not to loose the stereochemical integrity at C_{10} during the final steps of the synthesis, involving oxidation to a stereochemically labile triketone **29** and finally deprotection, leading to denticulatin A. An elegant solution for avoiding epimerization at the C_{10}-stereocenter was formulated by Paterson and Perkins.[7] They could handle epimeric

triketone **30**, obtained via Swern oxidation of aldol products **40** and **41** (**Scheme 10**, *vide infra*) under carefully defined conditions, without significant epimerization if chromatography was avoided. Under similar conditions, we obtained triketone **29** in nearly quantitative yield.[33] Although triketone **29** was not purified, the crude product was essentially pure and free of the corresponding C_{10} epimer as judged by ^{1}H and ^{13}C NMR analysis. Similar careful Swern oxidation of *anti* aldol **28** proved to be unproductive as no reaction had occurred. As an alternative procedure for mild oxidation of *anti* aldol **28** we explored the use of the Dess-Martin periodinane.[34] Under this set of conditions triketone **30**, intermediate in Paterson's denticulatin B (**1b**) synthesis,[7] was formed without observing epimerization at C_{10}, but the oxidation was accompanied by the formation of some unidentified minor by-products (TLC and ^{1}H NMR analysis). This served however to establish the configuration at C_{10} to be the one present in denticulatin B (**1b**).[33]

Paterson and Perkins obtained denticulatin B from triketone **30** *via* mild deprotection of the dioxasilinanyl protecting group with buffered hydrogen fluoride (commercial HF.pyridine, pyridine, THF, rt) followed by recrystallization in 54% yield.[7] Subjecting epimeric triketone **29** to these reaction conditions,[33] a 3:1 mixture of denticulatin A and B was obtained as an oil in 51% yield. Disappointed by this result, the possibility was explored of using a more hindered base to buffer the hydrogen fluoride pyridine complex (70% HF, 30% pyridine). However, the use of Hunigs base (i-Pr_2NEt) lead to a lower yield of a 2:1 mixture of denticulatin A and B (25% yield) together with an unidentified byproduct. Finally, it was found that the reaction conditions defined by Paterson and Perkins gave the best results if the workup procedure was slightly modified (washing with $CuSO_4$, phosphate buffer pH 7.4 and brine). Denticulatin A was thus obtained in 89% yield after flash chromatography with neutral silicagel (*Fluka* silicagel 60, *puriss.*, pH 7.0, 70-230 mesh ASTM), contaminated with 5% of denticulatin B (**1a**:**1b** = 20:1). As such, this represents the first stereocontrolled synthesis of denticulatin A.

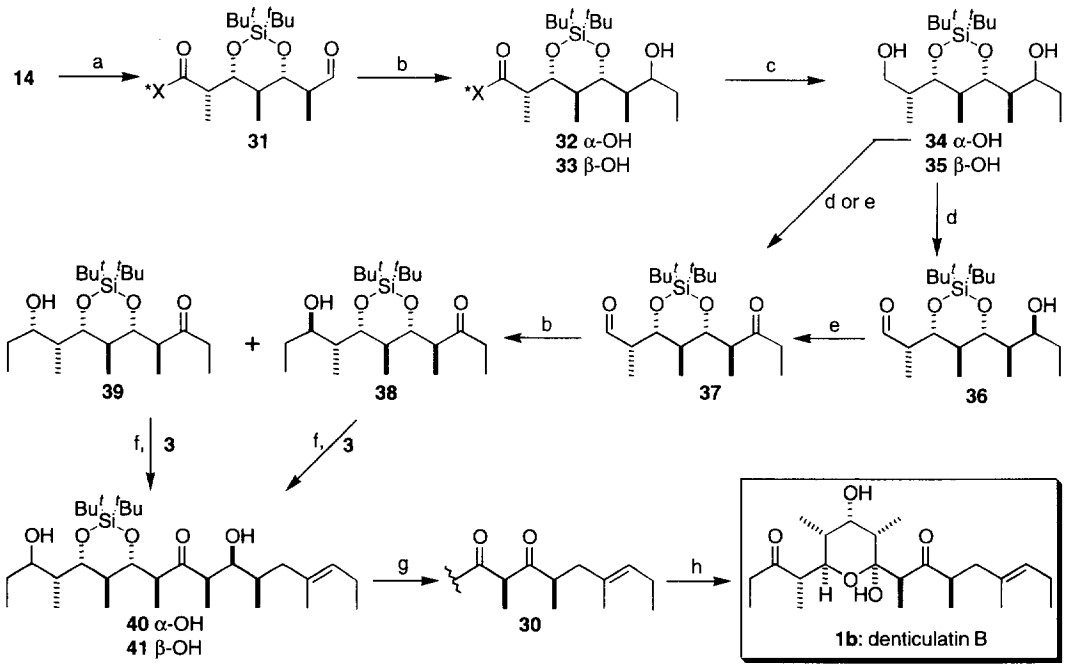
Synthesis of Denticulatin B *via* C_{10}-C_{11} Aldol Bond Construction

By choosing the appropriate disconnection for the retro aldol coupling reaction one should be able to obtain selectively denticulatin B (**1b**), as was demonstrated by Paterson and Perkins.[7] Using our methodology for the desymmetrization of *meso* dialdehydes and the alkylation of homochiral propionylsultams, applied to the synthesis of denticulatin A, we can have access to the same building blocks as the ones used in Paterson's synthesis of denticulatin B.

Thus, deprotection of the dithiolane **14** using a modification of the procedure reported by Bernardi *et al.*[25] (Hg(II)perchlorate, THF-buffer pH 7.4), gave the aldehyde **31** in 92% yield (**Scheme 10**). Reaction of aldehyde **31** with ethylmagnesium bromide in a 2:1 THF-Et_2O mixture at -100°C to -50°C provided the two epimeric alcohols **32** and **33** which were separated by flash chromatography for reasons of characterization (**32**: 23%, **33**: 72%). The auxiliary in **32** and **33** respectively, was then reductively cleaved ($LiEt_3BH$, THF, -78°C to rt), yielding diols **34** (94%) and **35** (90%). The same sequence of transformations was also done without

purification of the intermediates. Thus, starting from **14** an epimeric mixture of alcohols **34** and **35** was obtained. Purification of the crude mixture by flash chromatography gave 59% of **35**, 21% of epimeric alcohol **34** (80% overall yield from dithiolane **14**) and 70% of recovered (2*S*)-*N*-bornane-10,2-sultam.

The known crystalline diol **34** (m.p. 93°-94.5°C) was oxidized to **37** with PCC according to Paterson and Perkins.[7] However, subjecting the diastereomeric diol **35** to the same reaction conditions failed to afford dicarbonyl compound **37** giving instead the mono oxidized product, aldehyde **36** (97%). Excess of PCC reagent or higher temperatures and reaction times resulted in decomposition. Extensive investigation of oxidation conditions identified the Dess-Martin periodinane[34] as the oxidant of choice, providing **37** (63%), derived from alcohol **36**, with the same spectroscopic data as for **37** derived from diol **34**. Furthermore, oxidation of epimer **35** with the Dess-Martin periodinane[34] gave now in one step aldehyde **37** in 80% yield. The same conditions applied to epimeric alcohol **34** provided also aldehyde **37** (90%). This implies that the complete sequence to aldehyde **37** can be done without intermediate separation of the epimeric mixtures. Finally, addition of ethylmagnesium bromide to aldehyde **37** yielded an epimeric mixture of secondary alcohols **38** and **39** (100% crude), which upon flash chromatography afforded 21% of **38** and 60% of **39** (total yield 81%).



Scheme 10: (a) $Hg(OClO_3)_2$, THF/pH 7.4 buffer, room temperature; (b) EtMgBr, THF/Et_2O, -100 → -50°C; (c) $LiEt_3BH$, THF, -78°C → room temperature; (d) PCC, CH_2Cl_2, room temperature; (e) Dess-Martin periodinane[34], CH_2Cl_2, room temperature; (f) **38** or **39**, $TiCl_4$, *i*-Pr_2NEt, CH_2Cl_2, -78°C; **3**, CH_2Cl_2, -78°C; (g) $(COCl)_2$, DMSO, NEt_3, CH_2Cl_2, -78°C; (h) HF.pyridine, pyridine, THF, room temperature.

Aldol reaction of the *Z(O)*-titanium enolate derived from **39** [**39** (1 eq.), $TiCl_4$ (3 eq., 1 M in CH_2Cl_2, freshly prepared), CH_2Cl_2, -78°C, 30 min; *i*-Pr_2NEt (2.13 eq.), -78°C, 1 h] with aldehyde **3** (3 eq., CH_2Cl_2, -78°C, 1 h) gave the desired *syn* aldol **40** as one single isomer in 89%.[35] Similarly, aldol reaction between epimeric alcohol **38** and aldehyde **3** afforded the *syn* aldol product **41** as a single diastereomer (71%) together with 19% of recuperated ethyl ketone **38**.[35] Both C_3-epimeric diols **40** and **41** were quantitatively converted to diastereomerically pure triketone **30** *via* careful Swern oxidation provided chromatography was avoided.[7] As mentioned before, deprotection of the silyl protecting group in triketone **30** was reported by Paterson and Perkins to give denticulatin B (**1b**) in 54% yield.[7] Using the slightly modified workup procedure which proved to be superior for the final deprotection step leading to denticulatin A (see **Scheme 7**), a 12:1 epimeric mixture of denticulatin B and A was produced in essentially quantitative yield after purification by flash chromatography with high grade neutral silicagel. Recrystallization from pentane (m.p. 138-142°C) furnished denticulatin B with an improved yield of 78%, showing the same spectroscopic data as described in the literature.[5,7]

Conclusions

In summary, this represents the first enantioselective total synthesis of denticulatin A (**1a**) in 9 steps and 41% overall yield from *meso* dialdehyde **6**. **The key step** 4 + 6 → 8 **represents, to our knowledge, the first enantiotopic group differentiation in a *meso* dialdehyde by an aldolization reaction.** In addition, denticulatin B (**1b**) was obtained from the common intermediate **8** *en route* to denticulatin A in 10 steps and 35% overall yield. Finally, by careful fine-tuning the workup and purification conditions, the final steps of the first stereoselective denticulatin B synthesis,[7] could be greatly improved.

EXPERIMENTAL

General Experimental Methods. All reactions were carried out under Ar with magnetic stirring, unless otherwise specified. Solvents were dried by distillation from drying agents as follows: Et_2O (Na), THF (Na), toluene (Na), CH_2Cl_2, DMF and HMPA (CaH_2). Workup denotes extraction with an organic solvent, drying ($MgSO_4$) and evaporation. Column flash chromatography (FC): SiO_2 (*Merck* 9385) or Al_2O_3 neutral (*Fluka* 06300). GC: *Hewlett-Packard 5790A*, integrator *HP 3390*, capillary column (fused silica, 0.2 mm, 12 m, OV-1), 10 psi H_2. Chiral GC: *Hewlett-Packard 5890 Series II*, integrator *HP 3395*, Lipodex E column (0.25 mm, 25 m), 7 psi H_2. M.p.: *Kofler* hot stage, uncorrected. [α]: *Perkin-Elmer 241* polarimeter. NMR: *Bruker AMX* 400; ^{1}H-NMR at 400 MHz in $CDCl_3$, *J* in Hz; ^{13}C-NMR at 100.62 MHz (always combined with DEPT-spectra) in $CDCl_3$ unless otherwise specified, standard TMS (δ = 0 ppm); ^{1}H-200 MHz and ^{13}C-50 MHz spectra (always combined with APT-spectra) are recorded on a *Varian Gemini 200* spectrometer. MS: *m/z* (rel. %). IR *Perkin-*

Elmer 1600 Series FTIR spectrometer (cm^{-1}); solid compounds: KBr-plates, liquid compounds or oils: neat (KBr).

(2*R*, 3*R*, 4*S*)-2,4-Dimethyl-3-triisopropylsilanyloxy-pentanedial (7).

To a stirred solution of dimethallylalcohol (1.5 g, 13.4 mmol) in CH_2Cl_2 (100 ml) was added 2,6-lutidine (4 ml, 34.8 mmol) followed by triisopropylsilyltrifluoromethanesulfonate (4.7 ml, 17.4 mmol). After stirring for 12 h at rt, CH_2Cl_2 (50 ml) was added and the mixture was washed with 2% aq. HCl (2 ×), sat. aq. $NaHCO_3$ (1 ×), brine (1 ×) and dried. After concentration, the residue was purified by FC (EtOAc/hexane 1:4) to furnish 3.27 g (12.2 mmol, 91%) of (1-Isopropenyl-2-methyl-allyloxy)-triisopropyl-silane: IR 2943, 2866, 1464, 1383, 1370. ^{1}H-NMR: 1.03-1.09 (m, 21 H); 1.61 (bs, 6 H); 4.49 (bs, 1 H); 4.86 (m, 2 H); 5.05 (m, 2 H). CI HRMS: 225.1656 ($[C_{13}H_{25}OSi]^+$, calc. 225.1674).

To a stirred -90°C solution of 9-borabicyclo[3.3.1]nonane (9-BBN) (0.5 M in THF, 105 ml, 52.3 mmol) was added dropwise a solution of the silyl ether (4.67 g, 17.4 mmol) in THF (15 ml + 5 ml rince). After stirring for 2 h at -90°C, the mixture was placed in a dry ice\acetone bath (-78°C) and was then allowed to slowly reach rt over 12 h. After cooling the mixture to -40°C, aq. 20% NaOH (35 ml, 174 mmol) was added dropwise followed by a very slow addition (exothermic!) of aq. 30% H_2O_2 (20 ml, 174 mmol) whereby the temperature was kept below -20°C. After stirring for 15 min at -30°C and 2.5 h at rt, the aqueous phase was separated from the organic phase and neutralized with 4% aq. HCl until pH 7 and extracted with Et_2O (4 ×). The combined organic phases were washed with brine, dried and concentrated. Purification of the residue by FC (EtOAc/hexane 1:4 containing 1% MeOH to EtOAc/hexane 1:3 containing 1% MeOH) furnished 4.62 g (15.2 mmol, 87%) of *meso* diol (2*R*, 3*S*, 4*S*)-2,4-Dimethyl-3-triisopropylsilanyloxy-pentane-1,5-diol: IR 3521. ^{1}H-NMR: 1.01 (d, J = 7.0, 6 H); 1.09-1.15 (m, 21 H); 1.96-2.06 (m, 2 H); 2.13 (bs, 2 H(OH)); 3.59 (dd, J = 5.5/11.0, 2 H); 3.66 (dd, J = 7.0/11.0, 2 H); 4.06 (t, J = 4.4, 1 H). ^{13}C-NMR: 78.62, 65.90, 39.34, 18.27, 14.21, 13.06. CI HRMS: 243.1798 ($[C_{16}H_{36}O_3Si]^+$, calc. 243.1780). Anal. calc. for $C_{16}H_{36}O_3Si$: C, 63.10; H, 11.92; found: C, 62.88; H, 11.77.

