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Diastereoselective Reactions at Enantiomerically Pure, Sterically Congested Cyclohexanes as an Entry to Wailupemycins A and B: Total Synthesis of (+)-Wailupemycin B

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Abstract: Wailupemycin A (**1**) and B (**2**) are polyketide natural products with a highly substituted cyclohexanone core. Three different routes for the syntheses of these compounds were pursued, which commenced from either (*R*)-(−)-carvone (*ent*-**5**) or (*S*)-(+)-carvone (**5**). In the first approach it was attempted to construct the skeleton of wailupemycin A from triol **19** (nine steps from *ent*-**5**; 19% yield) by a sequence of diastereoselective epoxidation, nucleophilic ring opening at C-13 and carbonyl addition at C-5. The synthetic plan failed at the stage of the carbonyl addition to aldehyde **27**, which had been obtained in seven steps (18% yield) from triol **19**. The second route included an epoxide ring opening at C-13 and a carbonyl addition at C-7 as key steps. It could have led to either wailupemycin A or B depending on the diastereoselectivity of the addition step. Starting from allylic alcohol **30** (six steps from *ent*-**5**; 59% yield) the cyclohexanone **28** was obtained in five steps (54% yield). Unfortunately, the carbonyl addition failed also in this instance. In the eventually successful third attempt the skeleton of wailupemycin B was built from cyclohexanone **43** (eight steps from **5**; 53% yield) by highly diastereoselective carbonyl addition reactions at C-7 and C-12. The phenyl group at C-14 was introduced at a late stage of the synthetic sequence. Careful protecting group manipulation finally allowed for the total synthesis of (+)-wailupemycin B. The absolute and relative configuration of the natural product was unambiguously confirmed. The total yield of wailupemycin B amounted to 6% over 23 steps starting from (*S*)-(+)-carvone (**5**).

Keywords: antibiotics · asymmetric synthesis · ketones · polyketides · total synthesis

Introduction

Wailupemycin A (**1**) and wailupemycin B (**2**) are polyketide natural products the structures of which were elucidated by Davidson et al. in 1996 (Figure 1).[1] They were obtained together with other α-pyrone-containing metabolites from an actinomycete designated BD-26T(20). The organism was isolated from sediments collected at Wailupe beach park on the south-east shore of Oahu, Hawaii. From 40 L of fermentation broth 4 mg wailupemycin A and 7 mg wailupemycin B were obtained. Due to the limited amount of material a comprehensive antimicrobial assay was not possible. It was, however, shown in preliminary experiments that compound **1** shows inhibitory activity against *E. coli*. Our synthetic interest arose from the structurally unique, highly substituted cyclohexanone skeleton which is not precedented in common antibiotics.[2] Although the indication for antibacterial activity of either compound was limited, the possibility to establish a new class of antibiotics and the challenge to construct a sterically congested, enantiomerically pure six-membered ring was sufficient motivation for us to embark on a synthesis of the wailupemycins A and B. From a medicinal chemistry point of view, the possible decoration of the core with aromatic substituents different from phenyl (C-15 to C-21) and 6-oxopyran-2-yl (C1 to C5) could be a promising handle to further increase a potential activity of the wailupemycins.

According to the structure assignment by Davidson et al. wailupemycin A and B differ in the relative configuration at carbon atom C-7 and in the acetal part at C-14. Wailupemycin B (**2**) is characterized by a tricylic structure resulting from the formation of an intramolecular acetal between the *cis*-hydroxy groups at C-7 and C-9 and the carbonyl group at C-14. In wailupemycin A (**1**) an acetal formation is not feasible and the compound presents itself as a highly substi-

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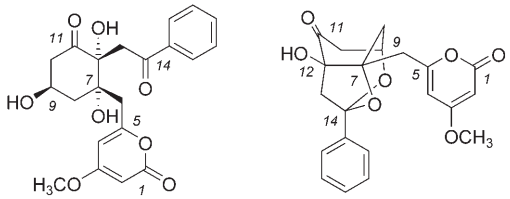
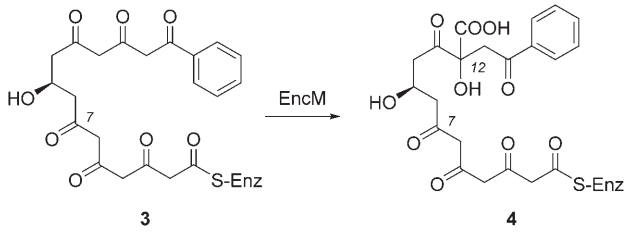


Figure 1. Proposed[1] structures of the natural products wailupemycin A and B isolated from the actinomycete BD-26T(20).



Scheme 1. Suggested[3] biosynthetic pathway to the biosynthetic wailupemycin precursor **4**.

tuted cyclohexanone. Biosynthetically, the compounds are formed by C–C bond formation between carbon atoms C-7 and C-12, that is, by cyclohexane ring closure from an open-chain precursor **4** (Scheme 1).[3] The linear octaketide **3**, which is derived from an uncommon benzoate starter[4] and seven malonate-SCoA units, undergoes a rare Favorskii-type oxidative rearrangement. The rearrangement accounts for the polarity reversal which is required for the crucial C-7/C-12 bond formation step in the biosynthesis of wailupemycin A and B. It is catalyzed by an oxidase ("favorskiiase") which is encoded by the gene encM,[5] a member of the enterocin gene cluster. The 21.3 kb Enc gene cluster from the marine bacterium *Streptomyces maritimus* has recently been cloned and sequenced.[6] Intermediate **4** is presumed to be also a key intermediate in the biosynthesis of the more abundant polyketide enterocin (vulgamycin)[7] and its deoxy-derivatives 5-deoxyenterocin and 3-*epi*-5-deoxyenterocin.

Despite the beauty of the natural pathway to wailupemycins A and B it appeared unlikely to implement the cyclization of an open-chain precursor into a laboratory synthesis. Our retrosynthetic analysis was therefore guided by the functional group pattern found in the target and by a structure-based analysis of possible starting materials. The central cyclohexane core of wailupemycins A and B is tetrasubstituted exhibiting a 1,2,3,5-relationship of substituents with stereogenic centers at three positions. Following this analysis, we were looking for a chiral pool starting material that would exhibit at least one defined stereogenic center and would allow for the direct functionalization of four positions in the above-mentioned relationship. The monoterpene carvone which is available in both enantiomeric forms **5** and *ent*-**5** (Figure 2) fulfilled this requirement almost ideally. The

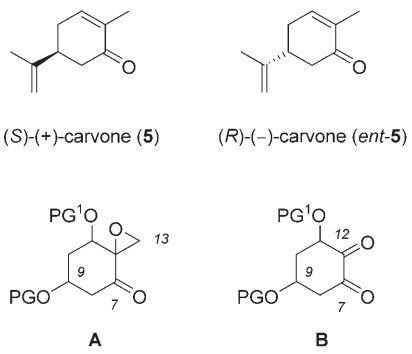


Figure 2. Structures of the two enantiomeric forms **5** and *ent*-**5** of carvone and of the general building blocks **A** and **B**.

isopropenyl substituent can be easily converted into a hydroxy group under retention of configuration[8] and the α,β-unsaturated ketone appeared to be an ideal starting point to establish functionality in a 1,2,3-pattern. In our synthetic endeavour, we followed two major strategies represented by the general structures **A** and **B** (Figure 2, PG = protective group). One strategy—represented by structure **A**—focussed on a C–C bond formation at C-7 by carbonyl addition and by epoxide ring opening at C-13 or vice versa. The other strategy—represented by structure **B**—aimed at a successive carbonyl addition at C-12 and at C-7. Concerning

Abstract in German: *Die Wailupemycine A (**1**) und B (**2**) sind polyketide Naturstoffe mit einem hochsubstituierten Cyclohexanongerüst. Zur Synthese dieser Verbindungen wurden drei verschiedene Routen eingeschlagen, die von natürlichem (R)-(−)-Carvon (ent-**5**) oder (S)-(+)-Carvon (**5**) ausgingen. Im ersten Anlauf wurde versucht, aus dem Triol **19** (neun Stufen aus ent-**5** in 19 % Ausbeute) über eine diastereoselektve Epoxiderung, eine nucleophile Ringöffnung an C-13 und eine Carbonyladdition an C-5 das Gerüst von Wailupemycin A aufzubauen. Die Reaktionssequenz scheiterte auf der Stufe der Carbonyladdition an Aldehyd **27**, der in sieben Stufen (18 % Ausbeute) aus dem Triol **19** erhalten worden war. Die zweite Route sah eine Epoxid-Ringöffnung an C-13 und eine Carbonyladdition an C-7 vor. Sie konnte je nach Diastereoselektivität des Additionsschritts zu Wailupemycin A oder B führen. Ausgehend von Allylalkohol **30** (sechs Stufen aus ent-**5** in 59 % Ausbeute) wurde das Cyclohexanon **28** in fünf Stufen (54 % Ausbeute) erhalten. Leider scheiterte auch hier die Carbonyladdition. Im schließlich erfolgreichen dritten Versuch wurde ausgehend von Cyclohexanon **43** (8 Stufen aus **5** in 53 % Ausbeute) das Gerüst des Wailupemycins B durch hoch diastereoselektive Carbonyladditionen an C-7 und C-12 aufgebaut. Die Phenylgruppe an C-14 wurde erst am Ende der Synthesesequenz eingeführt. Vorsichtige Schutzgruppenmanipulationen erlaubten schließlich die Totalsynthese des (+)-Wailupemycins B. Durch die Synthese wurden Relativ- und Absolutkonfiguration des Naturstoffs einwandfrei bestätigt. Die Gesamtausbeute betrug ausgehend von (S)-(+)-Carvon (**5**) 6 % über 23 Stufen.*

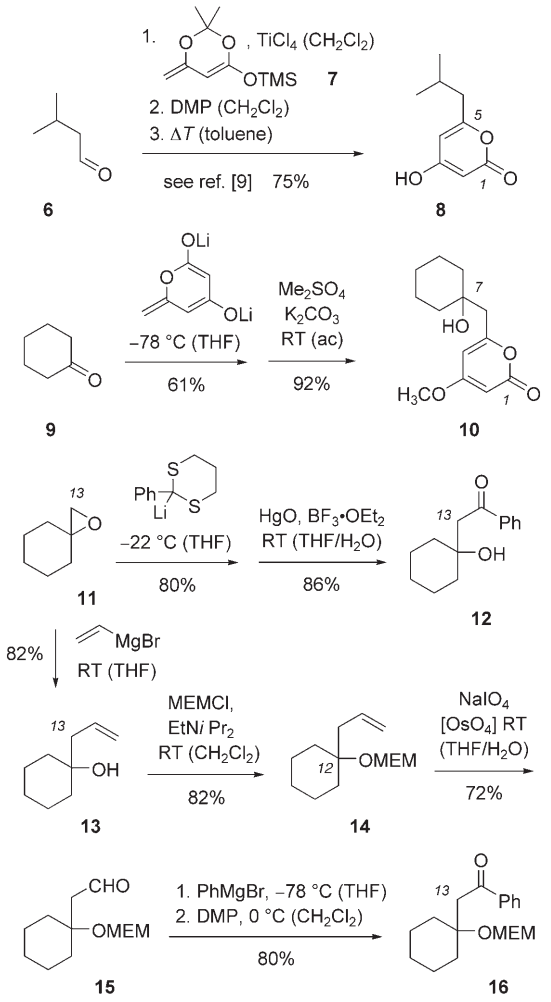
the protective groups PG and PG[1] we relied on orthogonal silyl ethers to protect the hydroxy groups at C-9 and C-11. The alcohol at C-9 was frequently protected with the robust *tert*-butyldiphenylsilyl (TBDPS) or triisopropylsilyl (TIPS) group, the alcohol at C-11 was often converted into the corresponding *tert*-butyldimethylsilyl (TBDMS) ether. Small protecting groups were used for the temporary protection of tertiary alcohols at C-7 and C-12 (Figure 1).

In the following sections we report the results of the individual approaches we followed. The study has provided several useful details on the reactivity of sterically congested cyclohexanes. While many of the synthetic approaches to wailupemycins A and B were performed parallel to each other they have to be now described in successive order. To keep this account within a reasonable page limit, several dead ends cannot be discussed extensively, some are not even mentioned. The story starts with our initial approaches according to a bond connection at C-7/C-13 and vice versa (strategy **A**). Subsequently, strategy **B** with a bond connection C-12/C-7 is discussed. It eventually culminated in a concise synthesis of enantiomerically pure wailupemycin B (**2**)[9] which served to unambiguously prove the absolute and relative configuration of the natural product.

Results and Discussion

Preliminary experiments were conducted to evaluate possible C–C-bond forming reactions at the different positions mentioned above (Scheme 2). Pyrone formation from different aldehydes was possible by addition of ketene acetal **7**,[10] oxidation with the Dess–Martin periodinane (DMP)[11] and ring closure.[12,13] Isovaleraldyde (**6**) for example was converted to pyrone **8** in 75% overall yield. Addition of an acetate enolate to a cyclohexanone at C-7 and subsequent reduction to an aldehyde would in combination with this three-step sequence allow for construction of the C-1/C-6 part of the wailupemycins. Alternatively, the direct introduction of a pyrone was attempted. The best method was found to be the addition of the dianion derived from 4-hydroxy-6-methyl-2*H*-pyran-2-one[14] to an appropriate ketone. Addition to cyclohexanone (**9**) and methylation for example yielded directly the desired pyrone **10**.

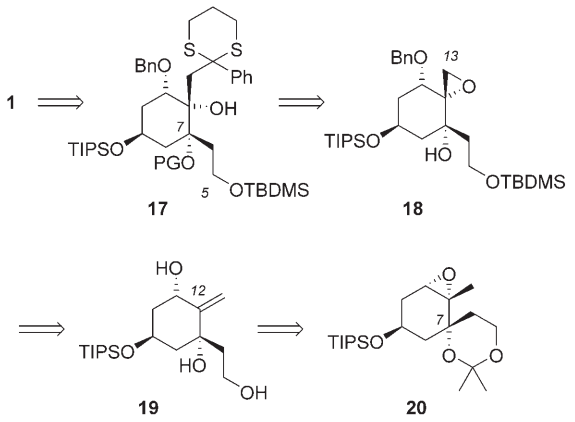
The epoxide ring opening at carbon atom C-13 with a benzoyl anion equivalent proceeded favorably by using a lithiated dithiane.[15] Removal of the dithiane was best achieved with HgO in the presence of $BF_3{\cdot}OEt_2$. Following this protocol, epoxide **11** was transformed into phenyl ketone **12** in an overall yield of 69%. An alternative sequence delivering the alcohol at carbon atom C-12 in protected form was feasible upon epoxide ring opening with vinyl magnesium bromide. The same alcohol **13** can of course be obtained by allyl metal addition to cyclohexanone, which is relevant to strategy **B** (see below). Methoxyethoxymethyl (MEM) protection[16] of alcohol **13** furnished the homoallylic ether **14** which was oxidized to aldehyde **15** and further converted into the protected β-hydroxyketone **16**. The ring opening of



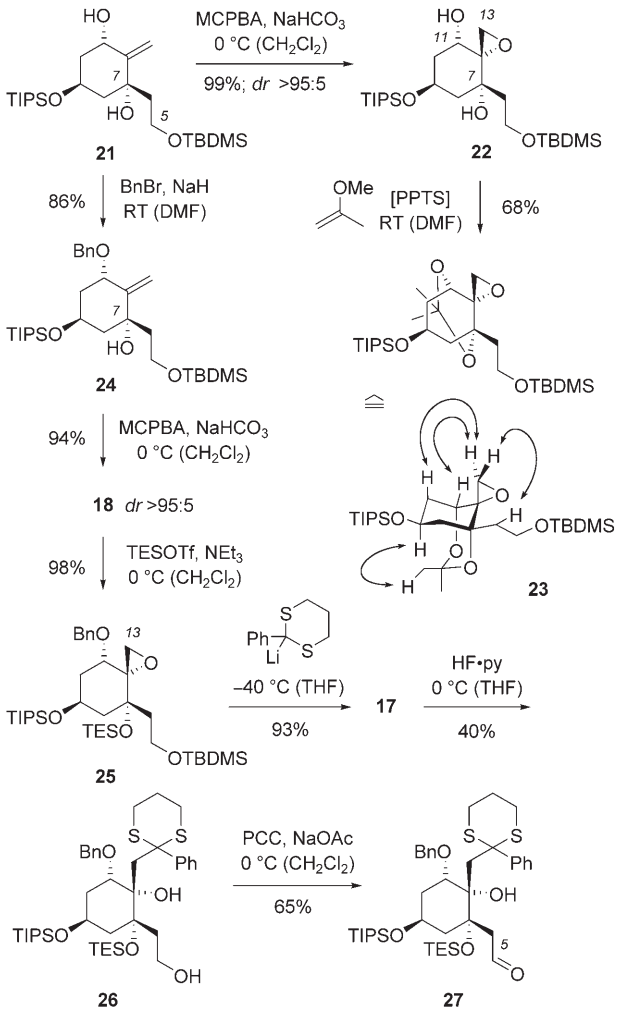
Scheme 2. Test reactions to evaluate possible C–C bond formation reactions at C-5, C-7 and C-13 of the wailupemycin skeleton.

epoxide **11** with an α-metalated styrene[17] was not possible under a variety of conditions.

C–C Bond formation at C-7, C-13 and C-5: Reactions at the double bond (e.g. epoxidation[18]) or at the carbonyl group (e.g. enolate addition[8a,19]) of carvone (**5**/*ent*-**5**) occur from the face opposite to the isopropenyl group.[20] Our initial plan relied on the hydroxy group at C-7 directing the epoxidation at C-11 and C-12 to establish the relative configuration of C-7 and C-12 in wailupemycin A.[21] Since the configuration at C-9 can be—after conversion of the isopropenyl into a hydroxy group—easily inverted (e.g. by a Mitsunobu reaction)[22] we envisaged a straightforward synthesis of wailupemycin A starting from (*R*)-(−)-carvone (*ent*-**5**). Enolate attack at the carbonyl group would establish the correct configuration at C-7, directed epoxidation would deliver the desired configuration at C-11 and C-12 and inversion at C-9 would adjust the configuration of the cyclohexane. As depicted in Scheme 3, wailupemycin A (**1**) was retrosynthetically traced back to the dithiane **17** which in turn was to be obtained from epoxide **18** by nucleophilic ring opening. Our



Scheme 3. Retrosynthetic analysis of wailupemycin A (**1**) based on a diastereoselective epoxidation and a C–C bond disconnection at C-4/C-5 and at C-13/C-14.



Scheme 4. Synthesis of the epoxides **18** and **23** from diol **21**, further conversion of epoxide **18** to aldehyde **25** and major NOESY contacts in epoxide **23**.

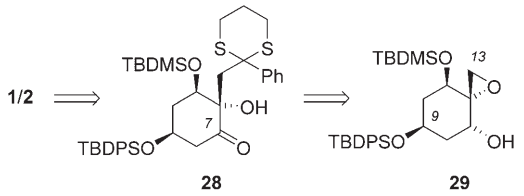
method for the construction of the α-pyrone from an aldehyde at C-5 (Scheme 2)[13] appeared to be compatible with the functional groups present in intermediate **17**. Epoxide **18** was to be prepared by directed epoxidation via allylic triol **19** which in turn was expected to evolve from epoxide **20** by elimination. The origin of the relative configuration in precursor **20** has already been explained (see above). Indeed, compound **20** had been prepared in an earlier study which aimed at an optimization of the desired epoxide elimination to an allylic alcohol.[23] It was obtained in eight steps from (*R*)-(−)-carvone (*ent*-**5**) with an overall yield of 31%.

