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Matched and mismatched pairings in B-secotaxane construction: a structure elucidation study

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Abstract—The synthesis of the basic B-seco taxoid skeleton was achieved through a C10–C11 coupling of the A-ring segment (14*S*)-**1** with the C-ring segments (10*S*) and (10*R*)-α-alkoxyorganolithium reagents, prepared in situ from **2** and **6** through *n*BuLi mediated transmetallation. The matched reactions of (14*S*)-**1** with (10*S*)-**2** and (10*S*)-**6** displays an outstanding diastereoselectivity providing **12** and **34**, respectively, as single isomers and hence allowing a convenient entry to highly functionalized taxoid diterpene frameworks. Significant mismatching was observed with the (10*R*)-epimer of **2** and **6** yielding little, if any, diastereoselectivity. The structures of B-secotaxanes were assigned on the basis of spatial proximity effects in the proton NMR spectrum. Assignment of the C10/C11 stereochemistry was made possible through conversion of the B-secotaxoid frameworks, derived from the matched and mismatched adducts, to the corresponding cyclic acetals. Configurational stability of α-alkoxyorganolithium derivatives was verified in all the cases investigated. Structure elucidation of these adducts was essential for the successful C1–C2 bonding via an intramolecular aldol reaction, given the fact that adducts containing a β-MOM substituent at C10 would be disfavored for such an endeavor.

1. Introduction

Recently, our laboratory reported an efficient A+C approach for assembling the taxoid ABC diterpene framework[1] based on Still's α-alkoxyorganolithium[2] mediated fragment coupling and an intramolecular aldol reaction for the crucial B-ring formation. This protocol has been applied to the construction of close precursors of all major taxoid representatives[3] thus demonstrating the suitability of the stannylation/destannylation-aldol protocol to access the key substructure **4**.

This approach was carried further using a five-step sequence, which introduced the oxygen functionalities at C-1 and C-5 and reduced the existing at C-14, thus transforming the key substructure **4** into the pivotal intermediate **5**. This resulted in the preparation of several tricyclic taxoid diterpene frameworks, close precursors of various representatives of the taxane family. The most accessible was the hitherto unsynthesized taxuspine D **9**,[4] and 7-deoxytaxanes **10** (taiwanxan) and **11** (taxuyunnanine C),[5] whose ABC substructures are quite close to **5** and **8**, respectively (Scheme 1). Our interest in this topic resulted from the need of an effective scaleable synthesis of the taxoid ABC-ring systems **4** and **8**, valuable precursors in the preparation of taxoids possessing medical applications other than oncological. First accomplished using the enantiomerically pure organostannane (10*S*)-**2** with racemic **1**, the A+C coupling revealed the existence of a high kinetic discrimination. With the above mentioned successful construction of the taxoid diterpene **4**, we became particularly interested in how reactions of (14*S*)-**1**[6] with (10*S*)-**6** and (10*R*)-**6** derived α-alkoxyorganolithium reagents would proceed in leading to either matched or mismatched B-secotaxanes, since, ultimately that could determine the aldol outcome during the crucial B-ring closure. We expected, from precedent in our work, to be able to generate 7-deoxytaxane (7-nor taxoid) ABC framework **8** and believed that we would also be able to introduce the right stereochemistry at C-11 by using the appropriate matched segments.

The two (10*S*)-α-alkoxyorganolithium reagents from **2** and **6** exhibited typical matched behavior with (14*S*)-**1** affording single AC adducts **12** (Scheme 2) and **34** (Scheme 5), respectively. Additions of α-alkoxyorganolithium reagents from (10*R*)-organostannanes, **2** and **6**,

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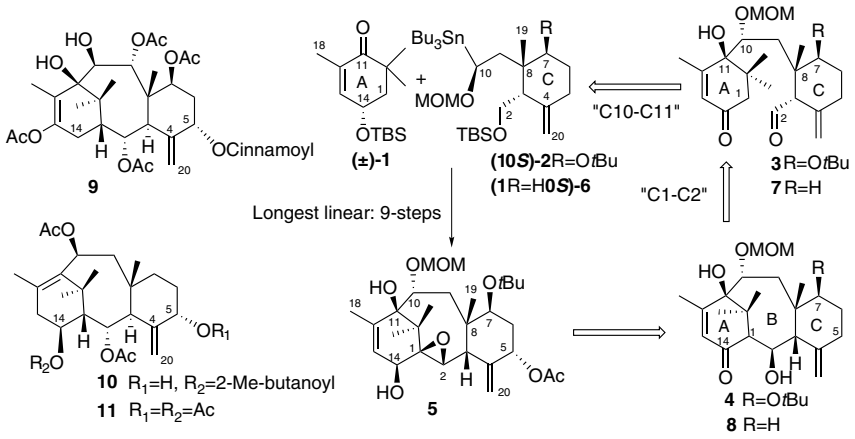
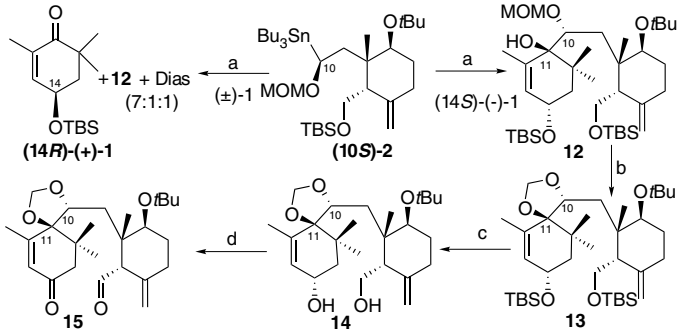


Scheme 1.



Scheme 2. Reagents and conditions: (a) *n*BuLi, THF, −78 °C, 20 min; (b) TMSOTf, collidine, −30 to 0 °C, 2 h; (c) TBAF–THF, 60 °C, 2.5 h; (d) Dess–Martin periodinane, dry CH_2Cl_2, py, 25 °C, 1.5 h.

on the other hand, were significantly mismatched. In each case, the adducts resulting from β-face attack accounted for nearly one-half of the total AC products. Since we were unable to obtain X-ray quality crystals of B-secotaxane frameworks synthesized their corresponding acetal derivatives proved ideal substrates for NOEDIFF experiments, and we were able to obtain excellent support for our assignments. This paper describes a series of experiments addressing these issues.

2. Results and discussion

The synthesis of C-ring fragments such as α-alkoxy stannanes **2** and **6** to be used as 'C-10 Nu^{-}' and TBS-protected phorenol **1** to be used as 'C-11 E^{+}' for the synthesis of the B-seco taxane derivatives has been described in previous work.[7] To accomplish the key fragment coupling (C10–C11), we opted to employ the Still transmetallation, in view of the high regio- and stereoselectivity this process is known to display. In each case, the appropriate tin acetal was converted to its corresponding α-alkoxy stabilized carbanion, which in turn was coupled with the A-ring precursor (14*S*)-**1** to produce the desired B-secotaxane framework. In the present study, we have used stereopure A and C-ring components in order to facilitate product characterization. In all cases investigated, this reaction was regioselective, with nucleophilic attack of the α-alkoxyorganolithium species occurring exclusively at the C-11 electrophilic terminus of **1**.[8]

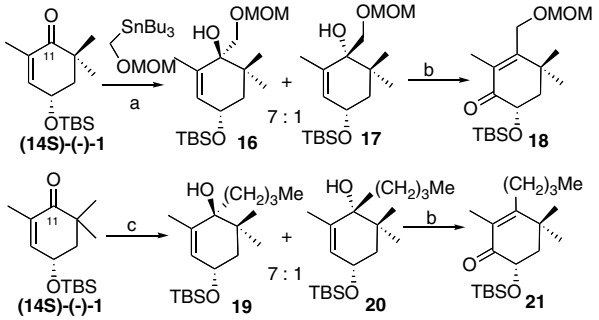
2.1. Linking of the subunits: preparation of B-secotaxanes

The matched double asymmetric reaction of Tin-MOM acetal (10*S*)-**2** with (14*S*)-**1** proceeded with an outstanding stereoselectivity and in excellent isolated yield (92%) affording **12** as the sole detectable adduct. At this stage, neither the C10 configuration of the organotin acetal nor the stereochemistry at C10 relative to C11 and C14 in **12** could be determined from NMR analysis. Therefore, the assignment of the absolute configuration of (10*S*)-**2** was based on the relative stereochemistry of the C-10 stereocenter in **4** (Scheme 1) and the assumption of retentive transmetallation,[9] which by inference, proved the C-10 configuration of **2**. We needed a more direct and reliable method to assign the configurations of the newly formed carbinol center at C11, resulting from the segment coupling. This was achieved through conversion of the B-secotaxoid frameworks to their corresponding acetals (e.g., **13**–**15**).

To check the reliability of the proposed structure correlation, full stereochemical assignment of the known **12** was achieved following conversion to its corresponding acetal **13** by treatment with TMSOTf in the presence

of collidine (TMSOTf, collidine, −30 to 0 °C, 2 h, 97%). The added rigidity in the molecule accompanying this transformation allowed for the successful measuring of proximity effects using NOE difference experiments (see below). This material was converted to enone-aldehyde **15** in a straightforward two-step sequence. First, acetal **13** was desilylated (nBu$_4$NF–THF, 60 °C, 2 h) to yield diol **14** (96%), which was then subjected to Dess–Martin oxidation (Dess–Martin periodinane, dry CH_2Cl_2, py, 25 °C, 1.5 h) to give **15** (85%).

With the outstanding match effect observed in the above reaction, we went on to check the inherent facial selectivity of (14*S*)-**1** with achiral organolithium reagents such as nBuLi and Bu_3SnCH_2OMOM. The latter was readily prepared using literature procedures from the corresponding aldehyde by condensation of lithium tributylstannylate followed by protection of the resulting alcohol using chloromethyl methyl ether in the presence of Hunig's base.[10] As portrayed in Scheme 3, the reactant **1** [racemic and (*S*)-form] in its reactions with achiral reaction partners revealed a 7:1 inherent diastereoselectivity. Furthermore, these reactions, like that of (10*S*)-**2** with (14*S*)-**1** (Scheme 2) were regioselective, with nucleophilic attack of the α-alkoxy carbanion occurring exclusively at the C-11 electrophilic terminus.



Scheme 3. Reagents and conditions: (a) nBuLi, Bu_3SnCH_2OMOM, THF, −78 °C, 20 min; (b) PCC, 4 Å MS, CH_2Cl_2, 25 °C, 12 h; (c) nBuLi, THF, −78 °C, 20 min.

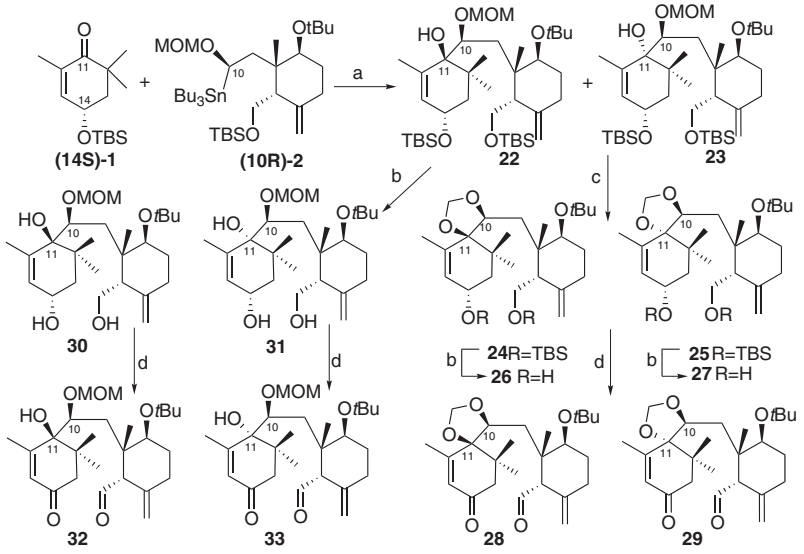
The reaction between enone (14*S*)-**1** and α-alkoxyorganolithium derived from Bu_3SnCH_2OMOM via transmetallation with nBuL*i* (nBuLi, Bu_3SnCH_2OMOM, THF, −78 °C, 20 min) gave a mixture of two diastereomeric products, **16** and **17** (84% in 7:1 ratio), which were separated by SiO_2 flash chromatography and isolated pure. Reaction between enone (14*S*)-**1** and nBuLi proceeded analogously (nBuLi, THF, −78 °C, 20 min), affording a 7:1 mixture of **19** and **20** (99% combined yield). Rather than separating the mixture (except small quantities for assigning the stereostructures), we preferred to proceed via an oxidative rearrangement affording the transposed α,β-unsaturated ketones **18** and **21**. The Dauben–Michno oxidative rearrangement[11] (PCC, 4 Å MS, CH_2Cl_2, 25 °C, 12 h) of the mixture (**16**+**17**) provided the transposed enone **18** (58%, 96% based on recovered starting material) possessing the olefin at C11-C12 position as required for the vast majority of taxanes. This transformation allows the C10 center to be introduced as a methoxymethyl ether, in a form suitable for subsequent elaboration into the taxoid diterpene framework. Similarly, the oxidation of the mixture **19**+**20** according to Dauben–Michno protocol, delivered enone **21** in 83% yield. These results show that reasonably high levels of control in face selectivity can be achieved with the TBS-protected derivative of phorenol **1** (both racemic and 14*S* forms).

While the matched double asymmetric reaction of (14*S*)-**1** with (10*S*)-**2** proceeded with excellent stereoselectivity affording a single diastereomer, significant mismatching was observed with the (10*R*)-epimer of **2**, yielding moderate diastereoselectivity, with a slight reversal in facial selectivity. With the configurational assignments of **12** secured by spatial proximity studies on the cyclic acetal derivatives, and the inherent facial selectivity of **1** found to be roughly 7:1, we went on to determine the identity of the AC adducts **22** and **23**. Hence, we set out on the sequence displayed in Scheme 4. Thus, proceeding under the same conditions as above, the mismatched reaction of (14*S*)-**1** with (10*R*)-**2** did not display any significant diastereoselectivity affording **22** and **23**, in 84% combined yield and in a 1:1.3 ratio (Scheme 4), easily separable by column chromatography on silica gel.

