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The domino chemistry approach to molecular complexity: high-yielding bis-hetero intramolecular Diels–Alder reactions with ketone components

Angeline Chanu, Isabel Castellote, Aurelien Commeureuc, Imad Safir and Siméon Arseniyadis*

Institut de Chimie des Substances Naturelles, CNRS, F-91198 Gif-sur-Yvette, France

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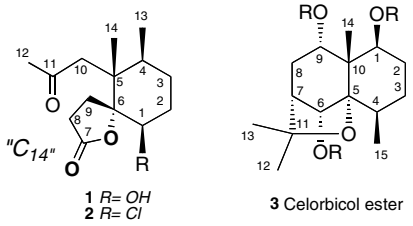
Abstract—The bis-keto-hetero-IMDA option, with two ketone components (both the heterodiene and heterodienophile moieties) has been examined in several representative domino templates with the aim of ultimately developing efficient methods for the synthesis of structurally complex natural products. The domino sequence could also be activated efficiently by utilizing the less toxic iodobenzene diacetate as the oxidative cleavage/[4+2] promoter while it is unbiased to the nature of substitution around the bicyclic framework.

1. Introduction

We have already shown in several publications that the reaction of $Pb(OAc)_4$ with selected ene-diols can lead to domino[1] reactions providing an entry into a range of molecular architectures.[2] Trying to satisfy Tietze's criteria[3] we explored several reagents capable of replacing toxic lead tetraacetate at least for the half of the domino process. An important experimental improvement since we first reported this reaction was that $Pb(OAc)_4$ could be replaced by $PhI(OAc)_2$ as the domino promoter, thus decreasing the toxicity of the oxidative/pericyclic process by half. Other alternatives to the $Pb(OAc)_4$ based oxidative cleavage included $NaBiO_3$, Ph_3BiCO_3, $Mn(OAc)_3$ and Dess–Martin periodinane, which were less effective at completing the oxidative cleavage, and in no case was the full cascade observed.[4]

The observation that the non-toxic $PhI(OAc)_2$[5] is a useful domino promoter for the successful elaboration of advanced subunits justifies the use of this reaction sequence in synthetic strategies, as the products of these domino reactions are potentially versatile intermediates. While optimizing the efficiency of the oxidative/pericyclic domino reaction (which we called 'half-cascade'), we discovered that the process was compatible with two ketone components as heterodiene–heterodienophile moieties.[6] We therefore decided to examine this transformation as a possible synthetic strategy for the ring construction with controllable patterns of selective oxygenation. Among the target molecules, spirolactone natural products such as pathylactone A **1**,[7] napalilactone **2**[8] and agarofuran sesquiterpenes[9] such as celorbicol ester **3** are shown in Figure 1.



1 *R= OH*
2 *R= Cl*

3 Celorbicol ester

Figure 1.

In preliminary studies we showed that a convenient method for synthesis of **III** ($R^1 = H$) involved a stoichiometry, reagent and/or solvent controlled domino reaction such as reacting **I** ($R^1 = H$) with 1 equiv of $Pb(OAc)_4$. We report herein that oxidative cleavage of unsaturated diol **I** (R^1, R^2, R^3#H) using 1 equiv of $PhI(OAc)_2$ gives the bis-heterodiene–dienophile motif **II** (hitherto unexplored), which collapses

* Corresponding author. Tel.: +33 169 82 30 29; fax: +33 169 07 72 47; e-mail: simeon.arseniyadis@icsn.cnrs-gif.fr