To a stirred solution of $(COCl)_2$ (3.89 ml, 45.3 mmol) in CH_2Cl_2 (150 ml) was added at -78°C DMSO (3.32 ml, 46.8 mmol). After stirring for 15 min at -78°C, a solution of the *meso* diol (4.6 g, 15.1 mmol) in CH_2Cl_2 (40 ml + 10 ml rince) was added dropwise at -78°C. After stirring for 40 min at -78°C, triethylamine (21 ml, 151 mmol) was slowly added over a 20 min period and stirring was continued for 1 h at -78°C. The reaction was allowed to reach rt and was diluted with toluene (200 ml) after which the precipitated triethylammonium hydrochloride was filtered over a path of celite. After concentration of the mother liquour, the residue was triturated with hexane (100 ml) and a second filtration over celite gave after concentration the crude *meso* dialdehyde **7** which was sufficiently pure for use in the next step without purification. IR 1727. ^{1}H-NMR: 1.05-1.11 (m, 21 H); 1.12 (d, J = 7.0, 6 H); 2.65 (ddq, J = 1.8/5.2/7.0, 2 H); 4.64 (t, J = 5.2, 1 H); 9.80

(d, J = 1.8, 2 H). ^{13}C-NMR (50 MHz): 203.66, 74.31, 51.95, 18.60, 13.27, 10.65. CI HRMS: 257.1552 ($[C_{13}H_{25}O_3Si]^+$, calc. 257.1573).

The same procedure was applied for the synthesis of *meso* dialdehyde **6** which could be distilled by bulb to bulb distillation (b.p. 140°C, 0.1 mmHg).

Desymmetrization of *Meso* Dialdehydes 6 and 7, General Procedure. To a stirred solution of triethylborane in hexane (1 M in hexane, 0.909 ml, 0.909 mmol) was added trifluoromethanesulfonic acid (72 µl, 0.826 mmol) and the mixture was gently heated to 40°C for 5 min and then cooled to -5°C after which a solution of the *N*-propionylsultam **4** or **5** (0.716 mmol) in CH_2Cl_2 (1 ml + 0.5 ml rince) was added followed by diisopropylethylamine (145 µl, 0.849 mmol). The mixture was stirred for 30 min at 0°C and then cooled to -78°C after which a solution of the *meso* dialdehyde **6** or **7** (0.551 mmol) in CH_2Cl_2 (1 ml + 0.5 ml rince) was added dropwise at -78°C. After stirring for 1-1.5 h at -78°C, the mixture was quenched by the addition of aq. phosphate buffer (pH 7, 3 ml), allowed to reach rt, and the aq. phase extracted with CH_2Cl_2 (3 ×). After drying and concentration, the residue was purified by FC (EtOAc/hexane 1:4) to yield the corresponding lactols **8**, **9** or **10**.

(2*S*)-*N*-{(2*S*)-2-[(2*R*,3*S*,4*S*,5*S*)-4-(*tert*-Butyl-dimethyl-silanyloxy)-6-hydroxy-3,5-dimethyl-tetra-hydropyran-2-yl]-propan-1-oyl}bornane-10,2-sultam (8): IR 3460, 1695. ^{1}H-NMR (mixture of anomers): equatorial anomer (6*R*): 0.04 (s, 3 H); 0.06 (s, 3 H); 0.84 (d, J =7.0, 3 H); 0.93 (s, 9 H); 0.97 (s, 3 H); 0.99 (d, J = 7.0, 3 H); 1.15 (s, 3 H); 1.28 (d, J = 7.0, 3 H); 1.25-1.45 (m, 2 H); 1.47-1.74 (m, 2 H); 1.80-1.95 (m, 3 H); 2.03-2.11 (m, 2 H); 2.92 (d, J = 5.5, 1 H(OH)); 3.20 (dq, J = 5.2/7.0, 1 H); 3.43 (d, J = 14.0, 1 H); 3.49 (d, J = 14.0; 1H); 3.74 (dd, J = 1.8/1.8, 1 H); 3.89 (dd, J = 6.3/6.3, 1 H); 4.12 (dd, J = 5.2/9.9, 1 H); 4.81 (dd, J = 5.5, 8.8, 1 H); axial anomer (6*S*): 0.10 (s, 3 H); 0.13 (s, 3 H); 0.90 (d, J = 7.0, 3 H); 0.96 (s, 9 H); 0.97 (s, 3 H); 1.05 (d, J = 7.0, 3 H); 1.16 (s, 3 H); 1.29 (d, J = 7.0, 3 H); 1.25-1.45 (m, 2 H); 1.47-1.74 (m, 2 H); 1.80-1.95 (m, 3 H); 2.03-2.11 (m, 2 H); 3.20 (dq, J = 5.9/7.0, 1 H); 3.43 (d, J = 14.0, 1 H); 3.50 (d, J = 14.0, 1 H); 3.83 (dd, J = 1.8/3.5, 1 H); 3.91 (dd, J = 6.3/6.3, 1 H); 4.33 (dd, J = 5.9/10.3, 1 H); 4.95 (dd, J = 1.8/11.0, 1 H); 5.03 (d, J = 11.0, 1 H(OH)). ^{13}C-NMR (mixture of anomers): 173.82, 173.49, 96.68, 96.63, 77.67, 77.21, 73.23, 66.49, 65.48, 65.37, 53.28, 53.21, 48.35, 47.79, 48.68, 44.12, 42.42, 42.17, 40.79, 40.64, 39.52, 38.50, 32.91, 26.45, 26.35, 26.26, 20.87, 20.84, 19.90, 18.61, 18.36, 16.25, 15.33, 14.91, 13.77, 13.68, 13.32, -3.21, -3.27, -3.41, -3.49. MS (ES): 552 ($[M+Na]^+$, 100).

(2*S*)-*N*-{(2*S*)-2-((2*R*,3*S*,4*S*,5*S*)-6-Hydroxy-3,5-dimethyl-4-triisopropylsilanyloxy-tetrahydropyran-2-yl)-propan-1-oyl}bornane-10,2-sultam (9): IR 3466, 1690. ^{1}H-NMR (mixture of anomers): equatorial anomer (6*R*): 0.92 (d, J = 7.0, 3 H); 0.97 (s, 3 H); 1.06 (d, J = 7.0, 3 H); 1.10-1.18 (m, 24 H); 1.30 (d, J = 7.0, 3 H); 1.25-1.45 (m, 2 H); 1.49-1.75 (m, 2 H); 1.82-1.96 (m, 3 H); 2.03-2.14 (m, 2 H); 2.76 (d, J = 5.9, 1 H(OH)); 3.21 (dq, J = 5.2/7.0, 1 H); 3.44 (d, J = 14.0, 1 H); 3.49 (d, J = 14.0, 1 H); 3.89 (dd, J = 6.3/6.3, 1 H); 4.0 (dd, J = 1.8/1.8, 1 H); 4.16 (dd, J = 5.2/9.9, 1 H); 4.89 (dd, J = 5.9/8.8, 1 H); axial anomer (6*S*): 0.97 (s, 3 H); 0.97 (d,

J = 7.0, 3 H); 1.10-1.18 (m, 27 H); 1.30 (d, *J* = 7.0, 3 H); 1.25-1.45 (m, 2 H); 1.49-1.75 (m, 2 H); 1.82-1.96 (*m*, 3 H); 2.03-2.14 (m, 2 H); 3.22 (dq, *J* = 5.9/7.0, 1 H); 3.43 (d, *J* = 13.6, 1 H); 3.50 (d, *J* = 13.6, 1 H); 3.90 (dd, *J* = 6.3/6.3, 1 H); 4.06 (dd, *J* = 1.8/3.5, 1 H); 4.36 (dd, *J* = 5.9/10.0, 1 H); 4.95 (dd, *J* = 2.5/11.0, 1 H); 5.04 (d, *J* = 11.0, 1 H(OH)). ^{13}C-NMR (50 MHz, mixture of anomers): 174.31, 173.95, 97.11, 96.93, 78.70, 77.81, 73.67, 66.92, 65.85 , 65.74, 53.70, 53.64, 48.76, 48.24, 45.05, 44.77, 43.00, 42.81, 41.64, 41.40, 40.16, 38.91, 33.32, 26.89, 21.33, 21.29, 20.36, 19.03, 18.97, 16.13, 15.25, 14.78, 14.50, 14.40, 14.17, 13.58. CI HRMS: 553.3258 ($[C_{29}H_{51}NO_5SSi]^+$, calc. 553.3257). Anal. calc for $C_{29}H_{53}NO_6SSi$: C, 60.91; H, 9.34; N, 2.45; found: C, 61.24; H, 9.29; N, 2.59.

(3*S*)-*N*-{(2*S*)-2-((2*R*,3*S*,4*S*,5*S*)-6-Hydroxy-3,5-dimethyl-4-triisopropylsilanyloxy-tetrahydropyran-2-yl)-propan-1-oyl}toluene-1,2-sultam (10): ^{1}H-NMR (mixture of anomers): equatorial anomer (6*R*): 0.97 (d, *J* = 7.0, 3 H); 1.07 (d, *J* = 7.0, 3 H); 1.07-1.15 (m, 21 H); 1.39 (d, *J* = 7.0, 3 H); 1.58 (ddq, *J* = 2.0/7.0/10.0, 1 H); 1.63 (d, *J* = 6.6, 3 H); 1.76 (ddq, *J* = 2.0/7.0/8.1, 1 H); 3.47 (dq, *J* = 5.5/7.0, 1 H); 4.01 (dd, *J* = 2.0/2.0, 1 H); 4.45 (dd, *J* = 5.5/10.0, 1 H); 4.89 (d, *J* = 8.1, 1 H); 5.44 (q, *J* = 6.6, 1 H); 7.43 (d, *J* = 7.7, 1 H); 7.58 (dd, *J* = 7.7/7.7, 1 H); 7.70 (dd, *J* = 7.7/7.7, 1 H); 7.79 (d, *J* = 7.7, 1 H); axial anomer (6*S*): 1.03 (d, *J* = 7.0, 3 H); 1.07-1.15 (m, 24 H); 1.38 (d, *J* = 7.0, 3 H); 1.58 (ddq, *J* = 2.0/7.0/10.3, 1 H); 1.65 (d, *J* = 6.6, 3 H); 1.86 (ddq, *J* = 2.0/2.5/7.0, 1 H); 3.48 (dq, *J* = 5.5/7.0, 1 H); 4.09 (dd, *J* = 2.0/2.0, 1 H); 4.48 (dd, *J* = 5.5/10.3, 1 H); 4.97 (dd, *J* = 2.5/11.0, 1 H); 5.10 (d, *J* = 11.0, 1 H(OH)); 5.45 (q, *J* = 6.6, 1 H); 7.43 (d, *J* = 7.7, 1 H); 7.58 (dd, *J* = 7.7/7.7, 1 H); 7.70 (dd, *J* = 7.7/7.7, 1 H); 7.79 (d, *J* = 7.7, 1 H).

(2*S*)-*N*-{(2*S*,3*R*,4*S*,5*S*,6*S*)-6-[1,3]Dithiolan-2-yl-3,5-dihydroxy-2,4-dimethyl-heptan-1-oyl}bornane-10,2-sultam (13). To a stirred solution of the lactol **8** (1.270 g, 2.40 mmol) and zinc(II) iodide (919 mg, 2.88 mmol) in CH_2Cl_2 (30 ml) was added ethanedithiol (9 ml). After stirring for 3 h at rt, the mixture was diluted with Et_2O (150 ml) and washed with 1 N aq. NaOH (2 ×). The aqueous phase was back extracted with Et_2O (1 ×) and the combined organic phases were dried and concentrated. The residue was recrystallized (CH_2Cl_2/hexane) to give 971 mg of the pure diol **13** as white crystals. Recrystallization of the mother liquour gave a second crop of crystals (110 mg). The combined yield was 92% (1.08 g, 2.20 mmol): M.p. 189°-190°C (CH_2Cl_2/hexane). $[\alpha]_D$ = +71.7 (c = 0.6, $CHCl_3$). IR 3414, 1670. ^{1}H-NMR: 0.88 (d, *J* = 7.0, 3 H); 0.98 (s, 3 H); 1.15 (s, 3 H); 1.19 (d, *J* = 7.0, 3 H); 1.27 (d, *J* = 7.0, 3 H); 1.31-1.46 (m, 2 H); 1.82-2.00 (m, 4 H); 2.30 (ddq, J= 4.1/6.6/7.0, 1 H); 3.09-3.25 (m, 4 H); 3.28 (dq, *J* = 1.0/7.0, 1 H); 3.45 (d, *J* = 14.0, 1 H); 3.50 (dd, *J* = 4.8/6.6, 1 H); 3.53 (d, *J* = 14.0, 1 H); 3.89 (dd, *J* = 6.3/6.3, 1 H); 3.96 (dd, *J* = 1.0/9.2, 1 H); 4.94 (d, *J* = 4.1, 1 H). ^{13}C-NMR (50 MHz): 177.66, 80.26, 75.22, 64.88, 55.03, 53.02, 48.45, 47.79, 44.58, 41.56, 40.77, 38.75, 38.21, 37.57, 32.84, 26.40, 20.81, 19.84, 14.44, 14.33, 10.78. MS (ES): 514 ($[M+Na]^+$, 100). Anal. calc. for $C_{22}H_{37}NO_5S_3$: C, 53.53; H, 7.58; N, 2.90; found: C, 53.74; H, 7.58; N, 2.85.