The epoxide fragmentation to the desired allylic alcohol was initiated by treatment of **20** with diethylaluminum 2,2,6,6-tetramethylpiperidide (DATMP).[24] Upon acidic work-up (1N HCl) triol **19** was obtained (61% yield) and was selectively TBDMS-protected (TBDMSCl, imidazole in DMF, RT) at the primary alcohol site (C-5) to yield diol **21** (93%). The relative configuration of triol **19** was proven by single crystal X-ray crystallography.[23] Directed epoxidation with *meta*-chloroperbenzoic acid (MCPBA)[25] in the presence of $NaHCO_3$ delivered epoxide **22** in quantitative yield (Scheme 4). Since preliminary experiments had clearly indicated that free hydroxy groups are not compatible with an attempted nucleophilic epoxide ring opening, a suitable protection for the alcohols at C-7 and C-11 was looked for. Even small protecting groups, such as trimethylsilyl (TMS) or acetyl (Ac), could not be properly installed and we therefore had to rely on an acetonide protection of the two axial hydroxy groups. The formation of the tricyclic product **23** was sluggish (68% yield) but it allowed for an unambiguous assignment of the relative configuration by ^{1}H NMR NOESY experiments (Scheme 4). The attempted ring opening with the lithiated 2-phenyl-1,3-dithiane proceeded smoothly at −40 °C.[15] The newly generated hydroxy group, however, led to unexpected complications upon work-up and purification. Isomerization to five-membered acetonides occurred and decomposition was observed. An isomerization to a single protected product was impossible and consequently a deprotected tetraol with free hydroxy groups at positions C-5, C-7, C-11 and C-12 was the only product to be obtained (55% yield) after treatment with 1N HCl and $BF_3{\cdot}OEt_2$. Given the fact that a further protection would have been extremely tedious we looked for an alternative route to intermediates of type **17** (Scheme 3). To this end, the secondary alcohol at C-11 was benzyl (Bn)-protected and the resulting alcohol **24** was stereoselectively epoxidized to the above-mentioned epoxyalcohol **18**. Its relative configuration was proven by ^{1}H NMR NOESY experiments. Triethylsilyl (TES) protection was feasible at the C-7 hydroxy group and the silylated epoxy ether **25** underwent smooth ring opening to dithiane **17** (PG = TES). Disappointingly, the projected route could not be successfully completed from this intermediate. Without mentioning every single experiment we performed the bottom line was that an attack of the carbonyl group at C-5 with any given nucleophile was impossible. As an example, the selective deprotection of the TDBMS group to diol **26** is depicted in Scheme 4. Oxidation with pyridinium chlorochromate (PCC)[26] gave aldehyde **27** which was inert toward all attempted nucleophilic addition

reactions. Even the addition of methyl lithium or the reduction with $LiAlH_4$ did not proceed. Attempts to selectively attack the aldehyde at C-5 after dithiane deprotection (at C-14) were not successful, either.

To summarize this section, the hydroxy-directed epoxidation of sterically congested double bonds proved to be a reliable method for introducing the stereogenic center at carbon atom C-12. One axially positioned hydroxy group was sufficient (cf. alcohol **24**) to guarantee high stereocontrol. The dithiane moiety could be introduced nicely, but its steric bulk prohibited further reactions at carbon atom C-5. The tertiary alcohol at C-7 which was introduced early in the synthesis by carbonyl addition to carvone caused complications because it a) was almost impossible to protect and b) suppressed in unprotected form several straightforward reactions. We believed that the complete introduction of the pyrone fragment C-1 to C-6 (Scheme 2) after formation of the C-13/C-14 bond could be a remedy to avoid these complications.

C–C Bond formation at C-13 and C-7: We identified ketone **28** as an ideal precursor to test the feasibility of a C-7 ketone addition at a later stage of the synthesis. Irrespective of the facial diastereoselectivity, both product diols could be used as intermediates towards the wailupemycins, either as *cis*-1,2-diol for the synthesis of wailupemycin A (**1**) or as *trans*-1,2-diol for the synthesis of wailupymycin B (**2**). As suitable epoxide for ring opening we planned to employ compound **29** which in turn was to be formed by directed epoxidation (Scheme 5).



Scheme 5. Retrosynthetic analysis of wailupemycin A and B (**1**/**2**) based on a C–C bond disconnection at C-13/C-14 and at C-6/C-7.

In selecting the epoxide precursor there was a choice of allylic alcohol precursors readily available from either enantiomer of carvone. The correct configuration at carbon atom C-9 was to be based on the use of (*R*)-(−)-carvone (*ent*-**5**) as starting material. Following established methodology,[27,28] the alcohols **30**–**32** were available in 42–59% overall yield from *ent*-**5** in six steps (Figure 3). While allylic alcohol **32** is apparently unsuited for the desired directed epoxidation at C-12, the two alcohols **30** and **31** both have a directing hydroxy group at carbon atom C-7 the relative configuration of which appeared to be in accord with the desired epoxide formation at carbon atom C-12. Only alcohol **30**, however, can adopt a single chair conformation in which the hydroxy group resides in an axial position. Alcohol **31** is conformationally more flexible and directed reactions were expected to proceed with less stereocontrol. Indeed, epoxidations

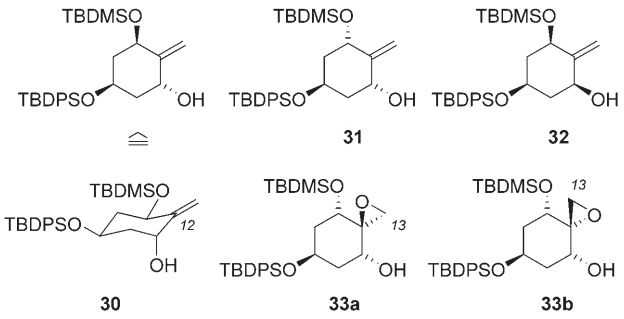
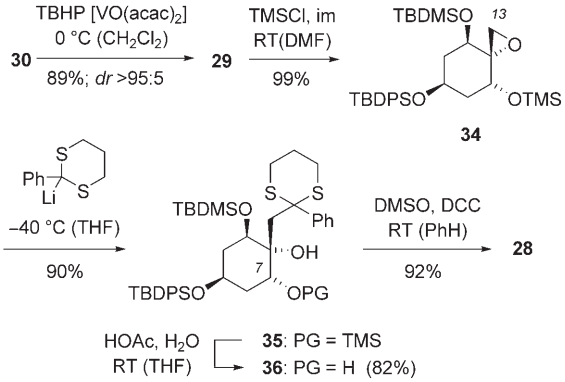


Figure 3. Structure of the allylic alcohols **30**–**32** obtained from (*R*)-(−)-carvone (*ent*-**5**)[28] and of the epoxidation products **33** of allylic alcohol **31**.

with either *tert*-butyl hydroperoxide (TBHP) and $VO(acac)_2$ (acac = acetyl acetone) as the catalyst[29] or with MCPBA led to a 1:1 mixture of diastereoisomers **33a** and **33b**.

In pleasant contrast to the latter observation, the epoxidation of allylic alcohol **30** proceeded with excellent facial diastereoselectivity. MCPBA epoxidation (0 °C, CH_2Cl_2) furnished the epoxide **29** as a single diastereoisomer in 71% yield. The $VO(acac)_2$-catalyzed reaction was even superior in this instance (Scheme 6) delivering the desired product in



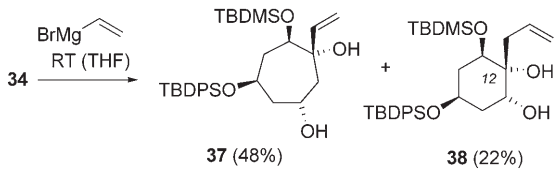
Scheme 6. Synthesis of ketone **28** from allylic alcohol **30** by diastereoselective epoxidation and nucleophilic epoxide ring opening.

89% yield.[29] TMS protection of the hydroxy group at C-7 proceeded quantitatively and paved the way for the desired ring opening. Again, lithiated 2-phenyl-1,3-dithiane proved to be a reliable reagent for the regio- and chemoselective epoxide ring opening and epoxide **34** was converted into tertiary alcohol **35** and, again, the hydroxy group protection was required to allow for the reaction. Alcohol **29** did not react with the lithiated dithiane. TMS deprotection was selectively attained by the use of aqueous acetic acid to yield secondary alcohol **36**. Pfitzner–Moffatt oxidation was the superior method for the oxidation to ketone **28**.[30,31] Cr^{VI} reagents led to glycol cleavage reactions and I^{V} oxidants attacked the dithiane part of the molecule. Attempts to temporarily protect (TMS, MEM, Ac) the sterically congested tertiary alcohol at C-12 in compounds **28** (after oxidation) or **35** (prior to oxidation) failed.

Disappointingly, the α-hydroxyketone **28** did not react with a nucleophile to allow for the desired C-6/C-7 bond formation. All synthetic equivalents for an α-metalated 4-methoxy-6-methyl-2*H*-pyran-2-one, including the dianion derived from 4-hydroxy-6-methyl-2*H*-pyran-2-one (Scheme 2), did not attack the carbonyl group. With 10 equivalents of this reagent elimination to an α,β-unsaturated cyclohexenone but no addition was observed. The reasons for the low electrophilicity of ketone **28** are linked either directly or indirectly to the steric bulk of the dithiane moiety. Based on ^{1}H NMR NOESY measurements compound **28** adopts a chair conformation with the silyloxy (C-9, C-11) and oxy (C-12) groups in equatorial position. The (2-phenyldithian-2-yl)methyl substituent resides in an axial position prohibiting the attack to the carbonyl group from the *Si* face. The *Re* face attack is impossible due to 1,3-diaxial interactions and due to Coulomb repulsion between the alkoxide (C-12) and the incoming nucleophile. The tertiary alcohol at C-12 in turn had to remain unprotected because the size of the dithiane did not allow a temporary protection.

In other experiments (see below), we noted that cyclohexanones which do *not* populate a chair conformation are much more difficult to attack by a nucleophile than conformationally restricted cyclohexanones.

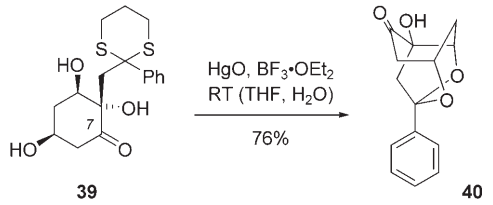
As a detour to build the required phenyl ketone, we briefly looked into the vinyl Grignard ring-opening sequence (**11** → **16**, Scheme 2) and attempted to open epoxide **34** with a vinyl magnesium reagent rather than with a lithiated dithiane. Surprisingly, the major pathway of this reaction was not the ring opening to homoallylic alcohol **38**. Instead, a pinacol-type rearrangement generated a β-hydroxyketone, which was subsequently trapped by the Grignard reagent to yield cycloheptanediol **37** (Scheme 7).



Scheme 7. Attempted ring opening of epoxide **34** with vinyl magnesium bromide.

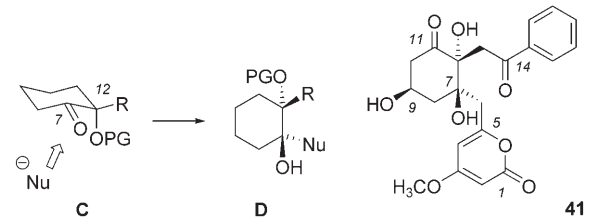
Although the ring opening product could be made the major product by conducting the epoxide attack in the presence of CuI (53% yield) we did not further follow this route. There were several reasons for this decision. First, the protection of the tertiary alcohol at C-12 would require a laborious protection/deprotection strategy if it could be protected at all. Secondly, the relative configuration of the O-protected ketone derived from alcohol **38** would not favor a single chair conformation. Thirdly, access to ketones of this type was easier to achieve by allyl magnesium addition to a C-12 ketone (strategy **B** in Figure 2).

The ketal ring closure to wailupemycin B was modelled in a final experiment of this series. Ketone **28** was silyl deprotected with HF·py (0 °C, THF) to yield triol **39**, which upon treatment with HgO and $BF_3{\cdot}OEt_2$ cyclized to the expected cyclic ketal **40** (Scheme 8). The result nicely illustrated the high preference for intramolecular ketal formation in triols of this type and encouraged further work directed towards the synthesis of wailupemycin B (**2**).



Scheme 8. Deprotection and intramolecular ketalization of dithiane **39**.

C–C Bond formation at C-12 and C-7: An analysis of the consecutive bond-formation steps according to strategy **B** (Figure 2) revealed that the *trans*-1,2-diol found in wailupemycin B is much more readily formed than the *cis*-1,2-diol of wailupemycin A. Attack with a reasonably large nucleophile, for example, the dianion derived from 4-hydroxy-6-methyl-2*H*-pyran-2-one, on a ketone of general structure **C** can only occur as an equatorial attack leading to the axial alcohol **D**. Even if R is an allyl or another relatively small carbon substituent, any attempt to override its preference for an equatorial position, for example, by enlarging the size of the O-PG group or by utilizing the relative configuration of the protected hydroxy groups at C-9 or C-11, appeared unsensible. On the contrary, it was our notion that a strong attempt should be made to choose the protected hydroxy groups at C-9 or C-11 so that a single chair conformation of an appropriate ketone was strongly preferred. For comparison, the open-chain isomer **41** of wailupemycin B is drawn in Scheme 9.



Scheme 9. Facial diastereoselectivity of a nucleophilic approach to cyclohexanone **C** and structure of the open-chain isomer **41**.

Another question to be addressed was related to the configuration at the stereogenic carbon atom C-12. It is defined in the diastereoselective addition step of a given acetophenone enolate equivalent to a chiral C-12 ketone. In our case, several ketones were available starting from either enantiomer of carvone. They are readily prepared from the abovementioned alkenes **30**–**32** (Figure 3) or their enantiomers by

TMS protection (C-7) and ozonolytic cleavage.[28] In preliminary experiments, only two ketones **42** and **43**—both prepared from (*S*)-(+)-carvone (**5**)—allowed for an unequivocal attack in favor of the correct absolute configuration at C-12 required for wailupemycin B (Figure 4). The question which

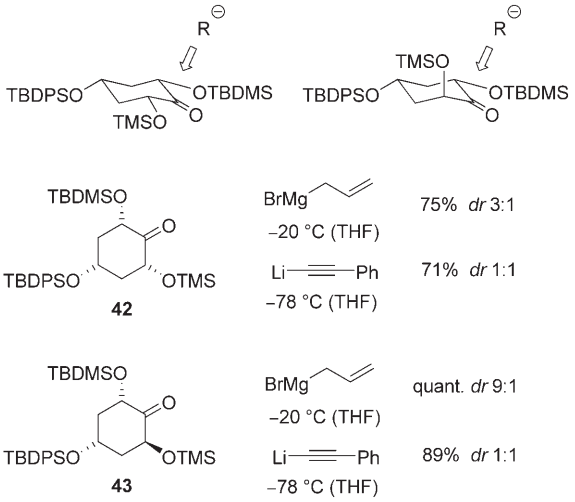
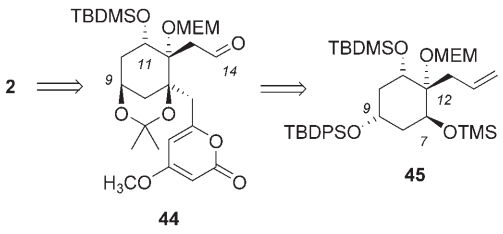


Figure 4. Facial diastereoselectivity of a nucleophilic approach to cyclohexanones **42** and **43** with allyl magnesium bromide and 2-phenylethynyl lithium.

acetophenone enolate equivalent was to be employed could also be answered in these studies. Allyl magnesium bromide gave much higher diastereoselectivities than 2-phenylethynyl lithium. The observation is in line with previous studies on the nucleophilic addition to cyclohexanones.[19,20,32] The sterically least congested equatorial trajectory is favored for large nucleophiles whereas small nucleophiles approach cyclohexanones axially. A surprising observation was the fact that the all-equatorial cyclohexanone **42** reacted with allyl magnesium bromide in lower yields and with lower diastereoselectivity than cyclohexanone **43**.

While it was tempting to introduce the phenyl ring already with a suitable allyl Grignard reagent, for example, with 2-phenylallyl magnesium bromide, we discarded this idea. Previous experience had shown that the substituent at C-12 should be as small as possible. Based on the preliminary work (Scheme 2) we were optimistic that the conversion of the allyl group to a benzoylmethyl substituent would succeed after MEM protection of the tertiary alcohol. Consequently, we adjusted our retrosyntethic plan aiming at allyl addition product **45** as initial key intermediate (Scheme 10). The second key intermediate **44** was certainly not envisioned with this set of protecting groups—they rather accommodated synthetic needs in the real synthesis - but it reflects the crucial synthetic steps: a) pyrone addition, b) inversion of configuration at C-9, c) complete protection of hydroxy groups and d) ozonolytic cleavage of the double bond. From intermediate **44** the completion of the synthesis by carbonyl addition, oxidation at C-14, deprotection and oxidation at C-11 as well as complete deprotection appeared

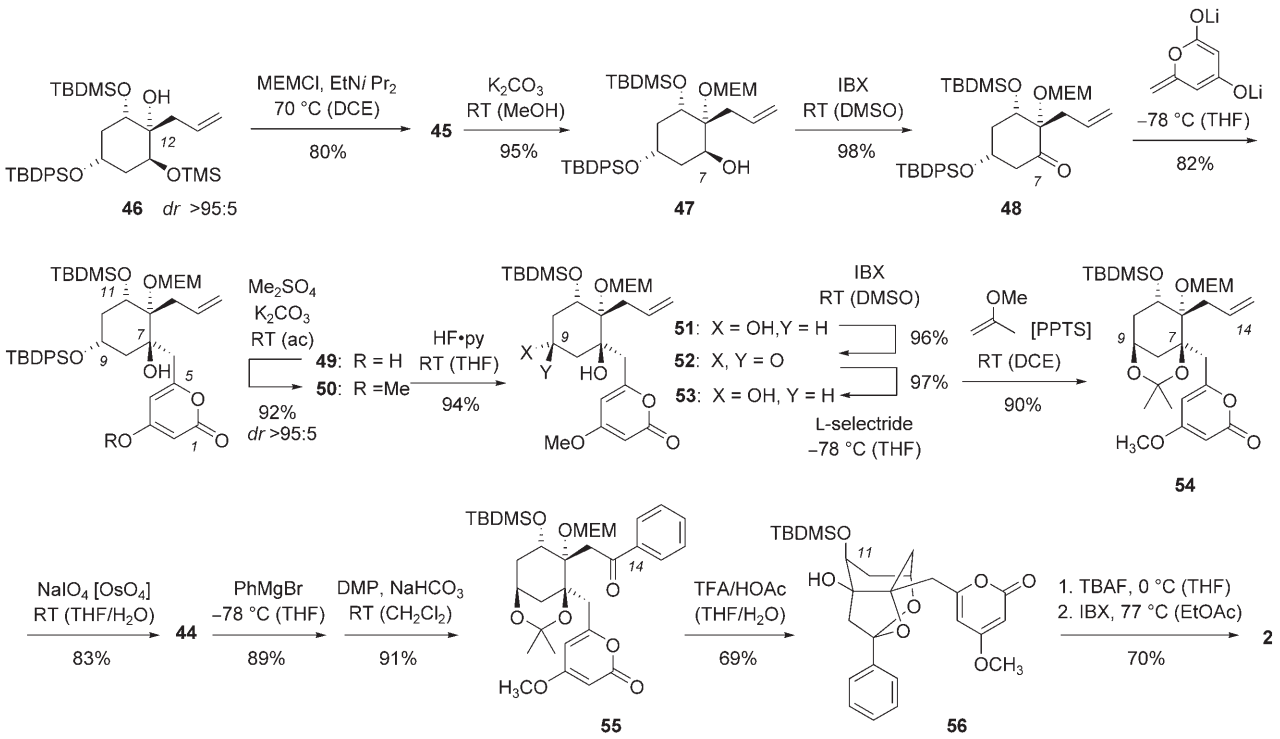


Scheme 10. Retrosynthetic analysis of wailupemycin B (**2**) based on a C–C bond disconnection at C-12/C-13, at C-6/C-7, and at C-14/C-15.

straightforward based on the facile ketalization we had earlier observed for the model system **40** (Scheme 8).

In a forward direction the synthesis commenced with the above-mentioned MEM ether **45** which was obtained from the allyl Grignard addition product **46** by MEM protection (Scheme 11).[33] The diastereomeric ratio (*dr*) was determined after MEM protection to be >95:5. Deprotection of the TMS ether at C-7 was achieved by treatment of compound **45** with K_2CO_3 in methanol. The secondary alcohol **47** was oxidized with 2-iodoxybenzoic acid (IBX)[34] to ketone **48**.[35,36] The dianion generated from 4-hydroxy-6-methyl-2*H*-pyran-2-one by deprotonation with *tert*-butyl lithium added diastereoselectively to this ketone and yielded the tertiary alcohol **49**. In order to achieve a high facial diastereoselectivity, the addition was conducted at low temperature (−78 °C), at which the reaction was slow. Even after 2 d it did not go to completion (64% yield) and starting material was recovered (22% yield). The unstable hydroxypyranone (*dr* 93:7) was immediately methylated with dimethyl sulfate in the presence of K_2CO_3. Product **50** obtained after methylation and purification was diastereomerically pure (*dr* >95:5).