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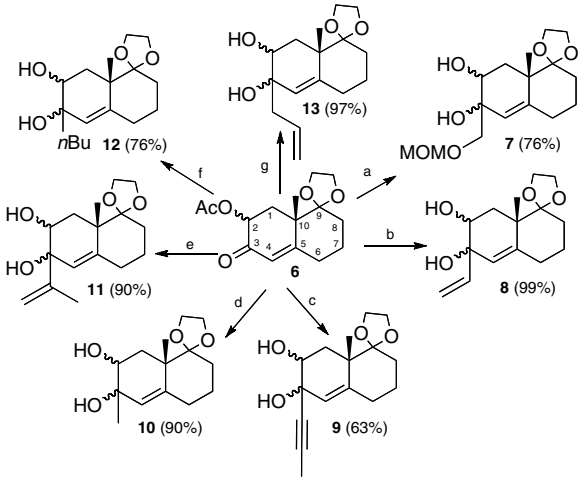
into the tricyclic enol ether **III**. This protocol satisfies the Tietze's criteria in that it uses non-toxic reagents, it produces high yields, there are no isomeric or byproducts and enantiomeric purity can be introduced at a very early stage.

A stereo-cleaning, generating stereochemical bias through the substrate's structure ensures that the cyclic ene-acetal (4 + 2 product) of type **III**, the sole product formed, has the two adjacent quaternary centres correctly set for **1**, **2** (C5, C6) and **3** (C5, C10). The cyclocondensation reaction can tolerate a remarkably broad range of functionality in both the heterodiene and heterodienophile components, while stereochemical control is realized through destruction–reconstruction of the hydroxy-bearing stereocentres (stereocleaning). In addition, the reaction proceeds through an intermediate with reactive functionalities (R^1, R^2, R^3) available for either in situ or subsequent modification.

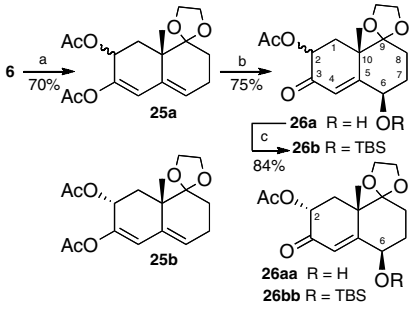


Scheme 1. Reagents and conditions: (a) Bu_3SnCH_2OMOM, *n*-BuLi, THF, −78 °C; (b) vinylMgBr, THF, −78 °C; (c) propyne, *n*-BuLi, HMPA, THF, −78 to 25 °C; (d) MeLi, THF, −78 °C; (e) isopropenylMgBr, THF, −78 °C; (f) *n*-BuLi, THF, −78 °C; (g) allylMgBr, THF, −78 °C.

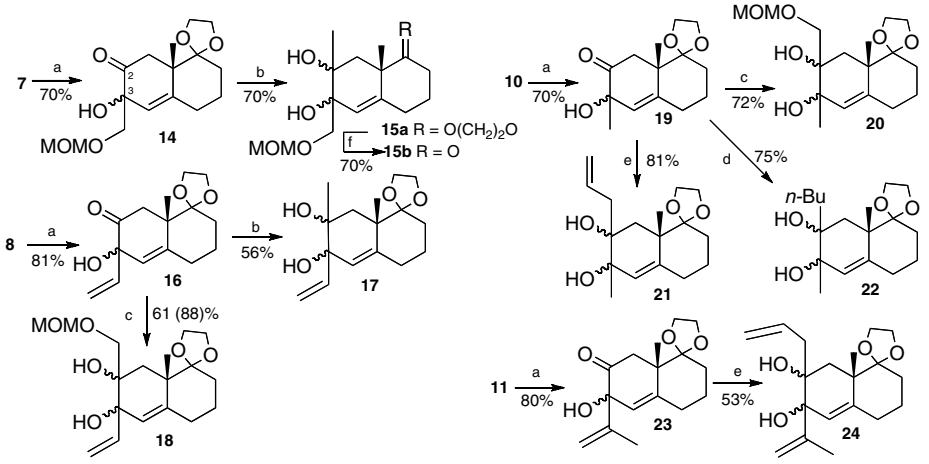
Although rare[10] due to steric and electronic reasons, such hetero-Diels–Alder reactions in the intramolecular version are part of an elegant multi-component domino sequence developed by Tietze et al.[11] The ready availability of a large array of bicyclic unsaturated diols provided the incentive for analysis of the scope of this one-pot multi-stage transformation chemistry, of which we provide the details and experimental procedures herein.