(2*S*)-*N*-{(2*S*)-2-[(4*R*,5*S*,6*S*)-2,2-Di-*tert*-butyl-6-((1*S*)-1-[1,3]dithiolan-2-yl-ethyl)-5-methyl-[1,3,2]dioxasilinan-4-yl]-propan-1-oyl}bornane-10,2-sultam (14). To a stirred solution of the diol **13** (962 mg, 1.96 mmol) in CH_2Cl_2 (33 ml) was added 2,6-lutidine (0.502 ml, 4.312 mmol) followed by di-*tert*.butyl ditriflate (0.786 ml, 2.155 mmol). After stirring for 12 h at rt, the reaction mixture was diluted with Et_2O (100 ml) and washed with 1 N aq. HCl (1 ×). The aq. phase was extracted with Et_2O (2 ×), dried and concentrated. The residue was purified by FC (EtOAc\hexane 1:5) to give 1.236 g (1.96 mmol, 100%) of the silylated product **14** which was recrystallized from hexane (92%): M.p. 167°-168°C (hexane). $[\alpha]_D$ = +66.6 (c = 0.59, $CHCl_3$). IR 1690. ^{1}H-NMR: 0.77 (d, *J* = 6.6, 3 H); 0.97 (s, 3 H); 1.03 (s, 9 H); 1.04 (s, 9 H); 1.15 (s, 3 H); 1.23 (d, *J* = 6.6, 3 H); 1.30 (d, *J* = 7.0, 3 H); 1.28-1.46 (m, 2 H); 1.84-1.97 (m, 4 H); 2.06-2.11 (m, 2 H); 2.28 (dddd, *J* = 1.8/6.6/6.6/9.6, 1 H); 3.07-3.20 (m, 4 H); 3.24 (dq, *J* = 5.5/7.0, 1 H); 3.45 (d, *J* = 14.0, 1 H); 3.51 (d, *J* = 14.0, 1 H); 3.81 (dd, *J* = 1.8/9.9, 1 H); 3.86 (dd, *J* = 6.3/6.3, 1 H); 4.31 (dd, *J* = 5.5/9.6, 1 H); 4.78 (d, *J* = 4.4, 1 H). ^{13}C-NMR: 173.83, 82.74, 78.05, 65.46, 53.61, 53.19, 48.40, 47.80, 44.80, 44.56, 41.28, 40.60, 38.91, 38.48, 38.15, 32.81, 27.91, 27.24, 26.45, 23.08, 20.78, 20.09, 19.89, 15.73, 13.85, 13.11. CI HRMS: 631.2816 ($[C_{30}H_{53}NO_5S_3Si]^+$, calc. 631.2855). Anal. calc. for $C_{30}H_{53}NO_5S_3Si$: C, 57.01; H, 8.45; N, 2.22; found: C, 57.01; H, 8.35; N, 2.38.

(2*R*)-2-[(4*S*,5*S*,6*S*)-2,2-Di-*tert*-butyl-6-((1*S*)-1-[1,3]dithiolan-2-yl-ethyl)-5-methyl-[1,3,2]dioxasilinan-4-yl]-propan-1-ol (15). To a stirred solution of the sultam **14** (959 mg, 1.52 mmol) in THF (40 ml) was added at -78°C lithium triethylborohydride (1 M in THF, 6 ml, 6 mmol). The mixture was stirred for 2 h at -78°C and was allowed to come to -40°C over 2 h after which 2 N aq. NaOH (50 ml) was added. The cooling bath was removed and when the mixture reached rt the phases were separated and the aq. phase was extracted with Et_2O (3 ×). The combined organic phases were washed with sat. aq. NH_4Cl (1 ×), dried and concentrated. The residue was purified by FC (EtOAc\hexane 1:6 containing 0.1% *n*-propanol) to give 600 mg (1.43 mmol, 94%) of the alcohol **15** and 294 mg (1.37 mmol, 90%) of the recovered (2*S*)-bornane-10,2-sultam: $[\alpha]_D$ = +17.2 (c = 0.808, $CHCl_3$). IR: 3419, 2965, 2937, 2857, 1473. ^{1}H-NMR: 0.78 (d, *J* = 7.0, 3 H); 1.02 (d, *J* = 7.0, 3 H); 1.04 (s, 9 H); 1.05 (s, 9 H); 1.25 (d, *J* = 7.0, 3 H); 1.88 (dddq, *J* = 2.2/2.9/5.5/7.0, 1 H); 2.04 (ddq, *J* = 7.0/9.6/10.0, 1 H); 2.28 (ddq, *J* = 1.8/5.1/7.0, 1 H); 2.64 (dd, *J* = 2.6/8.5, 1 H(OH)); 3.09-3.25 (m, 4 H); 3.71 (ddd, *J* = 5.5/8.5/10.7, 1 H); 3.79 (dd, *J* = 1.8/10.0, 1 H); 3.83 (ddd, *J* = 2.6/2.9/10.7, 1 H); 4.05 (dd, *J* = 2.2/9.6, 1 H); 4.80 (d, *J* = 5.1, 1 H). ^{13}C-NMR: 83.59, 83.32, 68.06, 53.67, 40.98, 38.77, 38.71, 38.33, 36.57, 27.96, 27.19, 23.19, 20.29, 16.17, 12.35, 8.78. CI HRMS: 363.1487 ($[C_{16}H_{31}O_3S_2Si]^+$, calc. 363.1484). Anal. calc. for $C_{20}H_{40}O_3S_2Si$: C, 57.09; H, 9.58; S, 15.24; found: C, 57.44; H, 9.36; S, 14.95.

(2*S*)-2-[(4*R*,5*S*,6*S*)-2,2-Di-*tert*-butyl-6-((1*S*)-1-[1,3]dithiolan-2-yl-ethyl)-5-methyl-[1,3,2]dioxasilinan-4-yl]-propionaldehyde (16). To a stirred solution of $(COCl)_2$ (215 µl, 2.5 mmol) in CH_2Cl_2 (28 ml) was added at -78°C DMSO (237 µl, 3.34 mmol). After stirring for 10 min at -78°C, a solution of the alcohol **15** (600 mg, 1.43

mmol) in CH_2Cl_2 (8 ml + 4 ml rince) was added dropwise over a 10 min period. After stirring for 45 min at -78°C, triethylamine (1.16 ml, 8.35 mmol) was added over a 10 min period. Stirring was continued for 1 h during which time the mixture was allowed to reach 0°C. Et_2O (150 ml) was added and the mixture was washed with 1 N aq. HCl (3 ×), brine (1 ×), dried and concentrated to give 588 mg (1.41 mmol, 98%) of the crude aldehyde **16** which was sufficiently pure for use in the next step without purification: IR 1732. ^{1}H-NMR: 0.83 (d, *J* = 7.0, 3 H); 1.02 (s, 18 H); 1.17 (d, *J* = 7.0, 3 H); 1.27 (d, *J* = 7.0, 3 H); 2.08 (ddq, *J* = 7.0/9.9/9.9, 1 H); 2.29 (ddq, *J* = 1.8/5.5/7.0, 1 H); 2.52 (dq, *J* = 2.2/7.0, 1 H); 3.10-3.26 (m, 4 H); 3.87 (dd, *J* = 1.8/9.9, 1 H); 4.43 (dd, *J* = 2.2/9.9, 1 H); 4.80 (d, *J* = 5.5, 1 H); 9.75 (s, 1 H). ^{13}C-NMR (50 MHz): 205.05, 83.57, 79.64, 54.14, 49.89, 41.65, 39.16, 38.86, 38.70, 28.38, 27.59, 23.67, 20.71, 16.86, 13.00, 6.58.

(2*S*)-2-[(4*R*,5*S*,6*S*)-2,2-Di-*tert*-butyl-6-((1*S*)-1-[1,3]dithiolan-2-yl-ethyl)-5-methyl-[1,3,2]dioxasilinan-4-yl]-pentan-3-one (17). To a stirred solution of the aldehyde **16** (588 mg, 1.41 mmol) in Et_2O (25 ml) was added at -78°C ethylmagnesium bromide (3 M in Et_2O, 0.94 ml, 2.82 mmol). After stirring for 2.5 h at -78°C, the mixture was allowed to reach rt and 2% aq. HCl (30 ml) was slowly added. The aq. phase was extracted with Et_2O (3 ×) and the combined organic phases were washed with brine, dried and concentrated to give 632 mg (1.41 mmol, 100%) of a 6.8:1 mixture of epimeric alcohols (^{1}H NMR) which was sufficiently pure for use in the next step without purification.

To a stirred solution of $(COCl)_2$ (181 µl, 2.12 mmol) in CH_2Cl_2 (28 ml) was added at -78°C DMSO (200 µl, 2.82 mmol). After stirring for 10 min at -78°C, a solution of epimeric alcohols (632 mg, 1.41 mmol) in CH_2Cl_2 (8 ml + 4 ml rince) was added dropwise over a 10 min period. After stirring for 1.5 h at -78°C, triethylamine (981 µl, 7.05 mmol) was added dropwise over a 10 min period. Stirring was continued for 1 h during which time the mixture was allowed to reach 0°C. Et_2O (150 ml) was added and the mixture was washed with 2% aq. HCl (2 ×), brine (1 ×), dried and concentrated. The residue was purified by FC (EtOAc\hexane 1:6) to give 562 mg (1.26 mmol, 89%) of the ethylketone **17**.

(2*S*)-2-[(4*R*,5*S*,6*S*)-2,2-Di-*tert*-butyl-6-((1*S*)-1-[1,3]dithiolan-2-yl-ethyl)-5-methyl-[1,3,2]dioxasilinan-4-yl]-thiopropionic acid S-benzyl ester (18). To a stirred solution of benzyl mercaptan (51 µl, 0.476 mmol) in Et_2O (2 ml) was added at 0°C *n*-butyl lithium (2.7 M in heptane, 0.176 ml, 0.476 mmol). After stirring for 5 min at 0°C, trimethylaluminum (2 M in toluene, 0.238 ml, 0.476 mmol) was added dropwise and stirring was continued for 20 min after which a pre-cooled solution (0°C) of sultam **14** (200 mg, 0.317 mmol) in toluene (2 ml + 2 ml rince) was added *via* cannula. After stirring for 12 h at 0°C, 2% aq. HCl (6 ml) was added and the aq. phase was extracted with Et_2O (3 ×). The combined organic layers were washed with brine (3 ×), dried and concentrated. The residue was purified by FC (CH_2Cl_2\hexane 1:4 to 1:2) to give 160 mg (0.296 mmol, 93%) of thioester **18**: $[\alpha]_D$ = -15.7 (c = 1.15, $CHCl_3$). IR 1698. ^{1}H-NMR: 0.80 (d, *J* = 7.0, 3 H), 0.96 (s, 9 H), 1.02

(s, 9 H), 1.24 (d, *J* = 7.0, 3 H), 1.25 (d, *J* = 6.6, 3 H), 2.00 (ddq, *J* = 7.0/9.6/9.6, 1 H), 2.27 (ddq, *J* = 1.8/5.2/6.6, 1 H), 2.87 (dq, *J* = 2.6/7.0, 1 H), 3.06-3.25 (m, 4 H), 3.81 (dd, *J* = 1.8/9.6, 1 H), 4.14 (s, 2 H), 4.36 (dd, *J* = 2.6/9.6, 1 H), 4.77 (d, *J* = 5.2, 1 H), 7.18-7.31 (m, 5 H). ^{13}C-NMR: 200.88, 137.89, 128.82, 128.49, 127.04, 83.05, 80.73, 53.68, 51.31, 41.14, 38.72, 38.61, 38.31, 32.89, 27.77, 27.14, 23.20, 20.18, 16.41, 12.50, 8.39. CI HRMS: 483.1513 ($[C_{23}H_{35}O_3S_3Si]^+$, calc. for 483.1518). Anal. calc. for $C_{27}H_{44}O_3S_3Si$: C, 59.95; H, 8.20; found: C, 60.14; H, 8.25.

(2*S*)-2-[(4*R*,5*S*,6*S*)-2,2-Di-*tert*-butyl-6-((1*S*)-1-[1,3]dithiolan-2-yl-ethyl)-5-methyl-[1,3,2]dioxasilinan-4-yl]-pentan-3-one (17). To a stirred solution of thioester **18** (79 mg, 0.146 mmol) in THF (2.5 ml) containing $Fe(acac)_3$ (5 mg) was added at -30°C ethylmagnesium bromide (1 M in THF, 0.190 ml, 0.190 mmol). After stirring for 50 min between -30 and -20°C, another 0.7 eq. of ethylmagnesium bromide (1 M in THF, 0.1 ml, 0.1 mmol) was added and stirring was continued for 1 h. The mixture was quenched by the slow addition of 2% aq. HCl (4 ml) after which the aq. phase was extracted with hexane (3 ×). The combined organic phases were washed with brine (2 ×), dried and concentrated to give a residue which was purified by FC (CH_2Cl_2\hexane 1:2 to 2:1) to give 55 mg (0.124 mmol, 85%) of pure ethyl ketone **17**: $[\alpha]_D$ = +4.9 (c = 0.61, $CHCl_3$). IR 1716. ^{1}H-NMR: 0.82 (d, *J* = 7.0, 3 H); 0.98 (s, 9 H); 1.02 (s, 9 H); 1.06 (dd, *J* = 7.3/7.3, 3 H); 1.16 (d, *J* = 7.0, 3 H); 1.26 (d, *J* = 7.0, 3 H); 2.02 (ddq, *J* = 7.0/9.6/9.6, 1 H); 2.28 (ddq, *J* = 1.8/7.0/7.0, 1 H); 2.53 (dq, *J* = 7.3/18.0, 1 H); 2.58 (dq, *J* = 7.3/18.0, 1 H); 2.62 (dq, *J* = 2.6/7.0, 1 H); 3.09-3.26 (m, 4 H); 3.82 (dd, *J* = 1.8/9.6, 1 H); 4.29 (dd, *J* = 2.6/9.6, 1 H); 4.79 (d, *J* = 5.2, 1 H). ^{13}C-NMR: 213.07, 83.08, 80.94, 53.68, 49.69, 41.13, 38.70, 38.64, 38.34, 33.37, 27.19, 27.10, 23.18, 20.21, 16.34, 12.52, 7.97, 7.73. CI HRMS: 389.1610 ($[C_{18}H_{33}O_3S_2Si]^+$, calc. 389.1640).

(2*S*)-2-[(4*S*,5*R*,6*R*)-2,2-Di-*tert*-butyl-5-methyl-6-((1*S*)-1-methyl-2-oxo-butyl)-[1,3,2]dioxasilinan-4-yl]-propionaldehyde (19). To a stirred solution of dithiolane **17** (87 mg, 0.195 mmol) in a mixture of THF (2.7 ml) and phosphate buffer pH 7.4 (0.55 ml) was added at rt dropwise freshly prepared aq. mercury(II) perchlorate[36] (4 M in H_2O, 98 µl, 0.39 mmol). After stirring for 15 min at rt, the mixture was diluted with Et_2O (30 ml) after which the cloudy mixture was filtered over celite, washed with phosphate buffer pH 7.0 (2 ×), dried and concentrated. The residue was purified by FC to give 59.3 mg (0.1603 mmol, 82%) of the aldehyde **19**: $[\alpha]_D$ = -10.9 (c = 0.92, $CHCl_3$). IR 1721. ^{1}H-NMR: 0.84 (d, *J* = 7.0, 3 H); 0.95 (s, 9 H); 0.99 (s, 9 H); 1.05 (dd, *J* = 7.0/7.0, 3 H); 1.15 (d, *J* = 7.0, 3 H); 1.30 (d, *J* = 7.0, 3 H); 1.93 (ddq, *J* = 7.0/9.9/10.3, 1 H); 2.51 (dq, *J* = 7.0/18.0, 1 H); 2.58 (dq, *J* = 7.0/18.0, 1 H); 2.62 (dq, *J* = 2.9/7.0, 1 H); 2.62 (ddq, *J* = 2.2/2.9/7.0, 1 H); 3.98 (dd, *J* = 2.2/10.3, 1 H); 4.32 (dd, *J* = 2.9/9.9, 1 H); 9.81 (d, *J* = 2.9, 1 H). ^{13}C-NMR: 212.94, 205.09, 81.92, 80.29, 49.54, 49.04, 38.66, 33.48, 27.59, 27.10, 23.10, 20.18, 12.26, 11.85, 7.88, 7.69. CI HRMS: 313.1831 ($[C_{16}H_{29}O_4Si]^+$, calc. 313.1835).