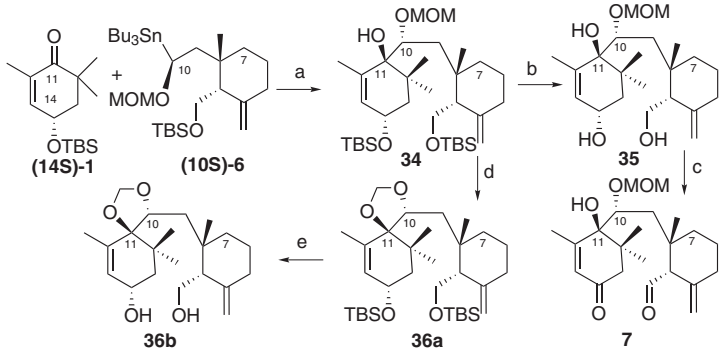
This reaction, like that of (10*S*)-**2** is regioselective with nucleophilic attack of α-alkoxy carbanion occurring exclusively at the C-11 electrophilic terminus. At that point, spectral analysis could not tell us, which of the two possible B-secotaxanes, C11(*S*)-**22** or C11(*R*)-**23**, was preferentially formed. To determine the identity of the AC adducts, we prepared as above, the corresponding acetals **24** and **25**, respectively in 82% yield. Further, removal of both TBS protecting groups (TBAF–THF, 60 °C, 2.5 h) in **24** and **25** gave the corresponding diols **26** (91%) and **27** (94%), respectively. Oxidation of the diol thus obtained with Dess–Martin periodinane (dry CH_2Cl_2, py, 25 °C, 1.5 h) afforded the intramolecularly linked aldol partners **28** (87%) and **29** (87%), on which we performed NOE studies. On the other hand, cleavage of the TBS-protected ethers **22** and **23** with TBAF and subsequent exposure of the derived diols **30** (80%) and **31** (83%) to Dess–Martin periodinane afforded the required enone-aldehydes **32** (84%) and **33** (86%), respectively.

2.2. The 7-deoxytaxane (7-nor) series

A parallel sequence of reactions was employed for the preparation of 7-nor-B-secotaxanes. As with (10*S*)-**2** and (10*R*)-**2**, (14*S*)-**1** experienced matching with (10*S*)-**6** to provide **34** as a single diastereomer and mismatching with (10*R*)-**6** to afford **37** and **38** in a nearly 1:1.3 ratio. Thus, exposure of (14*S*)-**1** to 10-(*S*)-α-alkoxyorganolithium, generated in situ from the tributyltinmethoxymethyl carbinol (10S)-**6** in the presence of nBuLi, afforded 7-nor B-secotaxane **34** in 87% isolated yield, with no trace of the isomer resulting from β-face attack, nor a trace of configurational reversal at C10. The crude reaction profile showed only one product, the one depicted in Scheme 5, indicating that a complete facial selectivity had occurred in that case. Full stereochemical



Scheme 4. Reagents and conditions: (a) *n*BuLi, THF, −78 °C, 20 min; (b) TBAF–THF, 60 °C, 2.5 h; (c) TMSOTf, collidine, −30 to 0 °C, 2 h; (d) Dess–Martin periodinane, dry CH_2Cl_2, py, 25 °C, 1.5 h.

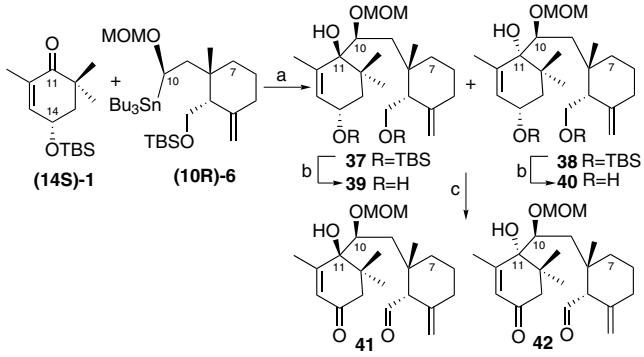


Scheme 5. Reagents and conditions: (a) *n*BuLi, THF, −78 °C, 20 min; (b) TBAF–THF, 60 °C, 2.5 h; (c) Dess–Martin periodinane, dry CH_2Cl_2, py, 25 °C, 1.5 h; (d) TMSOTf, collidine, −30 to 0 °C, 2 h; (e) TBAF–THF, 60 °C, 2.5 h.

assignment to **34** was made possible following its conversion to the corresponding acetals **36a** (84%) and **36b** (96%), prepared using exactly the same reactions as described in Scheme 4. Also, the synthesis of enone-aldehyde **7** was accomplished in two steps, starting with the fluoride deprotection (TBAF–THF, 60 °C, 2.5 h, 91%) followed by Dess–Martin oxidation (Dess–Martin periodinane, dry CH_2Cl_2, py, 25 °C, 1.5 h, 76%).

When the fragment coupling experiment was repeated with 10-(*R*)-organostannane **6**, a 1:1.3 mixture of the AC adducts **37** and **38** was formed, in 89% combined yield, free of any C-10 inversed adduct, signifying that the diastereoselectivity suffered only at C11 in mismatched cases. Following chromatographic separation, these compounds were subjected to the same sequence of functional group interconversions as were **22** and **23**. Accordingly, fluoride mediated TBS deprotection afforded **39** (87%) and **40** (89%) and subsequent Dess–Martin oxidation gave **41** (86%) and **42** (89%), respectively, as portrayed in Scheme 6.

Once again, the reaction of (14*S*)-phorenol derivative with (10*R*)-organostannane **2** was unselective, though



Scheme 6. Reagents and conditions: (a) *n*BuLi, THF, −78 °C, 20 min; (b) TBAF–THF, 60 °C, 2.5 h (96%); (c) Dess–Martin periodinane, dry CH_2Cl_2, py, 25 °C, 1.5 h.

such modest selectivity as did exist tended to favor the β-face attack leading to a slight preference for **38** relative to **37**. It should be pointed out that in none of the cases investigated thus far was 1,4-addition realized to a detectable extent.

2.3. Proof of stereochemistry of the resulting B-secotaxanes

At the outset, the steric director mode has been used to probe the effect of conformational bias on α-alkoxyorganolithium additions to **1**. The OTBS-group at C14 plays the role of conformational director by destabilizing conformers where the sterically demanding OTBS group occupies a quasi-axial position as portrayed in Figure 1. Thus, in our earlier work, we observed that the facial selectivity during the C10–C11 bonding was conformationally controlled, while the C-10*S* stereocenter, derived from the configurationally rigid α-alkoxyorganolithium reagents (perfectly stable at below zero temperatures between −78 and −40 °C), exhibited substantial preference for one of the two enantiomers of the racemic A-ring component. The favored sense of attack at C-11 was from the α-face, as indicated, leading to AC-linked **12** (stereochemistry as depicted in Scheme 2). Molecular mechanics calculations using Still's Macromodel program, with Allinger's MM3 force field and ^{1}H NMR on **1** were used to predict the face selectivity upon nucleophilic attack at C11. *J*-values calculated from MM3 for the lowest energy conformer **I** (Fig. 1) correlate fairly well with the experimentally determined values derived from the *J*-analysis (J_{calcd} H14–H1ax = 10.9 Hz, found: 9.5 Hz; J_{calcd} H14–H1eq = 5.1 Hz, found: 5.6 Hz; J_{calcd} H14–H13 = 2.7 Hz; found: 3.2 Hz). This is not the case with the second lower energy conformer **II**. Portrayed in the figure below are the two lowest energy conformers of (14*S*)-**1**, different by approximately 0.77 kcal/mol.

Furthermore, diagnostic NOE's between H-14 proton and the geminal methyl group confirms the adopted conformation, which sets the favored sense of attack at C-11 from the α-face. With this reasoning we investigated the inherent facial selectivity of the C11 electrophile (14*S*)-**1** and its match/mismatch combinations with the C10*S* and C10*R* nucleophilic partners **2** and **6**. Toward this aim, we carried out an elaborate series of nuclear Overhauser enhancement experiments using difference spectra, in order to establish the configuration of the key centers (C10, C11) in the AC linked substrates. In particular, we used the known AC adduct **12** and its acetal derivative **15** as a probe to test the method. In common with all other such products, the gross structure, as well as the stereochemistry, was proven in the following manner. Firstly, ^{1}H–^{1}H, ^{1}H–^{13}C correlation spectra allowed a definite assignment of the respective resonances due to all the protons and carbons of the molecules. The added rigidity accompanying this transformation allowed then for the successful measuring of proximity effects using 1D NOE difference experiments. The map of diagnostic NOE's is depicted in Figure 2 for the most significant effects (in the left-half of the figure, the C-ring part was omitted for clarity). Particularly revealing was the enhancement of the signals due to protons H-21b singlet at δ 4.96 ppm and H-10 doublet at δ 4.23 ppm upon irradiation of Me-15 singlet at δ 1.07 ppm, and vice versa. This confirmed that adduct **12** was the one obtained from α-face attack, thus showing a strong matched effect between (14*S*)-**1** and (10*S*)-**2**. On the other hand, enhancement of the signal due to proton H-21a at δ 5.23 ppm upon irradiation of Me-18 at δ 1.95 ppm identified the downfield proton singlet as H-21a and established that H-21a and Me-18 are cis.

The configurational relationships for the AC adducts **22** and **23** derived from the mismatched combination of reactants (14*S*)-**1** with (10*R*)-**2** have also been established through the ensuing enone-aldehyde products **28** and **29**, respectively. The map of diagnostic NOEs is depicted in Figure 3 for the most significant effects.

The sense of attack at C11 for **28** was determined as follows: methyl-18 doublet at δ 2.02 ppm showed a strong NOE on H-10 doublet, δ 3.74 ppm, and H-21a singlet at δ 4.98 ppm. NOE was also observed for H-10 doublet upon irradiation of Me-19 singlet at δ 0.81 ppm and vice versa.

The stereochemical relationships of the key stereogenic centers C10 and C11 followed from the NOE from H10 to Me18 (and its reverse), supporting the assignment of stereochemistry for **28**. However, this NOE enhancement is absent in isomer **29** resulting from a β-face attack. Further, the stereochemistry of the latter, shown in Figure 4, is assigned on the basis of the observation of strong enhancement of the signal due to proton H21b singlet at δ 5.14 ppm upon irradiation of

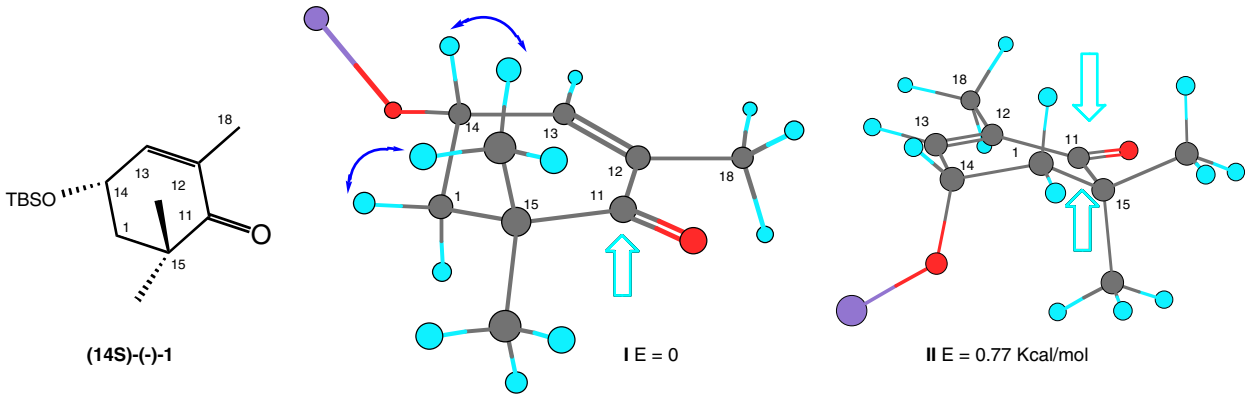


Figure 1. Facial selectivity in the fragment coupling reaction. Arrows indicate diagnostic NOEs (gray, carbon; red, oxygen; blue, hydrogen; violet, silicon; the *t*BuMe$_2$ part of the TBS group was omitted for clarity).

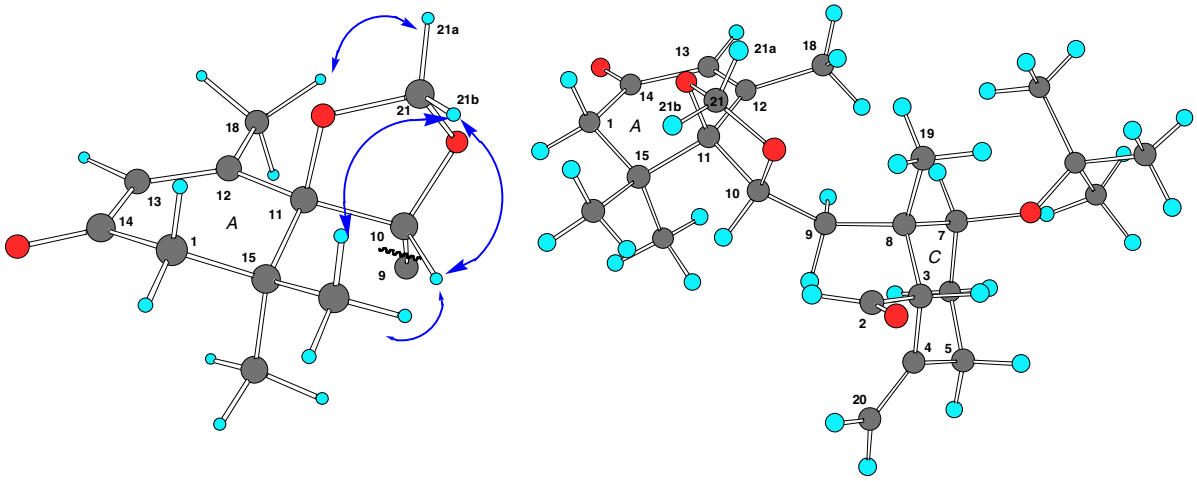


Figure 2. Chem3D drawing of the energy minimized structure of **15** (gray, carbon; red, oxygen; blue, hydrogen). Diagnostic NOEs are shown with blue arrows on A-ring moiety (in the left).