2. Results and discussion

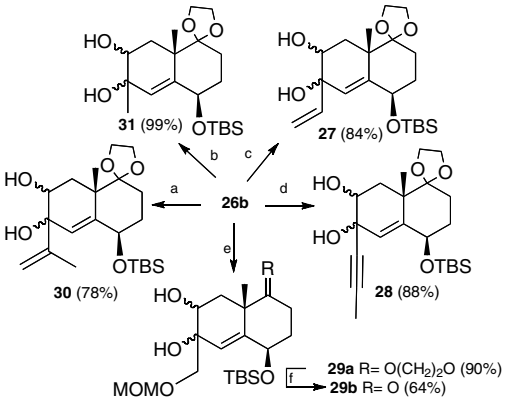
Since our primary concerns were the assessment of the outer limits of the domino strategy and the evaluation of new designs for higher molecular complexity, there was no need to operate with the enantiomerically homogeneous starting material. Accordingly we started with scalemic Wieland–Miescher ketone (ca. 71% ee). The conversion of the known enone **6**[4] to substrate-diols was conveniently realized by sequential nucleophilic addition, reoxidation of the resulting diol with IBX, the α-hydroxy-ketone thus obtained providing the setting for introduction of the second functionality, which was accomplished by nucleophilic addition in the same way (Schemes 1 and 2). With large amounts of **6** in hand, it proved an easy matter to add the allylic hydroxyl group and generate **26b** by making



Scheme 3. Reagents and conditions: (a) Ac_2O, Py, DMAP, reflux; (b) MTO, 30% H_2O_2, Py, CH_2Cl_2, 25 °C; (c) TBSCl, Imidazole, DMF, 60 °C.



Scheme 2. Reagents and conditions: (a) IBX, DMSO, 80 °C; (b) MeLi, THF, −78 °C; (c) Bu_3SnCH_2OMOM, *n*-BuLi, THF, −78 °C; (d) *n*-BuLi, THF, −78 °C; (e) allylMgBr, THF, −78 °C; (f) HCl 4 N, THF, 0 °C.