Originally, we had planned to subsequently remove the TBDMS group at C-11 and to form the C-11 ketone prior to inverting the configuration at C-9.[37] While the TBDMS and MEM deprotection was possible under acidic conditions ($ZnBr_2$, $CeCl_3$ in MeCN) leaving the TBDPS group untouched it turned out that the TBDPS-protecting group at C-9 was selectively cleaved under standard silyl deprotection conditions (HF·py in THF). Since the inversion of configuration at C-9 appeared feasible with alcohol **51** it was attempted by an oxidation–reduction sequence. Indeed, oxidation to ketone **52** proceeded smoothly and the subsequent hydride addition occurred selectively from the equatorial position if $LiHB(sBu)_3$ (L-selectride) was used as the reducing agent. $NaBH_4$ gave predominantly the starting material **51** (*dr* 80:20) approaching the conformationally locked cyclohexanone **52** from the axial position. The two axial hydroxy groups at C-7 and C-9 could be protected as the cyclic isopropylidene acetal **54** upon treatment of diol **53** with 2-methoxy propene in the presence of pyridinium *para*-toluene sulfonate (PPTS). At this stage the elaboration of the terminal olefin to the benzoyl group commenced. The oxidative double bond cleavage was conducted as in the previous model study (**14** → **15**, Scheme 2) by the Lemieux–Johnson method.[38] Grignard addition to aldehyde **44** and imme-



Scheme 11. Total synthesis of wailupemycin B (**2**) starting from the allyl addition product **46**, which in turn was obtained from (*S*)-(+)-carvone (**5**) in nine steps and 53% overall yield.

diate oxidation provided access to ketone **55**. The combination of Dess–Martin periodinane/$NaHCO_3$ was the only oxidant that effected the required oxidation but left the acetal protecting groups untouched.[39] Swern-,[40] PCC-,[26] and pyridinium dichromate(PDC) oxidation[41] led to concomitant deprotection reactions whereas IBX,[34–36] tetrapropylammonium perruthenate (TPAP),[42] 2,2,6,6-tetramethylpiperdine nitroxyl (TEMPO),[43] or MnO_2[44] did not oxidize the secondary alcohol and starting material was recovered. TBDMS deprotection at C-11 was impossible under basic conditions in the presence of the adjacent MEM ether and it was therefore decided to attempt the oxidation to the C-11 ketone after formation of the wailupemycin B skeleton. In the tricyclic core the TBDMSO group at C-11 should be in an exposed axial position. The acetal protecting groups could be completely removed under carefully selected conditions in a 1:2:2:4 mixture of trifluoroacetic acid (TFA), acetic acid, water, and THF and the cyclic ketal **56** was formed. Tetrabutylammonium fluoride (TBAF) effected the deprotection of the remaining silyl ether and an IBX oxidation to wailupemycin B (**2**) completed the synthesis. Conventional IBX oxidation in DMSO with an aqueous work-up and ether extraction was not favorable due to the low solubility of wailupemycin B in diethyl ether. Instead, the Finney protocol[45] was followed according to which the IBX oxidation is conducted in refluxing ethyl acetate.

Overall, the total synthesis proceeded in 23 steps starting from (*S*)-(+)-carvone (**5**) and in 6% overall yield. The identity of the synthetic material to the natural product was proven by comparison of the spectroscopic data (NMR, $[\alpha]_D^{20}$). The relative configuration of intermediates (e.g. **54**) was proven by ^{1}H NMR NOESY studies.[9]

The unexpected higher reactivity of the TBDPS group at C-9 as compared with the TBDMS group at C-11 in intermediate **50** may raise the question why the protection was not more conveniently conducted with a twofold TBDMS protection at C-9 and C-11. The corresponding ketone **57** was quickly prepared in analogy to ketone **48**. It failed, however, to provide the same selectivities in the subsequent addition step. While the dianion generated from 4-hydroxy-6-methyl-2*H*-pyran-2-one added to ketone **48** after 2 d in THF at −78 °C in 64% yield and with a *dr* 93:7, the addition to ketone **57** proceeded only in 52% yield and with a *dr* of 83:17.

The previously mentioned conformational arguments are important in all addition steps to these sterically congested cyclohexanones. Ketone **58** may serve as an example (Figure 5). NOESY studies and analysis of its coupling constants clearly indicated that this ketone does not adopt a chair conformation. A nucleophilic addition to the carbonyl group was impossible.

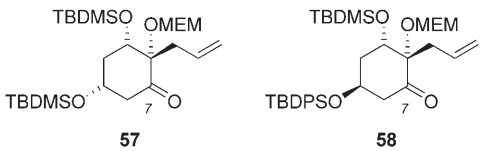
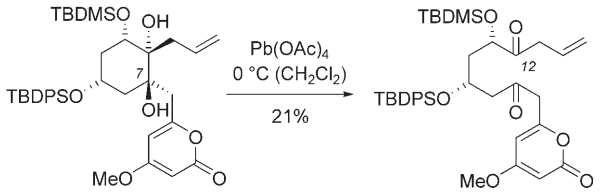


Figure 5. Structure of the ketones **57** and **58**, which were also tested for a diastereoselective C–C bond formation at carbon atom C-7.

Attempted C–C bond formation between C-12 and C-7: While strategy **B** had provided a straightforward entry to wailupemycin B (**2**), it appeared to be less suited for the synthesis of wailupemycin A (**1**). Since all other approaches had not led to a feasible synthetic route to **1**, either, we attempted as the final strategy a "biomimetic" approach aiming at a bond construction between carbon atoms C-12 and C-7. MEM deprotection of compound **50** yielded the diol **59** which could be oxidatively cleaved to diketone **60**. Due to the *trans*-diaxial relationship of the hydroxy groups at C-7 and C-12 the yield in the cleavage was not high but the amount of material was sufficient to attempt a reasonable number of pinacol coupling reactions. None of them, however, gave a hint on the formation of a diol, be it compound **59** or the desired diastereoisomer (Scheme 12).



59 **60**

Scheme 12. Preparation of the acyclic diketone **60** from diol **59** by diol cleavage.

Conclusion

In summary, three approaches to the synthesis of wailupemycins A and B have been described. They were all based on the use of enantiomerically pure carvone as starting material but differed in the chosen bond set. In the first approach, it was impossible to add a C_4 fragment to the aldehyde carbon atom C-5 of key intermediate **27**. The low reactivity of the electrophile was attributed to the steric shielding of the reaction center by the adjacent dithiane. In the second approach, attempts to introduce the 4-methoxy-6-oxopyran-2-ylmethyl group (C-1 to C-6) by addition to an appropriate ketone (**28**) were unsuccessful. Besides the steric bulk of the substituents at the cyclohexanone, the ring conformation was found to play a decisive role as to success of the carbonyl additions. Implementing these observations a final approach was conducted which aimed at successive bond formations at carbon atoms C-12 and C-7. By adjusting the configuration of the hydroxy substituents at C-9 and C-11, cyclohexanones were prepared starting from (*S*)-(+)-carvone (**5**), in which an unequivocal chair conformation was set up and in which an equatorial nucleophilic approach was possible. After appropriate protecting and functional group manipulations the strategy turned out to be successful and wailupemycin B was synthesized in 23 steps and an overall yield of 6% starting from (*S*)-(+)-carvone (**5**). An appealing aspect of our synthetic route is the possibility to replace the peripheral aromatic substituents by other arenes and hetarenes.

Experimental Section

General: All reactions involving water-sensitive chemicals were carried out in flame-dried glass ware with magnetic stirring under Ar. Common solvents [pentane (P), methanol (MeOH), ethanol (EtOH), ethyl acetate (EtOAc), tetrahydrofuran (THF), diethyl ether (Et_2O), CH_2Cl_2] were distilled prior to use. All other reagents and solvents were used as received. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ unless otherwise noted. Chemical sifts are reported relative to $CHCl_3$. Apparent multiplets which occur as a result of accidental equality of coupling constants to those of magnetically nonequivalent protons are marked as virtual (virt.). TLC was performed on aluminum sheets (0.2 mm silica gel 60 F_{254}) with detection by UV (254 nm) or by coloration with ceric ammonium molybdate (CAM). Flash chromatography[46] was performed on silica gel 60 (230–400 mesh) (ca. 50 g for 1 g of material to be separated), with the indicated eluent. Compounds **20**,[23] **30**,[28] and **43**[28] were prepared according to known procedures.

4-Methoxy-6-[(1-hydroxycyclohexyl)methyl]-2*H*-pyran-2-one (10): 4-Hydroxy-6-methyl-2*H*-pyran-2-one (630 mg, 5 mmol) was dissolved in THF (60 mL). The solution was cooled to −78 °C, and a solution of *t*BuLi in pentane (1.5 M; 10 mmol, 6.7 mL) was added dropwise. After stirring the orange solution for 15 min at −78 °C, the mixture was warmed to 0 °C. The solution was stirred for 20 min at 0 °C, then cooled to −78 °C. A solution of cyclohexanone (0.15 mL, 147 mg, 1.5 mmol) in THF (5 mL) was added. The reaction mixture was stirred for additional 20 min at −78 °C and then warmed to RT over a period of 3 h. The reaction was quenched by addition of sat. aqueous NH_4Cl (100 mL). The mixture was acidified with aqueous H_2SO_4 (10%) to pH 2. After addition of Et_2O (200 mL) and water (200 mL), the layers were separated. The aqueous layer was extracted with Et_2O (2×150 mL). The combined organic layers were washed with water (200 mL) and brine (200 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 30:70) to give 4-hydroxy-6-[(1-hydroxycyclohexyl)methyl]-2*H*-pyran-2-one as a yellow oil (205 mg, 0.92 mmol, 61%). R_f=0.05 (P/EA 50:50) [CAM]; ^1H NMR (250 MHz, [D$_6$]DMSO): δ= 1.53–1.96 (m, 10H), 2.85 (s, 2H), 3.75 (brs, 1H, OH), 4.72 (brs, 1H, OH), 5.60 (s, 1H), 6.32 (s, 1H); ^{13}C NMR (90.6 MHz, [D$_6$]DMSO): δ= 21.7 (t), 25.4 (t), 37.2 (t), 46.4 (t), 70.0 (s), 88.6 (d), 102.5 (d), 164.0 (s), 164.3 (s), 170.4 (s).

4-Hydroxy-6-[(1-hydroxycyclohexyl)methyl]-2*H*-pyran-2-one (180 mg, 0.8 mmol) was dissolved in dry acetone (10 mL) and was stirred with K_2CO_2 (300 mg) and dimethyl sulfate (0.15 mL, 202 mg, 1.6 mmol) at RT for 12 h. The mixture was diluted with Et_2O (150 mL) and water (150 mL), the layers were separated. The organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 50:50) to give **10** as a colorless oil (175 mg, 0.74 mmol, 92%). R_f=0.20 (P/EA 50:50) [CAM]; ^1H NMR (250 MHz): δ=1.17–1.36 (m, 1H), 1.41–1.55 (m, 9H), 2.14 (brs, 1H, OH), 2.53 (s, 2H), 3.73 (s, 3H), 5.36 (d, J=2.1 Hz, 1H), 5.84 (d, J= 2.1 Hz, 1H); ^{13}C NMR (62.9 MHz): δ=21.9 (t), 25.3 (t), 37.4 (t), 46.3 (t), 55.7 (q), 71.1 (s), 87.7 (d), 102.5 (d), 162.3 (s), 164.8 (s), 171.0 (s); IR (neat): $\tilde{\nu}$=3432 (brs, OH), 2933, 2858 (vs, C_{sp^3}-H), 1698 (vs sh, C=O), 1643 (s), 1565 (vs), 1456 (s), 1411 (s), 1249 (vs), 1146 (s), 1035 (s), 984 cm^{-1} (m); MS (EI, 70 eV): m/z (%): 238 (1) [M^+], 140 (100), 125 (8), 81 (10); elemental analysis calcd (%) for $C_{13}H_{18}O_4$ (238.28): C 65.53, H 7.61; found: C 65.81, H 7.75.

1-(2-Oxo-2-phenylethyl)cyclohexanol (12): A solution of *n*BuLi in hexanes (1.3 M, 2 mmol, 1.6 mL) was added at −40 °C to a solution of 2-phenyl-1,3-dithiane[15a] (392 mg, 2.0 mmol) in dry THF (6 mL). The resulting solution was stirred for 2 h at −30 °C. Then the orange solution was cooled to −78 °C. A solution of 1-oxaspiro[2.5]octane[47] (**11**) (168 mg, 1.5 mmol) in THF (2 mL) was added slowly. The reaction mixture was stirred for 1 h at −78 °C. Then the mixture was allowed to stand for 2 d at −22 °C. The reaction was quenched by addition of sat. aqueous NH_4Cl (25 mL). The mixture was extracted with CH_2Cl_2 (2×50 mL). The combined organic layers were washed with water (100 mL) and brine (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 90:10) to

give 1-(2-phenyl-1,3-dithian-2-ylmethyl)-1-cyclohexanol as a colorless oil (370 mg, 1.2 mmol, 80%). R_f=0.59 (P/EA 80:20) [CAM] [UV]; ^{1}H NMR (300 MHz): δ=1.29–1.63 (m, 10H), 2.02–2.10 (m, 3H), 2.51 (s, 2H), 2.81–2.89 (m, 4H), 7.24–7.39 (m, 1H), 7.46–7.51 (m, 2H), 8.02–8.05 (m, 2H); ^{13}C NMR (50.3 MHz): δ=22.3 (t), 25.1 (t), 25.9 (t), 28.3 (t), 39.3 (t), 55.5 (t), 57.2 (s), 73.5 (s), 127.7 (d), 128.9 (d), 129.1 (s), 142.5 (d).

A solution of 1-(2-phenyl-1,3-dithian-2-ylmethyl)-1-cyclohexanol (40.0 mg, 0.13 mmol) in THF (2 mL) was added dropwise to a suspension of red mercury(II) oxide (56.3 mg, 0.26 mmol) and BF_3·OEt_2 (0.07 mL, 36.9 mg, 0.26 mmol) in aqueous THF (2 mL, 15% in water) at RT. The mixture was stirred at RT for 30 min, diluted with Et_2O (10 mL). The layers were separated. The organic layer was washed with sat. aqueous $NaHCO_3$ (2×10 mL) and brine (20 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 70:30) to give the known compound **12**[48] as a colorless oil (24.3 mg, 0.11 mmol, 86%). R_f=0.28 (P/EA 80:20) [CAM] [UV]; ^{1}H NMR (250 MHz, [D$_6$]DMSO): δ=1.23–1.78 (m, 10H), 3.04 (s, 2H), 3.35 (br s, 1H, OH), 7.45–7.60 (m, 3H), 7.96–8.00 (m, 2H); ^{13}C NMR (50.3 MHz, [D$_6$]DMSO): δ=21.9, 25.6, 37.8, 47.6, 70.7, 128.7, 128.8, 133.1, 138.6, 200.3.

1-Allylcyclohexanol (13): A solution of vinylmagnesium bromide in THF (1.0 M, 10 mmol, 10 mL) was added at RT to a solution of 1-oxaspiro-[2.5]octane[47] (**11**) (1.12 g, 10 mmol) in dry THF (30 mL). The solution was stirred for 1 h at RT. The reaction was quenched by addition of sat. aqueous NH_4Cl (50 mL) and diluted with water (100 mL). The mixture was extracted with Et_2O (250 mL). The layers were separated. The organic layer was washed with water (100 mL) and brine (150 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 80:20) to give **13** as a colorless oil (1.15 g, 8.2 mmol, 82%). R_f=0.41 (P/EA 80:20) [CAM]. ^{1}H NMR (360 MHz): δ=1.30–1.62 (m, 10H), 1.67 (s, 1H, OH), 2.12 (d, J=7.5 Hz, 2H), 4.98–5.06 (m, 2H), 5.74–5.86 (m, 1H); ^{13}C NMR (90.6 MHz): δ=22.0 (t), 25.6 (t), 37.2 (t), 46.6 (t), 70.7 (s), 118.2 (t), 133.7 (d); IR (neat): $\tilde{\nu}$=3420 (br s, OH), 3077 (m, C_{sp^2}-H), 2928 (s, C_{sp^3}-H), 636 (s), 1460 (s), 971 (s), 932 cm^{-1} (vs); MS (EI, 70 eV): m/z (%): 140 (1) [M^+], 99 (100) [$M^+-C_3H_5$], 81 (95), 55 (64), 41 (28); elemental analysis calcd (%) for $C_9H_{16}O$ (140.22): C 77.09, H 11.50; found: C 76.43, H 11.40.

1-(2-Methoxyethoxymethoxy)-1-allylcyclohexane (14):[16] Diisopropylethylamine (3.6 mL, 21 mmol) and MEM chloride (1.6 mL, 14 mmol) were added at 0°C to a solution of **13** (1.0 g, 7.1 mmol) in 1,2-dichloroethane (20 mL). The solution was stirred for 15 h at RT. The reaction was quenched by addition of sat. aqueous $NaHCO_3$ (150 mL). The aqueous layer was extracted with Et_2O (2×150 mL). The layers were separated. The combined organic layers were washed with water (200 mL) and brine (200 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 90:10) to give **14** as a colorless oil (1.33 g, 5.8 mmol, 82%). R_f=0.48 (P/EA 80:20) [CAM]; ^{1}H NMR (360 MHz): δ=1.19–1.71 (m, 10H), 2.27 (dt, J=7.2, 1.2 Hz, 2H), 3.35 (s, 3H), 3.51 (t, J=5.0 Hz, 2H), 3.72 (t, J=5.0 Hz, 2H), 4.78 (s, 2H), 4.96–5.00 (m, 2H), 5.74–5.83 (m, 1H); ^{13}C NMR (90.6 MHz): δ=22.0 (t), 25.6 (t), 34.8 (t), 42.9 (t), 58.9 (q), 67.2 (t), 71.8 (t), 77.1 (s), 89.4 (t), 117.2 (t), 134.2 (d); IR (neat): $\tilde{\nu}$=3071 (m, C_{sp^2}-H), 2958, 2922 (vs, C_{sp^3}-H), 1470 (vs), 1055 cm^{-1} (vs br); MS (EI, 70 eV): m/z (%): 187 (5), 153 (7), 123 (15), 89 (100) [$CH_2OCH_2CH_2OCH_3^+$], 81 (32), 59 (98) [$CH_3OCH_2CH_2^+$]; elemental analysis calcd (%) for $C_{13}H_{24}O_3$ (228.33): C 68.38, H 10.59; found: C 68.38, H 10.50.

2-[1-(2-Methoxyethoxymethoxy)cyclohexyl]acetaldehyde (15):[38] Ether **14** (393 mg, 1.72 mmol) was dissolved in THF (10 mL) and water (10 mL) at RT. To this mixture was added a solution of OsO_4 in water (1%; 0.04 mL) and $NaIO_4$ (0.95 g, 4.4 mmol) subsequently. The mixture was stirred for 3 h at RT. The precipitate was filtered. The residue was washed with Et_2O (50 mL). The filtrate was diluted with Et_2O (100 mL) and water (100 mL). The layers were separated. The aqueous layer was extracted with Et_2O (2×100 mL). The combined organic layers were washed with sat. aqueous $NaHCO_3$ (200 mL) and brine (200 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 80:20) to give **15** as a colorless oil (285 mg, 1.24 mmol, 72%). R_f=0.24 (P/EA 80:20) [CAM]; ^{1}H NMR (360 MHz): δ=1.30–1.89 (m, 10H), 2.57 (d, J=2.9 Hz, 2H), 3.37 (s, 3H), 3.51 (t, J=4.6 Hz, 2H), 3.72 (t, J=4.6 Hz, 2H), 4.87 (s, 2H), 9.84 (br s, 1H); ^{13}C NMR (90.6 MHz): δ=21.8 (t), 25.2 (t), 35.3 (t), 51.5 (t), 59.0 (q), 67.4 (t), 71.6 (t), 76.3 (s), 89.6 (t), 202.8 (d); IR (neat): $\tilde{\nu}$=2932, 2863 (vs, C_{sp^3}-H), 1720 (vs, C=O), 1448 (w), 1104 (s), 1036 cm^{-1} (vs sh); MS (EI, 70 eV): m/z (%): 230 (1) [M^+], 154 (12), 125 (20), 89 (95) [$CH_2OCH_2CH_2OCH_3^+$], 81 (63), 59 (100) [$CH_3OCH_2CH_2^+$]; elemental analysis calcd (%) for $C_{12}H_{22}O_4$ (230.30): C 62.58, H 9.63; found: C 61.46, H 9.30.