(3*S*)-*N*-{*E*-(2*R*)-2,4-Dimethyl-hept-4-en-1-oyl}toluene-1,2-sultam (22). To a stirred solution of (3*S*)-*N*-propionyltoluene-1,2-sultam **5** (2.88 g, 12.07 mmol) in THF (35 ml) was added at -78°C sodium hexamethyldisilazide (1 M in THF, 14 ml, 14 mmol) over a 5 min period. After stirring for 1 h at -78°C, the allyl bromide **21** (2 g, 12.27 mmol) was added *via* syringe followed by HMPA (4.52 ml, 26 mmol). After stirring for 16 h at -65°C, the reaction mixture was poured into aqueous saturated NH_4Cl followed by extraction with Et_2O (3 ×). The combined organic phases were washed with aq. sat. NH_4Cl, dried and concentrated. The residue was purified by FC (EtOAc\hexane 1:5) to yield 2.76 g (8.59 mmol, 71%) of the alkylated sultam **22** as a colorless oil: GC: 98%, 9.7 min (140°, 2 min, 10°\min, 270°, OV). $[\alpha]_D$ = -19.7 (c = 1.17, $CHCl_3$). IR 2964, 1698, 1455. ^{1}H-NMR: 0.92 (dd, *J* = 7.4/7.4, 3 H); 1.24 (d, *J* = 6.6, 3 H); 1.59 (d, *J* = 6.3, 3 H); 1.70 (d, *J* = 0.7, 3 H); 1.95 (ddq, *J* = 7.0/7.4/14.4, 1 H); 2.01 (ddq, *J* = 7.0/7.4/14.4, 1 H); 2.11 (dd, *J* = 6.6/13.2, 1 H); 2.60 (dd, *J* = 7.7/13.2, 1 H); 3.46 (ddq, *J* = 6.6/6.6/7.7, 1 H); 5.24 (ddq, *J* = 0.7/7.0/7.0, 1 H); 5.46 (q, *J* = 6.3, 1 H); 7.43 (dd, *J* = 1.1/7.7, 1 H); 7.58 (dd, *J* = 7.7/7.7, 1 H); 7.70 (ddd, *J* = 1.1/7.7/7.7, 1 H); 7.80 (d, *J* = 7.7, 1 H). ^{13}C-NMR (50 MHz): 175.40, 137.66, 134.54, 134.17, 131.69, 130.07, 129.99, 124.74, 122.15, 55.83, 45.38, 39.83, 21.82, 21.72, 17.50, 16.20, 14.70. CI HRMS: 321.1374 ($[C_{17}H_{23}NO_3S]^{+\cdot}$, calc. 321.1399). Anal. calc. for $C_{17}H_{23}NO_3S$: C, 63.52; H, 7.21; N, 4.36; found: C, 63.76; H, 7.12; N, 4.40.

(2*S*)-*N*-{*E*-(2*R*)-2,4-Dimethyl-hept-4-en-1-oyl}bornane-10,2-sultam (23). The same procedure as described for the synthesis of toluenesultam **22** was employed using the following quantities: (2*S*)-*N*-propionylbornane-10,2-sultam (**4**) (3.48 g, 12.83 mmol) in THF (35 ml), NaHMDS (1 M in THF, 13.2 ml, 13.2 mmol), pre-cooled (-78°C) allyl bromide **21** (1.9 g, 11.66 mmol) in THF (5 ml)-HMPA (4.52 ml, 26 mmol). Workup gave crude crystalline sultam **23** (4.14 g, 11.7 mmol, 100%) which was >98.3% diastereomerically pure as judged by GC-analysis (OV_1; 140°C (2 min), 10°C/min increase, 270°C). The crude mixture was recrystallized from methanol to give after 3 recrystallizations 2.85 g (8.07 mmol, 69%) of the white crystalline product (100% pure; GC: OV_1): M.p. 110.5-112°C (MeOH). $[\alpha]_D$ = +56.3 (c = 1.23, $CHCl_3$). IR 1682. ^{1}H-NMR (200 MHz): 0.91 (t, *J* = 7.5, 3 H), 0.96 (s, 3 H), 1.12 (d, *J* = 6.6, 3 H), 1.13 (s, 3 H), 1.31-1.47 (m, 2 H), 1.63 (bs, 3 H), 1.80-2.13 (m, 8 H), 2.45 (dd, *J* = 8.3/12.6, 1 H), 3.30 (ddq, *J* = 6.6/6.6/8.3, 1 H), 3.40 (d, *J* = 13.7, 1 H), 3.50 (d, *J* = 13.7, 1 H), 3.88 (dd, *J* = 5.6/6.9, 1 H), 5.15 (bt, *J* = 7.0, 1 H). ^{13}C-NMR (50 MHz): 176.19, 131.39, 129.38, 65.27, 53.22, 48.15, 47.67, 45.62, 44.73, 38.49, 38.23, 32.85, 26.49, 21.17, 20.71, 19.86, 16.58, 15.40, 14.08. CI HRMS: 353.2027 ($[C_{19}H_{31}NO_3S]^{+\cdot}$, calc. 353.2025). Anal. calc. for $C_{19}H_{31}NO_3S$: C, 64.55; H, 8.84; N, 3.96; found: C, 64.37; H, 8.79; N, 4.03.

(*E*)-(4*R*)-2-Benzenesulfonyl-4,6-dimethyl-non-6-en-3-one (24). To a -78°C solution of ethyl phenyl sulfone (1.38 g, 8.1 mmol) in THF (20 ml) was added dropwise *n*-butyllithium (1.6 M in hexane, 10.13 ml, 16.2 mmol) followed by TMEDA (2.43 ml, 16.20 mmol). After stirring for 1 h at 0°C, the mixture was cooled to -78°C and a solution of the sultam **22** (2 g, 6.23 mmol) in THF (10 ml + 5 ml rince) was added dropwise. The mixture

was stirred 1.5 h at -78°C, 1 h at -60°C, 2 h at -50°C and 0.5 h at -35°C. The mixture was poured into 2% aq. HCl and an extraction was performed with Et_2O (3 ×). The combined organic phases were washed with brine (2 ×), dried and concentrated. The residue was purified by FC (EtOAc\hexane 1:4) to give 1.5 g (4.86 mmol, 78%) of a 1.7:1 mixture of epimeric sulfones **24** (^{1}H-NMR). The sultam was recovered (5.51 mmol, 88%) by rincing the column with 50% ethylacetate in hexane: ^{1}H-NMR (the underlined chemical shifts are for the minor isomer as far as they differ from the major isomer): 0.91 (t, *J* = 7.3, 3 H); 0.96 (t, *J* = 7.3, 3 H); 1.05 (d, *J* = 7.0, 3 H); 1.08 (d, *J* = 7.0, 3 H); 1.29 (d, *J* = 7.0, 3 H); 1.39 (d, *J* = 7.0, 3 H); 1.57 (s, 3 H); 1.67 (s, 3 H); 1.90-2.61 (m, 3 H); 2.21 (dd, *J* = 7.3/13.6, 1 H); 2.43 (dd, *J* = 7.3/13.6, 1 H); 3.11 (m, 1 H); 3.28 (m, 1 H); 4.26 (q, *J* = 7.0, 1 H); 4.36 (q, *J* = 7.0, 1 H); 5.11 (bt, *J* = 7.0, 1 H); 5.20 (bt, *J* = 7.0, 1 H); 7.50-7.64 (m, 2 H); 7.64-7.72 (m, 1 H); 7.72-7.83 (m, 2 H).

(*E*)-(2*R*)-2,4-Dimethyl-hept-4-enethioic acid S-benzyl ester (25). The same procedure as described for the synthesis of toluenesultam **22** was employed using the following quantities: benzyl mercaptan (49 µl, 0.412 mmol) in Et_2O (1.8 ml), *n*-butyllithium (1.6 M in hexane, 0.258 ml, 412 mmol), trimethylaluminum (2 M in hexane, 0.206 ml, 0.412 mmol), sultam **23** (97 mg, 0.275 mmol) in toluene (3.6 ml). Workup (extraction with CH_2Cl_2, washing with 2N aq. NaOH and sat. aq. NH_4Cl) and purification by FC (CH_2Cl_2\hexane 1:2) furnished 64 mg (0.244 mmol, 89%) of the pure thioester **25** as a clear oil. The bornane-10,2-sultam could be recuperated by rincing the column with EtOAc\hexane 1:1, giving 41 mg (0.193 mmol,70%) of recuperated bornane-10,2-sultam: $[\alpha]_D$ = -18.3 (c = 1.07, $CHCl_3$). IR 1688. ^{1}H-NMR: 0.93 (t, *J* = 7.3, 3 H), 1.14 (d, *J* = 7.0, 3 H), 1.59 (bs, 3 H), 1.98 (dq, *J* = 7.0/7.3, 2 H), 2.05 (dd, *J* = 8.1/13.6, 1 H), 2.44 (dd, *J* = 7.0/13.6, 1 H), 2.82 (ddq, *J* = 7.0/7.0/8.1, 1 H), 4.09 (d, *J* = 13.6, 1 H), 4.14 (d, *J* = 13.6, 1 H), 5.18 (bt, *J* = 7.0, 1 H), 7.22-7.33 (m, 5 H). ^{13}C-NMR: 202.69, 137.81, 130.83, 129.67, 128.78, 128.55, 127.11, 46.71, 44.13, 32.96, 21.19, 17.00, 15.60, 14.12. CI HRMS: 180.0608 ($[C_{10}H_{12}OS]^+$, calc. 180.0609), 171.0848 ($[C_9H_{15}OS]^+$, calc. 171.0844). Anal. cal. for $C_{16}H_{22}OS$: C, 73.24; H, 8.45; found: C, 73.40; H, 8.24.

(*E*)-(4*R*)-4,6-Dimethyl-non-6-en-3-one (2).

From phenylsulfone 24: *Method A.* To a stirred solution of the sulfone **24** (137 mg, 0.445 mmol) in THF-H_2O (10:1, 10 ml) was added Al(Hg) (Al-foil dipped in 2% aq. $HgCl_2$ for 30 sec, washed with EtOH and Et_2O) (680 mg). The mixture was refluxed for 20 h after which the slurry was filtered over celite and dried. After concentration, the residue was purified by FC (EtOAc\hexane 1:7) to give 54 mg (0.319 mmol, 72%) of the ketone **2** (95% ee). *Method B.* To a stirred solution of the sulfone **24** (1.4 g, 4.55 mmol) in THF (45 ml) was added at -78°C samarium iodide (0.1 M in THF, 140 ml, 14 mmol) *via* syringe pump over a 30 min period until a fainth blue color persisted. After stirring for 10 min at -78°C, pentane (200 ml) and Et_2O (100 ml) were added and the solution was washed with aq. sat. sodium thiosulphate (1% in HCl), aq. sat. sodium thiosulphate (1 ×), pH 7.0 phosphate buffer (2 ×), dried and concentrated. The residue was purified by FC (ether\hexane

1:20 to 1:10) to give 683 mg (4.07 mmol, 89%) of the ketone **2** (95% ee). Chiral GC (*lipodex E*, 70°C): ee = 95% (*R*-enantiomer (10.9 min): 87.9%, *S*-enantiomer (11.4 min): 2.0%; a racemic sample gave: *R*-enantiomer: 45.1%, *S*-enantiomer: 44.6%).

From thioester 25: To a stirred solution of the thioester **25** (55 mg, 0.21 mmol) in THF (3.5 ml) was added $Fe(acac)_3$ (7 mg), followed by the dropwise addition of ethylmagnesium bromide (1 M in THF, 0.252 ml, 0.252 mmol) at -35°C. After stirring for 1 h at -35°C, another 0.48 eq. of ethylmagnesium bromide (1 M in THF, 0.1 ml, 0.1 mmol) was added and stirring was continued for another 2 h. To the mixture was added dropwise 2% aq. HCl and the aq. layer was extracted with Et_2O (2 ×). The combined organic layers were washed with sat. aq. $NaHCO_3$ (2 ×), 2% aq. HCl (1 ×), sat. aq. NH_4Cl (1 ×), dried and concentrated. The residue was dissolved in hexane and washed with 2 N aq. NaOH (2 ×), 2% aq. HCl (1 ×), brine (1 ×), dried and concentrated to give the crude ketone **2** which was purified by FC (EtOAc\hexane 1:7) to give 35 mg (0.208 mmol, 99%) of the pure ethyl ketone **2**. Chiral GC (*Lipodex E*, 70°C): ee = 100% (*R*-enantiomer: 11.3 min; *S*-enantiomer: 12.0 min for a racemic sample and co-injection). $[\alpha]_D$ = -29.9 (c = 2.22, $CHCl_3$). IR 1710. ^{1}H-NMR: 0.92 (t, *J* = 7.3, 3 H); 1.01 (d, *J* = 7.0, 3 H); 1.03 (t, *J* = 7.3, 3 H); 1.58 (bs, 3 H); 1.93 (dd, *J* = 7.7/13.6, 1 H); 1.97 (dq, *J* = 7.0/7.3, 2 H); 2.30 (dd, *J* = 7.0/13.6, 1 H); 2.38-2.50 (m, 2 H); 2.70 (dq, *J* = 7.0/14.0, 1 H); 5.12 (bt, *J* = 7.0, 1 H). ^{13}C-NMR (50 MHz): 215.26, 131.45, 129.12, 44.28, 43.37, 34.45, 21.21, 16.14, 15.67, 14.25, 7.68. CI HRMS: 168.1513 ($[C_{11}H_{20}O]^+$, calc. 168.1514). Anal. calc. for $C_{11}H_{20}O$: C, 78.51; H, 11.98; found: C, 78.29; H, 11.74.