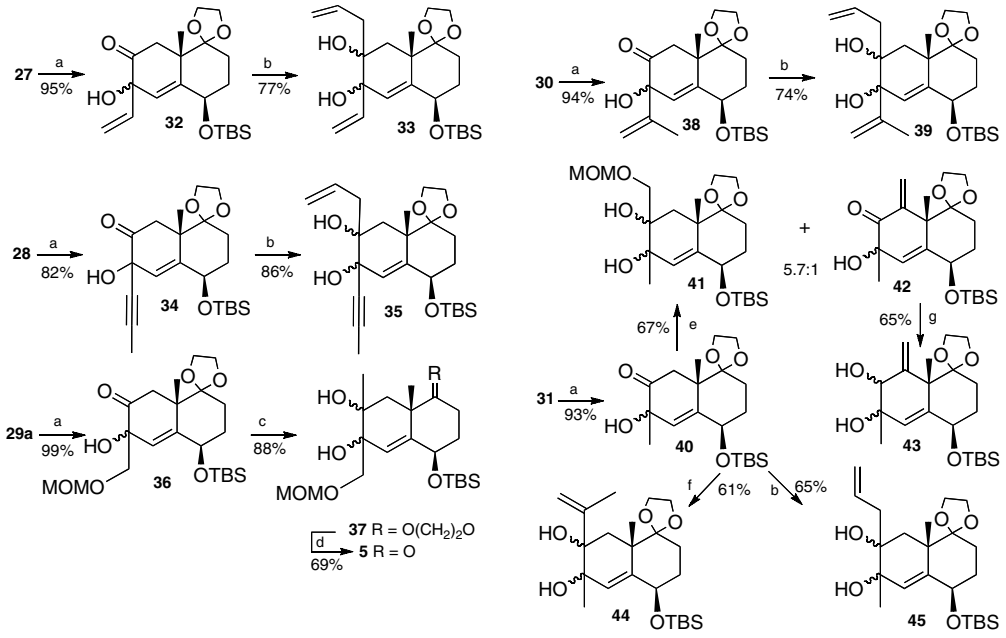


Scheme 4. Reagents and conditions: (a) isopropenylMgBr, THF, −78 °C; (b) MeLi, THF, −78 °C; (c) vinylMgBr, THF, −78 °C; (d) propyne, *n*-BuLi, HMPA, THF, −78 to 25 °C; (e) Bu_3SnCH_2OMOM, *n*-BuLi, THF, −78 °C; (f) PPTS, acetone/H_2O, reflux.

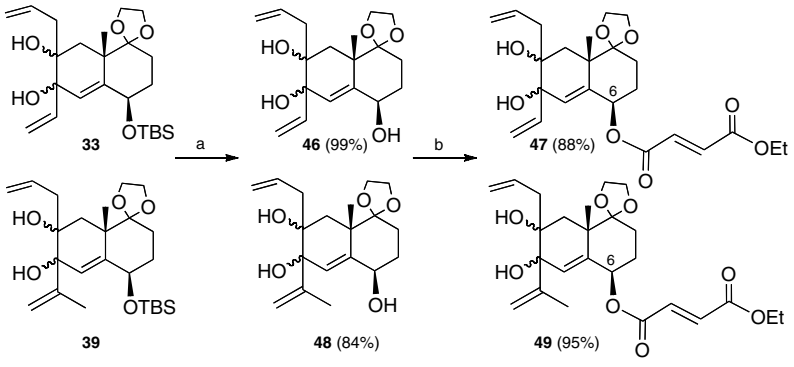
recourse to dienol acetate formation and its known oxidation (Scheme 3). The latter, possessing a β-hydroxy group at the C6 position, served as the key intermediate for the construction of all domino templates portrayed in Schemes 4–6 by a sequence of functional group interconversion. The steroidal diol framework was prepared straightforwardly from the acetoxy-enone derivative of 17-OTBS-protected testosterone **50** (Scheme 7).

2.1. Synthesis of the 'heterodiene–ketone' precursors; the C3-substitution

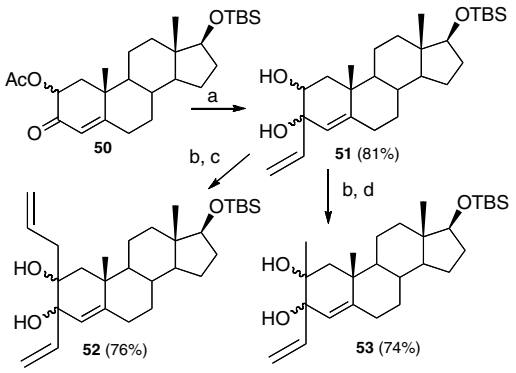
Targets **7**–**13** were selected so that they could be directly synthesized from readily available α-acetoxy-enone **6**, via literature procedures, and allow for further rearrangements during or after the domino reaction. The key compound **6** was obtained via selective ketal protection[12] of the Wieland–Miescher ketone **1**,[13] followed by acetoxylation



Scheme 5. Reagents and conditions: (a) IBX, DMSO, 80 °C; (b) allylMgBr, THF, −78 °C; (c) MeLi, THF, −78 °C; (d) PPTS, acetone/H_2O, reflux; (e) Bu_3SnCH_2OMOM, *n*-BuLi, THF, −78 °C; (f) isopropenylMgBr, THF, −78 °C; (g) $NaBH_4$, $CeCl_3{\cdot}7H_2O$, CH_2Cl_2/EtOH, 0 °C.