2-[1-(2-Methoxyethoxymethoxy)cyclohexyl]-1-phenylethanone (16): A solution of phenylmagnesium bromide in Et_2O (3 M; 0.33 mL, 1.0 mmol) at 0°C was added to a solution of aldehyde **15** (200 mg, 0.86 mmol) in THF (20 mL). The yellow solution was stirred for 1 h at 0°C. The reaction was quenched by addition of sat. aqueous NH_4Cl (150 mL). The mixture was extracted with Et_2O (2×200 mL). The combined organic layers were washed with water (150 mL) and brine (150 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 50:50) to give 2-[1-(2-methoxyethoxymethoxy)cyclohexyl]-1-phenylethanol as a colorless oil (225 mg, 0.73 mmol, 85%). R_f=0.44 (P/EA 50:50) [CAM]; ^{1}H NMR (360 MHz): δ=1.39–1.94 (m, 12H), 3.39 (s, 3H), 3.58 (t, J=4.5 Hz, 2H), 3.80 (t, J=4.5 Hz, 2H), 4.27 (br s, 1H, OH), 4.92 (s, 2H), 5.02 (dd, J=7.7, 4.5 Hz, 1H), 7.23–7.34 (m, 5H); ^{13}C NMR (90.6 MHz): δ=22.6 (t), 25.4 (t), 33.7 (t), 35.5 (t), 58.9 (q), 67.4 (t), 70.5 (d), 71.6 (t), 79.3 (s), 89.1 (t), 125.6 (d), 127.0 (d), 128.2 (d), 142.2 (s).

To a solution of 2-[1-(2-methoxyethoxymethoxy)cyclohexyl]-1-phenylethanol (120 mg, 0.39 mmol) in CH_2Cl_2 was added Dess–Martin periodinane[11] (191 mg, 0.45 mmol) in one portion. The mixture was stirred at 0°C. After 2 h, Et_2O (100 mL) and sat. aqueous $NaHCO_3$ (100 mL) containing 5% $Na_2S_2O_3$ were added. The mixture was stirred at RT until the formation of two clear layers was observed (~30 min). The layers were separated. The organic layer was washed with water (100 mL) and brine (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 80:20) to give **16** as a colorless oil (112 mg, 0.37 mmol, 94%). R_f=0.51 (P/EA 50:50) [CAM]; ^{1}H NMR (360 MHz): δ=1.23–1.88 (m, 10H), 3.22 (s, 3H), 3.30 (s, 2H), 3.41–3.44 (m, 2H), 3.64–3.66 (m, 2H), 4.82 (s, 2H), 7.39–7.53 (m, 3H), 7.92–7.94 (m, 2H); ^{13}C NMR (90.6 MHz): δ=22.0 (t), 25.4 (t), 34.9 (t), 46.5 (t), 58.9 (q), 67.2 (t), 71.8 (t), 77.1 (s), 89.8 (t), 128.3 (d), 128.4 (d), 132.7 (d), 138.6 (s), 198.8 (s); IR (neat): $\tilde{\nu}$=3059 (m, C_{sp^3}-H), 2930 (vs, C_{sp^3}-H), 1675 (vs, C=O), 1448 (vs), 1368 (m), 1208 (m), 1134 (s), 1100 (vs), 1040 (vs sh), 751 (s), 691 cm^{-1} (vs); MS (EI, 70 eV): m/z (%): 306 (1) [M^+], 200 (50), 105 (100) [$OCH_2OCH_2CH_2OCH_3^+$], 89 (91) [$CH_2OCH_2CH_2OCH_3^+$], 59 (94) [$CH_3OCH_2CH_2^+$]; elemental analysis calcd (%) for $C_{18}H_{26}O_4$ (306.40): C 70.56, H 8.55; found: C 70.66, H 8.55.

(1*R*,3*S*,5*S*)-1-(2-Hydroxyethyl)-5-triisopropysilyloxy-2-methylencyclohexane-1,3-diol (19): A solution of (6*R*,7*S*,8*S*,10*S*)-7,8-epoxy-2,2,7-trimethyl-10-triisopropylsilyloxy-1,3-dioxaspiro[5.5]undecane (**20**)[24] (1.74 g, 4.5 mmol) in benzene (40 mL) was treated with DATMP [15 mmol; prepared from 2,2,6,6-tetramethylpiperidine (15 mmol), a solution of *n*-butyllithium in hexane (2.5 M, 15 mmol), a solution of Et_2AlCl in toluene (1.8 M, 15 mmol) at 0°C] for 45 min at 0°C. The reaction was quenched by addition of saturated aqueous NH_4Cl (40 mL). The mixture was acidified with aqueous HCl (1 N, 100 mL) and stirred for 1 h at room temperature. After dilution with diethyl ether (100 mL), the layers were separated and extracted with ethyl acetate (2×50 mL). The combined organic layers were washed with water (100 mL) and brine (100 mL), dried (Na_2SO_4), filtered and concentrated. Flash chromatography (CH/EA 50:50) gave triol **19** as a colorless solid (945 mg, 2.75 mmol, 61%). R_f=0.13 (P/EA 50:50) [CAM]; m.p. 90–96°C; $[\alpha]_D^{20}$=−84.6 (c=0.23, CH_2Cl_2); ^{1}H NMR (360 MHz): δ=1.06 (s, 21H), 1.78–2.01 (m, 5H), 2.21 (d, J=6.1 Hz, 1H), 2.27 (ddd, J=15.0, 5.9, 3.9 Hz, 1H), 2.41 (t, J=4.6 Hz, 1H), 3.74 (s, 1H), 3.85–3.87 (m, 2H), 4.40 (virt. quint, J ≅ 4.9 Hz, 1H), 4.43–4.49 (m, 1H), 5.17 (s, 1H), 5.19 (s, 1H); ^{13}C NMR (90.6 MHz): δ=12.2 (d), 18.1 (q), 18.1 (q), 40.5 (t), 44.5 (t), 47.8 (t), 60.0 (t), 65.4 (d), 70.4 (d), 76.8 (s), 107.0 (t), 153.0 (s); IR (neat): $\tilde{\nu}$=3286 (vs br, OH), 2942 (vs), 2866 (s), 1384 (m), 1098 (m), 1058 (s), 914 (m), 674 cm^{-1} (m); MS (EI, 70 eV): m/z (%): 301 (43) [M^+-iPr], 283 (56), 265 (30), 153

(45), 135 (100), 107 (87), 103 (49), 81 (64), 75 (83), 59 (20), 43 (44) [iPr$^+$]; elemental analysis calcd (%) for $C_{18}H_{36}O_4Si$ (344.56): C 62.74, H 10.53; found: C 62.52, H 10.46.

(3*S*,4*R*,6*S*,8*S*)-4-(2-*tert*-Butyldimethylsilyloxyethyl)-4,8-dihydroxy-6-(triisopropyl)silyloxy-1-oxaspiro[2.5]octane (22): A solution of *tert*-butyldimethylsilyl chloride in toluene (2.9 M; 0.69 mL, 2.0 mmol) at 0 °C was added to a solution of triol **19** (675 mg, 1.96 mmol) and imidazole (170 mg, 2.5 mmol) in DMF (5 mL). The solution was stirred at RT for 15 h. The solution was diluted with water (150 mL) and Et_2O (100 mL). The layers were separated. The aqueous layer was extracted with Et_2O (2×50 mL). The combined organic layers were washed with water (100 mL) and brine (150 mL), dried (Na_2SO_4), filtered and concentrated. The crude product was purified by flash chromatography (P/EA 80:20) to give diol **21** as a colorless oil (836 mg, 1.83 mmol, 93%). R_f=0.56 (P/EA 80:20) [CAM]; ^{1}H NMR (360 MHz): δ=0.05 [s, 3H, $(CH_3)_3CSi(CH_3)_2$], 0.06 [s, 3H, $(CH_3)_3CSi(CH_3)_2$], 0.90 [s, 9H, $(CH_3)_3CSi(CH_3)_2$], 1.06 [s, 21H, $SiCH(CH_3)_2$], 1.72–1.89 (m, 4H), 1.99 (dt, J=12.7, 4.8 Hz, 1H), 2.25 (dt, J=15.2, 4.3 Hz, 1H), 2.40 (d, J=7.1 Hz, 1H, OH), 3.83 (virt. t, $J\cong$5.9 Hz, 2H), 4.37–4.40 (m, 2H), 4.85 (s, 1H, OH), 5.17 (s, 2H); ^{13}C NMR (90.6 MHz): δ=−5.7 [q, $(CH_3)_3CSi(CH_3)_2$], −5.6 [q, $(CH_3)_3CSi(CH_3)_2$], 12.3 [d, $SiCH(CH_3)_2$], 18.0 [q, $SiCH(CH_3)_2$], 18.1 [q, $SiCH(CH_3)_2$], 18.1 [s, $(CH_3)_3CSi(CH_3)_2$], 25.8 [q, $(CH_3)_3CSi(CH_3)_2$], 40.0 (t), 44.9 (t), 47.1 (t), 60.9 (t), 65.9 (d), 69.8 (d), 76.5 (s), 106.3 (t), 153.4 (s).

3-Chloroperbenzoic acid (444 mg, 1.8 mmol) and $NaHCO_3$ (210 mg, 2.5 mmol) were added at 0 °C to a solution of **21** (662 mg, 1.45 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred for 2 h at 0 °C. The mixture was filtered and diluted with sat. aqueous $NaHCO_3$ (20 mL) and CH_2Cl_2 (20 mL). The layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2×10 mL). The combined organic layers were washed with sat. aqueous $NaHCO_3$ (20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 80:20) to give **22** as a colorless oil (680 mg, 1.43 mmol, 99%; dr > 95:5). R_f=0.41 (P/EA 80:20) [CAM]; $[\alpha]_D^{20}$=−32.9 (c=0.52, $CHCl_3$); ^{1}H NMR (500 MHz): δ=0.03 [s, 6H, $(CH_3)_3CSi(CH_3)_2$], 0.84 [s, 9H, $(CH_3)_3CSi(CH_3)_2$], 1.04 [s, 21H, $SiCH(CH_3)_2$], 1.74 (virt. t, $J\cong$12.9 Hz, 1H), 1.81–1.92 (m, 3H), 2.02 (dt, J=12.9, 4.7 Hz, 1H), 2.22 (virt. quint, $J\cong$6.8 Hz, 1H, -OH), 3.00 (d, J=5.0 Hz, 1H), 3.03 (d, J=5.0 Hz, 1H), 3.79–3.89 (m, 2H), 4.03–4.08 (m, 1H, + OH), 4.32–4.34 (m, 2H); ^{13}C NMR (90.6 MHz): δ=−5.7 [q, $(CH_3)_3CSi(CH_3)_2$], −5.6 [q, $(CH_3)_3CSi(CH_3)_2$], 12.2 [d, $Si(CH(CH_3)_2)_3$], 17.9 [q, $Si(CH(CH_3)_2)_3$], 18.0 [s, $(CH_3)_3CSi(CH_3)_2$], 18.1 [s, $(CH_3)_3CSi(CH_3)_2$], 25.7 [s, $(CH_3)_3CSi(CH_3)_2$], 38.8 (t), 41.4 (t), 44.1 (t), 47.2 (t), 59.9 (t), 64.3 (s), 65.7 (d), 65.7 (d), 72.5 (s); IR (neat): $\tilde{\nu}$=3345 (vs br, OH), 2941 (vs), 2866 (s), 1386 (m), 1252 (m), 1095 (m), 1058 (s), 912 (m), 674 cm^{-1} (m); MS (EI, 70 eV): m/z (%): 431 (10) [$M^+-C_3H_7$], 399 (18), 299 (30), 255 (38), 151 (61), 105 (67), 75 (100) [$C_2H_7SiO^+$]; MS (CI): m/z (%): 475 (48) [M+H$^+$], 457 (66), 439 (27), 325 (100), 283 (52), 151 (25); elemental analysis calcd (%) for $C_{24}H_{50}O_5Si_2$ (474.82): C 60.71, H 10.61; found: C 60.42, H 10.55.

(3*S*,4*R*,6*S*,8*S*)-4-(2-*tert*-Butyldimethylsilyloxyethyl)-4,8-(dimethyl)methylendioxy-6-(triisopropyl)silyloxy-1-oxaspiro[2.5]octane (23): Molecular sieves (4 Á; 300 mg), 2-methoxypropene (1.00 mL, 757 mg, 10.5 mmol) and a catalytic amount of PPTS (~15 mg) were added successively at RT to a solution of diol **22** (500 mg, 1.05 mmol) in dry DMF (15 mL). The mixture was stirred at RT for 14 h, filtered and diluted with Et_2O (150 mL) and sat. aqueous $NaHCO_3$ (150 mL). The layers were separated. The aqueous layer was extracted with Et_2O (2×50 mL). The combined organic layers were washed with water (150 mL) and brine (150 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 90:10) to give **23** as a colorless oil (368 mg, 0.71 mmol, 68%). R_f=0.68 (P/EA 80:20) [CAM]; $[\alpha]_D^{20}$=−60.2 (c=0.20, $CHCl_3$); ^{1}H NMR (500 MHz): δ=0.02 [s, 6H, $(CH_3)_3CSi(CH_3)_2$], 0.86 [s, 9H, $(CH_3)_3CSi(CH_3)_2$], 1.05 [s, 21H, $SiCH(CH_3)_2$], 1.34 (s, 3H), 1.32–1.41 (m, 2H), 1.52–1.59 (m, 1H), 1.57 (s, 3H), 1.77 (ddd, J=13.7, 8.2, 5.4 Hz, 1H), 2.33–2.38 (m, 1H), 2.45 (ddd, J=12.9, 5.4, 2.2 Hz, 1H), 2.59 (d, J=4.3 Hz, 1H), 2.84 (d, J=4.3 Hz, 1H), 3.67 (dd, J=4.1, 1.6 Hz, 1H), 3.73–3.82 (m, 2H), 4.51 (virt. sept, $J\cong$5.4 Hz, 1H); ^{13}C NMR (90.6 MHz): δ=−5.3 [q, $(CH_3)_3CSi(CH_3)_2$], −5.3 [q, $(CH_3)_3CSi(CH_3)_2$], 12.4 [d, $Si(CH(CH_3)_2)_3$], 18.1 [q, $Si(CH(CH_3)_2)_3$], 18.1 [q, $Si(CH(CH_3)_2)_3$], 18.3 [s, $(CH_3)_3CSi(CH_3)_2$], 26.0 [s, $(CH_3)_3CSi(CH_3)_2$], 27.5 (q), 31.0 (q), 36.5 (t), 43.0 (t), 47.5 (t), 48.5 (t), 58.2 (t), 59.6 (s), 65.7 (d), 73.3 (d), 73.8 (s), 97.7 (s); IR (neat): $\tilde{\nu}$=2943 (vs), 2866 (s), 1464 (m), 1381 (m), 1369 (m), 1249 (s), 1113 (vs), 1046 (s), 1002 (s), 882 (s), 835 cm^{-1} (vs); MS (EI, 70 eV): m/z (%): 499 (16) [M^+-CH_3], 369 (50), 267 (38), 237 (58), 135 (50), 73 (100); MS (CI): m/z (%): 515 (40) [M+H$^+$], 457 (100), 439 (80), 325 (29), 283 (65), 253 (20), 151 (40); HRMS of fragment [M^+-CH_3]: m/z: calcd for $C_{26}H_{51}O_5Si_2$: 499.8511; found: 499.8509.

(1*R*,3*S*,5*S*)-1-(2-*tert*-Butyldimethylsilyloxyethyl)-3-benzyloxy-5-triisopropysilyloxy-2-methylencyclohexan-1-ol (24): Sodium hydride (60% in oil; 120 mg, 3 mmol) was added at 0 °C to a solution of diol **21** (1.26 g, 2.75 mmol) and benzyl bromide (0.36 mL, 513 mg, 3 mmol) in DMF (15 mL). The mixture was stirred for 20 min at 0 °C and then warmed to RT. After stirring for 1 h at RT, the mixture was diluted with Et_2O (150 mL) and water (200 mL). The layers were separated. The aqueous layer was extracted with Et_2O (3×50 mL). The combined organic layers were washed with water (150 mL) and brine (150 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 90:10) to give **24** as a yellow oil (1.30 g, 2.37 mmol, 86%). R_f=0.62 (P/EA 90:10) [CAM]; $[\alpha]_D^{20}$=−52.4 (c=0.25, $CHCl_3$); ^{1}H NMR (500 MHz): δ=0.06 [s, 6H, $(CH_3)_3CSi(CH_3)_2$], 0.90 [s, 9H, $(CH_3)_3CSi(CH_3)_2$], 1.04 [s, 21H, $SiCH(CH_3)_2$], 1.67–1.74 (m, 2H), 1.94 (ddd, J=14.9, 9.5, 5.1 Hz, 1H), 2.03 (dt, J=11.0, 2.8 Hz, 1H), 2.16 (dt, J=12.6, 4.4 Hz, 1H), 2.30 (dt, J=14.9, 3.5 Hz, 1H), 3.69–3.78 (m, 2H), 4.12 (dd, J=11.0, 4.4 Hz, 1H), 4.33–4.37 (m, 1H), 4.56 (d, J=12.0 Hz, 1H), 4.71 (d, J=12.0 Hz, 1H), 4.78 (s, 1H, OH), 5.32 (s, 1H), 5.38 (s, 1H), 7.25–7.34 (m, 5H); ^{13}C NMR (90.6 MHz): δ=−5.7 [q, $(CH_3)_3CSi(CH_3)_2$], −5.6 [q, $(CH_3)_3CSi(CH_3)_2$], 12.2 [d, $SiCH(CH_3)_2$], 18.1 [q, $SiCH(CH_3)_2$], 18.1 [q, $SiCH(CH_3)_2$], 18.1 [s, $(CH_3)_3CSi(CH_3)_2$], 25.8 [q, $(CH_3)_3CSi(CH_3)_2$], 40.7 (t), 42.5 (t), 47.3 (t), 60.9 (t), 66.4 (d), 71.2 (t), 74.7 (d), 76.3 (s), 106.5 (t), 127.5 (d), 127.5 (d), 128.4 (d), 138.6 (s), 151.3 (s); IR (neat): $\tilde{\nu}$=3486 (brs, OH), 2943 (vs), 2866 (vs), 1463 (m), 1255 (s), 1051 (vs br), 911 (vs), 837 cm^{-1} (vs); MS (EI, 70 eV): m/z (%): 530 (1) [M^+-H_2O], 397 (18), 383 (19), 209 (15), 91 (100) [$C_7H_7^+$]; elemental analysis calcd (%) for $C_{31}H_{56}O_4Si_2$ (548.94): C 67.83, H 10.28; found C 67.41, H 10.06.