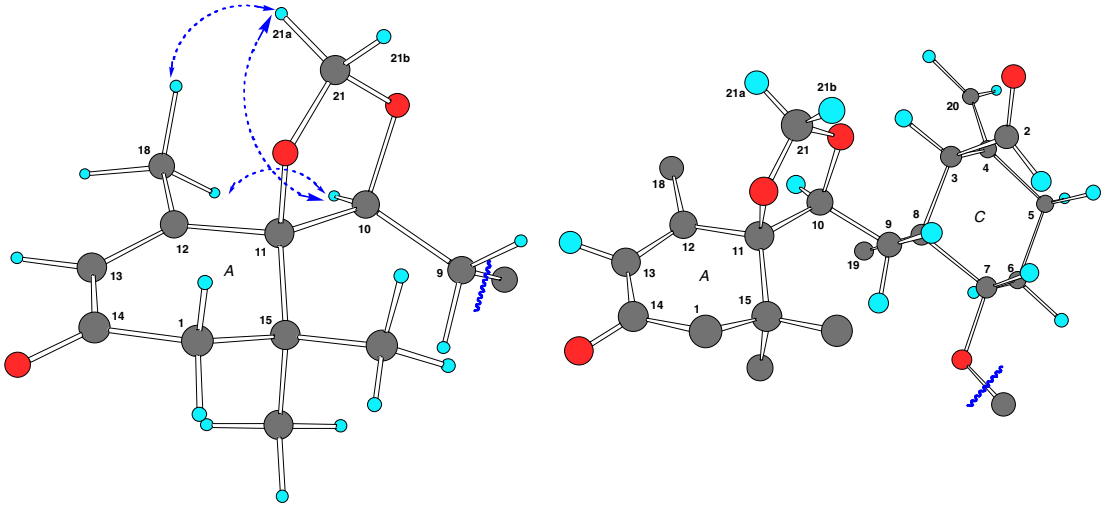


Figure 3. Chem3D drawing of the energy minimized structure of **28** showing key NOEs (dashed double-headed blue arrows, on the A-ring moiety; gray, carbon; red, oxygen; blue, hydrogen, *t*Bu group was omitted for clarity).

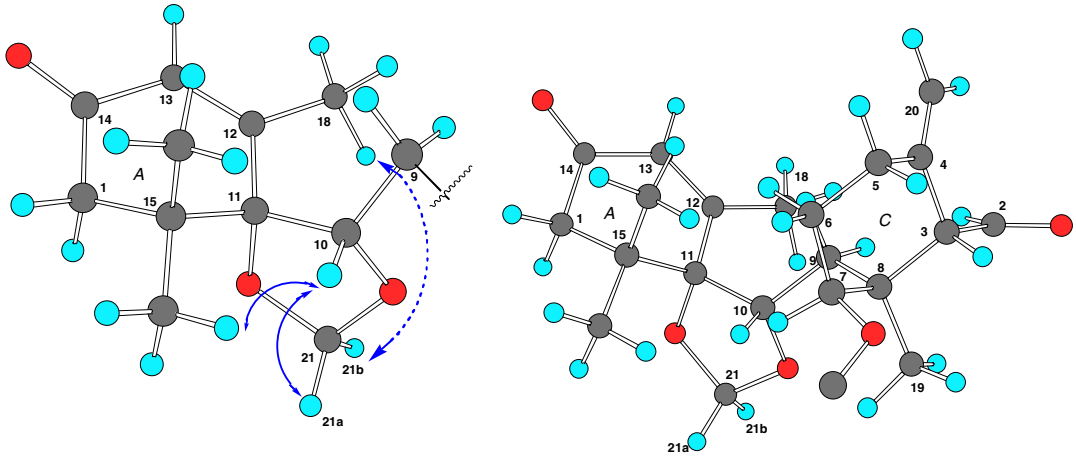


Figure 4. Chem3D drawing of the energy minimized structure of **29** showing key NOEs (double-headed blue arrows on the A-ring moiety; gray, carbon; red, oxygen; blue, hydrogen, *t*Bu group was omitted for clarity).

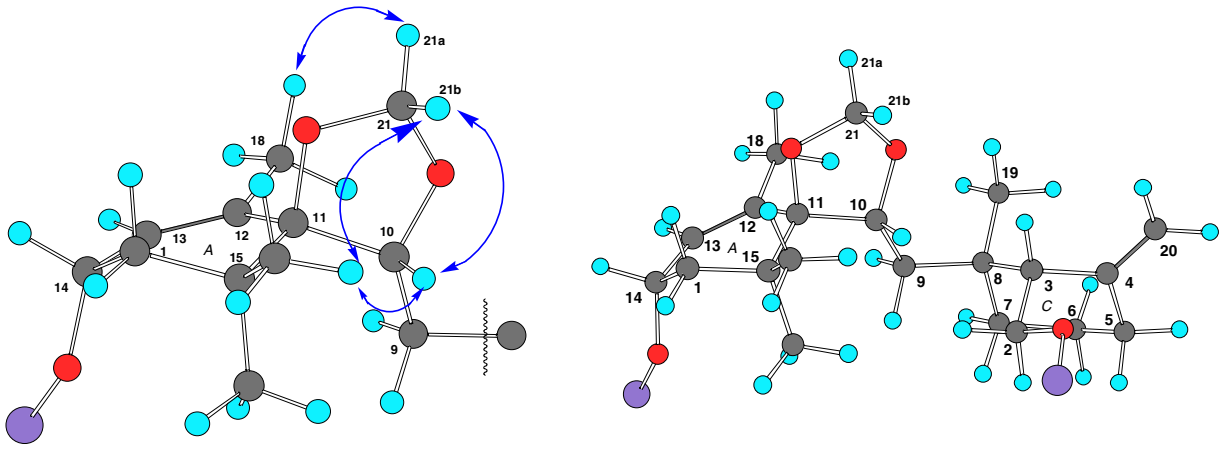


Figure 5. Chem3D drawing of the energy minimized structure of **36a** showing key NOEs (double-headed blue arrows; gray, carbon; red, oxygen; blue, hydrogen; violet, silicon, tBuMe$_2$ group was removed for clarity).

Me-18 singlet at δ 1.90 ppm. This is supported by an NOE from the methyl-15 singlet at δ 1.12 ppm to the H10 doublet at δ 4.41 ppm, as well as to H21a singlet at δ 4.95 ppm and the reverse in both cases. Experimental data from NOE studies on the acetal derivatives **28** (Fig. 3) and **29** (Fig. 4) enabled unequivocal stereochemical assignment and further confirmed the correctness of previous assignments of the organostannanes (10*S*)-**2** and (10*R*)-**2**.

The stereochemical assignments of the resultant B-secotaxoid frameworks in 7-nor series were again based on spatial proximity effects, measured by the 1D NOEDIFF technique, as for the corresponding 7-oxygenated analogs. Full stereochemical assignment to **34** was made possible following conversion to its corresponding acetal **36a**. The downfield methyl doublet Me18 at δ 1.71 ppm gave an NOE only to the downfield singlet H21a, at δ 4.80 ppm and naturally to H13 proton at 5.43 ppm. Additional diagnostic enhancements on H10 doublet at 4.14 ppm and highfield singlet H21b at 4.63 ppm were observed upon irradiation of the Me15 signals appearing both as a singlet at δ 1.06 ppm. This confirmed that adduct **34** was the one obtained from α-face attack, again illustrating an outstanding matched effect between (14*S*)-**1** and (10*S*)-**6** (Fig. 5).

The C10/C11 stereochemistry of A–C adducts **41** and **42** (Scheme 6) obtained from the mismatched pair of reactants (14*S*)-**1** with (10*R*)-**6** is assigned by analogy. The conformational difference between the two diastereomers, resulting from α and β-face attack, respectively, could provide a hint to the origin of the difference in facial selectivity, leading to an outstanding match effect for the (14*S*)-(10*S*) combinations. The (*S*)–(*S*) combination is a matched pair, probably because sterically demanding groups can be oriented away from each other and as a result there should exist few unfavorable steric interactions. In contrast, the (*S*)–(*R*) combination could suffer from a severe steric interaction between sterically demanding groups, since chelation with the metal during the α-alkoxyorganolithium addition could force these substituents to orient in the same direction. It is likely that the same argument developed to rationalize the exclusive 1,2-addition (the nucleophilic addition proceeds through a stable metal-chelated intermediate) could be used to explain the significant mismatch between (*S*) and (*R*). Minimization of non-bonded steric interactions on the internal chelate (five-membered ring Li–O bridging) as well as minimization of molecular dipole moment could explain the origin of the observed match effect.

3. Conclusion

The use of α-alkoxyorganostannanes (10*S*)-**2** and (10*S*)-**6** enables various B-secotaxanes to be obtained in quantity with a stereochemically defined C10/C11 coupling. Since we were unable to obtain X-ray quality crystals of A–C adducts **12**, **22**, **23**, and **34** their acetal derivatives **15**, **28**, **29**, **36a** (respectively) proved ideal substrates for NOEDIFF experiments, and we were able to obtain excellent support for our assignments. Complete diastereocontrol was achieved when there was a match between nucleophile (10*S*)-**2**, (10*S*)-**6** and electrophile (14*S*)-**1** configurations, while when there was a mismatch, (10*R*)-**2**, (10*R*)-**6** with (14*S*)-**1** mixture of adducts were obtained. Besides its use for stereochemical assignments, the presence of the acetal ring is expected to reduce the entropic cost of bringing the two reacting centers (C1–C2) together, lowering the activation energy of the reaction. An alternative intramolecular aldol reaction in which the C10, C11 hydroxyl groups are protected as acetals could provide additional opportunities for stereochemical control and synthetic efficiency.

4. Experimental

4.1. General

Solvents and reagents used in this work were purified according to standard literature techniques and stored under argon. Experiments, which required an inert atmosphere were carried out under dry argon in a flame dried glass system. Flash chromatographies were run on

silica gel (230–400 mesh) with the solvent mixture indicated. Thin layer chromatography was performed on commercial silica gel plates that were developed by immersion in 5% phosphomolybdic acid in 95% ethanol. 'Usual work up' means washing of the organic layer with brine, drying on anhydrous $MgSO_4$, and evaporating in vacuo with a rotary evaporator at aspirator pressure. Melting points were uncorrected. IR spectra were recorded with an FT-IR instrument through NaCl cell windows. NMR spectra were run in $CDCl_3$ unless otherwise noted. Experimental evidence favoring the structures investigated came from a comprehensive range of ^1H and ^{13}C NMR data (400–300–250 and 100–75–69.5 MHz, respectively, 1D and 2D experiments) and corroborated by spatial proximity (NOE) studies using mainly the 1D NOEDIFF technique.[12] ^1H (800 MHz) and ^{13}C NMR (200 MHz) experiments were carried out on a spectrometer, equipped with triple resonance H/C/N probeheads and a three-axis pulsed field gradient modules. Gradients were used for the coherence transfer pathway selection in HMBC and HMQC experiments. In the latter, broadband decoupling was performed by using adiabatic WURST-40 pulses. For all compounds investigated, multiplicities of ^{13}C resonances were assigned by the SEFT technique.[13] ^1H chemical shifts are expressed in parts per million downfield from TMS using the residual non-deuterated solvent as internal standard ($CDCl_3$ ^1H, 7.27 ppm; C_6D_6 ^1H, 7.15). ^{13}C spectra were measured at 62.5 and 75 MHz and the chemical shifts are reported relative to $CDCl_3$ or C_6D_6 triplet centered, respectively, at 77.0 and 128.0 ppm. Mass spectra acquired in the positive ion mode under electron spray ionization (ES^+) using a mobile phase of methanol, will be abbreviated as ESIMS (MeOH).

4.1.1. General procedure for transmetallation/A+C fragment linking: the Stille method. To a magnetically stirred solution of Tin-MOM acetal (1 mmol) in 5 mL of anhydrous THF cooled at −78 °C under argon, *n*BuLi (1.05 equiv) was added and the mixture was stirred at this temperature for 10 min before **1** (1 mmol) was added. After stirring 20 min at −78 °C, the reaction mixture was diluted with ether, and quenched with a saturated solution of NH_4Cl. Following usual work up ('Usual work up' means washing of the organic layer with brine, drying on anhydrous $MgSO_4$, and evaporating in vacuo with a rotary evaporator at aspirator pressure) the A+C adducts were isolated using SiO_2 column chromatography.

4.2. General procedure for TBS-deprotection

4.2.1. Desilylation. Fluoride deprotection of *tert*-butyldimethylsilyl ethers at C-14 and C-2 was carried out with *n*-Bu_4NF (TBAF, 1 M solution in THF, 4 equiv) in dry THF (5 mL/mmol) at 60 °C for 2 h. Ethyl acetate was then added and the mixture was washed with brine, dried on $MgSO_4$ and concentrated in vacuo. The residue was purified by chromatography (SiO_2, heptane–EtOAc, 1:1) to give the desired diols in high yields. It should be pointed out that some self-deprotection on standing was also observed.

4.2.2. General procedure for diol oxidation with Dess–Martin's periodinane. To a solution of the substrate alcohol (2.8 mmol) in dry methylene chloride (15 mL) and pyridine (9 mL) were added 356 mg (8.4 mmol) of periodinane and stirring continued at room temperature for 1 h 30 min. The reaction was then diluted with methylene chloride quenched with a saturated aqueous solution of sodium bicarbonate and worked up as usual.

4.2.3. General procedure for cyclic formaldehyde-acetal formation. Cyclic diol formals were produced by a Lewis acid catalyzed process, using TMSOTf in dry toluene in the presence of collidine at −30 to 0 °C for approximately 2 h (TLC monitoring) as follows. A dry flask was charged with the mono MOM-ether of the 1,2-diol (1 mmol), vacuumed, and flushed with argon several times. Toluene (dry, 10 mL) was added and the solution was cooled to −30 °C, followed by collidine (20 mmol) and, after 10–15 min, TMSOTf (10 mmol) while the temperature of the bath was raised to 0 °C. After consumption of the starting material, the reaction mixture was diluted with heptane and worked up as usual.

4.3. A+C coupling of the matched partners (14*S*)-1/(10*S*)-2

4.3.1. Preparation of 12 and its cyclic acetal 15. Using the general procedure for fragment coupling on a 10 mmol scale, **12** was obtained in 92% isolated yield (6.27 g) and as the sole diastereomer.