Scheme 6. Reagents and conditions: (a) TBAF, 60 °C; (b) fumaric acid monoester, DCC, DMAP, CH_2Cl_2, 0 °C.



Scheme 7. Reagents and conditions: (a) vinylMgBr, THF, −78 °C; (b) IBX, DMSO, 80 °C; (c) allylMgBr, THF, −78 °C; (d) MeMgBr, THF, −78 °C.

($Pb(OAc)_4$, PhH, reflux, 4 days).[14] Starting from **6**, nucleophilic addition (Grignard or RLi, THF, −78 °C) afforded the targets in high chemical yields. Thus, addition of the α-alkoxyorganolithium derived from Bu_3SnCH_2OMOM[15] via transmetallation with *n*-BuLi (Bu_3SnCH_2OMOM, in dry THF, −78 °C, 1 h)[16] to **6** gave **7** (76%). Vinylmagnesium bromide (1 M in dry THF, −78 °C for 3.5 h) addition on **6** afforded **8** (99%). Addition of propynyllithium (prepared in situ from propyne, *n*-BuLi, HMPA), in dry THF at −78 to 25 °C, overnight afforded **9** in 63% isolated yield. The methyl-carbinol **10** was prepared from **6** in 90% yield proceeding as in Ref. 4a, while **11** then **12** were prepared from **6** under the same conditions using the appropriate Grignard (isopropenylMgBr, 0.5 M in THF, −78 °C, 2 h, for the former), or organolithium (*n*-BuLi, 1.6 M in hexane, THF, −78 °C, 1 h, for the latter) in 90% and 76% yields, respectively. Finally, when **6** was reacted with excess allylmagnesium bromide (1.0 M in THF, 5 equiv) at −78 °C for 1 h, it furnished a 97% isolated yield of the carbinol **13**. Because the yields of the C3 substituted substrates were acceptable (from lowest 63% to nearly quantitative) and the recovered starting material completed the balance, no further efforts were made for optimization. The preparations of the heterodiene substituted precursors are summarized in Scheme 1.

2.2. Synthesis of the 'bis-ketone' precursors; the C2 substitution

To prepare the target substrates we needed to create conditions for the second nucleophilic addition leading to the C2 substitution. Having established a practical access to the keto-diene component (the C3 substitution) for the hetero-IMDA, we turned our attention to a viable route for an uneventful oxidation leading to the required α-ketol pattern. Based upon our earlier experience, care had to be taken at this stage to insure a clean C2 oxidation, avoiding C2–C3 cleavage (glycol fission).[4] This conversion was best achieved using 2-iodoxybenzoic acid (IBX), prepared using the Santagostino procedure (OXONE® oxidation).[17]

The tertiary–secondary diol frameworks **7**, **8**, **10** and **11** were converted to the corresponding α-ketols by oxidation with IBX (DMSO, 80 °C) in good yields (ca. 80% isolated). The ketal-protected **15a** was deketalized before the domino process (PPTS, acetone/H_2O, reflux) thus affording an additional free-keto template to be tested and further to be used in synthetic endeavours (vide infra, Fig. 3).

The subsequent step towards the bis-tertiary 1,2-unsaturated diol substrate was accomplished by nucleophilic addition as above (Scheme 2), setting the stage for ultimate conversion to the complex oxygen heterocycle of type **III** (Fig. 2).