(3*S*,4*R*,6*S*,8*S*)-4-(2-*tert*-Butyldimethylsilyloxyethyl)-8-benzyloxy-4-triethylsilyloxy-6-(triisopropyl)silyloxy-1-oxaspiro[2.5]octane (25): 3-Chloroperbenzoic acid (370 mg, 1.5 mmol) and $NaHCO_3$ (210 mg, 2.5 mmol) were added at 0 °C to a solution of **24** (554 mg, 1.01 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred for 2 h at 0 °C. The mixture was filtered and diluted with sat. aqueous $NaHCO_3$ (20 mL) and CH_2Cl_2 (20 mL). The layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2×10 mL). The combined organic layers were washed with sat. aqueous $NaHCO_3$ (20 mL) and brine (20 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 90:10) to give **18** as a colorless oil in (536 mg, 0.95 mmol, 94%). The obtained product was dissolved in CH_2Cl_2 (10 mL). To this solution were added triethylamine (0.28 mL, 202 mg, 2 mmol) and triethylsilyl trifluoromethanesulfonate (0.34 mL, 396.5 mg, 1.5 mmol) at 0 °C. The reaction mixture was stirred for 2 h at 0 °C. The mixture was diluted with Et_2O (150 mL). The layers were separated. The organic layer was washed with sat. aqueous $NaHCO_3$ (100 mL) and brine (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 98:2) to give **25** as a colorless oil (631 mg, 0.93 mmol, 98%) which decomposed slowly at RT. R_f=0.62 (P/EA 90:10) [CAM]; ^{1}H NMR (500 MHz): δ=0.00 [s, 3H, $(CH_3)_3CSi(CH_3)_2$], 0.01 [s, 3H, $(CH_3)_3CSi(CH_3)_2$], 0.55 [q, J=7.9 Hz, 6H, $Si(CH_2CH_3)_3$], 0.86 [s, 9H, $(CH_3)_3CSi(CH_3)_2$], 0.92 [t, J=7.9 Hz, 9H, $Si(CH_2CH_3)_3$], 1.03 [s, 21H, $SiCH(CH_3)_2$], 1.83 (virt. td, $J\cong$12.6, 2.9 Hz, 1H), 1.86 (ddd, J=14.5, 9.5, 4.7 Hz, 1H), 1.90 (dd, J=12.9, 3.8 Hz, 1H), 1.92 (virt. dt, J=12.9 Hz, $J\cong$2.5 Hz, 1H), 2.09 (dddd, J=12.6, 4.4, 3.1, 2.5 Hz, 1H), 2.52 (ddd, J=14.5, 9.5, 6.3 Hz, 1H), 2.90 (d, J=6.3 Hz, 1H), 3.00 (d, J=6.3 Hz, 1H), 3.62–3.70 (m, 2H), 4.11 (dd, J=11.7, 4.4 Hz, 1H), 4.28 (virt. quin, J=3.1 Hz, 1H), 4.50 (s, 2H), 7.21–7.28 (m, 5H); ^{13}C NMR (90.6 MHz): δ=−5.3 [q, $(CH_3)_3CSi(CH_3)_2$], −5.2 [q, $(CH_3)_3CSi$-

($CH_3)_2$], 6.9 [t, Si($CH_2CH_3)_3$], 7.1 [q, Si($CH_2CH_3)_3$], 12.1 [d, Si*C*H($CH_3)_2$], 18.1 [q, SiCH($CH_3)_2$], 18.2 [q, SiCH($CH_3)_2$], 18.3 [s, $(CH_3)_3C$Si($CH_3)_2$], 25.9 [q, $(CH_3)_3C$Si($CH_3)_2$], 37.3 (t), 44.4 (t), 44.5 (t), 46.4 (t), 59.0 (t), 63.7 (s), 66.5 (d), 70.1 (d), 72.0 (t), 74.1 (s), 127.5 (d), 127.6 (d), 128.3 (d), 138.4 (s).

2-{(1*S*,2*S*,3*S*,5*S*)-3-Benzyloxy-1-triethylsilyloxy-5-(triisopropyl)silyloxy-2-hydroxy-2-[(2-phenyl-1,3-dithian-2-yl)methyl]cyclohexyl}acetaldehyde (27): A solution of *n*BuLi in hexanes (2.5 M, 1.36 mL, 3.4 mmol) at −40 °C was added to a solution of 2-phenyl-1,3-dithiane[15a] (654 mg, 3.33 mmol) in dry THF (40 mL). The resulting orange solution was stirred for 2 h at −40 °C. A solution of epoxide **25** (1.25 g, 1.85 mmol) in THF (30 mL) was added slowly. The reaction mixture was stirred for 6 h at −40 °C. Then the mixture was allowed to warm to RT and stirring was continued for 30 min. The reaction was quenched by addition of sat. aqueous NH_4Cl (100 mL). The mixture was extracted with Et_2O (2× 80 mL). The combined organic layers were washed with water (100 mL) and brine (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 99:1) to give **17** as a colorless oil (1.51 g, 1.72 mmol, 93 %). Dithiane **17** could not be completely separated from the excess of 2-phenyl-1,3-dithiane and was directly used in the next step. To a solution of dithiane **17** in THF (20 mL) was added pyridine (20 mL) and HF·py (3 mL) at 0 °C subsequently. The solution was stirred at 0 °C for 5 h. The reaction was quenched by addition of sat. aqueous $NaHCO_3$ (200 mL) (**caution**: gas evolution). After stirring for 30 min at RT, Et_2O (100 mL) was added and the layers were separated. The aqueous layer was extracted with Et_2O (2×80 mL). The combined organic layers were washed with water (150 mL) and brine (150 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 85:15) to give the primary alcohol **26** (524 mg, 0.69 mmol, 40 %) which was directly used in the next step.

To a solution of **26** (524 mg, 0.69 mmol) in CH_2Cl_2 (15 mL) were added anhydrous sodium acetate (164 mg, 2 mmol) and pyridinium chlorochromate (323 mg, 1.5 mmol) at RT. After stirring for 60 min at RT, the mixture was filtered and concentrated. The residue was purified by flash chromatography (P/EA 90:10) to give the aldehyde **27** as a yellow oil (340 mg, 0.45 mmol, 65 %). R_f = 0.71 (P/EA 90:10) [CAM]; $[\alpha]_D^{20}$ = −32.6 (c = 0.78, $CHCl_3$); ^{1}H NMR (360 MHz): δ = 0.49 [q, J = 7.9 Hz, 6 H], 0.79 [t, J = 7.9 Hz, 9 H], 0.96 [s, 21 H], 0.94–1.03 (m, 1 H), 1.59 (dd, J = 13.7, 9.8 Hz, 1 H), 1.83–1.99 (m, 3 H), 2.02 (dd, J = 9.8, 2.5 Hz, 1 H), 2.20 (d, J = 15.0 Hz, 1 H), 2.41 (d, J = 15.0 Hz, 1 H), 2.50 (dd, J = 15.0, 4.0 Hz, 1 H), 2.55 (d, J = 15.0 Hz, 1 H), 2.61–2.71 (m, 3 H), 2.75–2.78 (m, 1 H), 3.73 (br s, 1 H, OH), 3.89–3.92 (m, 1 H), 4.20 (virt. sept, $J \cong$ 4.8 Hz, 1 H), 4.32 (d, J = 11.4 Hz, 1 H), 4.42 (d, J = 11.4 Hz, 1 H), 7.16–7.29 (m, 8 H), 7.88 (d, J = 7.5 Hz, 2 H), 9.86 (virt. d, $J \cong$ 4.0 Hz, 1 H); ^{13}C NMR (90.6 MHz): δ = 6.9 [t, Si($CH_2CH_3)_3$], 7.1 [q, Si($CH_2CH_3)_3$], 12.3 [d, Si*C*H($CH_3)_2$], 18.1 [q, SiCH($CH_3)_2$], 18.1 [q, SiCH($CH_3)_2$], 24.6 (t), 28.0 (t), 28.1 (t), 35.3 (t), 45.0 (t), 48.0 (t), 52.9 (t), 57.9 (s), 63.9 (d), 73.3 (t), 77.2 (s), 78.4 (d), 82.0 (s), 126.9 (d), 127.7 (d), 128.1 (d), 128.5 (d), 128.9 (d), 129.3 (d), 138.3 (s), 142.6 (s), 201.7 (d); IR (neat): $\tilde{\nu}$ = 3504 (s sh, OH), 2944 (vs), 2862 (vs), 1715 (vs, C=O), 1455 (m), 1097 (s), 909 (s), 734 cm^{-1} (vs); MS (EI, 70 eV): m/z (%): 758 (9) [M^+], 715 (4) [$M^+ - i$Pr], 607 (8), 385 (28), 195 (100) [$C_{10}H_{11}S_2^+$], 91 (92) [$C_7H_7^+$].

(3*R*,4*R*,6*R*,8*R*)-8-(*tert*-Butyldimethylsilyloxy)-6-(*tert*-butyldiphenylsilyloxy)-1-oxaspiro[2.5]octan-4-ol (29): $VO(acac)_2$ (67 mg, 0.25 mmol) and a solution of *tert*-butylhydroperoxide in decane (5 M; 3.4 mL, 17.2 mmol) was added at 0 °C to a solution of **30**[28] (4.3 g, 8.6 mmol) in CH_2Cl_2 (25 mL). The dark red solution was stirred for 15 h at RT. After addition of dimethylsulfide (0.5 mL), the mixture was stirred for additional 10 min at RT, then concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 90:10) to give **29** as sole diastereoisomer (3.92 g, 7.56 mmol, 89 %; dr > 95:5). R_f = 0.28 (P/EA 90:10) [CAM]; $[\alpha]_D^{20}$ = −17.2 (c = 0.50, $CHCl_3$); ^{1}H NMR (500 MHz): δ = −0.11 (s, 3 H, MeSiCH_3), −0.09 (s, 3 H, H_3CSiMe), 0.77 [s, 9 H, SiC($CH_3)_3$], 1.06 [s, 9 H, SiC($CH_3)_3$], 1.50 (virt. q, $J \cong$ 11.7 Hz, 1 H), 1.63–1.68 (m, 1 H), 1.99–2.03 (m, 1 H, +OH), 2.16–2.20 (m, 1 H), 2.46 (d, J = 5.4 Hz, 1 H), 3.04 (d, J = 5.4 Hz, 1 H), 3.48 (br s, 1 H), 3.95 (dd, J = 11.7, 4.7 Hz, 1 H), 4.19–4.27 (m, 1 H), 7.34–7.42 (m, 6 H), 7.67 (virt. t, $J \cong$ 8.2 Hz, 4 H); ^{13}C NMR (90.6 MHz): δ = −5.2 (q, MeSi*C*H$_3$), −5.1 (q, H_3CSiMe), 18.1 [s, Si*C*($CH_3)_3$], 19.1 [s, Si*C*($CH_3)_3$], 25.7 [q, SiC(*C*H$_3)_3$], 27.0 [q, SiC(*C*H$_3)_3$], 40.8 (t), 44.1 (t), 48.5 (t), 63.2 (d), 63.8 (s), 65.9 (d), 72.5 (d), 127.6 (d), 127.7 (d), 129.6 (d), 129.7 (d), 134.2 (s), 134.3 (s), 135.7 (d), 135.7 (d); IR (neat): $\tilde{\nu}$ = 3444 (vs br, OH), 3071 (m, C_{sp^2}-H), 2929, 2857 (vs, C_{sp^3}-H), 1472 (m), 1428 (s), 1388 (m sh), 1250 (s), 1112 (vs sh), 1028 (vs), 940 (s), 886 (s), 837 (vs), 780 (s), 739 (vs), 702 cm^{-1} (vs); MS (EI, 70 eV): m/z (%): 497 (1) [$M^+ - CH_3$], 455 (8) [$M^+ - t$Bu], 437 (10), 313 (15), 271 (22), 209 (31), 199 (100), 135 (60), 125 (35), 75 (38).

(3*R*,4*R*,6*R*,8*R*)-8-(*tert*-Butyldimethylsilyloxy)-6-(*tert*-butyldiphenylsilyloxy)-4-(trimethylsilyloxy)-1-oxaspiro[2.5]octane (34): Trimethylsilyl chloride (1.3 mL, 1.09 g, 10 mmol) was added at 0 °C to a solution of triol **30** (4.8 g, 9.4 mmol) and imidazole (884 mg, 13 mmol) in DMF (15 mL). The solution was stirred at RT for 3 h. The solution was diluted with water (200 mL) and Et_2O (200 mL). The layers were separated. The aqueous layer was extracted with Et_2O (2×100 mL). The combined organic layers were washed with water (200 mL) and brine (200 mL), dried ($MgSO_4$), filtered and concentrated. The crude product was purified by flash chromatography (P/EA 98:2) to give **34** as a colorless oil (5.4 g, 9.3 mmol, 99 %). R_f = 0.70 (P/EA 98:2) [CAM]; $[\alpha]_D^{20}$ = −33.7 (c = 1.49, $CHCl_3$); ^{1}H NMR (360 MHz): δ = −0.06 (s, 3 H, MeSiCH_3), −0.05 (s, 3 H, H_3CSiMe), −0.02 [s, 9 H, Si($CH_3)_3$], 0.81 [s, 9 H, SiC($CH_3)_3$], 1.07 [s, 9 H, SiC($CH_3)_3$], 1.50–1.62 (m, 2 H), 1.95 (dddd, J = 11.9, 5.5, 4.8, 1.4 Hz, 1 H), 2.10–2.17 (m, 1 H), 2.36 (d, J = 5.7 Hz, 1 H), 2.95 (d, J = 5.7 Hz, 1 H), 3.41 (dd, J = 3.6, 2.3 Hz, 1 H), 3.99 (dd, J = 11.6, 4.8 Hz, 1 H), 4.27 (virt. tt, $J \cong$ 10.9 Hz, $J \cong$ 4.7 Hz, 1 H), 7.35–7.44 (m, 6 H), 7.66–7.69 (m, 4 H); ^{13}C NMR (90.6 MHz): δ = −5.2 (q, MeSi*C*H$_3$), −5.1 (q, H_3CSiMe), 0.0 [q, Si($CH_3)_3$], 18.1 [s, Si*C*($CH_3)_3$], 19.1 [s, Si*C*($CH_3)_3$], 25.7 [q, SiC(*C*H$_3)_3$], 27.0 [q, SiC(*C*H$_3)_3$], 42.7 (t), 44.3 (t), 47.1 (t), 63.2 (d), 63.4 (s), 66.2 (d), 73.0 (d), 127.5 (d), 127.5 (d), 129.6 (d), 129.6 (d), 134.4 (s), 134.5 (s), 135.7 (d), 135.8 (d); IR (neat): $\tilde{\nu}$ = 3073 (m, C_{sp^2}-H), 2974, 2879 (vs, C_{sp^3}-H), 1436 (m), 1378(vs), 1267 (m), 1252 (m), 1193 (s), 1162 (s), 1101 (vs), 1050 (s), 979 (vs), 889 (vs), 812 cm^{-1} (vs); MS (EI, 70 eV): m/z (%): 237 (32), 177 (43), 135 (30), 119 (50), 97 (30), 68 (45), 43 (100); elemental analysis calcd (%) for $C_{32}H_{52}O_4Si_3$ (585.01): C 65.70, H 8.96; found: C 65.40, H 8.64.

(1*R*,2*R*,4*R*,6*R*)-2-(*tert*-Butyldimethylsilyloxy)-4-(*tert*-butyldiphenylsilyloxy)-1-[(2-phenyl-1,3-dithian-2-yl)methyl]-6-(trimethylsilyloxy)-cyclohexan-1-ol (35): A solution of *n*BuLi in hexanes (2.5 M, 1.80 mL, 4.5 mmol) was added at −40 °C to a solution of 2-phenyl-1,3-dithiane[15a] (882 mg, 4.5 mmol) in dry THF (20 mL). The resulting orange solution was stirred for 2 h at −40 °C. Then the orange solution was cooled to −78 °C. A solution of **34** (1.75 g, 3 mmol) in THF (20 mL) was added slowly. The reaction mixture was stirred for 1 h at −78 °C. Then the mixture was allowed to warm to −45 °C over 45 min. The reaction was quenched by addition of sat. aqueous NH_4Cl (100 mL). The mixture was extracted with Et_2O (3×100 mL). The combined organic layers were washed with brine (200 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 98:2) to give **35** as a colorless oil (90 %, 2.11 g, 2.7 mmol). R_f = 0.58 (P/EA 98:2) [CAM]; $[\alpha]_D^{20}$ = −38.5 (c = 1.26, $CHCl_3$); ^{1}H NMR (360 MHz): δ = −0.18 [s, 9 H, Si($CH_3)_3$], −0.15 (s, 3 H, MeSiCH_3), −0.06 (s, 3 H, H_3CSiMe), 0.81 [s, 9 H, SiC($CH_3)_3$], 1.01 [s, 9 H, SiC($CH_3)_3$], 1.35–1.45 (m, 2 H), 1.52–1.55 (m, 1 H), 1.70–1.74 (m, 1 H), 1.84–1.95 (m, 2 H), 2.05 (s, 1 H, OH), 2.23 (d, J = 15.4 Hz, 1 H), 2.60–2.81 (m, 4 H), 2.89 (d, J = 15.4 Hz, 1 H), 3.42 (dd, J = 12.3, 4.5 Hz, 1 H), 3.61 (br s, 1 H), 3.89–3.97 (m, 1 H), 7.19–7.37 (m, 9 H), 7.56–7.64 (m, 4 H), 7.93–7.95 (m, 2 H); ^{13}C NMR (90.6 MHz): δ = −4.8 (q, MeSi*C*H$_3$), −4.6 (q, H_3CSiMe), 0.1 [q, Si($CH_3)_3$], 18.1 [s, Si*C*($CH_3)_3$], 19.0 [s, Si*C*($CH_3)_3$], 24.9 (t), 25.9 [q, SiC(*C*H$_3)_3$], 26.9 [q, SiC(*C*H$_3)_3$], 27.9 (t), 28.0 (t), 38.8 (t), 41.3 (t), 42.9 (t), 57.6 (s), 66.0 (d), 71.5 (d), 72.6 (d), 77.1 (s), 126.7 (d), 127.5 (d), 127.5 (d), 128.2 (d), 128.9 (d), 129.5 (d), 129.5 (d), 134.4 (s), 134.5 (s), 135.7 (d), 135.7 (d), 142.4 (s); IR (neat): $\tilde{\nu}$ = 3564 (m sh, OH), 3070 (m, C_{sp^2}-H), 2953, 2856 (vs, C_{sp^3}-H), 1484 (m), 1428 (m), 1251 (s), 1075 (vs br), 927 (s), 838 (s sh), 777 (m), 740 (m), 701 cm^{-1} (s); MS (EI, 70 eV): m/z (%): 780 (10) [M^+], 723 (90) [$M^+ - t$Bu], 633 (18), 513 (70), 397 (12), 195 (100), 135 (63), 73 (92); elemental analysis calcd (%) for $C_{42}H_{64}O_4S_2Si_3$ (781.34): C 64.56, H 8.26; found: C 64.56, H 8.25.

(1*R*,2*R*,4*R*,6*R*)-2-(*tert*-Butyldimethylsilyloxy)-4-(*tert*-butyldiphenylsilyloxy)-1-[(2-phenyl-1,3-dithian-2-yl)methyl]-cyclohexan-1,6-diol (36): Dithiane **35** (1.05 g, 1.35 mmol) was dissolved in a mixture of THF (21 mL), water (7 mL) and acetic acid (7 mL). The mixture was stirred at RT for 14 h. To this mixture was added water (300 mL) and Et_2O (300 mL). The layers were separated; the organic layer was carefully washed with sat. aqueous $NaHCO_3$ (2×200 mL) and brine (150 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 90:10) to give **36** as a colorless oil (768 mg, 1.11 mmol, 82%). Due to the instability of the compound, an analytical sample was not obtained. R_f=0.29 (P/EA 90:10) [CAM]; ^{13}C NMR (90.6 MHz): δ=−4.7 (q, MeSi*C*H$_3$), −4.6 (q, H$_3$*C*SiMe), 18.0 [s, Si*C*-(CH$_3$)$_3$], 19.1 [s, Si*C*(CH$_3$)$_3$], 24.5 (t, SCH$_2$*C*H$_2$CH$_2$S), 25.9 [q, SiC(*C*H$_3$)$_3$], 27.0 [q, SiC(*C*H$_3$)$_3$], 27.7 (t), 28.1 (t), 36.9 (t), 40.7 (t), 42.4 (t), 57.4 (s), 65.8 (d), 71.1 (d), 71.6 (d), 77.2 (s), 127.3 (d), 127.3 (d), 127.5 (d), 128.6 (d), 128.7 (d), 129.5 (d), 129.5 (d), 134.2 (s), 134.5 (s), 135.7 (d), 135.7 (d), 142.1 (s).