(*E*)-(2*R*)-2,4-Dimethyl-hept-4-en-1-ol (26). To a stirred solution of the sultam **23** (2.1 g, 5.95 mmol) in THF (85 ml), was added at -78°C lithium triethylborohydride (1 M in THF, 14.88 ml, 14.88 mmol) dropwise *via* syringe. After stirring for 30 min at -78°C, the mixture was allowed to reach rt over a period of 30 min. After 15 min stirring at rt, 2% aq. HCl (100 ml) was slowly added and after separation of the layers, the aq. layer was extracted with Et_2O (3 ×). The combined organic layers were washed with 2 N aq. NaOH (2 ×), brine (1 ×), dried and concentrated to give an oil which was purified by FC (EtOAc\hexane 1:5) to furnish 788 mg (5.55 mmol, 93%) of the alcohol **26** as a clear colorless oil which was 100% pure as judged by GC. The sultam could be recuperated by rincing the column with EtOAc/hexane 1:1 giving 1.18 g (5.49 mmol, 92%) of the (S)-bornane-10,2-sultam. $[\alpha]_D$ = +5.7 (c = 1.93, $CHCl_3$); lit.[7] $[\alpha]_D$ = +5.1 (*c* = 2, $CHCl_3$) for a sample of 80% ee. IR 3339. ^{1}H-NMR (200 MHz): 0.87 (d, *J* = 6.4, 3 H), 0.94 (t, *J* = 7.5, 3 H), 1.60 (bs, 3 H), 1.67 (s, 1 H(OH)), 1.73-1.90 (m, 2 H), 1.90-2.15 (m, 3 H), 3.41 (dd, *J* = 5.7/10.4, 1 H), 3.50 (dd, *J* = 5.7/10.4, 1 H), 5.17 (bt, *J* = 7.0, 1 H). ^{13}C-NMR (50 MHz): 132.99, 128.30, 68.50, 44.26, 33.59, 21.14, 16.65, 15.70, 14.27. Anal. calc. for $C_9H_{18}O$: C, 76.00; H, 12.76; found: C, 75.10; H, 12.42.

(*E*)-(2*R*)-2,4-Dimethyl-hept-4-enal (3). To a stirred solution of the alcohol **26** (235 mg, 1.655 mmol) in CH_2Cl_2 (11 ml) was added portionwise PCC (624 mg, 2.9 mmol). After stirring for 1 h at rt, the mixture was diluted with Et_2O (20 ml) and the black gum triturated until it became a granular solid. Filtration of the mixture through florisil (which had been previously wet with Et_2O), eluting with Et_2O followed by concentration gave the crude aldehyde as an oil. Purification by FC (CH_2Cl_2) gave 185 mg (1.324 mmol, 88%) of the pure aldehyde **3** as an oil. This compound decomposed on storage and was best used immediatly in the subsequent step: $[\alpha]_D$ = -13.6 (c = 1.26, $CHCl_3$); lit.[7] $[\alpha]_D$ = -9.6 (*c* = 1.4, $CHCl_3$) for a sample of 80% ee. IR 1729. ^{1}H-NMR: 0.94 (t, *J* = 7.3, 3 H), 1.04 (d, *J* = 7.0, 3 H), 1.60 (s, 3 H), 1.97 (dd, *J* = 8.1/13.6, 1 H), 2.00 (dq, *J* = 7.3/7.3, 2 H), 2.41 (dd, *J* = 6.2/13.6, 1 H), 2.51 (dddq, *J* = 2.2/6.2/7.0/8.1, 1 H), 5.19 (bt, *J* = 7.3, 1 H), 9.62 (d, *J* = 2.2, 1 H). ^{13}C-NMR: 205, 130.63, 129.56, 44.37, 40.80, 21.20, 15.68, 14.18, 13.10. CI HRMS: 140.1191 ($[C_9H_{16}O]^{+\cdot}$, calc. 140.1201). Anal. calc. for $C_9H_{16}O$: C, 77.09; H, 11.50; found: C, 76.87; H, 11.39. A sample was transformed into ethyl ketone **2** *via* addition of EtMgBr followed by oxidation with PCC. The enantiomeric excess of **2** was determined by chiral phase GC (*lipodex E*, 70°C) (>99.9% ee).

***E*-(2*R*,3*S*,4*S*,6*R*)-2-[(4*R*,5*R*,6*R*)-2,2-Di-*tert*-butyl-5-methyl-6-((1*S*)-1-methyl-2-oxo-butyl)-[1,3,2]dioxasilinan-4-yl]-3-hydroxy-4,6,8-trimethyl-undec-8-en-5-one (28) and *E*-(2*R*,3*S*,4*R*,6*R*)-2-[(4*R*,5*R*,6*R*)-2,2-Di-*tert*-butyl-5-methyl-6-((1*S*)-1-methyl-2-oxo-butyl)-[1,3,2]dioxasili-nan-4-yl]-3-hydroxy-4,6,8-trimethyl-undec-8-en-5-one (27).** To a stirred solution of ketone **2** (40.4 mg, 0.241 mmol) in CH_2Cl_2 (1 ml) was added at -78°C dropwise a freshly prepared solution of titanium tetrachloride (1 M in CH_2Cl_2, 0.257 ml, 0.257 mmol) and the slightly yellow solution was stirred for 15 min at -78°C. Diisopropylethylamine (42.5 µl, 0.249 mmol) was then added dropwise (immediate red colour on addition of amine) and stirring was continued for 1 h at -78°C. A pre-cooled solution (-78°C) of aldehyde **19** (59.3 mg, 0.160 mmol) in CH_2Cl_2 (0.5 ml + 0.5 ml rince) was then added *via* cannula. After stirring for 2 h at -78°C, the mixture was quenched by adding 2% aq. HCl (0.2 ml) followed by phosphate buffer pH 7.0 (6 ml) and distilled water (4 ml). The aq. phase was extracted with Et_2O (3 ×) and the combined organic phases were washed with distilled water (1 ×), phosphate buffer pH 7.0 (1 ×) and brine (1 ×), dried and concentrated. The residue was purified by FC (EtOAc\hexane 1:12 to 1:10) to give 7.5 mg (0.01394 mmol, 8.7%) of the less polar anti-diastereomer **28** and 69 mg (0.1283, 80%) of the more polar syn-diastereomer **27** (ratio syn:anti = 9.2:1). The major isomer **27** had $[\alpha]_D$ = -23.9 (c = 0.52, $CHCl_3$). IR 3506, 1704. ^{1}H-NMR: 0.81 (d, *J* = 6.6, 3 H); 0.92 (t, *J* = 7.3, 3 H); 0.96 (d, *J* = 7.0, 3 H); 0.97 (s, 9 H); 0.98 (s, 9 H); 1.04 (d, *J* = 7.0, 3 H); 1.05 (t, *J* = 7.3, 3 H); 1.06 (d, *J* = 7.0, 3 H); 1.14 (d, *J* = 7.0, 3 H); 1.59 (bs, 3 H); 1.92 (dd, *J* = 7.3/13.6, 1 H); 1.89-2.01 (m, 1 H); 1.98 (dq, *J* = 7.0/7.3, 2 H); 2.32 (dd, *J* = 7.0/13.6, 1 H); 2.41 (ddq, *J* = 6.6/9.9/9.9, 1 H); 2.52 (dq, *J* = 7.0/17.7, 1 H); 2.58 (dq, *J* = 7.0/17.7, 1 H); 2.60 (dq, *J* = 2.9/7.0, 1 H); 2.72 (dq, *J* = 1.5/7.0, 1 H); 2.81 (d, *J* = 2.2, 1H(OH)); 2.88 (ddd, *J* = 7.0/7.0/7.3, 1 H); 3.80 (dd, *J* = 1.6/9.9, 1 H); 4.19 (ddd, *J* = 1.5/2.2/9.2, 1 H); 4.20 (dd, *J* = 2.9/9.9, 1 H); 5.14 (bt, *J* = 7.0, 1 H). ^{13}C-NMR

(50 MHz): 220.60, 214.18, 131.62, 129.93, 85.39, 81.94, 70.17, 50.25, 46.99, 44.07, 43.32, 39.76, 37.82, 33.89, 28.13, 27.70, 23.62, 21.70, 20.78, 17.13, 16.77, 16.28, 14.67, 13.22, 8.42, 8.37, 8.24. Anal. calc. for $C_{31}H_{58}O_5Si$: C, 69.10; H, 10.85; found: C, 68.86; H, 10.68.

The minor isomer **28** had ^{1}H-NMR: 0.80 (d, *J* = 7.0, 3 H); 0.94 (t, *J* = 7.3, 3 H); 0.98 (s, 9 H); 1.00 (s, 9 H); 1.02 (d, *J* = 7.0, 3 H); 1.06 (t, *J* = 7.3, 3 H); 1.07 (d, *J* = 7.0, 3 H); 1.21 (d, *J* = 7.0, 3 H); 1.25 (d, *J* = 7.0, 3 H); 1.61 (bs, 3 H); 1.74 (bq, *J* = 7.0, 1 H); 1.82 (dd, *J* = 8.8/13.2, 1 H); 1.89-2.07 (m, 2 H); 2.07 (ddq, *J* = 7.0/9.7/9.9, 1 H); 2.31 (dd, *J* = 5.9/13.2, 1 H); 2.52 (dq, *J* = 7.3/18.0, 1 H); 2.59 (dd, *J* = 7.3/18.0, 1 H); 2.67 (dq, *J* = 2.9/7.0, 1 H); 2.79-2.92 (m, 2 H); 3.52 (s, 1 H(OH)); 3.89 (dd, *J* = 1.5/9.9, 1 H); 4.15 (d, *J* = 9.9, 1 H); 4.31 (dd, *J* = 2.9/9.7, 1 H); 5.16 (bt, *J* = 7.0, 1 H). ^{13}C-NMR: 217.61, 212.95, 131.00, 129.68, 86.29, 81.13, 70.55, 49.72, 49.38, 43.95, 43.06, 38.23, 35.65, 33.43, 27.83, 27.10, 23.15, 21.27, 19.96, 15.96, 15.60, 14.97, 14.17, 11.83, 11.50, 8.10, 7.74.

***E*-(2*S*,4*S*,6*R*)-2-[(4*S*,5*S*,6*R*)-2,2-Di-*tert*-butyl-5-methyl-6-((1*S*)-1-methyl-2-oxo-butyl)-[1,3,2]dioxasilinan-4-yl]-4,6,8-trimethyl-undec-8-ene-3,5-dione (29).** To a stirred solution of $(COCl)_2$ (1 M in CH_2Cl_2, freshly prepared, 0.335 ml, 0.335 mmol) in CH_2Cl_2 (2 ml) was added at -78°C DMSO (47.4 µl, 0.669 mmol) and the mixture was stirred for 15 min at -78°C. To this mixture was added dropwise a solution of the alcohol **27** (60 mg, 0.112 mmol) in CH_2Cl_2 (1 ml + 0.5 ml rince) at -78°C and stirring was continued for 1 h after which triethylamine (155 µl, 1.115 mmol) was added dropwise. Stirring was continued at -78°C for 30 min and the mixture was warmed to -5°C for 5 min. The reaction was quenched by the addition of aq. sat. NH_4Cl, allowed to warm to rt and extracted with a 1:1 mixture of Et_2O \hexane (3 ×). The combined organic phases were washed with sat. aq. NH_4Cl (2 ×), dried and concentrated to give an oil. This residue was triturated with pentane, filtered to remove insoluble triethylammonium hydrochloride and concentrated to give 60 mg of the triketone **29** (0.1115, mmol, 100%). This crude triketone was sufficiently pure to be used in the next step without purification: IR 1722, 1707. ^{1}H-NMR: 0.75 (d, *J* = 6.6, 3 H); 0.92 (t, *J* = 7.3, 3 H); 0.96 (s, 9 H); 0.98 (s, 9 H); 1.05 (t, *J* = 7.3, 3 H); 1.07 (d, *J* = 7.0, 3 H); 1.14 (d, *J* = 6.6, 3 H); 1.24 (d, *J* = 7.0, 3 H); 1.27 (d, *J* = 7.0, 3 H); 1.59 (bs, 3 H); 1.85-2.00 (m, 1 H); 1.89 (dd, *J* = 7.0/13.2, 1 H); 1.97 (dq, *J* = 7.0, 7.3, 2 H); 2.28 (dd, *J* = 6.9/13.2, 1 H); 2.51 (dq, *J* = 7.3/18.0, 1 H); 2.55 (dq, *J* = 7.3/18.0, 1 H); 2.59 (dq, *J* = 2.7/7.0, 1 H); 2.87 (ddq, *J* = 6.9/7.0/7.0, 1 H); 2.92 (dq, *J* = 4.4/6.6, 1 H); 3.99 (q, *J* = 7.0, 1 H); 4.08 (dd, *J* = 4.4/9.5, 1 H); 4.30 (dd, *J* = 2.7/9.7, 1 H); 5.14 (bt, *J* = 7.0, 1 H). ^{13}C-NMR (50 MHz): 212.89, 211.11, 207.52, 130.87, 129.82, 81.25, 80.33, 60.11, 51.24, 49.41, 43.28, 43.18, 39.50, 33.39, 27.54, 27.10, 23.00, 21.20, 20.01, 16.57, 15.69, 14.15, 13.41, 12.53, 12.48, 7.79, 7.70. CI HRMS: 479.3160 ($[C_{27}H_{47}O_5Si]^+$, calc. 479.3193).

***E*-(2*S*,4*R*,6*R*)-2-[(4*S*,5*S*,6*R*)-2,2-Di-tert-butyl-5-methyl-6-((1*S*)-1-methyl-2-oxo-butyl)-[1,3,2]dioxasilinan-4-yl]-4,6,8-trimethyl-undec-8-ene-3,5-dione (30).** To a stirred solution of **28** (17.7 mg, 0.033 mmol) in CH_2Cl_2 (0.5 ml) was added at rt Dess-Martin periodinane[34] (21 mg, 0.049 mmol). After stirring at rt for 20

min, Et_2O (5 ml) and solid $Na_2S_2O_3.5H_2O$ were added and stirring was continued for 30 min. The mixture was then filtered over celite and washed with sat. aq. NH_4Cl (1 ×), pH 7.0 phosphate buffer (2 ×), brine (1 ×), dried and concentrated to give 18 mg (0.033 mmol, 100%) of the crude triketone **30** which showed the same ^1H and ^{13}C-NMR as for triketone **30** prepared from **40** or **41**.