4.3.1.1. Compound 12. Mp: 78 °C (heptane–ether). $[\alpha]_D^{20} = +16$ (*c* 2.0, $CHCl_3$). IR (film): 3519, 2954, 2928, 2893, 2855, 1644, 1471, 1462, 1386, 1360, 1251, 1193, 1059, 1005, 912, 866, 834, 773 cm^{-1}. ^1H NMR (500 MHz): 0.01 (6H, s, Me_2Si), 0.05 (6H, s, Me_2Si), 0.82 (9H, s, *t*Bu), 0.88 (3H, s, Me-15), 0.90 (9H, s, *t*Bu), 1.01 (3H, s, Me-19), 1.04 (3H, s, Me-15), 1.17 (9H, s, *t*Bu), 1.39 (1H, d, $J = 15.7$ Hz, H9), 1.57 (1H, s, OH), 1.60 (2H, dd, $J = 13.2$, 6.9 Hz, H1), 1.72 (2H, d, $J = 9.4$ Hz, H6,6), 1.74 (3H, s, Me-18), 1.80–1.82 (1H, m, H9), 2.08–2.10 (1H, m, H5), 2.30–2.32 (1H, m, H5), 2.48–2.52 (1H, m, H3), 3.46 (3H, s, MeO), 3.77 (1H, dd, $J = 8.6$, 3.9 Hz, H7), 3.78 (2H, d, $J = 6.3$ Hz, H2,2), 3.89 (1H, d, $J = 10.7$ Hz, H10), 4.21–4.23 (1H, m, H14), 4.57 (1H, s, H20), 4.69 (1H, s, H21), 4.78 (1H, s, H21), 4.80 (1H, s, H20), 5.39 (1H, s, H13).^{13}C NMR (125 MHz): −5.1 ($2Me_2Si$), −4.6 ($2Me_2Si$), 18.2 ($2Me_3CSi$), 19.7 (Me18), 25.2 (Me19), 25.9 ($2 \times 3C$, *t*Bu), 26.6 (2Me15), 29.4 (3C, *t*Bu) 28.9 (C5), 29.7 (C6), 30.7 (C9), 39.0 (C8), 42.3 (C15), 45.2 (C1), 52.1 (C3), 56.9 (MeO), 60.6 (C2), 66.1 (C14), 72.8 (C7+*Cq*tBu), 77.6 (C10), 84.6 (C11), 96.6 (C21), 100.7 (C20), 128.8 (C13), 136.8 (C12), 146.7 (C4). TOFMSES$^+$ (MEOH): 705 ($[MNa]^+$, 100). HRESIMS (MeOH) calcd for $C_{38}H_{74}O_6NaSi_2$ 705.4922; found 705.4954. Anal. Calcd for $C_{38}H_{74}O_6Si_2$: C, 68.25; H, 10.84. Found: C, 68.47; H, 10.95.

4.3.2. Preparation of cyclic formaldehyde-acetals 13–15. Using the general procedure for cyclic formaldehyde-acetal formation (646 mg, 0.98 mmol) of **12**,

afforded, after silica gel flash chromatography (heptane–Et_2O, 99:1), 600 mg (97%) of **13**: $[\alpha]_D^{20} = +14$ (*c* 1.1, $CHCl_3$). IR (film): 2956, 2930, 2857, 1472, 1252, 1105, 1066, 835, 774 cm^{-1}. ^1H NMR (500 MHz): 0.02 (6H, s, Me_2Si), 0.06 (6H, s, Me_2Si), 0.87 (9H, s, *t*Bu), 0.91 (9H, s, *t*Bu), 1.01 (3H, s, Me15), 1.05 (3H, s, Me19), 1.07 (3H, s, Me15), 1.17 (9H, s, *t*Bu), 1.39 (1H, d, $J = 15.7$ Hz, H9), 1.50 (1H, dd, $J = 13.4$, 9.2 Hz, H1), 1.55–1.77 (3H, m, H1, H6,6), 1.72 (3H, s, Me18), 1.77 (1H, dd, $J = 15.5$, 11.0 Hz, H9), 2.11–2.34 (2H, m, H5,5), 2.48 (1H, dd, $J = 8.9$, 3.7 Hz, H3), 3.45 (1H, dd, $J = 8.6$, 3.9 Hz, H7), 3.70 (1H, dd, $J = 10.3$, 3.8 Hz, H2), 3.77 (1H, t, $J = 9.0$ Hz, H2), 4.19 (1H, m, H10), 4.23 (1H, m, H14), 4.66 (1H, s, H20), 4.80 (1H, s, H20), 4.89 (1H, s, H21), 5.14 (1H, s, H20), 5.40 (1H, s, H13). ^{13}C NMR (75 MHz): −5.2 ($2Me_2Si$), −4.6 ($2Me_2Si$), 18.3 ($2Me_3CSi$), 20.5 (Me-18), 20.8 (Me19), 25.2 (Me15), 25.9 (Me15 + 2 × 3C, *t*Bu), 29.4 (3C, *t*Bu), 30.2 (C5), 30.6 (C6), 37.8 (C15), 39.3 (C9), 41.6 (C8), 44.9 (C1), 52.8 (C3), 60.5 (C2), 66.2 (C14), 72.1 (C7+*Cq*tBu), 76.9 (C10), 87.8 (C11), 95.1 (C21), 110.2 (C20), 128.2 (C13), 137.5 (C12), 146.2 (C4). HRESIMS (MeOH) calcd for $C_{37}H_{70}O_5NaSi_2$ 673.4660; found 673.4689. Anal. Calcd for $C_{37}H_{70}O_5Si_2$: C, 68.25; H, 10.84. Found: C, 68.47; H, 10.95.

Performed according to the general procedure, TBS deprotection of **13** (533 mg, 0.82 mmol) afforded, after silica gel flash chromatography (heptane–AcOEt, 2:1 to 1:2), 332 mg (96%) of diol **14**: $[\alpha]_D^{20} = +51$ (*c* 1.3, $CHCl_3$). IR (film): 3375, 2972, 2930, 2874, 1099, 1008, 757 cm^{-1}. ^1H NMR (500 MHz): 1.00 (3H, s, Me15), 1.01 (3H, s, Me15), 1.05 (3H, s, Me19), 1.16 (9H, s, *t*Bu), 1.38 (1H, dd, $J = 13.5$, 9.4 Hz, H1), 1.43 (1H, d, $J = 15.3$ Hz, H9), 1.62 (1H, m, H6), 1.71 (3H, t, $J = 1.6$ Hz, Me18), 1.74–1.83 (3H, m, H6, H9, OH), 1.87 (1H, ddd, $J = 13.5$, 6.9, 1.5 Hz, H1), 2.15 (1H, m, H5), 2.32 (1H, m, H5), 2.45 (1H, m, H3), 3.46 (1H, m, H7), 3.64–3.82 (2H, m, H2,2), 4.19 (3H, m, H14, H10, OH), 4.78 (1H, s, H20), 4.91 (1H, s, H20), 4.97 (1H, s, H21), 5.08 (1H, s, H21), 5.56 (1H, s, H13). ^{13}C NMR (125 MHz): 20.5 (Me18, Me19), 24.0 (Me15), 25.2 (Me15), 29.1 (3C, *t*Bu), 30.0 (C5), 30.1 (C6), 36.7 (C2), 39.8 (C15), 41.8 (C8), 43.9 (C1), 52.0 (C3), 59.2 (C2), 65.4 (C14), 72.2 (C7), 73.0 (*Cq*tBu), 76.5 (C10), 88.0 (C11), 94.8 (C21), 110.6 (C20), 127.7 (C13), 138.8 (C12), 146.6 (C4). HRESIMS (MeOH) calcd for $C_{25}H_{42}O_5Na$ 445.2930; found 445.2952. Anal. Calcd for $C_{25}H_{42}O_5$, 1 H_2O: C, 68.15; H, 10.07. Found: C, 68.02; H, 9.73.

Periodinane oxidation of **14** (307 mg, 0.78 mmol), achieved according to the general procedure, afforded after silica gel flash chromatography (heptane–AcOEt, 9:1 to 3:1), 260 mg (85%) of enone-aldehyde **15**: $[\alpha]_D^{20} = -84$ (*c* 1.2, $CHCl_3$). IR (film): 2975, 1718, 1666, 1365, 1266, 1097, 739 cm^{-1}. ^1H NMR (800 MHz): 1.03 (3H, s, Me19), 1.07 (3H, s, Me15), 1.12 (9H, s, *t*Bu), 1.13 (3H, s, Me15), 1.61 (1H, dddd, $J = 13.5$, 11.5, 9.5, 4.7 Hz, H6), 1.69 (2H, m, H9,9), 1.77 (1H, dq, $J = 13.5$, 4.5 Hz, H6), 1.95 (3H, d, $J = 1.4$ Hz, Me18), 2.02 (1H, dt, $J = 14.1$, 5.2 Hz, H5), 2.18 (1H, dd, $J = 17.6$, 1.2 Hz, H1), 2.33 (1H, dt, $J = 14.1$, 4.8 Hz, H5), 2.42 (1H, d, $J = 17.6$ Hz, H1), 3.31 (1H, d, $J = 1.9$ Hz, H3), 3.77 (1H, dd, $J = 9.5$, 4.1 Hz, H7), 4.23 (1H, dd, $J = 8.9$, 4.6 Hz, H10), 4.86 (1H, s, H20a), 4.96 (1H, s, H21b), 5.04 (1H, s, H20b), 5.23 (1H, s, H21a), 5.92 (1H, t, $J = 1.2$ Hz, H13), 9.68 (1H, d, $J = 2.2$ Hz, H2). Diagnostic NOEs: {Me-19}: H-3, H-10; {Me-15}: H-1, H-10, H-21b; {Me-18}: H-13, H-21a; {H-21b}: H-10, H-21a (NOE *gem*); {H-10}: H-21b. {H-3}: H-10, H-20a. ^{13}C NMR (200 MHz): 19.2 (Me-19), 21.6 (Me-18), 24.5 (Me-15), 25.9 (Me-15), 29.0 (3C, *t*Bu), 30.1 (C6), 30.7 (C5), 37.6 (C9), 40.2 (C15), 41.7 (C8), 48.9 (C1), 64.3 (C3), 72.7 (C7), 73.3 (*Cq*tBu), 77.0 (C10), 88.1 (C11), 95.4 (C21), 114.8 (C20), 127.6 (C13), 140.4 (C4), 163.3 (C20), 197.2 (C14), 201.3 (C2). HRESIMS (MeOH) calcd for $C_{25}H_{38}O_5Na$ 441.2617; found 441.2638. Anal. Calcd for $C_{25}H_{38}O_5$: C, 71.94; H, 9.15. Found: C, 71.91; H, 9.22.

4.4. Reactions of 1 with achiral nucleophiles; looking for the inherent facial selectivity

4.4.1. Reactions of 1 with Tin-MOM acetal. Use of the general procedure for transmetallation with Bu_3SnCH_2-OMOM (5.0 g, 13.72 mmol) and (14*S*)-(−)-**1** (1.84 g, 6.86 mmol) gave 1.98 g (84%) of the expected products **16**+**17** (in 7:1 ratio), separated by flash-chromatography (heptane–Et_2O, 95:5). The taxoid A-ring precursor **1** was used both in its racemic and enantiomerically homogeneous form (for the purpose of description of specific rotations).

4.4.1.1. Compound 16. $[\alpha]_D^{20} = -5$ (*c* 1.1, $CHCl_3$). IR (film): 3565, 2955, 2929, 2857, 1472, 1255, 1068, 1040, 835 cm^{-1}. ^1H NMR (300 MHz): 0.06 (3H, s, Me_2Si), 0.07 (3H, s, Me_2Si), 0.88 (9H, s, *t*Bu), 0.97 (6H, s, Me15), 1.62 (1H, d, $J = 8.7$ Hz, H1), 1.64 (1H, dd, $J = 7.2$, 1.2 Hz, H1), 1.76 (3H, t, $J = 1.7$ Hz, Me18), 2.78 (1H, s, OH), 3.37 (3H, s, CH_3O), 3.47 (1H, d, $J = 10.1$ Hz, H10), 3.77 (1H, d, $J = 10.1$ Hz, H10), 4.23 (1H, dddd, $J = 8.7$, 7.2, 1.7, 1.3 Hz, H14), 4.62 (1H, d, $J = 6.4$ Hz), 4.65 (1H, d, $J = 6.4$ Hz), 5.42 (1H, q, $J = 1.3$ Hz, H13). ^{13}C NMR (75 MHz): −4.5 (Me_2Si), 18.3 (Me_3CSi), 18.6 (Me18), 23.1 (Me15), 25.1 (Me15), 26.0 (3C, *t*Bu), 39.4 (Cq-15), 44.8 (C1), 55.7 (CH_3O), 66.4 (C14), 70.9 (C10), 75.8 (C11), 97.2, 129.0 (C13), 138.2 (C12). HRESIMS (MeOH) calcd for $C_{18}H_{36}O_4NaSi$ 367.2281; found 367.2269. Anal. Calcd for $C_{18}H_{36}O_4Si$+0.25 C_7H_{16}: C, 64.18; H, 10.91. Found: C, 64.11; H, 10.93.

4.4.1.2. Compound 17. $[\alpha]_D^{20} = -40$ (*c* 0.8, $CHCl_3$). IR (film): 3501, 2955, 2927, 2857, 1463, 1255, 1044, 835 cm^{-1}. ^1H NMR (400 MHz): 0.05 (3H, s, Me_2Si), 0.06 (3H, s, Me_2Si), 0.83 (9H, s, *t*Bu), 0.94 (3H, s, Me15), 1.08 (3H, s, Me15), 1.65 (1H, d, $J = 6.3$ Hz, H1), 1.68 (1H, d, $J = 10.2$ Hz, H1), 1.79 (3H, t, $J = 1.5$ Hz, Me18), 3.37 (3H, s, CH_3O), 3.53 (1H, d, $J = 10.0$ Hz, H10), 3.61 (1H, d, $J = 10.0$ Hz, H10), 4.16 (2H, m, OH), 4.63 (2H, s), 5.45 (1H, br s, H13). ^{13}C NMR (100 MHz): −4.6 (Me_2Si), 18.3 (Me_3CSi), 19.3 (Me18), 23.8 (Me15), 25.1 (Me15), 25.9 (3C, *t*Bu), 40.0 (Cq-15), 43.6 (C1), 55.8 (CH_3O), 65.3 (C14), 70.6

(C10), 74.7 (C11), 97.2, 129.2 (C13), 138.3 (C12). HRESIMS (MeOH) calcd for $C_{18}H_{36}O_4NaSi$ 367.2281; found 367.2258.

4.4.2. The Dauben–Michno rearrangement on allylic alcohols 16+17. To a stirring solution of the allylic tertiary alcohol **16+17** (370 mg, 1.07 mmol) as a mixture, in dry CH_2Cl_2 (5 mL), were added 400 mg of MS 4 Å and PCC (463 mg, 2.14 mmol). The reaction mixture was stirred at room temperature overnight, Et_2O was added, the suspension was applied to fluorisil column, and eluted with Et_2O. The eluate was concentrated and the residue was purified by silica gel flash chromatography (hexane–EtOAc, 1:9) affording the corresponding α,β-unsaturated ketone **18** (211 mg, 58%) as a colorless oil along with recovered starting material **16+17** (110 mg, 38%).