(2*S*,3*R*,5*S*)-3-(*tert*-Butyldimethylsilyloxy)-5-(*tert*-butyldiphenylsilyloxy)-2-[(2-phenyl-1,3-dithian-2-yl)methyl]-2-hydroxycyclohexan-1-one (28):[30] DMSO (3 mL), pyridine (0.04 mL, 41 mg, 0.53 mmol), trifluoroacetic acid (15 μL, 24 mg, 0.21 mmol) and dicyclohexylcarbodiimide (289 mg, 1.4 mmol) were added successively to a stirred solution of alcohol **36** (250 mg, 0.35 mmol) in benzene (3 mL). The mixture was stirred for 1 d at RT and filtered. The filtrate was diluted with Et_2O (20 mL) and water (20 mL). The layers were separated. The organic layer was washed with brine (20 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 95:5) to give **28** as a colorless oil (228 mg, 0.322 mmol, 92%). R_f=0.49 (P/EA 90:10) [CAM]; $[\alpha]_D^{20}$=−61.8 (c=1.21, $CHCl_3$); ^{1}H NMR (360 MHz): δ=−0.17 (s, 3H, MeSi*CH*$_3$), −0.03 (s, 3H, *H*$_3$CSiMe), 0.82 [s, 9H, SiC-(CH$_3$)$_3$], 1.03 [s, 9H, SiC(CH$_3$)$_3$], 1.72–1.99 (m, 4H), 2.31 (ddd, J=12.5, 5.2, 2.0 Hz, 1H), 2.44 (virt. t, J ≅ 12.5 Hz, 1H), 2.59–2.75 (m, 5H), 2.95 (dd, J=11.6, 5.2 Hz, 1H), 3.13 (d, J=15.4 Hz, 1H), 3.46–3.57 (m, 1H), 3.52 (s, 1H, OH), 7.19–7.39 (m, 9H), 7.51–7.59 (m, 4H), 7.83–7.86 (m, 2H); ^{13}C NMR (90.6 MHz): δ=−5.3 (q, MeSi*C*H$_3$), −4.7 (q, H$_3$*C*SiMe), 18.1 [s, Si*C*(CH$_3$)$_3$], 19.0 [s, Si*C*(CH$_3$)$_3$], 24.7 (t, SCH$_2$*C*H$_2$CH$_2$S), 25.8 [q, SiC(*C*H$_3$)$_3$], 26.8 [q, SiC(*C*H$_3$)$_3$], 27.7 (t), 28.2 (t), 41.5 (t), 46.0 (t), 47.6 (t), 57.0 (s), 66.3 (d), 75.8 (d), 83.2 (s), 127.4 (d), 127.7 (d), 127.7 (d), 128.4 (d), 129.7 (d), 129.9 (d), 129.9 (d), 133.3 (s), 133.5 (s), 135.6 (d), 135.6 (d), 140.9 (s), 208.1 (s); IR (neat): $\tilde{\nu}$=3478 (m, OH), 3071 (w, C$_{sp^2}$-H), 2953, 2857 (vs, C$_{sp^3}$-H), 1712 (s, C=O), 1471 (m), 1428 (m), 1250 (m), 1105 (vs sh), 909 (s), 837 (s), 824 (s), 734 (vs), 702 cm^{-1} (vs); MS (EI, 70 eV): m/z (%): 706 (8) [M^+], 649 (10) [M^+−*t*Bu], 255 (22), 209 (84), 195 (100), 135 (25), 103 (28); elemental analysis calcd (%) for $C_{39}H_{54}O_4S_2Si_2$ (707.15): C 66.24, H 7.70; found: C 66.39, H 7.80.

(1*R*,2*R*,4*R*,6*R*)-1-Allyl-2-(*tert*-butyldimethylsilyloxy)-4-(*tert*-butyldiphenylsilyloxy)-cyclohexan-1,6-diol (38): A solution of vinylmagnesium bromide in THF (1.0 M, 1 mmol, 1 mL) was added at RT to a solution of **34** (150 mg, 0.29 mmol) in dry THF (5 mL). The solution was stirred for 12 h at RT. The reaction was quenched by addition of sat. aqueous NH_4Cl (20 mL) and diluted with Et_2O (20 mL). The layers were separated. The organic layer was washed with water (10 mL) and brine (10 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 90:10) to give **38** as a colorless oil (34.5 mg, 0.064 mmol, 22%). R_f=0.30 (P/EA 90:10) [CAM]; $[\alpha]_D^{20}$=−5.0 (c=0.31, $CHCl_3$); ^{1}H NMR (360 MHz): δ=−0.13 (s, 3H, MeSi*CH*$_3$), −0.07 (s, 3H, *H*$_3$CSiMe), 0.83 [s, 9H, SiC(CH$_3$)$_3$], 1.06 [8s, 9H, SiC(CH$_3$)$_3$], 1.49 (virt. q, J ≅ 11.6 Hz, 1H), 1.58–1.64 (m, 1H), 1.74–1.82 (m, 1H), 2.06–2.11 (m, 1H), 2.12 (s, 1H, OH), 2.21 (dd, J=14.8, 8.8 Hz, 1H), 2.36 (brs, 1H, OH), 2.57 (dd, J=14.8, 6.1 Hz, 1H), 3.72 (dd, J=12.2, 4.5 Hz, 1H), 3.79 (virt. t, J ≅ 3.0 Hz, 1H), 4.15 (virt. septett, J ≅ 4.9 Hz, 1H), 5.04–5.12 (m, 2H), 5.80–5.91 (m, 1H), 7.34–7.40 (m, 6H), 7.63–7.69 (m, 4H); ^{13}C NMR (90.6 MHz): δ=−5.0 (q, MeSi*C*H$_3$), −4.5 (q, H$_3$*C*SiMe), 17.9 [s, Si*C*(CH$_3$)$_3$], 19.1 [s, Si*C*(CH$_3$)$_3$], 25.8 [q, SiC-(*C*H$_3$)$_3$], 27.0 [q, SiC(*C*H$_3$)$_3$], 35.7 (t), 36.9 (t), 40.9 (t), 62.2 (d), 70.9 (d), 71.4 (d), 75.9 (s), 118.3 (t), 127.6 (d), 127.6 (d), 129.6 (d), 129.7 (d), 133.7 (d), 134.2 (s), 134.5 (s), 135.7 (d), 135.7 (d); IR (neat): $\tilde{\nu}$=3563 (brs, OH), 3072 (m, C$_{sp^2}$-H), 2932 (s, C$_{sp^3}$-H), 1471 (s), 1428 (s), 1385 (m), 1254 (m), 1112 cm^{-1} (s br); MS (EI, 70 eV): m/z (%): 499 (4) [M^+−C$_3$H$_5$], 483 (8) [M^+−*t*Bu], 465 (22), 405 (22), 327 (18), 267 (25), 209 (42), 199 (96), 135 (100), 107 (32), 73 (88); elemental analysis calcd (%) for $C_{31}H_{48}O_4Si_2$ (540.88): C 68.84, H 8.94; found: C 68.94, H 9.06.

Diol **37** was obtained as major product (75 mg, 0.14 mmol, 48%). R_f=0.24 (P/EA 80:20) [CAM]; ^{1}H NMR (500 MHz): δ=−0.11 (s, 3H, MeSi*CH*$_3$), −0.07 (s, 3H, *H*$_3$CSiMe), 0.81 [s, 9H, SiC(CH$_3$)$_3$], 1.04 [s, 9H, SiC(CH$_3$)$_3$], 1.56 (brs, 1H, OH), 1.60 (dd, J=14.2, 9.2 Hz, 1H), 1.78–1.82 (m, 1H), 1.83–1.87 (m, 1H), 1.91–1.97 (m, 1H), 2.04 (virt. dt, J ≅ 14.2 Hz, J ≅ 3.5 Hz, 1H), 2.08 (dd, J=14.2, 3.5 Hz, 1H), 2.69 (brs, 1H, OH), 3.47 (dd, J=9.8, 3.5 Hz, 1H), 4.00 (brs, 1H), 4.13–4.16 (m, 1H), 5.15 (d, J=10.8 Hz, 1H), 5.32 (d, J=17.3 Hz, 1H), 6.09 (dd, J=17.3, 10.8 Hz, 1H), 7.34–7.42 (m, 6H), 7.63–7.66 (m, 4H); ^{13}C NMR (90.6 MHz): δ=−5.0 (q, MeSi*C*H$_3$), −4.3 (q, H$_3$*C*SiMe), 17.9 [s, Si*C*-(CH$_3$)$_3$], 19.1 [s, Si*C*(CH$_3$)$_3$], 25.8 [q, SiC(CH$_3$)$_3$], 27.0 [q, SiC(*C*H$_3$)$_3$], 43.0 (t), 43.8 (t), 45.3 (t), 65.6 (d), 66.6 (d), 75.9 (d), 76.3 (s), 114.2 (t), 127.6 (d), 127.7 (d), 129.6 (d), 129.7 (d), 134.2 (s), 134.2 (s), 135.8 (d), 135.9 (d), 140.3 (d).

(1*R*,2*S*,4*S*,6*S*)-1-Allyl-2-(*tert*-butyldimethylsilyloxy)-4-(*tert*-butyldiphenylsilyloxy)-6-trimethylsilyloxycyclohexanol (46): A stirred solution of **43**[28] (5.0 g, 8.8 mmol) in THF (150 mL) was cooled to −20 °C and allylmagnesium chloride (1 M in Et_2O; 13.2 mL, 13.2 mmol) was added dropwise. The clear solution was stirred for 1 h at −78 °C. The reaction was quenched by the addition of saturated aqueous NH_4Cl solution (300 mL), and allowed to warm to ambient temperature. The mixture was diluted with Et_2O (300 mL). After separation, the aqueous layer was extracted with Et_2O (2×200 mL). The organic extracts were combined, washed with water (400 mL) and brine (300 mL), dried (Na_2SO_4), filtered, and concentrated to give the crude product (*dr* 90:10, determined by ^{1}H NMR) as a yellow oil. The residue was purified by flash chromatography (P/EA 98:2) to yield **46** and its epimer as inseparable mixture of diastereoisomers (5.4 g, 8.8 mmol, quant.; *dr* 90:10, determined by ^{1}H NMR); R_f=0.65 (P/EA 90:10); $[\alpha]_D^{20}$ = 10.5 (c=0.94, $CHCl_3$); ^{1}H NMR (360 MHz): δ=−0.11 (s, 3H), −0.06 (s, 12H), 0.85 (s, 9H), 1.05 (s, 9H), 1.63–1.78 (m, 2H), 1.83 (virt d, J ≅ 13.1 Hz, 1H), 1.97 (virt dt, J ≅ 1.9 Hz, J ≅ 13.1 Hz, 1H), 2.06 (s, 1H, OH), 2.21 (dd, J=14.2, 8.0 Hz, 1H), 2.38 (dd, J=14.2, 6.2 Hz, 1H), 3.49 (dd, J=10.7, 5.4 Hz, 1H), 3.86 (virt. s, 1H), 3.98 (virt. sept, J ≅ 6.0 Hz 1H), 5.02–5.09 (m, 2H), 5.84–5.95 (m, 1H), 7.34–7.40 (m, 6H), 7.63–7.69 (m, 4H); ^{13}C NMR (90.6 MHz): δ=−5.0 (q), −4.2 (q), 0.28 (q), 17.9 (s), 19.1 (s), 25.8 (q), 26.9 (q), 37.7 (t), 39.2 (t), 40.1 (t), 65.8 (d), 70.9 (d), 71.0 (d), 74.0 (s), 117.6 (t), 127.5 (d), 127.5 (d), 129.5 (d), 129.6 (d), 134.2 (s), 134.3 (s), 134.6 (d), 135.8 (d); IR (neat): $\tilde{\nu}$=3572 (m, sh), 3072 (m), 2954, 2856 (s), 1471 (s), 1428 (s), 1379 (m), 1361 (m), 1251 (s), 1068 (s, br), 941 (s), 838 (s), 776 cm^{-1} (s); MS (EI, 70 eV): m/z (%): 571 (5) [M^+−C$_3$H$_5$], 465 (50), 339 (52), 209 (48), 135 (65), 73 (100); elemental analysis calcd (%) for $C_{34}H_{56}O_4Si_3$ (612.349): C 66.61, H 9.21; found: C 66.27, H 9.17.

(1*R*,2*S*,4*S*,6*S*)-1-Allyl-1-(2-methoxyethoxymethoxy)-2-(*tert*-butyldimethylsilyloxy)-4-(*tert*-butyldiphenylsilyloxy)-6-trimethylsilyloxycyclohexane (45): A solution of tertiary alcohol **46** (5.4 g, 8.8 mmol) in 1,2-dichloroethane (40 mL) was treated with *N*,*N*-diisopropylethylamine (2.3 mL, 1.7 g, 13.2 mmol) and MEMCl (1.0 mL, 1.0 g, 8.8 mmol) at 0 °C. After stirring for 4 h at 70 °C, *N*,*N*-diisopropylethylamine (2.3 mL, 1.7 g, 13.2 mmol) and MEMCl (1.0 mL, 1.0 g, 8.8 mmol) were added to the orange-colored solution. The reaction mixture was stirred for additional 4 h at 70 °C, cooled to room temperature, and diluted with CH_2Cl_2 (100 mL) and saturated aqueous NH_4Cl solution (100 mL). The aqueous layer was extracted with CH_2Cl_2 (100 mL), the combined organic layers were washed with water (100 mL) and brine (100 mL), dried (Na_2SO_4), filtered, and concentrated. Purification by flash chromatography (P/EA 98:2) gave **45** (4.9 g, 7.0 mmol, 80%) as a yellow oil. R_f=0.47 (P/EA 90:10); $[\alpha]_D^{20}$= 6.8 (c=1.10, $CHCl_3$); ^{1}H NMR (500 MHz): δ=−0.15 (s, 3H), −0.08 (s, 3H), −0.07 (s, 9H), 0.84 (s, 9H), 1.06 (s, 9H), 1.73 (virt. dt, J ≅ 11.8, 4.6 Hz, 1H), 1.75–1.86 (m, 2H), 2.04 (virt. dt, J ≅ 2.2, 11.1 Hz, 1H), 2.13 (dd, J=15.5, 7.9 Hz, 1H), 2.80 (dd, J=15.5, 6.0 Hz, 1H), 3.44 (s, 3H), 3.52 (dd, J=12.0, 4.6 Hz, 1H), 3.62 (t, J=5.4 Hz, 2H), 3.74–3.86 (m, 3H), 3.97 (virt. sept, J ≅ 4.6 Hz, 1H), 5.03–5.13 (m, 4H), 5.86–5.95 (m, 1H), 7.34–7.40 (m, 6H), 7.61–7.69 (m, 4H); ^{13}C NMR (90.6 MHz): δ=−5.3 (q), −4.6 (q), 0.27 (q), 17.8 (s), 19.1 (s), 25.7 (q),

26.9 (q), 32.7 (t), 37.5 (t), 40.1 (t), 59.0 (q), 66.6 (d), 67.6 (t), 71.1 (d, C2), 71.6 (d, C4), 71.8 (t), 78.9 (s, C1), 90.8 (t), 117.5 (t), 127.4 (d), 127.5 (d), 129.4 (d), 129.5 (d), 133.6 (d), 134.3 (s), 134.7 (s), 135.7 (d); IR (neat): $\tilde{\nu}$ = 3072 (m), 2955, 2893, 2857 (s), 1472 (s), 1427 (s), 1379 (m), 1361 (m), 1251 (vs), 1112 (vs), 1070 (vs, br), 1024 (vs), 914 (s), 838 cm^{-1} (s); MS (EI, 70 eV): *m/z* (%): 443 (6) [$M^+ - t$Bu], 553 (5), 463 (9), 369 (20), 339 (30), 257 (64), 213 (18), 133 (100), 89 (54), 59 (48) [$CH_3OCH_2CH_2^+$]; elemental analysis calcd (%) for $C_{38}H_{64}O_6Si_3$ (700.401): C 65.09, H 9.20; found: C 65.13, H 9.21.

(1*S*,2*R*,3*S*,5*S*)-2-Allyl-3-(*tert*-butyldimethylsilanyl-oxy)-5-(*tert*-butyldiphenylsilyloxy)-2-(2-methoxyethoxymethoxy)cyclohexanol (47): K_2CO_3 (1.8 g) was added at 0 °C to a solution of **45** (4.9 g, 7.0 mmol) in MeOH (60 mL). The mixture was allowed to warm to room temperature. After 12 h saturated aqueous NH_4Cl solution (400 mL) and CH_2Cl_2 (400 mL) were added. The aqueous layer was separated and extracted with CH_2Cl_2 (300 mL). The organic extracts were combined, washed with water (400 mL) and brine (400 mL), dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography (P/EA 90:10) to give **47** as a colorless oil (4.2 g, 6.7 mmol, 95 %). R_f = 0.17 (P/EA 90:10); $[\alpha]_D^{20} = -0.4$ (c = 2.02, $CHCl_3$); ^{1}H NMR (360 MHz): $\delta = -0.12$ (s, 3H), −0.07 (s, 3H), 0.84 (s, 9H), 1.07 (s, 9H), 1.41 (br d, J = 4.3 Hz, 1H, OH), 1.63–1.74 (m, 2H), 1.80 (virt. q, $J \cong$ 11.4 Hz, 1H), 1.96 (ddd, J = 14.8, 11.4, 2.9 Hz, 1H), 2.08 (dd, J = 15.5, 9.3 Hz, 1H), 2.86 (dd, J = 15.5, 5.0 Hz, 1H), 3.42 (s, 3H), 3.51–3.58 (m, 3H), 3.62–3.68 (m, 1H), 3.71–3.75 (m, 1H), 3.76–3.82 (m, 1H), 3.99 (virt. sept, $J \cong$ 4.8 Hz, 1H), 4.89 (d, J = 6.1 Hz, 1H), 5.03–5.12 (m, 2H), 5.18 (d, J = 6.1 Hz, 1H), 5.93–6.09 (m, 1H), 7.33–7.40 (m, 6H), 7.61–7.71 (m, 4H); ^{13}C NMR (90.6 MHz): $\delta = -5.1$ (q), −4.5 (q), 17.8 (s), 19.1 (s), 25.8 (q), 26.9 (q), 34.7 (t), 37.3 (t), 40.1 (t), 59.0 (q), 66.6 (d), 67.5 (t), 70.7 (d), 71.9 (t), 72.3 (d), 78.8 (s), 91.1 (t), 117.4 (t), 127.5 (d), 127.5 (d), 129.5 (d), 129.5 (d), 134.5 (d), 134.6 (s), 134.8 (s), 135.7 (d), 135.8 (d); IR (neat): $\tilde{\nu}$ = 3478 (m, br), 3071 (m), 2955, 2930, 2892, 2857 (s), 1472 (s), 1427 (m), 1374 (m), 1361 (m), 1251 (s), 1111 (vs), 1061 (vs, br), 1025 (vs), 835 (s), 702 cm^{-1} (s); MS (EI, 70 eV): *m/z* (%): 587 (1) [$M^+ - C_3H_5$], 571 (5) [$M^+ - t$Bu], 495 (8), 465 (10), 297 (18), 257 (100), 133 (68), 89 (52), 59 (58) [$CH_3OCH_2CH_2^+$]; elemental analysis calcd (%) for $C_{35}H_{56}O_6Si_2$ (628.362): C 66.83, H, 8.97; found: C 66.78, H 8.97.

(2*S*,3*S*,5*R*)-2-Allyl-3-(*tert*-butyldimethylsilyloxy)-5-(*tert*-butyldiphenylsilyloxy)-2-(2-methoxyethoxymethoxy)cyclohexanone (48): Alcohol **47** (4.1 g, 6.5 mmol) was dissolved in DMSO (30 mL), and IBX[34] (3.6 g, 13 mmol) was added in one portion. The resulting solution was stirred for 12 h at room temperature, then poured into a mixture of Et_2O (300 mL) and saturated aqueous $NaHCO_3$ solution (300 mL). The layers were separated, the aqueous layer was extracted with Et_2O (150 mL). The combined organic layers were washed with water (2 × 400 mL), dried over Na_2SO_4, filtered, and concentrated. Flash chromatography (P/EA 95:5) of the crude oil gave the title compound **48** (4.0 g, 6.4 mmol, 98 %) as a colorless oil. R_f = 0.34 (P/EA 90:10); $[\alpha]_D^{20}$ = 10.1 (c = 0.98, $CHCl_3$); ^{1}H NMR (500 MHz): $\delta = -0.12$ (s, 3H), −0.10 (s, 3H), 0.85 (s, 9H), 1.07 (s, 9H), 1.86 (ddt, J = 11.9, 1.7, 4.4 Hz, 1H), 2.30 (virt. q, $J \cong$ 11.9 Hz, 1H), 2.49 (dd, J = 14.2, 7.3 Hz, 1H), 2.52 (ddd, J = 12.8, 5.2, 1.7 Hz, 1H), 2.77 (dd, J = 14.2, 6.6 Hz, 1H), 3.17 (dd, J = 12.8, 11.2 Hz, 1H), 3.29 (dd, J = 11.9, 4.4 Hz, 1H), 3.41 (s, 3H), 3.57 (t, J = 4.6 Hz, 2H), 3.69 (virt. sept, $J \cong$ 4.9 Hz, 1H), 3.72–3.82 (m, 2H), 4.92 (d, J = 6.3 Hz, 1H), 4.94 (d, J = 6.3 Hz, 1H), 5.03 (dd, J = 10.2, 1.9 Hz, 1H), 5.12 (dd, J = 17.3, 1.9 Hz, 1H), 5.64–5.73 (m, 1H), 7.33–7.42 (m, 6H), 7.59–7.68 (m, 4H); ^{13}C NMR (90.6 MHz): $\delta = -4.9$ (q), −4.0 (q), 17.9 (s), 19.0 (s), 25.8 (q), 26.9 (q), 32.8 (t), 39.1 (t), 47.5 (t), 58.9 (q), 65.9 (d), 67.7 (t), 71.1 (d), 71.7 (t), 83.9 (s), 91.3 (t), 118.2 (t), 127.7 (d), 127.7 (d), 129.8 (d), 129.8 (d), 133.4 (d), 133.5 (s), 133.8 (s), 135.6 (d), 135.7 (d), 205.7 (s); IR (neat): $\tilde{\nu}$ = 3072 (m), 2931, 2857 (s), 1721 (s), 1472 (s), 1427 (s), 1377 (m), 1255 (s), 1113 (vs), 1021 (vs), 837 (s), 703 cm^{-1} (s); MS (EI, 70 eV): *m/z* (%): 626 (1) [M^+], 569 (5) [$M^+ - C(CH_3)_3$], 493 (2), 370 (10), 281 (15), 257 (48), 199 (32), 133 (46), 89 (100), 59 (80) [$CH_3OCH_2CH_2^+$]; elemental analysis calcd (%) for $C_{35}H_{54}O_6Si_2$ (626.346): C 67.05, H 8.68; found: C 66.90, H 8.73.