***E*-(2*S*,4*R*)-2-[(3*S*,4*S*,5*R*,6*R*)-2,4-Dihydroxy-3,5-dimethyl-6-((1*S*)-1-methyl-2-oxo-butyl)-tetrahydro-pyran-2-yl]-4,6-dimethyl-non-6-en-3-one (denticulatin A, 1a).** The crude triketone **29** (60 mg, 0.112 mmol) was stirred in a solution of freshly prepared buffered pyridinium hydrofluoride (0.35 ml) (stock solution prepared from dry THF (5 ml), pyridine (2.5 ml) and commercially available pyridinium hydrofluoride (1.05 g)) for 4 h at rt. The reaction was then diluted with Et_2O (20 ml) and successively washed with aq. sat. $CuSO_4$ (4 ×), pH 7.4 phosphate buffer (2 ×), brine (1 ×), dried and concentrated to give 54 mg of the crude denticulatin A. ^1H-NMR analysis of the crude mixture showed that this was actually a mixture of denticulatin A (**1a**) and B (**1b**) in a 20:1 ratio. Purification by FC (*Fluka* silica gel 60, *puriss.*, pH 7.0, 70-230 mesh ASTM, EtOAc\hexane 2:8) gave 39.4 mg (0.100 mmol, 89%) of denticulatin A (**1a**) as the same 20:1 mixture. $[\alpha]_D$ = -47.2 (c = 0.5, $CHCl_3$); lit.[7]: $[\alpha]_D$ = -35.1 (c = 0.4, $CHCl_3$); lit.[5]: $[\alpha]_D$ = -30.7 (c = 1.49, $CHCl_3$); lit.[6]: $[\alpha]_D$ = -43.1 (c = 0.33, $CHCl_3$) for a 6:1 mixture of denticulatin A and B. IR 3400, 1714, 1704. ^1H-NMR: 0.92 (d, *J* = 7.0, 3 H), 0.93 (t, *J* = 7.3, 3 H), 0.96 (d, *J* = 6.6, 3 H), 1.02 (t, *J* = 7.3, 3 H), 1.04 (d, *J* = 7.0, 3 H), 1.10 (d, *J* = 7.0, 3 H), 1.19 (d, *J* = 7.3, 3 H), 1.59 (bs, 3 H), 1.59-1.70 (m, 1 H), 1.74 (dd, *J* = 9.6/13.6, 1 H), 1.79 (ddq, *J* = 1.1/2.6/7.0, 1 H), 1.99 (dq, *J* = 7.0/7.3, 2 H), 2.19 (dd, *J* = 4.8/13.6, 1 H), 2.45 (dq, *J* = 7.3/18.0, 1 H), 2.53 (dq, *J* = 2.9/7.0, 1 H), 2.55 (dq, *J* = 7.3/18.0, 1 H), 2.76 (q, *J* = 7.3, 1 H), 2.95 (ddq, *J* = 4.8/7.0/9.6, 1 H), 3.46 (d, *J* = 8.8, 1 H(OH)), 3.62 (dt, *J* = 2.6, 8.8, 1 H), 4.38 (dd, J = 2.9/10.8, 1 H), 5.14 (bt, *J* = 7.0, 1 H), 6.10 (d, *J* = 1.1, 1 H(OH)). ^1H-NMR (C_6D_6): 6.28 (d, J = 1.1, 1 H(OH)), 5.27 (bt, J = 7.0, 1 H), 4.35 (dd, J = 2.9/10.7, 1 H), 3.28 (dt, J = 2.6/8.5, 1 H), 3.01 (d, J = 8.5, 1 H(OH)), 2.95 (ddq, J = 4.4/7.0/9.2, 1 H), 2.55 (q, J = 7.3, 1 H), 2.48 (dq, J = 7.3/18.0, 1 H), 2.41 (dd, J = 4.4/13.6, 1 H), 2.20 (dq, J = 2.9/7.0, 1 H), 2.15 (dq, J = 7.3/18.0, 1 H), 2.01 (dq, J = 7.0/7.3, 2 H), 1.92 (dd, J = 9.2/13.6, 1 H), 1.67 (bs, 3 H), 1.44 (ddq, J = 1.1/2.6/7.0, 1 H), 1.25 (ddq, J = 2.6/6.6/10.7, 1 H), 1.16 (t, J = 7.3, 3 H), 1.07 (d, J = 7.0, 3 H), 1.06 (d, J = 7.0, 3 H), 1.05 (d, J = 7.3, 3 H), 1.01 (d, J = 7.0, 3 H), 0.97 (t, J = 7.3, 3 H), 0.82 (d, J = 6.6, 3 H). ^{13}C-NMR: 219.59, 211.98, 131.09, 129.42, 102.60, 75.49, 69.60, 50.02, 47.16, 42.61, 42.04, 38.59, 37.58, 32.83, 21.21, 15.78, 15.53, 14.18, 13.47, 13.27, 11.77, 7.81, 7.72. ^{13}CNMR (C_6D_6, 50 MHz): 218.98, 209.80, 131.70, 129.54, 103.02, 75.43, 69.70, 50.56, 47.26, 42.83, 42.56, 38.73, 37.74, 32.70, 21.63, 15.87, 15.65, 14.46, 13.54, 13.50, 11.90, 8.11, 7.93. CI HRMS: 378.2756 ($[C_{23}H_{38}O_4]^{+\cdot}$, calc. 378.2770). ES: 419 ($[M+Na]^{+\cdot}$, 72).

(2*S*)-*N*-{(2*S*)-2-[(4*R*,5*R*,6*S*)-2,2-Di-*tert*-butyl-5-methyl-6-((1*S*)-1-methyl-2-oxo-ethyl)-[1,3,2]dioxasilinan-4-yl]-propan-1-oyl}bornane-10,2-sultam (31). Using the same procedure and concentrations as for the synthesis

of **19**, dithiolane **14** (956 mg, 1.515 mmol) gave after purification by FC (EtOAc\hexane 1:6) 770 mg (1.387 mmol, 92%) of the white crystalline aldehyde **31** which could be recrystallized from CH_2Cl_2\hexane (82%): M.p. 177-179°C. $[\alpha]_D$ = + 66.7 (c = 1.47, $CHCl_3$). IR 1728, 1687. ^{1}H-NMR: 0.82 (d, *J* = 6.6, 3 H), 0.97 (s, 9 H), 0.98 (s, 3 H), 1.04 (s, 9 H), 1.16 (s, 3 H), 1.27 (d, *J* = 7.0, 3 H), 1.29 (d, *J* = 7.0, 3 H), 1.30-1.47 (m, 2 H), 1.84-1.97 (m, 4 H), 2.04-2.15 (m, 2 H), 2.64 (ddq, *J* = 1.8/2.6/7.0, 1 H), 3.25 (dq, *J* = 5.2/7.0, 1 H), 3.45 (d, *J* = 13.6, 1 H), 3.51 (d, *J* = 13.6, 1 H), 3.86 (dd, *J* = 5.9/5.9, 1 H), 3.99 (dd, *J* = 1.8/10.3, 1 H), 4.37 (dd, *J* = 5.2/9.6, 1 H), 9.83 (d, *J* = 2.6, 1 H). ^{13}C-NMR (50 MHz): 204.92, 173.55, 81.75, 77.33, 65.38, 53.11, 49.08, 48.39, 47.77, 44.49, 44.35, 41.03, 38.43, 32.75, 27.68, 27.11, 26.42, 22.97, 20.74, 20.02, 19.85, 13.44, 12.83, 11.77. CI HRMS: 499.2466 ($[C_{24}H_{41}O_6NSSi]^+$, calc. 499.2424). Anal. calc. for $C_{28}H_{49}O_6NSSi$: C, 60.50; H, 8.88; N, 2.52; found: C, 60.18; H, 8.84; N, 2.80.

(2*S*)-*N*-{(2*S*)-2-[(4*R*,5*R*,6*R*)-2,2-Di-*tert*-butyl-6-((1*R*,2*R*)-2-hydroxy-1-methyl-butyl)-5-methyl-[1,3,2]dioxasilinan-4-yl]-propan-1-oyl}bornane-10,2-sultam (32) and (2*S*)-*N*-{(2*S*)-2-[(4*R*,5*R*,6*R*)-2,2-Di-*tert*-butyl-6-((1*R*,2*S*)-2-hydroxy-1-methyl-butyl)-5-methyl-[1,3,2]-dioxasilinan-4-yl]-propan-1-oyl}bornane-10,2-sultam (33). To a stirred solution of aldehyde **31** (680 mg, 1.225 mmol) in a 2 : 1 THF- Et_2O mixture (15 ml) was added at -100°C ethylmagnesium bromide (1 M in THF, 1.47 ml, 1.47 mmol). After stirring for 15 min at -100°C, the mixture was allowed to reach -50°C over a 1 h period and 2% aq. HCl (15 ml) was slowly added. The aq. layer was extracted with Et_2O (4 ×) and the combined organic layers were washed with sat. aq. $NaHCO_3$ (1 ×), sat. aq. NH_4Cl (1 ×), dried and concentrated. The residue was purified by FC (EtOAc\hexane 1:6) to give 519 mg (0.887 mmol, 72%) of the less polar isomer **33** (r.f. 0.26) and 167 mg (0.285 mmol, 23%) of the more polar isomer **32** (r.f. 0.1). The major isomer **33** had $[\alpha]_D$ = +49.1 (c = 1.13, $CHCl_3$). IR 3526, 1694. ^{1}H-NMR (200 MHz): 0.72 (d, *J* = 6.9, 3 H), 0.91 (t, *J* = 7.3, 3 H), 0.98 (s, 3 H), 1.02 (s, 9 H), 1.05 (s, 9 H), 1.08 (d, *J* = 7.0, 3 H), 1.17 (s, 3 H), 1.31 (d, J= 7.0, 3 H), 1.22-1.48 (m, 3 H), 1.60 (ddq, *J* = 7.0/7.3/14.0, 1 H), 1.78-2.05 (m, 5 H), 2.05-2.14 (m, 2 H), 3.27 (dq, *J* = 5.6/7.0, 1 H), 3.44 (d, *J* = 13.7, 1 H), 3.53 (d, J= 13.7, 1 H), 3.64 (s, 1 H(OH)), 3.82-3.90 (m, 1 H), 3.89 (dd, *J* = 6.6/6.6, 1 H), 3.97 (dd, *J* = 1.5/9.7, 1 H), 4.36 (dd, *J* = 5.6/9.7, 1 H). ^{13}C-NMR (50 MHz): 173.72, 85.59, 78.13, 71.35, 65.40, 53.15, 48.39, 47.78, 44.83, 44.48, 40.80, 38.42, 36.03, 32.77, 27.85, 27.51, 27.13, 26.42, 23.00, 20.75, 19.86, 19.79, 13.98, 12.90, 10.77, 10.38. CI HRMS: 526.2639 ($[C_{26}H_{44}O_6NSSi]^+$, calc. 526.2659).

The minor isomer **32** had $[\alpha]_D$ = +50.8 (c = 0.66, $CHCl_3$). IR 3539, 1694. ^{1}H-NMR (200 MHz): 0.80 (d, *J* = 6.8, 3 H), 0.96 (t, *J* = 7.3, 3 H), 1.00 (s, 12 H), 1.02 (d, *J* = 7.0, 3 H), 1.03 (s, 9 H), 1.18 (s, 3 H), 1.28 (d, *J* = 7.0, 3 H), 1.24-1.53 (m, 3 H), 1.70 (ddq, *J* = 2.6/7.3/14.0, 1 H), 1.81-2.03 (m, 5 H), 2.04-2.12 (m, 2 H), 3.24 (dq, *J* = 5.3/7.0, 1 H), 3.42 (d, *J* = 13.7, 1 H), 3.50 (d, *J* = 13.7, 1 H), 3.66 (ddd, *J* = 2.6/5.7/8.7, 1 H), 3.84 (dd, *J* = 2.4/9.7, 1 H), 3.85 (dd, *J* = 6.6/6.6, 1 H), 4.29 (dd, J= 5.3/9.7, 1 H). ^{13}C-NMR (50 MHz): 173.75, 84.51, 78.40, 74.43, 65.38, 53.12, 48.35, 47.76, 44.58, 44.48, 42.22, 40.14, 38.45, 32.75, 27.97, 27.86, 27.24,

26.42, 23.02, 20.74, 19.96, 19.86, 16.09, 13.62, 13.32, 10.24. CI HRMS: 510.2715 ($[C_{26}H_{44}O_5NSSi]^{+\cdot}$, calc. 510.2709). Anal. calc. for $C_{30}H_{55}O_6NSSi$: C, 61.50; H, 9.46; N, 2.39; found: C, 61.24; H, 9.35; N, 2.30.

(2*R*,3*R*)-2-[(4*R*,5*S*,6*S*)-2,2-Di-*tert*-butyl-6-((1*R*)-2-hydroxy-1-methyl-ethyl)-5-methyl-[1,3,2]dioxasilinan-4-yl]-pentan-3-ol (34). To a stirred solution of the minor diastereomer **32** (161 mg, 0.275 mmol) in THF (5 ml) was added at -78°C lithium triethylborohydride (1 M in THF, 0.908 ml, 0.908 mmol). After stirring for 3 h at -78°C, the mixture was allowed to reach rt over a 3 h period and sat. aq. NH_4Cl (10 ml) and 2% aq. HCl (2 ml) were added successively. The aq. layer was separated and extracted with CH_2Cl_2 (4 ×). The combined organic layers were washed with sat. aq. NH_4Cl, dried and concentrated to give an oil which was purified by FC (CH_2Cl_2\hexane 8:1 + 0.5% MeOH) to give 53 mg (0.248 mmol, 90%) of the recovered bornane-10,2-sultam and 96.5 mg (0.258 mmol, 94%) of the white crystalline diol **34** which could be recrystallized from pentane (90%): M.p. 93-94.5°C (pentane); lit.[7]: m.p. 95-96°C (pentane). $[\alpha]_D$ = -3.9 (c = 0.76, $CHCl_3$); lit.[7]: $[\alpha]_D$ = -2.7 (c = 1.0, $CHCl_3$). IR 3382. ^{1}H-NMR: 0.80 (d, *J* = 7.0, 3 H), 0.98 (t, *J* = 7.3, 3 H), 1.00 (d, *J* = 7.0, 3 H), 1.01 (s, 9 H), 1.03 (d, *J* = 7.0, 3 H), 1.04 (s, 9 H), 1.43 (ddq, *J* = 7.3/8.8/14.3, 1 H), 1.71 (ddq, *J* = 2.6/7.3/14.3, 1 H), 1.83-1.92 (m, 1 H), 1.94 (ddq, *J* = 2.2/7.0/7.0, 1 H), 2.15 (ddq, *J* = 7.0/9.7/9.7, 1 H), 3.66-3.74 (m, 2 H), 3.78-3.84 (m, 2 H), 4.02 (dd, *J* = 2.2/9.7, 1 H). ^{13}C-NMR: 84.94, 84.06, 74.05, 68.04, 40.32, 39.73, 36.59, 28.03, 27.91, 27.20, 23.13, 20.18, 16.00, 12.54, 10.03, 8.75. MS (ES): 397 ($[M+Na]^{+\cdot}$, 100). CI HRMS: 317.2116 ($[C_{16}H_{33}O_4Si]^{+\cdot}$, calc. 317.2148), 299.2041 ($[C_{16}H_{31}O_3Si]^{+\cdot}$, calc., 299.2043).