4.4.2.1. Compound 18. $[\alpha]_D^{20} = -122$ (*c* 1.5, $CHCl_3$). IR (film): 2953, 2929, 2886, 2858, 1692, 1471, 1363, 1249, 1152, 1103, 939, 920, 857, 837 cm^{-1}. ^1H NMR (500 MHz): −0.09 (3H, s, Me_2Si), −0.03 (3H, s, Me_2Si), 0.75 (9H, s, *t*Bu), 1.03 (3H, s, Me15), 1.09 (3H, s, Me15), 1.70 (3H, s, Me18), 1.72–1.83 (2H, m, H1,1), 3.25 (3H, s, MeO), 3.98 (2H, d, $J = 1.8$ Hz, H10,10), 4.17 (1H, dd, $J = 12.4$, 6.2 Hz, H14), 4.50 (2H, s). ^{13}C NMR (125 MHz): −5.3 (MeSi), −4.4 (MeSi), 11.8 (Me18), 18.6 (Cq *t*Bu), 25.5 (Me15), 25.8 (3C, *t*Bu), 29.1 (Me15), 36.8, 46.8 (C1), 55.8 (MeO), 64.1 (C10), 71.1 (C14), 96.7, 133.1 (C12), 155.8 (C11), 199.1 (C13). ESIMS (MeOH): 365.2 ($[MH]^+$, 100). HRESIMS (MeOH) calcd for $C_{18}H_{34}O_4NaSi$ 365.2124; found 365.2112. Anal. Calcd for $C_{18}H_{34}O_4Si$: C, 63.11; H, 10.00. Found: C, 63.65; H, 10.16.

4.4.3. Reaction of [±]-1 and (14*S*)-(−)-1 with *n*Buli. To a stirring solution of (14*S*)-(−)-**1** (1.00 g, 3.7 mmol) in THF (7 mL) were added, at −78 °C under argon, *n*BuLi 1.6 M in hexane (3.5 mL, 5.6 mmol). The reaction mixture was stirred 25 min at −78 °C (TLC monitoring), then diluted with ether, quenched with a saturated solution of NH_4Cl extracted with Et_2O, and worked up as usual. After purification by flash chromatography (heptane–Et_2O, 99:1 to 9:1), were obtained 1.20 g (99%) of **19** and **20** as a 7:1 mixture. Only **19** was obtained pure and characterized, **20** could not be efficiently separated and thus not characterized.

4.4.3.1. 1-Butyl-4-(*tert*-butyl-dimethyl-silanyloxy)-2,6,6-trimethyl-cyclohex-2-enol 19. IR (film): 3498, 2957, 2930, 2858, 1068, 835, 773 cm^{-1}. ^1H NMR (300 MHz): 0.06 (6H, 2s, Me_2Si), 0.89 (9H, s, *t*Bu), 0.92 (3H, m, Me10), 0.95 (3H, s, Me6), 0.97 (3H, s, Me6), 1.20–1.43 (5H, m, H8,8, H9,9, OH), 1.58 (1H, dd, $J = 15.5$, 13.8 Hz, H7), 1.60 (1H, ddd, $J = 13.5$, 6.9, 1.5 Hz, H5), 1.70 (1H, dd, $J = 13.1$, 9.3 Hz, H5), 1.73 (1H, ddd, $J = 15.5$, 8.4, 7.2 Hz, H7), 1.73 (3H, t, $J = 1.7$ Hz, Me2), 4.22 (1H, dddd, $J = 9.3$, 6.9, 1.7, 1.3 Hz, H4), 5.38 (1H, q, $J = 1.3$ Hz, H3). ^{13}C NMR (75 MHz): −4.4 (Me_2Si), 14.0 (Me10), 18.3 (Me_3CSi) 18.8 (Me2), 23.8 (Me6), 23.9 (C9), 24.8 (Me6), 26.0 (3C, *t*Bu), 28.1 (C8), 37.8 (C7), 40.0 (C6), 45.0 (C5), 66.5 (C4), 77.8 (C1), 127.9 (C3), 139.1 (C2). HRESIMS (MeOH) calcd for $C_{19}H_{38}O_2SiNa$ 349.2539, found 349.2522. Anal. Calcd for $C_{19}H_{38}O_2Si$+0.1 C_7H_{16}: C, 70.29; H, 11.86. Found: C, 70.37; H, 11.77.

Performed as above, the Dauben–Michno rearrangement on allylic alcohols **19**+**20** (111 mg, 0.35 mmol, from (14*S*)-(−)-**1**) afforded after silica gel flash chromatography (hexane–EtOAc, 98:2) the corresponding α,β-unsaturated ketone **21** (92 mg, 83%) as a colorless oil, along with unreacted starting material (9 mg, 9%).

4.4.3.2. 3-Butyl-6-(*tert*-butyl-dimethyl-silanyloxy)-2,4,4-trimethyl-cyclohex-2-enone 21. $[\alpha]_D^{20} = -125$ (*c* 1.4, $CHCl_3$). IR (film): 2957, 2930, 2858, 1685, 1472, 1248, 1152, 1039, 836, 779 cm^{-1}. ^1H NMR (300 MHz): 0.08 (3H, s, Me_2Si), 0.16 (3H, s, Me_2Si), 0.87–0.89 (3H, m, Me10), 0.89 (9H, s *t*Bu), 1.16 (3H, s, Me4), 1.20 (3H, s, Me4), 1.35–1.43 (4H, m, H8,8, H9,9), 1.76 (3H, s, Me2), 1.91 (1H, d, $J = 8.0$ Hz, H5), 1.91 (1H, d, $J = 10.5$ Hz, H5), 2.14 (2H, m, H7,7), 4.27 (1H, dd, $J = 10.5$, 8.0 Hz, H6). ^{13}C NMR (75 MHz): −5.4 (MeSi), −4.4 (MeSi), 11.8 (Me2), 13.8 (Me10), 18.6 (Me_3CSi), 23.6 (C9), 25.9 (3C, *t*Bu+Me4), 29.4 (Me4), 30.5 (C7), 31.0 (C8), 37.6 (C4), 47.0 (C5), 71.1 (C6), 129.0 (C2), 163.8 (C3), 198.7 (C1). HRESIMS (MeOH) calcd for $C_{19}H_{36}O_2NaSi$ 347.2382; found 347.2387. Anal. Calcd for $C_{19}H_{36}O_2$: C, 70.31; H, 11.18. Found: C, 70.51; H, 11.31.

4.5. Coupling of the mismatched partners (14*S*)-1/(10*R*)-2

Starting from (10*R*)-**2** (1.38 g, 1.96 mmol) and (14*S*)-**1** (406 mg, 1.96 mmol) the Stille method was repeated to afford, after SiO_2 column chromatography (eluent heptane–ether, 30:1), a mixture of two A+C adducts **22** and **23** (1.12 g, 84% combined) yield as a 1:1.3 mixture.

4.5.1. Slower eluting adduct 22. $[\alpha]_D^{20} = +286$ (*c* 1.35, $CHCl_3$). IR (film): 3472, 2955, 2920, 2853, 1470, 1462, 1385, 1359, 1256, 1192, 1068, 1054, 1024, 866, 835, 773, 667, 626 cm^{-1}. ^1H NMR (500 MHz): 0.03 (3H, s, MeSi), 0.04 (3H, s, MeSi), 0.05 (3H, s, MeSi), 0.07 (3H, s, MeSi), 0.86 (3H, s, Me15), 0.86 (9H, s, *t*Bu), 0.87 (9H, s, *t*Bu), 0.94 (3H, s, Me15), 1.11 (3H, s, Me19), 1.13 (9H, s, *t*Bu), 1.46–1.55 (3H, m), 1.70 (3H, s, Me18), 1.76–1.80 (1H, m), 1.86 (1H, dd, $J = 12.8$, 10.0 Hz, H1), 1.98 (1H, d, $J = 14.7$ Hz), 2.12–2.15 (2H, m), 2.25–2.32 (1H, m), 3.50 (3H, s, CH_3O), 3.58 (1H, dd, $J = 9.4$, 3.9 Hz), 3.82 (1H, d, $J = 11.5$ Hz), 3.88 (1H, dd, $J = 9.7$, 3.5 Hz), 3.91 (1H, q, $J = 9.7$ Hz, OH), 4.20–4.24 (2H, m), 4.52 (1H, s), 4.60 (1H, d, $J = 6.4$ Hz, H20), 4.68 (1H, s), 4.78 (1H, d, $J = 6.4$ Hz, H20), 5.50 (1H, s, H13). ^{13}C NMR (125 MHz): −5.4 (MeSi), −5.3 (MeSi), −4.7 (MeSi), −4.5 (MeSi), 18.1 (Me18), 18.3 (Me_3CSi), 18.4 (Me_3CSi), 25.6 (2 × 3C, *t*Bu), 27.2 (Me15), 27.7 (Me15), 29.4 (Me19), 29.6 (3C, *t*Bu), 30.5 (C5), 31.0 (C6), 36.1 (C15), 40.2 (C9), 42.1 (C8), 45.6 (C1), 54.2 (C3), 56.9 (CH_3O), 62.8 (C2), 66.5 (C14), 72.2 (C10), 73.8 (*C*q*t*Bu), 78.7 (C11), 89.8 (C7), 101.2 (OCH_2), 109.8 (C20), 131.6 (C13), 136.7 (C12), 147.9 (C4). TOFMSES$^+$ (MEOH): 705 ($[MNa]^+$, 100). HRESIMS (MeOH) calcd for $C_{38}H_{74}O_6NaSi_2$ 705.4922; found 705.4913. Anal. Calcd

for $C_{38}H_{74}O_6Si_2$: C, 66.81; H, 10.92. Found: C, 65.73; H, 10.91.

4.5.2. Faster eluting adduct 23. $[\alpha]_D^{20} = -53$ (*c* 1.90, $CHCl_3$). IR (film): 3519, 2952, 2930, 2884, 2853, 1470, 1460, 1385, 1359, 1254, 1189, 1145, 1098, 1063, 935, 884, 835, 773 cm^{-1}. ^1H NMR (500 MHz): 0.005 (3H, s, MeSi), 0.01 (3H, s, MeSi), 0.02 (3H, s, MeSi), 0.03 (3H, s, MeSi), 0.87 (9H, s, *t*Bu), 0.88 (9H, s, *t*Bu), 0.90 (3H, s, Me15), 0.96 (3H, s, Me15), 1.14 (9H, s, *t*Bu), 1.15 (3H, s, Me19), 1.37 (1H, dd, $J = 15.7$, 10.7 Hz, H1), 145–1.51 (2H, m), 1.58–1.62 (1H, m), 1.77–1.80 (2H, m), 1.82 (3H, t, $J = 1.3$ Hz, Me18), 1.95 (1H, dd, $J = 15.1$, 6.3 Hz, H1), 2.08–2.10 (1H, m, H5), 2.14–2.18 (1H, m, H5), 2.30–2.38 (1H, m, H3), 3.42 (3H, s, CH_3O), 3.50 (1H, dd, $J = 10.7$, 4.4 Hz), 3.82 (1H, t, $J = 10.1$ Hz), 3.90 (1H, dd, $J = 9.5$, 3.1 Hz), 3.98 (1H, br s, OH), 4.15–4.18 (1H, m), 4.56 (1H, s), 4.64 (1H, d, $J = 6.3$ Hz, H20), 4.70 (1H, s), 4.88 (1H, d, $J = 6.3$ Hz, H20), 5.42–5.45 (1H, m, H13). ^{13}C NMR (125 MHz): − 5.5 (MeSi), −5.4 (MeSi), −4.8 (MeSi), −4.7 (MeSi), 18.1 (Me_3CSi), 18.2 (Me_3CSi), 20.2 (Me18), 24.9 (Me15), 25.8 (Me15), 25.9 ($2 \times 3C$, *t*Bu), 27.8 (Me19), 29.2 (3C, *t*Bu), 30.1 (C5), 30.9 (C6), 35.9 (C15), 37.9 (C9), 41.9 (C8), 43.9 (C1), 54.4 (C3), 56.9 (CH_3O), 62.1 (C2), 64.4 (C14), 72.2 (C10), 73.0 (*C*q*t*Bu), 77.2 (C11), 85.9 (C7), 101.1 (OCH_2), 110.6 (C20), 127.3 (C13), 137.8 (C12), 147.3 (C4). TOFMSES$^+$ (MEOH): 705 ($[MNa]^+$, 100). HRESIMS (MeOH) calcd for $C_{38}H_{74}O_6NaSi_2$ 705.4922; found 705.4925. Anal. Calcd for $C_{38}H_{74}O_6Si_2$: C, 66.81; H, 10.92. Found: C, 66.71; H, 10.94.

4.6. Preparation of cyclic formaldehyde-acetals 24–29

Starting from **23** the general procedure for cyclic formaldehyde-acetal formation was repeated on a 1 mmol scale to afford 533 mg of **25** (82%).

4.6.1. Compound 25. $[\alpha]_D^{20} = -79$ (*c* 2.1, $CHCl_3$). IR (film): 2950, 2927, 2852, 1470, 1460, 1385, 1359, 1254, 1191, 1096, 1072, 1018, 1018, 979, 917, 884, 833, 773, 661 cm^{-1}. ^1H NMR (500 MHz): 0.03 (3H, s, MeSi), 0.04 (3H, s, MeSi), 0.06 (3H, s, MeSi), 0.09 (3H, s, MeSi), 0.90 (18H, s, 2*t*Bu), 0.94 (3H, s, Me15), 1.00 (3H, s, Me15), 1.15 (9H, s, *t*Bu), 1.18 (3H, s, Me19), 1.48 (1H, dd, $J = 11.2$, 4.5 Hz), 1.55 (1H, d, $J = 14.7$ Hz), 1.58–1.70 (2H, m), 1.75 (3H, s, Me18), 1.86–1.90 (2H, m), 2.16–2.20 (1H, m), 2.34 (1H, dd, $J = 7.2$, 3.4 Hz, H1), 2.43 (1H, dt, $J = 13.6$, 5.6 Hz, H3), 3.70 (1H, dd, $J = 10.5$, 4.9 Hz, H7), 3.90 (1H, dd, $J = 9.8$, 3.7 Hz, H2), 4.02 (1H, dd, $J = 9.8$, 7.5 Hz, H2), 4.16–4.20 (2H, m, H10, H14), 4.61 (1H, s, H20), 4.74 (1H, s, H20), 4.90 (1H, s, H21), 5.15 (1H, s, H21), 5.46–5.48 (1H, m, H13). ^{13}C NMR (125 MHz): −5.4 (MeSi), −5.3 (MeSi), −4.7 (MeSi), −4.5 (MeSi), 18.1 (Me_3CSi), 18.2 (Me_3CSi), 20.5 (Me19), 25.3 (Me18), 25.8 (3C, *t*Bu), 25.9 (3C, *t*Bu), 26.7 (Me15), 29.1 (3C, *t*Bu), 29.7 (Me15), 30.6 (C6), 31.1 (C5), 35.5 (*C*q15), 36.8 (C9), 41.6 (C8), 43.2 (C1), 54.5 (C3), 63.0 (C2), 64.3 (C14), 72.1 (C7), 73.0 (*C*q, *t*Bu), 77.2 (C10), 87.3 (C11), 94.9 (C21), 110.2 (C20), 126.7 (C13), 138.2 (C12), 148.1 (C4). TOFMSES$^+$ (MEOH): 673 ($[MNa]^+$, 100). HRESIMS (MeOH) calcd for $C_{37}H_{70}O_5NaSi_2$ 673.4660; found 673.4701. Anal. Calcd for $C_{37}H_{70}O_5Si_2$: C, 68.25; H, 10.84. Found: C, 68.73; H, 11.41.