4-Hydroxy-6-([(1*R*,2*S*,3*S*,5*R*)-2-allyl-3-(*tert*-butyldimethylsilyloxy)-5-(*tert*-butyldiphenylsilyloxy)-1-hydroxy-2-(2-methoxyethoxymethoxy)cyclohexyl]methyl)-2*H*-pyran-2-one (49): 4-Hydroxy-6-methyl-2*H*-pyran-2-one (334 mg, 2.65 mmol) was dissolved in THF (60 mL). The solution was cooled to −78 °C, and a solution of *t*BuLi in pentane (1.5 M; 5.83 mmol, 3.89 mL) was added dropwise. After stirring the orange solution for 15 min at −78 °C, the mixture was warmed to 0 °C. The dark red solution was stirred for 20 min at 0 °C, then cooled to −78 °C. A solution of **48** (665 mg, 1.06 mmol) in THF (10 mL) was added dropwise. The reaction mixture was stirred for 2 d at −78 °C. The reaction was quenched by addition of sat. aqueous NH_4Cl (100 mL). The mixture was acidified with aqueous H_2SO_4 (10 %) to pH 2. After addition of Et_2O (200 mL) and water (200 mL), the layers were separated. The aqueous layer was extracted with Et_2O (2 × 150 mL). The combined organic layers were washed with water (200 mL) and brine (200 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 30:70) to give the title compound as a yellow oil (510 mg, 0.68 mmol, 64 %; *dr* 93:7; 82 % based on recovered starting material). The starting material **48** was recovered as a pure compound (144 mg, 0.23 mmol). The product **49** showed limited stability at RT and was directly methylated. R_f = 0.13 (P/EA 60:40) [CAM]; $[\alpha]_D^{20}$ = 13.5 (c = 0.22, MeOH); ^{1}H NMR (360 MHz): $\delta = -0.06$ (s, 3H, MeSiCH_3), −0.05 (s, 3H, H_3CSiMe), 0.84 [s, 9H, SiC$(CH_3)_3$], 1.03 [s, 9H, SiC$(CH_3)_3$], 1.46 (dd, J = 12.9, 4.5 Hz, 1H), 1.75–1.88 (m, 3H + OH), 2.08 (br s, 1H, OH), 2.55 (dd, J = 14.7, 9.5 Hz, 1H), 2.79 (d, J = 14.3 Hz, 1H), 2.90 (d, J = 14.3 Hz, 1H), 3.02 (dd, J = 14.7, 4.8 Hz, 1H), 3.41 (s, 3H), 3.59–3.68 (m, 3H), 3.81–3.94 (m, 3H), 4.86 (d, J = 6.3 Hz, 1H), 5.00–5.19 (m, 2H), 5.23 (d, J = 5.9 Hz, 1H), 5.60 (d, J = 1.8 Hz, 1H), 5.82–5.89 (m, 2H), 7.28–7.39 (m, 6H), 7.58–7.70 (m, 4 H_r); ^{13}C NMR (90.6 MHz): $\delta = -5.0$ (q, MeSiCH_3), −4.0 (q, H_3CSiMe), 17.9 [s, Si$C(CH_3)_3$], 19.0 [s, Si$C(CH_3)_3$], 25.8 [q, SiC$(CH_3)_3$], 27.0 [q, SiC$(CH_3)_3$], 33.2 (t), 39.6 (t), 40.8 (t), 41.5 (t), 59.0 (q), 66.3 (d), 67.7 (t), 70.4 (d), 71.9 (t), 78.3 (s), 80.9 (s), 90.4 (d), 91.3 (t), 104.0 (d), 117.6 (t), 127.5 (d), 127.5 (d), 129.6 (d), 129.8 (d), 134.1 (s), 134.4 (s), 135.6 (d), 135.6 (d), 135.7 (d), 163.8 (s), 166.8 (s), 171.1 (s); IR (neat): $\tilde{\nu}$ = 3426 (br s, OH), 3072 (m, C_{sp^2}-H), 2955 (s), 2857 (s, C_{sp^3}-H), 1694 (s sh, C=O), 1567 (s), 1472 (m), 1428 (m), 1254 (s), 1112 (vs), 1072 (s), 1028 (s), 872 (m), 836 cm^{-1} (s); MS (EI, 70 eV): *m/z* (%): 695 (1) [$M^+ - t$Bu], 651 (20), 347 (42), 257 (100), 199 (18), 133 (85), 89 (40) [$CH_2OCH_2CH_2OCH_3^+$], 73 (32); elemental analysis calcd (%) for $C_{41}H_{60}O_9Si_2$ (753.08): C 65.39, H 8.03; found: C 65.40, H 8.00.

4-Methoxy-6-([(1*R*,2*S*,3*S*,5*R*)-2-allyl-3-(*tert*-butyldimethylsilyloxy)-5-(*tert*-butyldiphenylsilyloxy)-1-hydroxy-2-(2-methoxyethoxymethoxy)cyclohexyl]methyl)-2*H*-pyran-2-one (50): Pyranone **49** (410 mg, 0.54 mmol) was dissolved in dry acetone (20 mL) and was stirred with K_2CO_2 (500 mg) and dimethyl sulfate (0.11 mL, 151 mg, 1.2 mmol) at RT for 12 h. After 12 h, methanol (1 mL) and sodium acetate (200 mg) were added to the mixture and stirring was continued for 20 min. The mixture was diluted with Et_2O (250 mL) and water (250 mL), the layers were separated. The organic layer was dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 50:50) to give **50** as a colorless oil (377 mg, 0.50 mmol, 92 %). R_f = 0.36 (P/EA 50:50) [CAM]; $[\alpha]_D^{20}$ = 18.2 (c = 0.16, $CHCl_3$); ^{1}H NMR (500 MHz): $\delta = -0.08$ (s, 3H, MeSiCH_3), −0.07 (s, 3H, H_3CSiMe), 0.83 [s, 9H, SiC$(CH_3)_3$], 1.03 [s, 9H, SiC$(CH_3)_3$], 1.44 (dd, J = 12.9, 5.2 Hz, 1H), 1.80–1.98 (m, 3H), 2.04 (s, 1H, OH), 2.55 (dd, J = 15.1, 9.6 Hz, 1H), 2.79 (d, J = 14.4 Hz, 1H), 2.88 (d, J = 14.4 Hz, 1H), 3.03 (dd, J = 15.1, 5.7 Hz, 1H), 3.40 (s, 3H), 3.59 (t, J = 4.6 Hz, 2H), 3.65–3.71 (m, 1H), 3.80–3.96 (m, 6H), 4.86 (d, J = 6.6 Hz, 1H), 5.07 (d, J = 10.2 Hz, 1H), 5.17 (d, J = 17.0 Hz, 1H), 5.24 (d, J = 6.6 Hz, 1H), 5.43 (d, J = 2.3 Hz, 1H), 5.74 (d, J = 2.3 Hz, 1H), 5.84–5.95 (m, 1H), 7.28–7.39 (m, 6H), 7.58–7.70 (m, 4H); ^{13}C NMR (90.6 MHz): $\delta = -5.0$ (q, MeSiCH_3), −4.1 (q, H_3CSiMe), 17.9 [s, Si$C(CH_3)_3$], 19.0 [s, Si$C(CH_3)_3$], 25.8 [q, SiC$(CH_3)_3$], 27.0 [q, SiC$(CH_3)_3$], 33.2 (t), 39.6 (t), 40.7 (t), 41.1 (t), 55.7 (q), 59.1 (q), 66.3 (d), 67.7 (t), 70.3 (d), 71.9 (t), 78.2 (s), 80.7 (s), 87.9 (d), 91.2 (t), 102.8 (d), 117.4 (t), 127.4 (d), 127.5 (d), 129.5 (d), 129.5 (d), 134.3 (s), 134.4 (s), 135.6 (d), 135.7 (d), 135.7 (d), 162.4 (s), 164.4 (s), 170.7 (s); IR (neat): $\tilde{\nu}$ = 3538 (m sh, OH), 3072 (m, C_{sp^2}-H), 2930 (s), 2857 (s, C_{sp^3}-H), 1724 (s sh, C=O), 1648 (s), 1567 (s), 1456 (m), 1410 (m), 1249 (s), 1112 (vs), 1071 (s), 1033 (s), 872 (m), 835 cm^{-1} (s); MS (EI, 70 eV): *m/z* (%): 766 (1) [M^+], 709 (100) [$M^+ - t$Bu], 616 (40), 589 (39), 257 (50), 199 (73), 135 (88), 73 (92); elemental analysis calcd (%) for $C_{42}H_{62}O_9Si_2$ (767.11): C 65.76, H 8.15; found: C 65.70, H 8.48.

4-Methoxy-6-([(1*R*,2*S*,3*S*,5*R*)-2-allyl-3-(*tert*-butyldimethylsilyloxy)-1,5-dihydroxy-2-(2-methoxyethoxymethoxy)cyclohexyl]methyl)-2*H*-pyran-2-one (51): TBDPS ether **50** (402 mg, 0.52 mmol) was dissolved in THF (8 mL). To this solution were added pyridine (0.5 mL) and HF·py (1 mL) at 0 °C. The mixture was allowed to warm to RT and stirred for 12 h (until TLC analysis indicated complete conversion). The mixture was cooled to 0 °C and diluted with EtOAc (50 mL) and sat. aqueous $NaHCO_3$. Stirring was continued at RT until gas evolution stopped. The layers were separated, the aqueous layer was extracted with EtOAc (2× 50 mL). The combined organic layers were washed with sat. aqueous $NaHCO_3$ (100 mL), water (100 mL) and brine (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 50:50) to give the title compound as a colorless oil (257 mg, 0.49 mmol, 94 %). R_f = 0.12 (P/EA 50:50) [CAM]; $[\alpha]_D^{20}$ = 28.0 (c = 0.51, $CHCl_3$); ^{1}H NMR (360 MHz): δ = 0.09 (s, 3H, MeSiCH_3), 0.11 (s, 3H, H_3CSiMe), 0.88 [s, 9H, SiC$(CH_3)_3$], 1.61–1.81 (m, 4H), 2.00–2.04 (m, 1H), 2.37 (s, 1H, OH), 2.59 (dd, J = 14.8, 9.7 Hz, 1H), 2.85 (d, J = 14.3 Hz, 1H), 2.96 (d, J = 14.3 Hz, 1H), 3.11 (dd, J = 14.8, 5.0 Hz, 1H), 3.39 (s, 3H), 3.56 (t, J = 4.7 Hz, 2H), 3.62–3.67 (m, 1H), 3.78 (s, 1H), 3.79–3.88 (m, 2H), 4.18 (dd, J = 11.4, 4.3 Hz, 1H), 4.87 (d, J = 6.6 Hz, 1H), 5.13–5.29 (m, 3H), 5.41 (d, J = 2.3 Hz, 1H), 5.82 (d, J = 2.3 Hz, 1H), 5.90–5.95 (m, 1H); ^{13}C NMR (90.6 MHz): δ = −4.9 (q, MeSiCH_3), −3.9 (q, H_3CSiMe), 17.9 [s, Si$C(CH_3)_3$], 25.8 [q, SiC$(CH_3)_3$], 33.2 (t), 39.2 (t), 40.6 (t), 41.2 (t), 55.7 (q), 59.0 (q), 65.0 (d), 67.8 (t), 70.5 (d), 71.9 (t), 78.3 (s), 80.8 (s), 87.9 (d), 91.2 (t), 103.1 (d), 117.8 (t), 135.5 (d), 162.4 (s), 164.6 (s), 170.9 (s); IR (film): $\tilde{\nu}$ = 3414 (m br, OH), 3070 (w, C_{sp^2}-H), 2929 (m), 2855 (m, C_{sp^3}-H), 1702 (s sh, C=O), 1641 (m), 1565 (s), 1457 (m), 1411 (m), 1249 (s), 1115 (s br), 1070 (s), 1035 (s sh), 874 (m), 837 cm^{-1} (s); MS (EI, 70 eV): m/z (%): 528 (5) [M^+], 471 (12) [$M^+ - t$Bu], 395 (20), 365 (30), 211 (22), 133 (84), 125 (70), 89 (95) [$CH_2OCH_2CH_2OCH_3^+$], 59 (100) [$CH_3OCH_2CH_2^+$]; elemental analysis calcd (%) for $C_{26}H_{44}O_9Si$ (528.71): C 59.06, H 8.39; found: C 59.02, H 8.31.

4-Methoxy-6-([(1*S*,2*S*,3*S*)-2-allyl-3-(*tert*-butyldimethylsilyloxy)-1-hydroxy-2-(2-methoxyethoxymethoxy)-5-oxocyclohexyl]methyl)-2*H*-pyran-2-one (52): IBX[34] (178 mg, 0.63 mmol) at RT was added to a solution of alcohol **51** (224 mg, 0.42 mmol) in DMSO (3 mL). After stirring for 4 h at RT, the solution was diluted with Et_2O (50 mL) and water (50 mL). The layers were separated, the aqueous layer was extracted with Et_2O (2× 30 mL). The combined organic layers were washed with sat. aqueous $NaHCO_3$ (2×80 mL) and brine (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 60:40) to give the title compound as a colorless oil (214 mg, 0.41 mmol, 96 %). R_f = 0.29 (P/EA 50:50) [CAM]; $[\alpha]_D^{20}$ = 85.2 (c = 0.25, $CHCl_3$); ^{1}H NMR (360 MHz): δ = 0.07 (s, 3H, MeSiCH_3), 0.08 (s, 3 H_3CSiMe), 0.87 [s, 9H, SiC$(CH_3)_3$], 2.08 (dd, J = 14.8, 1.6 Hz, 1H), 2.52–2.56 (m, 1H), 2.64–2.73 (m, 2 H + OH), 2.85–2.89 (m, 1H), 2.89 (d, J = 14.3 Hz, 1H), 2.99 (d, J = 14.3 Hz, 1H), 3.20 (dd, J = 15.2, 5.0 Hz, 1H), 3.36 (s, 3H), 3.53–3.56 (m, 2H), 3.62–3.68 (m, 1H), 3.76 (s, 1H), 3.80–3.84 (m, 1H), 4.44 (dd, J = 10.5, 5.5 Hz, 1H), 4.92 (d, J = 6.8 Hz, 1H), 5.16 (virt. d, $J \cong$ 10.0 Hz, 1H), 5.23 (virt. d, $J \cong$ 16.7 Hz, 1H), 5.30 (d, J = 6.8 Hz, 1H), 5.39 (d, J = 2.1 Hz, 1H), 5.80 (d, J = 2.1 Hz, 1H), 5.90–5.96 (m, 1H); ^{13}C NMR (90.6 MHz): δ = −5.0 (q, MeSiCH_3), −4.2 (q, H_3CSiMe), 17.8 [s, Si$C(CH_3)_3$], 25.7 [q, SiC$(CH_3)_3$], 33.2 (t), 40.4 (t), 46.8 (t), 48.1 (t), 55.8 (q), 59.0 (q), 67.9 (t), 70.9 (d), 71.7 (t), 78.5 (s), 80.8 (s), 88.1 (d), 91.5 (t), 103.3 (d), 118.3 (t), 134.4 (d), 161.1 (s), 164.2 (s), 170.6 (s), 206.4 (s); IR (neat): $\tilde{\nu}$ = 3416 (m br, OH), 3070 (w, C_{sp^2}-H), 2926 (s, C_{sp^3}-H), 1721 (vs sh, C=O), 1649 (m), 1567 (vs), 1459 (m), 1412 (m), 1250 (s sh), 1107 (s br), 1018 (s sh), 837 (s), 828 (m), 777 cm^{-1} (m); MS (EI, 70 eV): m/z (%): 526 (3) [M^+], 469 (12) [$M^+ - t$Bu], 133 (60), 125 (40), 89 (100) [$CH_2OCH_2CH_2OCH_3^+$], 59 (78) [$CH_3OCH_2CH_2^+$]; elemental analysis calcd (%) for $C_{26}H_{42}O_9Si$ (526.69): C 59.29, H 8.04; found: 59.31, H 7.92.

4-Methoxy-6-([(1*R*,2*S*,3*S*,5*S*)-2-allyl-3-(*tert*-butyldimethylsilyloxy)-2-(2-methoxyethoxymethoxy)-1,5-dihydroxycyclohexyl]methyl)-2*H*-pyran-2-one (53): A solution of L-selectride in THF (1 M; 0.34 mL, 0.34 mmol) dropwise at −78 °C was added to a solution of ketone **52** (180 mg, 0.34 mmol) in THF (7 mL). The solution was stirred at −78 °C for 2 h. Then, methanol (0.6 mL), aqueous NaOH (2 M; 0.6 mL) and aqueous H_2O_2 (30 %; 0.6 mL) were added subsequently. The mixture was warmed to 0 °C. After stirring for 30 min at 0 °C, the mixture was diluted with water (50 mL) and Et_2O (50 mL). The layers were separated and the aqueous layer was extracted with Et_2O (50 mL). The combined organic layers were washed with water (70 mL) and brine (70 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (CH_2Cl_2/MeOH 95:5) to give the title compound as a colorless oil (175 mg, 0.33 mmol, 97 %). R_f = 0.26 (CH_2Cl_2/MeOH 95:5) [CAM]; $[\alpha]_D^{20}$ = 56.3 (c = 0.90, $CHCl_3$); ^{1}H NMR (360 MHz): δ = 0.07 (s, 3H, MeSiCH_3), 0.07 (s, 3H, H_3CSiMe), 0.86 [s, 9H, SiC$(CH_3)_3$], 1.51 (dd, J = 14.3, 2.9 Hz, 1H), 1.90–1.95 (m, 2H), 2.04 (dd, J = 14.3, 3.4 Hz, 1H), 2.61 (dd, J = 14.8, 8.4 Hz, 1H), 2.79–2.85 (m, 2H), 3.11 (dd, J = 14.8, 5.9 Hz, 1H), 3.39 (s, 3H), 3.52 (br s, 1H, OH), 3.53 (t, J = 3.9 Hz, 2H), 3.58–3.61 (m, 1H), 3.77 (s, 1H), 3.78–3.83 (m, 1H), 3.84 (s, 1H, OH), 4.07–4.09 (m, 1H), 4.37 (br s, 1H), 4.84 (d, J = 6.6 Hz, 1H), 5.07–5.18 (m, 3H), 5.36 (d, J = 2.3 Hz, 1H), 5.86 (d, J = 2.3 Hz, 1H), 6.02 (br s, 1H); ^{13}C NMR (90.6 MHz): δ = −5.0 (q, MeSiCH_3), −4.1 (q, H_3CSiMe), 17.9 [s, Si$C(CH_3)_3$], 25.8 [q, SiC$(CH_3)_3$], 32.9 (t), 36.1 (t), 37.8 (t), 40.7 (t), 55.7 (q), 58.9 (q), 67.1 (d), 67.7 (t), 68.2 (d), 71.7 (t), 80.1 (s), 81.9 (s), 87.6 (d), 91.2 (t), 103.2 (d), 116.8 (t), 135.6 (d), 162.7 (s), 165.0 (s), 171.1 (s); IR (neat): $\tilde{\nu}$ = 3398 (br s, OH), 3070 (w, C_{sp^2}-H), 2928 (s, C_{sp^3}-H), 1693 (s sh, C=O), 1644 (s), 1565 (vs), 1458 (s), 1411 (m), 1249 (s), 1033 (s sh), 837 cm^{-1} (s); MS (EI, 70 eV): m/z (%): 528 (5) [M^+], 471 (12) [$M^+ - t$Bu], 395 (20), 365 (28), 289 (38), 133 (62), 125 (75), 89 (95) [$CH_2OCH_2CH_2OCH_3^+$], 59 (100) [$CH_3OCH_2CH_2^+$]; elemental analysis calcd (%) for $C_{26}H_{44}O_9Si$ (528.71): C 59.06, H 8.39; found: C 58.67, H 8.48.