(2*R*,3*S*)-2-[(4*R*,5*S*,6*S*)-2,2-Di-*tert*-butyl-6-((1*R*)-2-hydroxy-1-methyl-ethyl)-5-methyl-[1,3,2]dioxasilinan-4-yl]-pentan-3-ol (35). Using the same procedure and concentrations as described for the synthesis of **34**, diastereomer **33** (956 mg, 1.515 mmol) gave after purification by FC (EtOAc\hexane 1:6 + 0.5% MeOH to EtOAc\hexane 1:2) 299 mg (0.799 mmol, 90%) of the diol **35** as a clear colorless oil and 168 mg (0.780 mmol, 88%) of the recovered (2*S*)-bornane-10,2-sultam: $[\alpha]_D$ = +8.3 (c = 0.77, $CHCl_3$). IR 3454. ^{1}H-NMR: 0.73 (d, *J* = 7.0, 3 H), 0.93 (t, *J* = 7.3, 3 H), 1.02 (d, *J* = 6.6, 3 H), 1.03 (s, 9 H), 1.06 (s, 9 H), 1.10 (d, *J* = 7.0, 3 H), 1.39 (ddq, *J* = 7.0/7.3/14.3, 1 H), 1.62 (ddq, *J* = 7.0/7.3/14.3, 1 H), 1.86 (bdq, *J* = 1.0/7.0, 1 H), 1.86-1.96 (m, 1 H), 2.07 (ddq, *J* = 6.6/9.6/9.8, 1 H), 2.44 (bd, *J* = 5.2, 1 H(OH)), 3.56 (s, 1 H(OH)) , 3.69-3.83 (m, 2 H), 3.92 (dd, *J* = 7.0/7.0, 1 H), 3.96 (dd, *J* = 1.0/9.6, 1 H), 4.10 (dd, *J* = 1.8/9.8, 1 H). ^{13}C-NMR: 86.17, 83.02, 71.42, 67.61, 38.08, 36.84, 36.13, 27.97, 27.51, 27.09, 23.15, 19.99, 12.06, 10.78, 10.39, 8.82. MS (ES): 398 ($[MH+Na]^{+\cdot}$, 30), 397 ($[M+Na]^{+\cdot}$, 100). Anal. calc. for $C_{20}H_{42}O_4Si$: C, 64.12; H, 11.30; found: C, 63.95; H, 11.19.

Transformation of 14 to 31 to 32 and 33 to 34 and 35 without intermediate purifications. A stirred solution of **14** (882 mg, 1.398 mmol in a THF (19 ml)-pH 7.4 phosphate buffer (4 ml) mixture was treated with an aq. mercury(II) perchlorate[36] solution (4 M, 0.734 ml, 2.936 mmol) to give after work up (no FC) 774 mg

(1.395 mmol) of the crude aldehyde **31**. A solution of the crude aldehyde **31** (774 mg) in a THF (11 ml)- Et_2O (5.5 ml) mixture was then treated with ethylmagnesium bromide (1 M in THF, 2.1 ml, 2.1 mmol) as described above to give a mixture of epimeric alcohols **32** and **33** which were not separated but used crude in the next step. Reduction of the unpurified mixture of alcohols **32** and **33** (800 mg) with lithium triethylborohydride (1 M in THF, 4.6 ml, 4.6 mmol) as described above gave after work up and FC (EtOAc\hexane 1:6 for epimer **35** to 1:3 for epimer **34**) 309 mg (0.826 mmol, 59%) of **35** and a mixture of **34** and bornane-10,2-sultam which were separated by FC (CH_2Cl_2\EtOAc 8:1 + 0.5% MeOH) to give 210 mg (0.9765 mmol, 70%) of recovered bornane-10,2-sultam and 112 mg (0.229 mmol, 21%) of **34**.

(2*S*)-2-[(4*R*,5*R*,6*R*)-2,2-Di-tert-butyl-6-((1*R*,2*S*)-2-hydroxy-1-methy-butyl)-5-methyl-[1,3,2]dioxasilinan-4-yl]-propionaldehyde (36). Treating a solution of the diol **35** (290 mg, 0.775 mmol) in CH_2Cl_2 (10 ml) with PCC (750 mg, 3.5 mmol) as described for the epimeric diol **34**, gave after 3 h reaction time followed by workup 278 mg (0.751 mmol, 97%) of the hydroxyaldehyde **36** which was sufficiently pure to be used in the next step without purification: $[\alpha]_D$ = +22.8 (c = 0.88, $CHCl_3$). IR 3538, 1736, 1474. ^{1}H-NMR (200 MHz): 0.78 (d, J= 6.8, 3 H), 0.93 (t, *J* = 7.5, 3 H), 0.99 (s, 9 H), 1.03 (s, 9 H), 1.11 (d, *J* = 7.0, 3 H), 1.19 (d, *J* = 7.0, 3 H), 1.37 (ddq, *J* = 7.0/7.5/14.3, 1 H), 1.61 (ddq, *J* = 7.0/7.5/14.3, 1 H), 1.87 (dq, *J* = 1.8/7.0, 1 H), 2.10 (ddq, *J* = 7.0/9.7/9.9, 1 H), 2.53 (dq, *J* = 2.4/7.0, 1 H), 3.52 (s, 1 H(OH)), 3.91 (dd, *J* = 7.0/7.0, 1 H), 4.02 (dd, *J* = 1.8/9.7, 1 H), 4.48 (dd, *J* = 2.4/9.9, 1 H), 9.75 (s, 1 H). ^{13}C-NMR (50 MHz): 204.19, 85.83, 79.24, 71.38, 49.36, 37.66, 36.20, 27.91, 27.51, 27.00, 23.14, 19.92, 12.24, 10.78, 10.41, 6.15. CI HRMS: 315.1992 ($[C_{16}H_{31}O_4Si]^+$, calc. 315.1992).

(2*S*)-2-[(4*R*,5*S*,6*S*)-2,2-Di-*tert*-butyl-5-methyl-6-((1*S*)-1-methyl-2-oxo-butyl)-[1,3,2]dioxasilinan-4-yl]-propionaldehyde (37).

From diol 34. *Method A:* To a stirred solution of diol **34** (87 mg, 0.233 mmol) in CH_2Cl_2 (2.5 ml) was added portionwise PCC (167 mg, 0.755 mmol) at rt. After stirring for 1.5 h at rt, the mixture was diluted with Et_2O (6 ml) and the black gum triturated until it became a granular solid. Filtration of the mixture through florisil (which had been previously wet with Et_2O), eluting with Et_2O and concentration gave 83 mg (0.224 mmol, 96%) of the crude aldehyde **37** as an oil. The aldehyde was sufficiently pure to be used in the next step without purification. *Method B:* Treatment of a solution of the diol **34** (112 mg, 0.299 mmol) in CH_2Cl_2 (3 ml) with Dess-Martin periodinane[34] (317 mg, 0.748 mmol) gave after work up (addition of solid $Na_2S_2O_3.5H_2O$, stirr 10 min at rt, add $MgSO_4$ and filtre, FC over florisil with CH_2Cl_2) 100 mg (0.270 mmol, 90%) of **37**: $[\alpha]_D$ = -2.2 (c = 0.87, $CHCl_3$). IR 1732, 1704. ^{1}H-NMR: 0.86 (d, *J* = 6.7, 3 H), 0.93 (s, 9 H), 1.01 (t, *J* = 7.1, 3 H), 1.02 (s, 9 H), 1.14 (d, *J* = 7.0, 3 H), 1.35 (d, *J* = 7.1, 3 H), 1.90 (ddq, *J* = 6.7/9.8/9.9, 1 H), 2.50 (dq, *J* = 2.2/7.0, 1 H), 2.51 (dq, *J* = 7.1/18.7, 1 H), 2.63 (dq, *J* = 7.1/18.7, 1 H), 2.78 (dq, *J* = 2.6/7.1, 1 H), 3.98 (dd, *J* = 2.6/9.8, 1 H), 4.43 (dd, *J* = 2.2/9.9, 1 H), 9.73 (s, 1 H). ^{13}C-NMR (50 MHz): 213.28, 204.49, 82.66, 78.71, 49.68,

49.32, 38.36, 35.00, 27.80, 26.91, 23.09, 20.01, 14.30, 12.56, 7.27, 5.97. CI HRMS: 313.1827 ($[C_{16}H_{29}O_4Si]^+$, calc. 313.1835).

From diol 35. To a stirred solution of diol **35** (288 mg, 0.77 mmol) in CH_2Cl_2 (10 ml) was added portionwise Dess-Martin periodinane[34] (816 mg, 1.925 mmol) at rt. After stirring for 1 h, solid $Na_2S_2O_3.5H_2O$ was added and stirring continued for 10 min. Et_2O (50 ml) was added and the mixture was filtrated and washed with distilled water (2 ×), brine (1 ×), dried and concentrated. The residue was purified by FC over florisil (CH_2Cl_2) to give 228 mg (0.616 mmol, 80%) of **37** which was sufficiently pure to be used in the next step without further purification.

From hydroxyaldehyde 36: To a stirred solution of alcohol **36** (76 mg, 0.204 mmol) in CH_2Cl_2 (2 ml) was added Dess-Martin periodinane[34] (87 mg, 0.206 mmol) and the mixture was stirred at rt for 30 min after which another equivalent of the periodinane (87 mg, 0.206 mmol) was added. After additional stirring for 2 h at rt, solid $Na_2S_2O_3.5H_2O$ was added and the mixture stirred for 10 min. Filtration over florisil (CH_2Cl_2) gave 48 mg (0.13 mmol, 64%) of the ketone **37** together with 4 mg (0.0107 mmol, 5%) of starting material **36**.

(2*S*)-2-[(4*S*,5*S*,6*S*)-2,2-Di-*tert*-butyl-6-((1*R*,2*R*)-2-hydroxy-1-methyl-butyl)-5-methyl-[1,3,2]dioxasilinan-4-yl]-pentan-3-one (38) and (2*S*)-2-[(4*S*,5*S*,6*S*)-2,2-Di-*tert*-butyl-6-((1*R*,2*S*)-2-hydroxy-1-methyl-butyl)-5-methyl-[1,3,2]dioxasilinan-4-yl]-pentan-3-one (39). To a stirred solution of aldehyde **37** (328 mg, 0.8865 mmol) in a 2:1 mixture of Et_2O/THF (30 ml) was added dropwise ethylmagnesium bromide (1 M in THF, 1.33 ml, 1.33 mmol) at -78°C. After stirring for 2 h at -78°C, the reaction was quenched by the dropwise addition of 1N aq. HCl (10 ml) and aq. sat. NH_4Cl (30 ml) after which an extraction was performed with Et_2O (3 ×). The combined organic phases were washed with sat. aq. NH_4Cl (2 ×), dried and concentrated to give an oil which was purified by FC (CH_2Cl_2\Et_2O 99:1) to give 213.5 mg (0.534 mmol, 60%) of the less polar epimer **39** and 73.5 mg (0.184 mmol, 21%) of the more polar epimer **38**, both as an oil. The major isomer **39** had $[\alpha]_D$ = -18.0 (c = 1.08, $CHCl_3$); lit.[7]: $[\alpha]_D$ = -16.4 (c = 1, $CHCl_3$). IR 3534, 1704. ^{1}H-NMR: 0.82 (d, *J* = 6.7, 3 H), 0.92 (d, *J* = 7.0, 3 H), 0.94 (t, *J* = 7.5, 3 H), 0.96 (s, 9 H), 1.01 (t, *J* = 7.2, 3 H), 1.06 (s, 9 H), 1.33 (d, *J* = 7.0, 3 H), 1.40 (ddq, *J* = 5.7/7.5/13.7, 1 H), 1.61 (ddq, *J* = 7.5/7.5/13.7, 1 H), 1.73 (bq, *J* = 7.0, 1 H), 1.92 (ddq, *J* = 6.7/9.7/9.8, 1 H), 2.50 (dq, *J* = 7.2/18.7, 1 H), 2.61 (dq, *J* = 7.2/18.7, 1 H), 2.77 (dq, *J* = 2.8/7.0, 1 H), 3.77 (bdd, *J* = 5.7/7.5, 1 H), 3.84 (s, 1 H(OH)), 3.93 (dd, *J* = 2.8/9.7, 1 H), 4.03 (dd, *J* = 2.0/9.8, 1 H). ^{13}C-NMR (50 MHz): 213.04, 86.74, 82.70, 78.34, 49.75, 38.92, 37.80, 34.96, 27.82, 27.73, 26.95, 23.08, 20.08, 14.20, 12.50, 10.56, 7.28, 4.44. CI HRMS: 343.2295 ($[C_{18}H_{35}O_4Si]^+$, calc. 343.2305). Anal. calc. for $C_{22}H_{44}O_4Si$: C, 65.95; H, 11.07; found: C, 65.84; H, 11.00.

The minor isomer **38** had $[\alpha]_D$ = -18.4 (c = 0.88, $CHCl_3$). IR 3522, 1704. ^{1}H-NMR: 0.89 (d, *J* = 6.6, 3 H), 0.96 (s, 9 H), 0.98 (t, *J* = 7.0, 3 H), 1.01 (t, *J* = 7.0, 3 H), 1.04 (d, *J* = 7.0, 3 H), 1.05 (s, 9 H), 1.33 (d, *J* = 7.3, 3 H), 1.50-1.69 (m, 2 H), 1.76 (ddq, *J* = 2.0/5.1/7.0, 1 H), 1.91 (ddq, *J* = 6.6/9.7/9.8, 1 H), 2.50 (dq, *J* =

7.0/18.7, 1 H), 2.62 (dq, *J* = 7.0/18.7, 1 H), 2.77 (dq, *J* = 2.8/7.3, 1 H), 3.11 (d, *J* = 8.1, 1 H(OH)), 3.47 (dddd, *J* = 5.1/5.1/8.1/8.1, 1 H), 3.93 (dd, *J* = 2.8/9.7, 1 H), 4.21 (dd, *J* = 2.0/9.8, 1 H). ^{13}C-NMR (50 MHz): 213.2, 82.76, 80.37, 77.60, 49.81, 38.71, 37.74, 34.96, 28.78, 27.78, 27.05, 23.06, 20.12, 14.20, 12.39, 10.67, 10.56, 7.31. CI HRMS: 343.2282 ($[C_{18}H_{35}O_4Si]^+$, calc., 343.2305). Anal. calc. for $C_{22}H_{44}O_4Si$: C, 65.95; H, 11.07; found: C, 65.77; H, 10.82.