Starting from **22** the general procedure for cyclic formaldehyde-acetal formation was repeated on a 0.24 mmol scale to afford 126 mg of **24** (81%).

4.6.2. Compound 24. $[\alpha]_D^{20} = +5$ (*c* 1.1, $CHCl_3$). IR (film): 2952, 2927, 2853, 1469, 1460, 1387, 1360, 1254, 1190, 1098, 1067, 1020, 1005, 953, 918, 873, 834 cm^{-1}. ^1H NMR (500 MHz): 0.04 (3H, s, MeSi), 0.06 (3H, s, MeSi), 0.07 (3H, s, MeSi), 0.09 (3H, s, MeSi), 0.89 (3H, s, Me15), 0.90 (18H, s, 2*t*Bu), 0.96 (3H, s, Me15), 1.07 (3H, s, Me19), 1.19 (9H, s, *t*Bu), 1.53–1.66 (2H, m), 1.76 (3H, s, Me18), 1.81 (1H, dd, $J = 8.6$, 4.4 Hz), 1.89–1.99 (2H, m), 2.14–2.26 (2H, m), 2.35 (1H, dd, $J = 13.0$, 5.6 Hz, H1), 2.42 (1H, dd, $J = 7.5$, 3.4 Hz, H3), 3.69 (1H, dd, $J = 9.7$, 4.4 Hz, H7), 3.88 (1H, dd, $J = 13.4$, 1.4 Hz, H10), 3.90 (1H, dd, $J = 10.0$, 3.6 Hz, H2), 4.02 (1H, dd, $J = 9.9$, 7.5 Hz, H2), 4.26–4.30 (1H, m, H14), 4.61 (1H, s, H20), 4.74 (1H, s, H20), 4.88 (1H, s, H21), 5.17 (1H, s, H21), 5.55 (1H, s, H13). ^{13}C NMR (125 MHz): −5.4 (MeSi), −5.3 (MeSi), −4.7 (MeSi), −4.6 (MeSi), 18.2 (Me18), 18.3 (Me_3CSi), 18.8 (Me_3CSi), 25.9 (2Me15), 25.9 ($2 \times 3C$, *t*Bu) 29.4 (Me19), 29.5 (3C, *t*Bu), 30.7 (C6), 31.1 (C5), 32.5 (C15), 39.7 (C9), 42.1 (C8), 43.8 (C1), 53.6 (C3), 63.2 (C2), 66.4 (C14), 72.2 (C7), 73.2 (*C*q*t*Bu), 79.2 (C10), 86.4 (C11), 94.5 (C21), 109.8 (C20), 131.7 (C13), 135.5 (C12), 148.3 (C4). TOFMSES$^+$ (MEOH): 673 ($[MNa]^+$, 100). HRESIMS (MeOH) calcd for $C_{37}H_{70}O_5NaSi_2$ 673.4660; found 673.4694. Anal. Calcd for $C_{37}H_{70}O_5Si_2$, 0.38 CH_2Cl_2: C, 67.02; H, 10.65. Found: C, 66.99; H, 10.95.

4.7. Fluoride deprotection of 24 and 25

Use of the general procedure for TBS-deprotection on **24** (500 mg, 0.77 mmol) gave 295 mg (91%) of **26**.

4.7.1. Compound 26. $[\alpha]_D^{20} = +24$ (*c* 0.5, $CHCl_3$). IR (film): 3430, 2965, 2926, 2855, 1095, 1006 cm^{-1}. ^1H NMR (800 MHz): 0.87 (3H, s, Me19), 0.95 (3H, s, Me15), 1.05 (3H, s, Me15), 1.19 (9H, s, *t*Bu), 1.54 (1H, OH), 1.60 (1H, m, H6), 1.77 (3H, t, $J = 1.4$ Hz, Me18), 1.78 (1H, dd, $J = 13.4$, 5.9 Hz, H1), 1.80 (2H, m, H5,5), 1.84 (1H, dd, $J = 14.6$, 9.5 Hz, H9), 1.88 (1H, dd, $J = 13.4$, 9.3 Hz, H1), 2.18 (1H, m, H6), 2.27 (1H, d, $J = 14.6$ Hz, H9), 2.46 (1H, dd, $J = 9.4$, 4.5 Hz, H3), 3.49 (1H, dd, $J = 10.2$, 4.5 Hz, H7), 3.62 (1H, t, $J = 9.8$ Hz, H2), 3.83 (1H, d, $J = 9.5$ Hz, H10), 4.07 (1H, dd, $J = 9.8$, 4.2 Hz, H2), 4.27 (1H, m, H14), 4.77 (1H, br s, H20a), 4.90 (1H, br s, H20b), 4.91 (1H, s, H21a), 5.20 (1H, s, H21b), 5.65 (1H, m, H13). Diagnostic NOEs: {Me-19}: H-3, H-10, H-9, H-6; {Me-18}: H-10, H-13, H-21a; {H-3}: H-20a; {H-10}: Me-18, H-21a; {H-21a}: H-10, H-21b (NOE *gem*). ^{13}C NMR (200 MHz): 18.2 (Me18), 18.9 (Me19), 25.9 (2C, Me15), 29.3 (3C, *t*Bu), 29.4 (C6), 30.7 (C5), 33.4 (C9), 40.0 (Cq15), 41.6 (Cq8), 43.6 (C1), 54.9 (C3), 60.0 (C2), 65.7 (C14), 72.1 (C7), 73.5 (*C*q, *t*Bu), 78.7 (C10),

86.4 (Cq 11), 94.7 (C21), 112.2 (C20), 130.2 (C13), 137.4 (C12), 146.4 (C4). HRESIMS (MeOH) calcd for $C_{25}H_{42}O_5Na$ 445.2930; found 445.2930. Anal. Calcd for $C_{25}H_{42}O_5$+0.3 C_7H_{16}: C, 71.91; H, 10.42. Found: C, 72.09; H, 10.55.

Use of the general procedure for TBS-deprotection on **25** (500 mg, 0.77 mmol) gave 306 mg (94%) of **27**.

4.7.2. Compound 27. $[\alpha]_D^{20} = -70$ (*c* 0.8, $CHCl_3$). IR (film): 3400, 2959, 2926, 2855, 1094, 1008 cm^{-1}. ^1H NMR (300 MHz): 0.87 (3H, s, Me19), 0.94 (3H, s, Me15), 1.05 (9H, s, *t*Bu), 1.13 (3H, s, Me15), 1.37 (1H, dd, $J = 16.0$, 11.0, H9), 1.55–1.73 (3H, m, H6, H1, H9), 1.70 (3H, s, Me12), 1.78–1.86 (3H, m, H6, H1, OH), 2.13 (3H, m, H5,5, OH), 2.36 (1H, dd, $J = 11.5$, 6.4 Hz, H3), 3.31 (1H, dd, $J = 10.7$, 4.8 Hz, H7), 3.46 (1H, t, $J = 9.7$ Hz, H2), 4.01 (1H, dd, $J = 9.8$, 4.5 Hz, H2), 4.08 (1H, br s, H14), 4.14 (1H, d, $J = 9.9$ Hz, H10), 4.72 (1H, s, H20), 4.82 (1H, s, H20), 4.84 (1H, s, H21), 5.13 (1H, s, H21), 5.55 (1H, s, H13). ^{13}C NMR (75 MHz): 18.5 (Me19), 20.7 (Me18), 25.3 (Me15), 26.6 (Me15), 29.1 (3C, *t*Bu), 39.7 (C5), 30.7 (C6), 35.5 (C15), 37.1 (C9), 41.2 (C8), 42.8 (C1), 55.9 (C3), 59.8 (C2), 64.4 (C14), 71.8 (C7), 73.4 (*C*q, *t*Bu), 77.1 (C10), 87.2 (C11), 95.1 (C21), 112.7 (C20), 126.0 (C13), 140.2 (C12), 146.0 (C4). HRESIMS (MeOH) calcd for $C_{25}H_{42}O_5Na$ 445.2930; found 445.2953. Anal. Calcd for $C_{25}H_{42}O_5$+0.5 C_7H_{16}: C, 72.42; H, 10.66. Found: C, 72.44; H, 10.88.

4.8. Periodinane oxidation of 26 and 27

The general procedure was repeated as above on **26** (228 mg, 0.54 mmol) to afford after chromatography (heptane–EtOAc, 2:1) **28** (197 mg, 87%).

4.8.1. Enone-aldehyde 28. $[\alpha]_D^{20} = -165$ (*c* 1.2, $CHCl_3$). IR (film): 2971, 1719, 1660, 1097, 1068 cm^{-1}. ^1H NMR (800 MHz): 0.81 (3H, s, Me19), 1.04 (3H, s, Me15), 1.06 (3H, s, Me15), 1.15 (9H, s, *t*Bu), 1.54 (1H, ddd, $J = 13.3$, 4.6, 2.5 Hz, H6), 1.84 (1H, dtd, $J = 13.1$, 4.8, 2.9 Hz, H6), 1.93 (1H, m, H9), 2.02 (3H, d, $J = 1.4$ Hz, Me18), 2.10 (1H, m, H5), 2.20 (1H, dd, $J = 18.6$, 1.1 Hz, H1), 2.24 (1H, m, H5), 2.41 (1H, dd, $J = 14.1$, 11.7 Hz, H9), 2.71 (1H, d, $J = 18.6$ Hz, H1), 3.43 (1H, s, H3), 3.74 (1H, dd, $J = 11.7$, 1.3 Hz, H10), 4.08 (1H, dd, $J = 10.9$, 4.6 Hz, H7), 4.92 (1H, t, $J = 1.8$ Hz, H20a), 4.98 (1H, s, H21a), 5.03 (1H, t, $J = 1.9$ Hz, H20b), 5.26 (1H, s, H21b), 5.98 (1H, t, $J = 1.3$ Hz, H13), 9.47 (1H, d, $J = 1.6$ Hz, H2). Diagnostic NOEs: {Me-19}: H-3, H-10; {Me-15}: H-1, H-1, H-9; {Me-18}: H-10, H-13, H-21a; {H-3}: H-20a; {H-10}: Me-18, H-21a, Me-19; {H-21a}: H-10, H-21b (NOE *gem*). ^{13}C NMR (200 MHz): 16.9 (M-19), 19.5 (Me18), 24.7 (Me15), 27.3 (Me-15), 29.3 (3C, *t*Bu), 30.1 (C5), 30.5 (C6), 32.7 (C9), 40.2 (C15), 41.1 (C8), 49.0 (C1), 65.8 (C3), 72.1 (C7), 73.3 (*C*q, *t*Bu), 80.6 (C10), 86.7 (C11), 95.5 (C21), 115.8 (C20), 128.4 (C13), 139.6 (C4), 161.9 (C12), 197.3 (C14), 199.5 (C2). HRESIMS (MeOH) calcd for $C_{25}H_{38}O_5Na$ 441.2617; found 441.2609.

The general procedure was repeated as above on **27** (176g, 0.42 mmol) to afford after chromatography (heptane–EtOAc, 2:1) **29** (152 mg, 87%).

4.8.2. Enone-aldehyde 29. $[\alpha]_D^{20} = -248$ (*c* 1.2, $CHCl_3$). IR (film): 2971, 2933, 2874, 1720, 1668, 1364, 1190, 1096, 1067 cm^{-1}. ^1H NMR (800 MHz): 0.91 (3H, s, Me19), 1.09 (9H, s, *t*Bu), 1.10 (3H, s, Me15), 1.12 (3H, s, Me15), 1.54 (1H, tdd, $J = 13.7$, 11.5, 4.6 Hz, H6), 1.67 (1H, d, $J = 14.9$ Hz, H9), 1.78 (1H, m, H6), 1.81 (1H, d, $J = 15.0$ Hz, H9), 1.90 (3H, s, Me18), 2.06 (1H, br t, $J = 14.4$ Hz, H5), 2.20 (1H, bd, $J = 14.1$ Hz, H5), 2.22 (1H, d, $J = 17.5$ Hz, H1), 2.29 (1H, d, $J = 17.5$ Hz, H1), 3.42 (1H, s, H3), 4.00 (1H, dd, $J = 11.0$, 4.6 Hz, H7), 4.41 (1H, d, $J = 10.5$ Hz, H10), 4.92 (1H, s, H20a), 4.95 (1H, s, H21a), 5.01 (1H, s, H20b), 5.14 (1H, s, H21b), 5.93 (1H, s, H13), 9.418 (1H, s, H2). Diagnostic NOEs: {Me-19}: H-6, H-9, H-10; {Me-15}: H-10; {Me-18}: H-13, H-21b; {H-10}: H-21a, Me-19; {H-3}: H-20a, Me-19H; {H-20a}: H-3, H-20b (NOE *gem*); {H-21a}: H-10, H-21b (NOE *gem*). ^{13}C NMR (200 MHz): 17.0 (Me19), 21.7 (Me18), 24.7 (Me-15), 25.8 (Me15), 29.0 (3C, *t*Bu), 30.0 (C5), 30.5 (C6), 37.0 (C9), 40.4 (C8), 40.6 (C15), 49.4 (C1), 65.9 (C3), 71.8 (C7), 73.4 (*C*q, *t*Bu), 77.3 (C10), 87.7 (C11), 95.5 (C21), 115.9 (C20), 127.7 (C13), 139.5 (C4), 163.9 (C12), 196.8 (C14), 199.0 (C2). HRESIMS (MeOH) calcd for $C_{25}H_{38}O_5Na$ 441.2617; found 441.2601.

4.9. Preparation of enone-aldehydes 32 and 33

The deprotection of *tert*-butyldimethylsilyl ethers at C-14 and C-2 on A+C adducts **22** and **23** is done according to the general procedure on a 0.5 mmol scale affording after the usual work up and SiO_2 flash chromatography (heptane–EtOAc, 2:1 to 1:3) the corresponding triols **30** (182 mg, 80%) and **31** (188 mg, 83%), respectively.