4-Methoxy-6-([(1*R*,2*S*,3*S*,5*S*)-2-allyl-3-(*tert*-butyldimethylsilyloxy)-2-(2-methoxyethoxymethoxy)-1,5-(dimethyl)methylendioxycyclohexyl]-methyl)-2*H*-pyran-2-one (54): Diol **53** (175 mg, 0.33 mmol) was dissolved in 1,2-dichloroethane (10 mL). At 0 °C, a catalytic amount of PPTS (< 2 mg) was added followed by a slow addition of 2-methoxypropene (67 μL, 50 mg). The solution was stirred for 15 min at 0 °C, then warmed to RT. After 3 h at RT, triethylamine (0.6 mL) was added at once. The mixture was diluted with Et_2O (100 mL) and sat. aqueous $NaHCO_3$ (100 mL). The layers were separated and the aqueous layer was extracted with Et_2O (50 mL). The combined organic layers were washed with water (100 mL) and brine (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 50:50) to give the title compound as a colorless oil (169 mg, 0.29 mmol, 90 %). R_f = 0.28 (P/EA 50:50) [CAM]; $[\alpha]_D^{20}$ = 76.7 (c = 0.97, $CHCl_3$); ^{1}H NMR (400 MHz): δ = 0.09 (s, 3H, MeSiCH_3), 0.09 (s, 3H, H_3CSiMe), 0.89 [s, 9H, SiC$(CH_3)_3$], 1.17 (s, 3H), 1.27 (s, 3H), 1.67 (ddd, J = 12.5, 11.1, 1.6 Hz, 1H), 1.96–2.03 (m, 1H), 2.27 (dd, J = 15.0, 1.8 Hz, 1H), 2.31 (ddd, J = 15.0, 4.5, 2.0 Hz, 1H), 2.55 (dd, J = 15.4, 7.0 Hz, 1H), 2.83 (d, J = 13.9 Hz, 1H), 2.85 (d, J = 13.9 Hz, 1H), 3.03 (dd, J = 15.4, 7.3 Hz, 1H), 3.37 (s, 3H), 3.55 (t, J = 4.8 Hz, 2H), 3.62 (dt, J = 10.7, 4.8 Hz, 1H), 3.76–3.81 (m, 1H), 3.79 (s, 1H), 4.20–4.28 (m, 1H), 4.33 (dd, J = 11.1, 5.0 Hz, 1H), 4.86 (d, J = 6.5 Hz, 1H), 4.97 (dd, J = 10.2, 1.6 Hz, 1H), 5.08 (dd, J = 17.0, 1.6 Hz, 1H), 5.20 (d, J = 6.5 Hz, 1H), 5.41 (d, J = 2.1 Hz, 1H), 5.82 (d, J = 2.1 Hz, 1H), 6.02 (dddd, J = 17.0, 10.2, 7.3, 7.0 Hz, 1H); ^{13}C NMR (90.6 MHz): δ = −4.8 (q, MeSiCH_3), −3.9 (q, H_3CSiMe), 18.0 [s, Si$C(CH_3)_3$], 25.9 (t, C8), 26.0 [q, SiC$(CH_3)_3$], 31.4 (q, H_3CCCH_3), 31.8 (q, H_3CCCH_3), 33.5 (t), 38.7 (t), 40.3 (t), 55.8 (q), 59.0 (q), 66.5 (d), 67.7 (t), 70.3 (d), 71.9 (t), 79.2 (s), 81.9 (s), 87.8 (d), 91.5 (t), 98.2 (s), 104.0 (d), 115.3 (t), 135.5 (d), 162.5 (s), 164.9 (s), 170.9 (s); IR (neat): $\tilde{\nu}$ = 3078 (m, C_{sp^2}-H), 2930 (vs), 2857 (vs, C_{sp^3}-H), 1728 (s, C=O), 1649 (s), 1569 (vs), 1457 (s), 1411 (s), 1248 (vs), 1197 (m), 1028 (s sh), 1098 (s), 1073 (s), 1026 (vs), 992 (s), 836 cm^{-1} (s); MS (EI, 70 eV): m/z (%): 568 (4) [M^+], 511 (10) [$M^+ - t$Bu], 421 (18), 221 (15), 133 (34), 125 (37), 89 (100) [$CH_2OCH_2CH_2OCH_3^+$], 59 (68) [$CH_3OCH_2CH_2^+$]; elemental analysis calcd (%) for $C_{29}H_{48}O_9Si$ (568.772): C 61.24, H 8.51; found: C 61.07, H 8.55.

2-{(1*S*,2*R*,4*S*,6*S*)-6-(*tert*-Butyldimethylsilyloxy)-2,4-(dimethyl)methylendioxy-1-(2-methoxyethoxymethoxy)-2-[(4-methoxy-6-oxopyran-2-yl)methyl]cyclohexyl}acetaldehyde (44): Acetonide **54** (700 mg, 1.24 mmol) was dissolved in THF (20 mL) and an aqueous solution of sodium acetate in water (1.5 g in 20 mL) at RT. To this mixture was added a solution of OsO_4 in water (1 %; 0.08 mL) and $NaIO_4$ (1.07 g, 5 mmol) subsequently.

The mixture was stirred for 3 h at RT. The precipitate was filtered off. The residue was washed with Et_2O (80 mL). The filtrate was diluted with Et_2O (150 mL) and water (150 mL). The layers were separated. The aqueous layer was extracted with Et_2O (2×100 mL). The combined organic layers were washed with sat. aqueous $NaHCO_3$ (250 mL) and brine (250 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 50:50) to give **44** as a colorless oil (605 mg, 1.06 mmol, 85%). R_f=0.21 (P/EA 50:50) [CAM]; $[\alpha]_D^{20}$ = 94.0 (c=1.58, CH_2Cl_2); ^{1}H NMR (360 MHz, [D$_6$]benzene): δ=0.06 (s, 3H, MeSiCH_3), 0.11 (s, 3H, H_3CSiMe), 0.90 [s, 9H, SiC(CH$_3$)$_3$], 1.22 (s, 6H), 1.62 (ddd, J=12.3, 11.0, 1.6 Hz, 1H), 1.99–2.07 (m, 1H), 2.13 (dd, J=15.0, 1.6 Hz, 1H), 2.48 (ddd, J=15.0, 4.8, 2.0 Hz, 1H), 2.89 (d, J=13.9 Hz, 1H), 2.96 (dd, J=13.2, 4.8 Hz, 1H), 2.98 (s, 3H), 3.04 (d, J=13.9 Hz, 1H), 3.23 (s, 3H), 3.40 (dd, J=13.2, 2.0 Hz, 1H), 3.41–3.44 (m, 2H), 3.51–3.55 (m, 1H), 3.76–3.84 (m, 1H), 4.02–4.06 (m, 1H), 4.67 (dd, J=11.0, 5.0 Hz, 1H), 4.88 (d, J=7.0 Hz, 1H), 5.31 (d, J=2.3 Hz, 1H), 5.46 (d, J=7.0 Hz, 1H), 5.82 (d, J=2.3 Hz, 1H), 10.00 (dd, J=4.8, 2.0 Hz, 1H); ^{13}C NMR (90.6 MHz, [D$_6$]benzene]): δ=−4.7 (q, MeSiCH_3), −4.1 (q, H$_3$CSiMe), 18.2 [s, SiC(CH$_3$)$_3$], 26.1 (t), 26.1 [q, SiC(CH_3)$_3$], 31.2 (q), 31.8 (q), 38.8 (t), 41.0 (t), 43.9 (t), 55.0 (q), 58.8 (q), 66.4 (d), 68.2 (t), 71.2 (d), 72.3 (t,, 79.1 (s), 83.0 (s), 88.2 (d), 92.3 (t), 99.2 (s), 103.9 (d), 162.0 (s), 163.4 (s), 170.5 (s), 197.4 (d): IR (neat): $\tilde{\nu}$=3072 (m, C_{sp^2}-H), 2930 (s, C_{sp^3}-H), 1726 (s sh, C=O), 1649 (s), 1565 (s), 1456 (s), 1410 (s), 1248 (s), 1028 (s), 1095 (s), 1073 (s), 1026 cm^{-1} (s); MS (EI, 70 eV): m/z (%): 570 (2) [M^+], 555 (6) [M^+ −CH$_3$], 513 (9) [M^+−tBu], 423 (10), 349 (28), 221 (25), 133 (24), 125 (52), 89 (100) [CH$_2$OCH$_2$CH$_2$OCH$_3^+$], 59 (55) [CH$_3$OCH$_2$CH$_2^+$], 44 (28).

2-{(1*S*,2*R*,4*S*,6*S*)-6-(*tert*-Butyldimethylsilyloxy)-2,4-(dimethyl)methylendioxy-1-(2-methoxyethoxymethoxy)-2-[(4-methoxy-6-oxopyran-2-yl)methyl]cyclohexyl}-1-phenylethanone (55): A solution of phenylmagnesium bromide in Et_2O (3 M; 0.43 mL, 1.3 mmol) at −78 °C was added to a solution of aldehyde **44** (580 mg, 1.02 mmol) in THF (50 mL). The yellow solution was stirred for 1 h at −78 °C. The cold reaction mixture was quenched by addition of sat. aqueous NH_4Cl (200 mL). The mixture was extracted with Et_2O (2×200 mL). The combined organic layers were washed brine (400 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 50:50) to give the secondary alcohol as a mixture of epimers (588 mg, 0.91 mmol, 89%; dr 4:1 according to ^{1}H NMR). The epimeric mixture (588 mg, 0.91 mmol) was dissolved in CH_2Cl_2 (30 mL). To this solution were added $NaHCO_3$ (1 g) and Dess–Martin periodinane (678 mg, 1.6 mmol) subsequently. The mixture was stirred at RT. After 3 h, Et_2O (100 mL) and sat. aqueous $NaHCO_3$ (100 mL) containing 5% $Na_2S_2O_3$ were added. The biphasic mixture was stirred at RT until the formation of two clear layers was observed (~30 min). The layers were separated. The organic layer was washed with water (100 mL) and brine (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 50:50) to give **55** as a colorless oil (536 mg, 0.83 mmol, 91%). R_f=0.23 (P/EA 50:50) [CAM]; $[\alpha]_D^{20}$= 101.2 (c=1.06, $CHCl_3$); ^{1}H NMR (360 MHz, [D$_6$]benzene]): δ=0.37 (s, 3H, MeSiCH_3), 0.40 (s, 3H, H_3CSiMe), 1.01 [s, 9H, SiC(CH$_3$)$_3$], 1.07 (s, 3H), 1.33 (s, 3H), 1.72 (ddd, J=12.5, 11.1, 1.6 Hz, 1H), 2.16 (dd, J=15.0, 1.6 Hz, 1H), 2.16–2.23 (m, 1H), 2.58 (ddd, J=15.0, 4.8, 2.3 Hz, 1H), 2.77 (s, 3H), 2.86 (d, J=13.9 Hz, 1H), 2.94 (d, J=13.9 Hz, 1H), 3.16 (s, 3H), 3.36–3.43 (m, 1H), 3.48–3.56 (m, 2H), 3.61 (d, J=12.7 Hz, 1H), 3.90–3.96 (m, 1H), 4.06 (d, J=12.7 Hz, 1H), 4.11 (tt, J=4.8, 1.6 Hz, 1H), 4.84 (d, J=2.3 Hz, 1H), 4.92 (d, J=7.3 Hz, 1H), 5.21 (d, J=2.3 Hz, 1H), 5.26 (dd, J=11.1, 5.0 Hz, 1H), 5.83 (d, J=7.3 Hz, 1H), 7.24–7.27 (m), 8.00–8.03 (m); ^{13}C NMR (90.6 MHz, [D$_6$]benzene]): δ=−4.5 (q, MeSiCH_3), −4.3 (q, H$_3$CSiMe), 18.4 [s, SiC(CH$_3$)$_3$], 26.3 [q, SiC(CH_3)$_3$], 26.5 (t), 30.3 (q), 31.9 (q), 35.6 (t), 39.4 (t), 40.6 (t), 54.8 (q), 58.8 (q), 66.5 (d), 67.8 (t), 70.5 (d), 72.5 (t), 79.0 (s), 84.8 (s), 88.1 (d), 92.2 (t), 99.5 (s), 103.5 (d), 128.8 (d), 129.0 (d), 132.0 (d), 141.0 (s), 162.3 (s), 163.4 (s), 170.4 (s), 198.1 (s); IR (neat): $\tilde{\nu}$=3072 (m, C_{sp^2}-H), 2928 (s, C_{sp^3}-H), 1731 (vs sh, C=O), 1681 (s), 1649 (s), 1568 (s), 1454 (s), 1412 (s), 1336 (s), 1249 (s), 1195 (s), 1027 (s sh), 1018 (s), 931 (s), 836 cm^{-1} (s); MS (EI, 70 eV): m/z (%): 646 (1) [M^+], 555 (2) [M^+−CH$_3$], 513 (18) [M^+−tBu], 499 (22), 483 (20), 425 (42), 221 (23), 125 (68), 105 (100) [C$_7$H$_5$O$^+$], 89 (94) [CH$_2$OCH$_2$CH$_2$OCH$_3^+$], 59 (80) [CH$_3$OCH$_2$CH$_2^+$]; elemental analysis calcd (%) for $C_{34}H_{50}O_{10}Si$ (646.84): C 63.13, H 7.79;found: C 63.15, H 7.84.

6-{(1*R*,3*S*,4*S*,6*S*,8*R*)-[4-(*tert*-Butyldimethylsilyloxy)-3-hydroxy-1-phenyl-9,10-dioxatricyclo[4.3.1.0][3,8]dec-8-yl]methyl}-4-methoxy-2*H*-pyran-2-one (56): A mixture of water (10 mL), acetic acid (10 mL) and trifluoroacetic acid (5 mL) was added to a solution of ketone **55** (350 mg, 0.54 mmol) in THF (20 mL). The resulting mixture was stirred at RT for 1 h, and then the mixture was poured into ice-cold sat. aqueous $NaHCO_3$ (200 mL). The mixture was neutralized with K_2CO_3 and diluted with Et_2O (200 mL) and water (100 mL). The layers were separated. The aqueous layer was extracted with Et_2O (2×100 mL). The combined organic layers were washed with water (300 mL) and brine (300 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 50:50) to give **56** as a colorless oil (185 mg, 0.37 mmol, 69%). R_f=0.58 (P/EA 50:50) [CAM]; $[\alpha]_D^{20}$ = 88.9 (c=0.24, $CHCl_3$); ^{1}H NMR (360 MHz, [D$_6$]benzene]): δ=−0.05 (s, 3H, MeSiCH_3), 0.00 (s, 3H, H_3CSiMe), 0.91 [s, 9H, SiC(CH$_3$)$_3$], 1.69 (dd, J=15.7, 5.9 Hz, 1H), 2.28–2.38 (m, 3H), 2.35 (d, J=12.9 Hz, 1H), 2.51 (s, 1H, OH), 2.52 (d, J=12.9 Hz, 1H), 2.63 (d, J=14.5 Hz, 1H), 2.83 (s, 3H), 3.14 (d, J=14.5 Hz, 1H), 4.11 (d, J=6.4 Hz, 1H), 4.20–4.24 (m, 1H), 5.16 (d, J=2.3 Hz, 1H), 5.92 (d, J=2.3 Hz, 1H), 7.19–7.28 (m, 3H), 7.82–7.87 (m, 2H); ^{13}C NMR (90.6 MHz, [D$_6$]benzene]): δ=−4.9 (q, MeSiCH_3), −4.6 (q, H$_3$CSiMe), 18.1 [s, SiC(CH$_3$)$_3$], 26.0 [q, SiC(CH_3)$_3$], 34.9 (t), 39.0 (t), 40.8 (t), 52.3 (t), 54.8 (q), 68.7 (d), 73.7 (d), 81.4 (s), 83.3 (s), 88.2 (d), 102.4 (d), 103.7 (s), 125.7 (d), 127.6 (d), 128.4 (d), 141.0 (s), 162.2 (s), 163.4 (s), 170.6 (s); IR (neat): $\tilde{\nu}$=3455 (m br, OH), 3072 (w, C_{sp^2}-H), 2928 (s, C_{sp^3}-H), 1699 (s sh, C=O), 1645 (s), 1567 (s), 1456 (s), 1412 (m), 1360 (m), 1251 (s), 1093 (vs sh), 1019 (s), 922 (m), 828 cm^{-1} (m); MS (EI, 70 eV): m/z (%): 500 (5) [M^+], 443 (40) [M^+−tBu], 343 (18), 292 (22), 105 (100) [C$_7$H$_5$O$^+$], 73 (30), 40 (28); elemental analysis calcd (%) for $C_{27}H_{36}O_7Si$ (500.66): C 64.77, H 7.25; found: C 64.79, H 7.20.

(7*R*,9*R*,12*R*,14*R*)-(+)-Wailupemycin B (2): A solution of TBAF in THF (1 M; 0.3 mL, 0.3 mmol) at 0 °C was slowly added to a solution of **56** (102 mg, 0.20 mmol) in THF (15 mL). Stirring was continued at 0 °C for 20 min, and then sat. aqueous NH_4Cl (150 mL) and EtOAc (150 mL) were added. The layers were separated. The aqueous layer was extracted with EtOAc (100 mL). The combined organic layers were washed with water (200 mL) and brine (200 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product was directly used in the next step. The crude alcohol was dissolved in EtOAc (10 mL). To this solution was added IBX (280 mg, 1 mmol). The mixture refluxed for 4 h, cooled to RT, filtered and concentrated in vacuo. The crude product was purified by flash chromatography (P/EA 50:50) to give wailupemycin B **(2)** as a colorless oil (54 mg, 0.14 mmol, 70%). R_f=0.22 (P/EA 50:50) [CAM]; $[\alpha]_D^{20}$= 79.0 (c=0.09, MeOH); natural product:[1] $[\alpha]_D^{20}$= 77.7 (c=0.07, MeOH); ^{1}H NMR (600 MHz): δ=1.62 (d, J=13.3 Hz, 1H, C8H_aH), 2.41 (ddd, J=13.3, 5.0, 2.6 Hz, 1H, C8HH_b), 2.55 (d, J=13.6 Hz, 1H, C13H_aH), 2.73 (dd, J=18.7, 5.3 Hz, 1H, C10H_aH), 2.76 (d, J=13.6 Hz, 1H, C13HH_b), 2.85 (d, J=14.9 Hz, 1H, C6H_bH), 3.03 (d, J=14.9 Hz, 1H, C6HH_b), 3.14 (br d, J=18.7 Hz, 1H, C10HH_b), 3.80 (s, 3H, OCH$_3$), 4.01 (br s, 1H, OH), 4.76 (virt. t, J ≅ 5.0 Hz, 1H, H9), 5.43 (d, J=2.3 Hz, 1H, H2), 6.02 (d, J=2.0 Hz, 1H, H4), 7.36–7.41 (m, 3H, H$_{Ar}$), 7.59 (d, J=7.5 Hz, 2H, H$_{Ar}$); ^{13}C NMR (90.6 MHz): δ=36.1 (t, C8), 38.7 (t, C6), 43.7 (t, C10), 54.7 (t, C10), 55.8 (q, OCH$_3$), 69.0 (d, C9), 85.0 (s, C12), 85.4 (s, C7), 88.2 (d, C2), 103.2 (d, C4), 106.0 (s, C14), 125.0 (d), 128.3 (d), 128.9 (d), 138.5 (s), 160.5 (s, C5), 164.3 (s, C1), 171.0 (s, C3), 208.9 (s, C11); IR (neat): $\tilde{\nu}$=3450 (br s, OH), 3072 (m), 3013 (m, C_{sp^2}-H), 2957 (s, C_{sp^3}-H), 1723 (s sh, C=O), 1647 (s), 1567 (vs), 1456 (s), 1411 (m), 1328 (m), 1248 (s), 1119 (s), 1072 (m), 1020 (m), 943 (m), 758 cm^{-1} (vs); MS (EI, 70 eV): m/z (%): 384 (15) [M^+], 356 (50), 209 (52), 140 (100), 125 (48), 105 (90) [C$_7$H$_5$O$^+$], 77 (32), 40 (20); HRMS: m/z: calcd for $C_{21}H_{20}O_7$: 384.1209, found 384.1206.

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