***E*-(2*S*,4*R*,5*S*,6*R*)-2-[(4*S*,5*S*,6*S*)-2,2-Di-*tert*-butyl-6-((1*R*,2*S*)-2-hydroxy-1-methyl-butyl)-5-methyl-[1,3,2]-dioxasilinan-4-yl]-5-hydroxy-4,6,8-trimethyl-undec-8-en-3-one (40).** The procedure as described by Paterson and Perkins[7] was used using the following quantities: ketone **39** (70 mg, 0.175 mmol) in CH_2Cl_2 (5 ml), $TiCl_4$ (1 M in CH_2Cl_2, freshly prepared, 0.525 ml, 0.525 mmol), *i*-Pr_2NEt (64 µl, 0.372 mmol), pre-cooled solution (-78°C) of aldehyde **3** (73.5 mg, 0.525 mmol) in CH_2Cl_2 (1 ml). Purification by FC (Et_2O\hexane 3:7) gave 83.6 mg (0.155 mmol, 89%) of the pure aldol adduct **40** as a clear oil: $[\alpha]_D$ = +24.3 (c = 0.84, $CHCl_3$); lit.[7]: $[\alpha]_D$ = +21.7 (c = 1.8, $CHCl_3$). IR 3478, 1704. ^{1}H-NMR: 0.76 (d, *J* = 6.6, 3 H), 0.90 (d, *J* = 6.6, 3 H), 0.93 (d, J= 7.0, 3 H), 0.945 (t, *J* = 7.4, 3 H), 0.95 (t, *J* = 7.4, 3 H), 1.00 (s, 9 H), 1.05 (s, 9 H), 1.15 (d, *J* = 7.0, 3 H), 1.25 (d, *J* = 7.0, 3 H), 1.40 (dddq (apparent septuplet), *J* = 7.4, 1 H), 1.56 (s, 3 H), 1.55-1.66 (m, 2 H), 1.66-1.77 (m, 2 H), 1.90-2.08 (m, 4 H), 2.98 (dq, *J* = 2.9/7.3, 1 H), 3.01 (dq, *J* = 4.0/6.6, 1 H), 3.02 (d, *J* = 2.9, 1 H(OH)), 3.59 (ddd, *J* = 2.9/2.9/7.4, 1 H), 3.78 (bt, *J* = 6.6, 1 H), 3.81 (s, 1 H(OH)), 4.04 (dd, *J* = 2.2/9.6, 1 H), 4.06 (dd, *J* = 4.0/9.6, 1 H), 5.14 (bt, *J* = 7.0, 1 H). ^{1}H-NMR (C_6D_6): 0.55 (d, *J* = 6.6, 3 H), 0.99 (t, *J* = 7.5, 3 H), 1.05 (d, *J* = 7.0, 3 H), 1.10 (s, 9 H), 1.11 (s, 9 H), 1.14 (t, *J* = 7.0, 3 H), 1.15 (d, *J* = 6.6, 6 H), 1.19 (d, *J* = 7.0, 3 H), 1.42 (dddq, *J* = 4.0/7.0/7.0/7.4, 1 H), 1.58 (ddq, *J* = 1.6/2.2/7.0, 1 H), 1.60 (s, 3 H), 1.73-1.93 (m, 3 H), 1.96-2.08 (m, 3 H), 2.17 (dd, *J* = 4.0/12.5, 1 H), 2.81 (dq, *J* = 3.7/7.0, 1 H), 2.83 (d, *J* = 3.3, 1 H(OH)), 2.94 (dq, *J* = 3.7/7.0, 1 H), 3.58 (s, 1 H(OH)), 3.80 (ddd, *J* = 3.3/3.7/7.0, 1 H), 3.84 (ddd, *J* = 1.6/4.9/8.6, 1 H), 3.96 (dd, *J* = 2.2/9.6, 1 H), 4.00 (dd, *J* = 3.7/9.6, 1 H), 5.29 (bt, *J* = 7.0, 1 H). ^{13}C-NMR: 217.02, 132.12, 128.83, 86.51, 81.32, 78.28, 74.50, 50.32, 46.80, 43.62, 39.26, 37.82, 33.42, 27.80, 27.11, 23.09, 21.19, 20.14, 15.50, 15.24, 14.26, 13.67, 12.68, 10.56, 10.07, 4.52. ^{13}C-NMR (C_6D_6): 215.85, 132.65, 128.95, 86.40, 81.78, 78.02, 74.64, 50.35, 47.50, 44.32, 39.44, 38.89, 33.98, 28.49, 27.92, 27.34, 23.20, 21.55, 20.32, 15.65, 15.34, 14.46, 13.95, 12.54, 10.91, 10.67, 5.26. MS (ES): 563 ($[M+Na]^+$, 100). Anal. calc. for $C_{27}H_{51}O_5Si$: C, 68.84; H, 11.18; found: C, 68.89; H, 11.19.

***E*-(2*S*,4*R*,5*S*,6*R*)-2-[(4*S*,5*S*,6*S*)-2,2-Di-*tert*-butyl-6-((1*R*,2*R*)-2-hydroxy-1-methyl-butyl)-5-methyl-[1,3,2]-dioxasilinan-4-yl]-5-hydroxy-4,6,8-trimethyl-undec-8-en-3-one (41).** Using the same procedure as described above, 51 mg of ethyl ketone **38** (0.128 mmol) and 38 mg of the aldehyde **3** (0.270 mmol) gave 48.9 mg (0.091 mmol, 71%) of the pure aldol adduct **41** as a clear oil and 9.8 mg (0.0245mmol, 19%) of recovered starting material **38**: $[\alpha]_D$ = +21.1 (c = 0.7, $CHCl_3$); lit.[7]: $[\alpha]_D$ = +23.6 (c = 1.9, $CHCl_3$). IR 3466, 1702. ^{1}H-NMR:

0.75 (d, *J* = 6.6, 3 H), 0.90 (d, *J* = 6.3, 3 H), 0.95 (t, *J* = 7.4, 3 H), 0.99 (t, *J* = 7.3, 3 H), 1.01 (s, 9 H), 1.05 (d, *J* = 7.0, 3 H), 1.05 (s, 9 H), 1.15 (d, *J* = 7.4, 3 H), 1.26 (d, *J* = 7.0, 3 H), 1.57 (s, 3 H), 1.54-1.66 (m, 3 H), 1.66-1.79 (m, 2 H), 1.90-2.08 (m, 4 H), 2.99 (dq, *J* = 2.6/7.4, 1 H), 3.01 (dq, *J* = 4.0/7.0, 1 H), 3.05 (d, *J* = 2.6, 1 H(OH)), 3.07 (d, *J* = 8.1, 1 H(OH)), 3.48 (dddd, *J* = 5.1/5.1/8.1/8.1, 1 H), 3.60 (ddd, *J* = 2.6/2.6/7.7, 1 H), 4.06 (dd, *J* = 4.0/9.8, 1 H), 4.23 (dd, *J* = 2.2/9.6, 1 H), 5.14 (bt, *J* = 7.0, 1 H). ^{13}C-NMR (50 MHz): 217.31, 132.03, 128.81, 81.40, 80.22, 77.46, 74.50, 50.14, 46.70, 43.48, 39.14, 37.70, 33.25, 28.77, 27.70, 27.17, 23.02, 21.18, 20.14, 15.45, 15.27, 14.31, 13.80, 12.56, 10.68, 10.48, 9.95. MS (ES): 563 ([M+Na]$^+$, 100).

***E*-(2*S*,4*R*,6*R*)-2-[(4*S*,5*S*,6*R*)-2,2-Di-*tert*-butyl-5-methyl-6-((1*S*)-1-methyl-2-oxo-butyl)-[1,3,2]dioxasilinan-4-yl]-4,6,8-trimethyl-undec-8-ene-3,5-dione (30).**

From aldol 40: Using the same procedure and concentrations as described for the synthesis of **29**, diol **40** (83.6 mg, 0.155 mmol) gave 84 mg (0.155 mmol, 100%) of essentially pure triketone **30**.

From aldol 41: Using the same experimental procedure, diol **41** (43 mg, 0.0796 mmol) gave 43 mg (0.0796 mmol, 100%) of essentially pure triketone **30**: IR 1716. ^{1}H-NMR: 0.79 (d, *J* = 6.7, 3 H), 0.92 (t, *J* = 7.5, 3 H), 0.956 (s, 9 H), 0.965 (s, 9 H), 0.97 (d, *J* = 6.8, 3 H), 1.04 (t, *J* = 7.3, 3 H), 1.13 (d, *J* = 7.0, 3 H), 1.26 (d, *J* = 7.3, 3 H), 1.31 (d, *J* = 7.3, 3 H), 1.57 (bs, 3 H), 1.90 (ddq, J = 6.7/9.6/9.9, 1 H), 1.93 (dd, J = 8.8/13.5, 1 H), 1.93-2.05 (m, 2 H), 2.38 (dd, *J* = 5.5/13.5, 1 H), 2.50 (dq, J = 7.3/17.9, 1 H), 2.56 (dq, *J* = 7.3/17.9, 1 H), 2.60 (dq, *J* = 2.6/7.0, 1 H), 2.84 (dq, *J* = 2.9/7.3, 1 H), 2.92 (ddq, *J* = 5.5/7.0/8.8, 1 H), 3.96 (dd, *J* = 2.9/9.6, 1 H), 4.10 (q, *J* = 7.0, 1 H), 4.28 (dd, *J* = 2.6/9.9, 1 H), 5.17 (bt, *J* = 7.0, 1 H). ^{13}C-NMR (50 MHz): 212.99, 211.53, 208.55, 130.80, 129.89, 82.20, 80.63, 57.75, 49.83, 49.52, 43.24, 42.45, 38.82, 33.39, 27.74, 27.10, 23.11, 21.22, 20.01, 16.26, 15.58, 14.15, 14.01, 13.57, 12.48, 7.86, 7.69. CI HRMS: 479.3188 ([$C_{27}H_{47}O_5Si$]$^+$, calc. 479.3193).

***E*-(2*R*,4*R*)-2-[(3*S*,4*S*,5*R*,6*R*)-2,4-Dihydroxy-3,5-dimethyl-6-((1*S*)-1-methyl-2-oxo-butyl)-tetrahydro-pyran-2-yl]-4,6-dimethyl-non-6-en-3-one (denticulatin B, 1b).** Using the same procedure as described for the synthesis of denticulatin A (**1a**), stirring of triketone **30** (crude from the Swern oxidation step) (84 mg, 0.155 mmol) in freshly prepared buffered pyridiunium hydrofluoride (0.5 ml) gave after workup 73 mg of the crude denticulatin B. ^{1}H-NMR-analysis revealed that this was actually a mixture of denticulatin B (**1b**) and A (**1a**) in a 12:1 ratio. FC (Fluka silica gel 60, puriss., pH 7.0, 70-230 mesh ASTM, EtOAc\Hexane 2:8) followed by recrystallization from pentane gave 47.8 mg (0.121 mmol, 78%) of pure denticulatin B (**1b**): M.p. 138-142°C (pentane); lit.[7]: m.p. 135-137°C (pentane); lit.[5]: 137-141°C. $[\alpha]_D$ = -32.7 (c = 0.4, $CHCl_3$); lit.[5]: $[\alpha]_D$ = -26.4 (c = 0.39, $CHCl_3$); lit.[7]: $[\alpha]_D$ = -29.3 (c = 0.4, $CHCl_3$); lit.[6]: $[\alpha]_D$ = -32.0 (c = 0.44, $CHCl_3$ for a 8:1 mixture of denticulatin B and A). IR 3400, 1714, 1704. ^{1}H-NMR: 0.92 (d, *J* = 7.0, 3 H), 0.94 (t, *J* = 7.3, 3 H), 0.96 (d, *J* = 7.0, 3 H), 1.01 (d, *J* = 7.0, 3 H), 1.05 (t, *J* = 7.3, 3 H), 1.16 (d, *J* = 7.0, 3 H), 1.20 (d, *J* = 7.0, 3 H), 1.61 (bs, 3

H), 1.63 (ddq, J = 2.6/7.0/10.7, 1 H), 1.69 (ddq, J = 1.5/2.6/7.0, 1 H), 1.72 (dd, J = 10.3/13.6, 1 H), 2.00 (dq, J = 7.3/7.3, 2 H), 2.29 (dd, J = 3.7/13.6, 1 H), 2.42 (dq, J = 7.0/17.7, 1 H), 2.52 (dq, J = 7.3/17.7, 1 H), 2.54 (dq, J = 3.0/7.0, 1 H), 2.70 (ddq, J = 3.7/7.0/10.3, 1 H), 2.94 (q, J = 7.0, 1 H), 3.21 (d, J = 8.8, 1 H(OH)), 3.56 (dt, J = 2.6/8.8, 1 H), 4.41 (dd, J = 3.0/10.7, 1 H), 5.18 (bt, J = 7.0, 1 H), 5.38 (d, J = 1.5, 1 H(OH)). ^{13}C-NMR: 219.40, 211.18, 131.34, 129.33, 102.00, 76.51, 69.18, 51.38, 46.90, 43.30, 42.11, 41.65, 37.57, 32.64, 21.23, 15.28, 14.68, 14.65, 14.24, 13.26, 12.67, 7.81, 7.44. CI HRMS: 378.2742 ($[C_{23}H_{38}O_4]^{+\cdot}$, calc. 378.2770).

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32. It was mentioned that also the nature of the protecting group of the β-oxygen bearing substituent plays a significant role, giving an attenuation of 1,3-stereoinduction with a *t*-butyldimethylsilyl protecting group relative to a *p*-methoxybenzyl ether: see ref. 31b.

33. We are indebted to Dr. Ian Paterson for kindly providing reference spectra and experimental details.

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35. Paterson and Perkins described the same aldol reaction but due to the lower enantiomeric purity of their aldehyde **3** (80% ee) aldol products **40** and **41** were obtained contaminated with C_{12}-epimeric aldol products in a 5 : 1 ratio (90%) and 3:1 ratio (80%) respectively.[7]

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