4.9.1. Triol 30. $[\alpha]_D^{20} = +71$ (*c* 1.0, $CHCl_3$). IR (film): 3435, 2971, 1650, 1461, 1388, 1362, 1190, 1083, 1053, 1025, 949, 887, 754 cm^{-1}. ^1H NMR (500 MHz): 0.92 (3H, s, Me15), 0.95 (3H, s, Me15), 1.09 (3H, s, Me19), 1.17 (9H, s, *t*Bu), 1.28–1.32 (2H, m, OH, H9), 1.36 (1H, br s, OH), 1.55–1.62 (2H, m, H6,6), 1.70 (1H, br s, OH), 1.75 (3H, s, Me18), 1.81 (2H, d, $J = 7.9$ Hz, H1,1), 2.02 (1H, d, $J = 14.6$ Hz, H9), 2.16–2.21 (1H, m, H5), 2.28–2.34 (2H, m, H3, H5), 3.41 (1H, dd, $J = 7.8$, 3.8 Hz, H7), 3.46 (3H, s, MeO), 3.63 (1H, t, $J = 10.2$ Hz, H2), 3.76 (1H, d, $J = 10.6$ Hz, H2), 3.99 (1H, dd, $J = 10.2$, 3.9 Hz, H10), 4.15–4.26 (1H, m, H14), 4.62 (1H, d, $J = 6.5$ Hz, H20), 4.69 (1H, s, H21), 4.82 (1H, d, $J = 6.5$ Hz, H20), 4.87 (1H, s, H21), 5.59 (1H, s, H13). ^{13}C NMR (75 MHz): 18.5 (Me18), 20.3 (Me15), 26.6 (Me15), 26.9 (Me19), 29.2 (3C, *t*Bu), 29.8 (C5), 30.2 (C6), 37.2 (C15), 40.6 (C9), 41.8 (C8), 44.8 (C1), 54.0 (C3), 57.0 (CH_3O), 59.8 (C2), 65.6 (C14), 71.7 (C10), 73.3 (*C*q*t*Bu), 78.9 (C11), 88.2 (C7), 101.0 (OCH_2), 110.1 (C20), 130.0 (C13), 138.4 (12), 147.6 (C4). CIMS: 455 ($[MH]^+$, 30), 437 (86), 419 (35), 405 (31), 163 (100). Analysis: calcd for $C_{26}H_{46}O_6$ C, 68.69; H, 10.20, found: C, 68.51; H, 9.99. TOFMSES$^+$ (MEOH): 477 ($[MNa]^+$, 100). HRESIMS

(MeOH) calcd for $C_{26}H_{46}O_6Na$ 477.3192; found 477.3195.

4.9.2. Triol 31. $[\alpha]_D^{20} = -62$ (*c* 1.1, $CHCl_3$). IR (film): 3401, 2972, 1649, 1460, 1388, 1378, 1362, 1190, 1050, 1025, 933, 887, 753 cm^{-1}. ^1H NMR (500 MHz): 0.94 (3H, s, Me18), 1.00 (3H, s, Me15), 1.12 (9H, s, *t*Bu), 1.16 (3H, s, Me15), 1.22–1.38 (4H, m, H9, OH, H6,6), 1.60–1.66 (2H, m, OH, H1), 1.84 (1H, d, $J = 15.7$ Hz, H1), 1.86 (3H, s, Me18), 2.02 (1H, dd, $J = 15.3$, 6.7 Hz, H9), 2.20–2.26 (3H, m, H3, H5,5), 3.35 (1H, dd, $J = 10.5$, 4.3 Hz, H7), 3.51 (3H, s, OMe), 3.53–3.57 (1H, m, H2), 3.93–3.99 (2H, m, H10, H2), 4.12 (1H, dd, $J = 10.4$, 4.3 Hz, H14), 4.16 (1H, br s, OH), 4.70 (1H, d, $J = 6.1$ Hz, H20), 4.75 (1H, s, H21), 4.89 (1H, d, $J = 6.1$ Hz, H20), 4.92 (1H, br s, H21), 5.64 (1H, br s, H13). ^{13}C NMR (75 MHz): 18.6 (Me18), 20.0 (Me15), 24.8 (Me15), 27.8 (Me19), 28.9 (C5), 29.0 (3C, *t*Bu), 30.6 (C6), 36.0 (C15), 37.9 (C9), 41.5 (C8), 43.4 (C1), 55.7 (C3), 56.9 (CH_3O), 59.3 (C2), 64.3 (C14), 71.7 (C10), 73.2 (*C*q*t*Bu), 77.1 (C11), 84.5 (C7), 100.7 (OCH_2), 112.5 (C20), 126.8 (C13), 139.1 (C12), 145.9 (C4). TOFMSES$^+$ (MEOH): 477 ([MNa]$^+$, 100). HRESIMS (MeOH) calcd for $C_{26}H_{46}O_6Na$ 477.3192; found 477.3202.

Dess–Martin periodinane oxidation of triols **30** and **31** is achieved according to the general procedure on a 0.2 mmol scale leading, after silica gel column chromatography using heptane–EtOAc, 3:1 as eluent, to **32** (76 mg, 84%) and **33** (78 mg, 86%), respectively.

4.9.3. Enone-aldehyde 32. $[\alpha]_D^{20} = -111$ (*c* 1.6, $CHCl_3$). IR (film): 3435, 2971, 2933, 1719, 1666, 1471, 1455, 1416, 1389, 1364, 1309, 1270, 1249, 1214, 1190, 1147, 1085, 1054, 1018, 905 cm^{-1}. ^1H NMR (300 MHz): 0.79 (3H, s), 1.03 (3H, s), 1.09 (9H, s), 1.14 (3H, s), 1.16–2.28 (6H, m), 1.98 (3H, s), 2.18 (1H, d, $J = 17.9$ Hz), 2.73 (1H, d, $J = 17.9$ Hz), 3.02 (1H, s), 3.52 (3H, s), 3.79 (1H, d, $J = 10.0$ Hz), 3.94 (1H, dd, $J = 10.4$, 4.3 Hz), 4.68 (1H, s), 4.71 (1H, d, $J = 6.5$ Hz), 4.80 (1H, d, $J = 6.5$ Hz), 4.82 (1H, br s), 4.98 (1H, br s), 5.98 (1H, s), 9.56 (1H, t, $J = 1.7$ Hz). ^{13}C NMR (75 MHz): 17.4, 19.7, 26.2, 27.8, 29.2 (3C), 30.0, 30.4, 36.2, 40.9, 41.8, 50.6, 57.3, 65.3, 71.9, 73.3, 79.8, 89.0, 101.0, 115.1, 129.3, 140.0, 162.5, 198.2, 198.7. ESIMS (MeOH): 489 ([MK]$^+$, 22), 473 ([MNa]$^+$, 100). HRESIMS (MeOH) calcd for $C_{26}H_{42}O_6Na$ 473.2879; found 473.2872.

4.9.4. Enone-aldehyde 33. $[\alpha]_D^{20} = -242$ (*c* 2.3, $CHCl_3$). IR (film): 3470, 2972, 2877, 1722, 1716, 1661, 1622, 1469, 1455, 1440, 1389, 1372, 1315, 1281, 1248, 1189, 1082, 1068, 1050, 1027, 1011, 909 cm^{-1}. ^1H NMR (300 MHz): 0.94 (3H, s), 1.08 (9H, s), 1.12 (3H, s), 1.13 (3H, s), 1.46–2.08 (3H, m), 1.67 (1H, dd, $J = 15.2$, 10.5 Hz), 1.87 (1H, d, $J = 15.2$ Hz), 2.00 (3H, s), 2.21 (1H, d, $J = 17.9$ Hz), 2.55 (1H, d, $J = 17.9$ Hz), 3.08 (1H, s), 3.51 (3H, s), 3.95 (1H, dd, $J = 11.0$, 4.5 Hz), 4.10 (1H, d, $J = 10.3$ Hz), 4.52 (1H, s), 4.78 (1H, d, $J = 6.6$ Hz), 4.81 (1H, br s), 4.82 (1H, d, $J = 6.6$ Hz), 4.86 (1H, br s), 5.00 (1H, br s), 5.96 (1H, s), 9.56 (1H, d, $J = 1.8$ Hz). ^{13}C NMR (75 MHz): 17.4, 21.0, 24.1, 27.6, 29.0 (3C), 30.0, 30.2, 38.0, 40.0, 40.9, 50.4, 57.2, 65.6, 71.8, 73.5, 78.1, 85.9, 100.6, 115.4, 128.3, 139.9, 162.9, 197.6, 198.4. ESIMS (MeOH): 489 ([MK]$^+$, 8), 473 ([MNa]$^+$, 100). HRESIMS (MeOH) calcd for $C_{26}H_{42}O_6Na$ 473.2879; found 473.2872.

4.10. Preparation of the matched 7-nor B-secotaxoids 7 and 36

The procedure of Still was repeated as above on (10*S*)-**6** (177 mg, 0.28 mmol) and (14*S*)-**1** (75.3 mg, 0.28 mmol) to afford after SiO_2 column chromatography (eluent heptane–ether, 25:1) gave 150 mg (87%) of **34**.

4.10.1. Compound 34. $[\alpha]_D^{20} = -20$ (*c* 1.6, $CHCl_3$). IR (film): 3513, 2954, 2929, 2856, 1652, 1471, 1462, 1360, 1255, 1144, 1060, 884, 835, 773 cm^{-1}. ^1H NMR (300 MHz): 0.01 (3H, s), 0.02 (3H, s), 0.04 (3H, s), 0.06 (3H, s), 0.86 (9H, s), 0.88 (9H, s), 1.00 (6H, s), 1.04 (3H, s), 1.16–2.41 (12H, m), 1.76 (3H, s), 3.46 (3H, s), 3.68 (1H, dd, $J = 10.2$, 3.7 Hz), 3.80–3.94 (2H, m), 4.19–4.29 (1H, m), 4.55 (1H, br s), 4.64 (1H, d, $J = 6.2$ Hz), 4.76 (1H, br s), 4.78 (1H, d, $J = 6.2$ Hz), 5.41 (1H, br s). ^{13}C NMR (75 MHz): −5.4 (2C), −4.6 (2C), 18.1, 19.9, 23.0, 25.0, 25.8, 25.9 (6C), 26.7, 33.6, 35.1, 37.1, 39.2, 42.5, 45.3, 56.9 (2C), 62.6, 65.8, 76.6, 85.0, 100.7, 107.1, 109.3, 128.2, 137.2, 148.9. ESIMS (MeOH): 649 ([MK]$^+$, 14), 633 ([MNa]$^+$, 100). HRESIMS (MeOH) calcd for $C_{34}H_{66}O_5NaSi_2$ 633.4347; found 633.4340.

The deprotection of *tert*-butyldimethylsilyl ethers at C-14 and C-2 of **34** (73 mg, 0.12 mmol) using the general procedure afforded, after the usual work up and SiO_2 flash chromatography (heptane–EtOAc, 1:1), 41 mg (91%) of triol **35**: $[\alpha]_D^{20} = +2$ (*c*1.8, $CHCl_3$). IR (film): 3401, 2931, 1646, 1455, 1379, 1358, 1248, 1209, 1142, 1083, 1055, 1022, 984, 911, 890, 754 cm^{-1}. ^1H NMR (300 MHz): 1.02 (9H, s), 1.21–2.16 (11H, m), 1.25 (1H, t, $J = 7.2$ Hz), 1.79 (3H, s), 2.63 (2H, br s), 3.46 (3H, s), 3.62 (1H, dd, $J = 10.7$, 7.7 Hz), 3.84 (1H, dd, $J = 10.7$, 5.2 Hz), 3.88 (1H, d, $J = 10.0$ Hz), 4.16–4.27 (1H, m), 4.64 (1H, d, $J = 6.1$ Hz), 4.73 (1H, br s), 4.78 (1H, d, $J = 6.1$ Hz), 4.87 (1H, s), 5.56 (1H, br s). ^{13}C NMR (75 MHz): 19.7, 22.7, 24.8, 25.0, 26.4, 32.6, 34.5, 37.0, 39.3, 43.0, 44.7, 56.9, 58.0, 60.6, 65.0, 77.5, 84.5, 100.4, 110.6, 127.9, 138.4, 147.9. ESIMS (MeOH): 421 ([MK]$^+$, 16), 405 ([MNa]$^+$, 100). HRESIMS (MeOH) calcd for $C_{22}H_{38}O_5Na$ 405.2617; found 405.2619.

The oxidation of triol **35** (37 mg, 0.10 mmol) was carried out by addition of Dess–Martin periodinane (266 mg, 0.63 mmol) according to the general procedure. The usual work up allowed, after filtration through a short silica gel column using heptane–EtOAc, 3:1 as eluent, 28 mg (76%) of the desired enone-aldehyde **7**: $[\alpha]_D^{20} = -64$ (*c* 1.3, $CHCl_3$). IR (film): 3467, 2935, 1718, 1661, 1442, 1373, 1335, 1276, 1146, 1087, 1062, 1024, 906, 755 cm^{-1}. ^1H NMR (300 MHz): 1.04 (3H, s), 1.12 (6H, s), 1.15–2.27 (8H, m), 2.04 (3H, d, $J = 1.2$ Hz), 2.63 (1H, d, $J = 18.5$ Hz), 2.78 (1H, d, $J = 2.5$ Hz),

3.50 (3H, s), 3.99 (1H, dd, $J = 8.8$, 3.0 Hz), 4.39 (1H, br s), 4.68 (1H, d, $J = 6.5$ Hz), 4.69 (1H, s), 4.80 (1H, s), 4.82 (1H, d, $J = 6.5$ Hz), 4.99 (1H, s), 5.98 (1H, s), 9.71 (1H, d, $J = 2.7$ Hz). ^{13}C NMR (75 MHz): 21.2, 22.3, 24.1, 24.6, 27.7, 33.2, 35.4, 37.7, 40.0, 40.6, 50.2, 57.0, 67.0, 78.5, 85.6, 100.4, 113.6, 128.2, 141.8, 163.3, 198.0, 201.3. ESIMS (MeOH): 417 ([MK]$^+$, 8), 401 ([MNa]$^+$, 100). HRESIMS (MeOH) calcd for $C_{22}H_{34}O_5Na$ 401.2304; found 401.2301.

4.11. Preparation of cyclic formaldehyde-acetals 36a and 36b

Using the general procedure for cyclic formaldehyde-acetal formation (27 mg, 0.044 mmol) of **34**, afforded, after silica gel flash chromatography (heptane–Et_2O, 25:1), 25 mg (84%) of **36a**.

4.11.1. Compound 36a. $[\alpha]_D^{20} = +10$ (c 1.1, $CHCl_3$). IR (film): 2951, 2925, 2853, 1470, 1460, 1362, 1256, 1099, 1062, 1026, 1005, 974, 866, 835, 773 cm^{-1}. ^{1}H NMR (800 MHz): 0.03 (3H, s, MeSi), 0.06 (3H, s, MeSi), 0.08 (3H, s, MeSi), 0.09 (3H, s, MeSi), 0.88 (9H, s, tBu), 0.91 (9H, s, tBu), 1.01 (3H, s, Me19), 1.06 (6H, s, 2Me15), 1.42–1.68 (8H, m), 1.71 (3H, t, $J = 1.6$ Hz, Me18), 1.94 (1H, t, $J = 5.9$ Hz, H3), 2.04 (1H, td, $J = 13.5$, 5.1 Hz, H1), 2.11 (1H, m, H1), 3.72 (2H, d, $J = 6.0$ Hz, H2,2), 4.14 (1H, d, $J = 9.9$ Hz, H10), 4.16–4.18 (1H, m, H14), 4.63 (1H, d, $J = 2.2$ Hz, H21b), 4.80 (1H, s, H21a), 4.90 (1H, s, H20a), 5.14 (1H, s, H20b), 5.43 (1H, s, H13). Diagnostic NOEs: {Me-18}: H-13, H-21a; {Me-15}: H-10, H-21b; {H-21b}: H-10, H-21a (NOE *gem*). ^{13}C NMR (125 MHz): −5.0 (MeSi), −4.9 (MeSi), −3.9 (MeSi), −3.8 (MeSi), 18.2 (*C*q, tBu), 18.5 (*C*q, tBu), 20.9 (Me18), 23.5 (C6), 25.4 (Me19), 25.5 (Me15), 25.6 (Me15), 26.3 (3C, tBu), 26.5 (3C, tBu), 33.7 (C5), 35.5 (C9), 37.8 (C15), 39.6 (C8), 40.4 (C7), 45.0 (C1), 56.8 (C3), 62.2 (C2), 66.3 (C14), 77.6 (C10), 88.4 (C11), 95.4 (C21), 110.1 (C21), 128.1 (C13), 138.3 (12), 148.6 (C4). HRESIMS (MeOH) calcd for $C_{33}H_{62}O_4NaSi_2$ 601.4084; found 601.4099. Anal. Calcd for $C_{33}H_{62}O_4Si_2 \times 0.22\ CH_2Cl_2$: C, 66.68; H, 10.52. Found: C, 66.69; H, 10.66

Use of the general procedure for TBS-deprotection on **36a** (25 mg, 0.043 mmol) gave 15 mg (96%) of **36b.**

4.11.2. Compound 36b. $[\alpha]_D^{20} = +38$ (c 1.1, $CHCl_3$). IR (film): 3354, 2930, 2869, 1454, 1376, 1216, 1100, 1007, 971, 891, 755 cm^{-1}. ^{1}H NMR (800 MHz): 1.02 (3H, s, Me15), 1.04 (3H, s, Me15), 1.08 (3H, s, Me19), 1.42 (1H, dd, $J = 9.4$ Hz, H1), 1.44–1.65 (8H, m), 1.72 (3H, s, Me18), 1.88 (1H, ddd, $J = 13.4$, 6.9, 1.4 Hz, H1), 2.12 (1H, dd, $J = 9.9$, 4.3 Hz, H3), 2.13–2.16 (2H, m), 3.66 (1H, t, $J = 10.3$ Hz, H2), 3.78 (1H, dd, $J = 10.4$, 4.3 Hz), 4.24 (1H, t, $J = 5.7$ Hz, H10), 4.26–4.30 (1H, m, H14), 4.78 (1H, s, H21), 4.95 (1H, s, H20), 4.86 (1H, s, H21), 5.12 (1H, s, H20), 5.58 (1H, s, H13). Diagnostic NOEs: {Me-18}: H-13, H-21a; {Me-15}: H-10, H-21b; {H-21b}: H-10, H-21a (NOE *gem*). ^{13}C NMR (200 MHz): 20.5 (Me19), 22.6 (C6), 24.4 (Me18), 24.9 (Me15), 25.5 (Me15), 32.0 (C5), 34.7 (C9), 37.0 (C15), 39.6 (C8), 40.5 (C7), 44.0 (C1), 56.2 (C3), 59.4 (C2), 65.6 (C14), 77.2 (C10), 87.8 (C11), 94.9 (C21), 111.7 (C20), 127.5 (C13), 139.1 (C12), 147.1 (C4). HRESIMS (MeOH) calcd for $C_{21}H_{34}O_4Na$ 373.2355; found 373.2360. Anal. Calcd for $C_{21}H_{34}O_4$: C, 71.96; H, 9.78. Found: C, 71.97; H, 9.97.

4.12. Coupling of the mismatched partners (14*S*)-1/(10*R*)-6; preparation of B-secotaxoids 37–42

Use of the general procedure for fragment coupling (10*R*)-**6** (316 mg, 0.50 mmol) and (14*S*)-**1** (134 mg, 0.50 mmol) afforded, after SiO_2 column chromatography (eluent heptane–ether, 25:1), a mixture of two A+C adducts **37** and **38** as a 1:1.3 mixture in a 89% combined yield.

4.12.1. Compound 37 (faster eluting isomer). $[\alpha]_D^{20} = +14$ (c 1.3, $CHCl_3$). IR (film): 3487, 2954, 2929, 2856, 1648, 1472, 1462, 1395, 1361, 1255, 1088, 1063, 1041, 1026, 1005, 870, 835, 774 cm^{-1}. ^{1}H NMR (500 MHz): 0.02 (3H, s), 0.03 (3H, s), 0.05 (3H, s), 0.06 (3H, s), 0.87 (9H, s), 0.89 (9H, s), 0.97 (6H, s), 0.99–1.06 (2H, m), 1.10 (3H, m), 1.13–1.16 (1H, m), 1.42–1.48 (1H, m), 1.55 (2H, dd, $J = 9.7$, 4.2), 1.60–1.64 (2H, m), 1.72 (3H, s), 1.91–1.98 (2H, m), 2.05–2.10 (1H, m), 2.16–2.23 (1H, m), 3.49 (3H, s), 3.74 (1H, t, $J = 9.7$ Hz), 4.00 (1H, dd, $J = 9.7$, 3.8 Hz), 4.27 (1H, m), 4.33 (1H, s), 4.61 (1H, br s), 4.64 (1H, d, $J = 6.6$ Hz), 4.78 (1H, s), 4.85 (1H, d, $J = 6.6$ Hz), 5.47 (1H, br s). ^{13}C NMR (125 MHz): −5.3 (2C), −4.5 (2C), 18.1, 18.2, 18.4, 22.9, 24.9, 25.9 (6C), 27.1, 27.3, 32.4, 35.8, 36.9, 40.7, 40.8, 45.2, 55.5, 56.9, 61.0, 66.0, 78.6, 88.8, 101.4, 110.2, 130.8, 137.0, 147.2. ESIMS (MeOH): 649 ([MK]$^+$, 32), 633 ([MNa]$^+$, 100). HRESIMS (MeOH) calcd for $C_{34}H_{66}O_5NaSi_2$ 633.4347; found 633.4346.

4.12.2. Compound 38 (slower eluting isomer). $[\alpha]_D^{20} = -55$ (c 1.1, $CHCl_3$). IR (film): 3514, 2953, 2929, 2856, 1648, 1472, 1462, 1386, 1360, 1255, 1146, 1088, 1062, 1037, 939, 835, 773 cm^{-1}. ^{1}H NMR (250 MHz): 0.02 (6H, s), 0.05 (6H, s), 0.83 (9H, s), 0.87 (9H, s), 0.96 (3H, s), 0.98 (3H, s), 1.14 (3H, s), 0.82–2.21 (12H, m), 1.83 (3H, s), 3.48 (3H, s), 3.58–4.34 (4H, m), 4.59 (1H, br s), 4.64 (1H, d, $J = 6.3$ Hz), 4.79 (1H, br s), 4.83 (1H, d, $J = 6.3$ Hz), 5.46 (1H, br s). ^{13}C NMR (62.5 MHz): −5.4 (2C), −4.7, −4.6, 18.1, 18.2, 20.2, 23.2, 24.9, 25.5, 25.9 (6C), 27.9, 32.7, 35.7, 35.8, 37.0, 41.6, 44.5, 56.1, 56.9, 61.4, 64.2, 77.2, 85.4, 101.0, 110.1, 127.4, 137.4, 147.9. ESIMS (MeOH): 649 ([MK]$^+$, 12), 633 ([MNa]$^+$, 100). HRESIMS (MeOH) calcd for $C_{34}H_{66}O_5NaSi_2$ 633.4347; found 633.4349.

The deprotection of *tert*-butyldimethylsilyl ethers at C-14 and C-2 of **37** and **38** on a 0.3 mmol scale using the general procedure afforded, after the usual work up and SiO_2 flash chromatography (heptane–EtOAc, 2:1 to 1:3), 96 mg (87%) of triol **39** and 98 mg (89%) of triol **40**, respectively.

4.12.3. Compound 39. $[\alpha]_D^{20} = +54$ (c 1.1, $CHCl_3$). IR (film): 3400, 2930, 1648, 1472, 1443, 1380, 1215, 1145, 1088, 1065, 1026, 945, 892, 849 cm^{-1}. ^{1}H NMR

(300 MHz): 0.92 (3H, s), 0.96 (3H, s), 1.10 (3H, s), 1.21–2.17 (11H, m), 1.75 (3H, s), 2.48 (2H, br s), 3.50 (3H, s), 3.61 (1H, dd, $J = 10.9$, 7.0 Hz), 3.73 (1H, d, $J = 10.1$ Hz), 3.86–3.97 (1H, m), 4.19–4.31 (1H, m), 4.34 (1H, s), 4.63 (1H, d, $J = 6.6$ Hz), 4.72 (1H, s), 4.82 (1H, d, $J = 6.6$ Hz), 4.86 (1H, s), 5.62 (1H, br s). ^{13}C NMR (75 MHz): 18.4, 22.5, 24.3, 26.9, 27.1, 32.2, 33.6, 36.7, 41.1, 42.5, 44.5, 57.0, 57.3, 61.3, 65.5, 78.9, 88.2, 101.1, 110.6, 129.7, 138.8, 148.4. ESIMS (MeOH): 421 ($[MK]^+$, 18), 405 ($[MNa]^+$, 100).

4.12.4. Compound 40. $[\alpha]_D^{20} = -70$ (c 1.3, $CHCl_3$). IR (film): 3584, 3401, 2931, 1645, 1454, 1380, 1147, 1060, 1024, 929, 891 cm^{-1}. ^{1}H NMR (300 MHz): 0.98 (3H, s), 0.99 (3H, s), 1.15 (3H, s), 1.18–2.18 (13H, m), 1.85 (3H, s), 3.49 (3H, s), 3.54 (1H, d, $J = 10.2$ Hz), 3.83–3.92 (2H, m), 4.02 (1H, s), 4.04–4.11 (1H, m), 4.66 (1H, d, $J = 6.3$ Hz), 4.74 (1H, br s), 4.85 (1H, d, $J = 6.3$ Hz), 4.94 (1H, br s), 5.62 (1H, br s). ^{13}C NMR (75 MHz): 20.1, 22.7, 24.7, 24.8, 28.1, 31.1, 35.2, 35.7, 36.7, 42.2, 44.0, 56.2, 57.0, 59.5, 64.2, 77.2, 84.7, 100.8, 112.3, 126.6, 139.2, 147.1. ESIMS (MeOH): 421 ($[MK]^+$, 22), 405 ($[MNa]^+$, 100).

Dess–Martin periodinane oxidation of triols **39** (63 mg, 0.16 mmol) and **40** (37 mg, 0.10 mmol) is achieved according to the general procedure leading, after silica gel column chromatography using heptane–EtOAc, 3:1 as eluent, to **41** (48 mg, 86%) and **42** (32 mg, 89%), respectively.

4.12.5. Enone-aldehyde 41. $[\alpha]_D^{20} = -68$ (c 1.9, $CHCl_3$). IR (film): 3584, 3435, 2931, 1716, 1667, 1443, 1414, 1371, 1309, 1214, 1149, 1087, 1063, 1018, 904 cm^{-1}. ^{1}H NMR (300 MHz): 0.86 (3H, s), 1.04 (3H, s), 1.15 (3H, s), 0.87–2.26 (9H, m), 1.99 (3H, d, $J = 0.8$ Hz), 2.71 (1H, d, $J = 18.3$ Hz), 2.77 (1H, s), 3.52 (3H, s), 3.78 (1H, d, $J = 10.4$ Hz), 4.68 (1H, d, $J = 6.6$ Hz), 4.75 (1H, s), 4.78 (1H, s), 4.81 (1H, d, $J = 6.6$ Hz), 4.97 (1H, s), 5.99 (1H, br s), 9.68 (1H, d, $J = 2.6$ Hz). ^{13}C NMR (75 MHz): 19.8, 22.1, 23.4, 25.9, 27.9, 32.1, 35.3, 36.5, 40.4, 41.7, 50.3, 57.3, 65.1, 79.4, 88.3, 100.8, 114.3, 129.4, 141.6, 162.8, 198.4, 199.9. ESIMS (MeOH): 417 ($[MK]^+$, 32), 401 ($[MNa]^+$, 100).

4.12.6. Enone-aldehyde 42. $[\alpha]_D^{20} = -221$ (c 1.1, $CHCl_3$). IR (film): 3459, 2938, 1719, 1662, 1442, 1376, 1334, 1308, 1273, 1149, 1085, 1063, 1016, 907, 755 cm^{-1}. ^{1}H NMR (250 MHz): 0.98 (3H, s), 1.11 (3H, s), 1.13 (3H, s), 1.19–2.06 (6H, m), 1.43 (1H, d, $J = 15.2$ Hz), 1.74 (1H, d, $J = 10.6$ Hz), 2.01 (3H, d, $J = 1.0$ Hz), 2.21 (1H, d, $J = 18.3$ Hz), 2.50 (1H, d, $J = 18.3$ Hz), 2.87 (1H, s), 3.50 (3H, s), 4.08 (1H, d, $J = 10.4$ Hz), 4.58 (1H, s), 4.70 (1H, d, $J = 6.4$ Hz), 4.81 (1H, s), 4.83 (1H, d, $J = 6.4$ Hz), 4.99 (1H, s), 5.98 (1H, s), 9.63 (1H, d, $J = 2.6$ Hz). ^{13}C NMR (62.5 MHz): 21.3, 22.2, 23.9, 24.1, 27.7, 31.8, 35.4, 36.6, 39.8, 42.1, 50.4, 57.2, 65.4, 78.1, 85.7, 100.6, 114.7, 128.3, 141.7, 163.2, 197.7, 200.0. ESIMS (MeOH): 417 ($[MK]^+$, 58), 401 ($[MNa]^+$, 100). HRESIMS (MeOH) calcd for $C_{22}H_{34}O_5Na$ 401.2304; found 401.2307.

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