2.3. Synthesis of the 6-oxo precursors, the C3, then C2 substitution

The allylically substituted diols **27**–**31** were synthesized by an analogous route. First, acetoxy-enone **6** was transformed into the dienol acetate **25a** using known procedures as indicated in Scheme 3. **25a**, obtained by heating **6** in pyridine in the presence of acetic anhydride and 4-DMAP (in 70% yield, 90% based on recovered starting acetoxy-enone), was subjected to epoxidation using methyltrioxorhenium (MTO)[18] as catalyst and aqueous hydrogen peroxide as terminal oxidant (75% isolated yield). The resulting mixture (C2-epimers) was protected at C6 (steroid numbering) by treatment with TBSCl in the presence of imidazole in DMF, at 60 °C under argon, affording cleanly the desired *tert*-butyldimethylsilylether **26b**, in 84% yield. It should be pointed out that the C6 stereogenic centre was obtained completely stereoselectively, without any detectable α-epimer, while in the C9–O*t*Bu series the α-epimer was present, albeit as a minor component.[19] Evidence that C6 carbon has a β-hydroxyl group came from the NOE experiments. Small quantities of the stereopure compounds **26aa** and **26bb** were isolated by chromatography only for characterization (the stereochemistry at the secondary hydroxyl groups is not important since it is destroyed in the generation of the [4+2] intermediate **II**, Fig. 2).

Starting from key intermediate **26b**, the keto-heterodiene precursors **27**–**31** were synthesized as above by addition of the appropriate nucleophile. VinylMgBr gave **27**

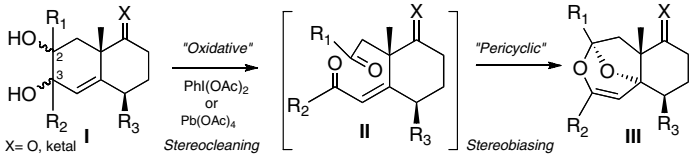


Figure 2.

(84%), propynyllithium **28** (88%), lithiated Tin-MOM acetal **29a** (90%), isopropenylMgBr **30** (78%) and finally methyllithium afforded **31** in 99% isolated yield (Scheme 4).

The resulting tertiary–secondary carbinols were then transformed into their corresponding bis-tertiary diols, ready for the oxidative cleavage, by the same two-step protocol as for the C6-nor series (Scheme 5). A clean reaction ensued in each case investigated, when the resulting carbinols were subjected to oxidation with IBX in DMSO (>90% isolated yields), and the products had ^{1}H and ^{13}C NMR spectra concordant with the expected α-ketols (no glycol fission detected).

Application of the same conditions as above for the nucleophilic substitution at C2 completed the two-step construction of the required templates in good isolated yields (Scheme 5). Insofar as formation of **42** is concerned, it is reasonable to assume a basic behaviour of the nucleophile resulting in the enolate formation (nucleophilic aldol partner) and on the other hand in situ re-formation of formaldehyde from the initial adduct $RCH(O^{-})CH_2OMOM$, which serves as an electrophilic aldol partner. The intermediate aldol thus obtained finally crotonizes to give **42**. In order to assess the relative reactivity of the heterodienophile created by the oxidative cleavage and a conventional doubly-activated dienophile at C-6, we needed to carry out an experiment, which would allow the two dienophiles to compete directly for a diene (two adducts could potentially form from the competing IMDA reactions). The probes were prepared straightforwardly as portrayed in Scheme 6. Thus, fluoride deprotection of **33** (TBAF, 60 °C) furnished the required free alcohol **46** (99%), which was selectively esterified at C6 with ethyl fumarate (fumaric acid monoester, DCC, DMAP, CH_2Cl_2, 0 °C) affording the target molecule **47** (88%). In a similar fashion compound **39** was readily transformed into the free allylic alcohol **48** (84%), which in turn was converted into the corresponding ester **49** (95%).

2.4. Synthesis of the steroidal templates

To gauge the scope of this methodology, a number of steroidal diols were synthesized and subjected to reaction with both $PhI(OAc)_2$ and $Pb(OAc)_4$ under the same reaction conditions. The preparation of **52** and **53**, considered to be challenging substrates for the domino transformations, was achieved straightforwardly. As before, the synthesis began with α-acetoxylation and subsequent alkylation of the known steroidal enone, derived from commercially available testosterone (Scheme 7). Conversion of **50** into the C3 substituted **51** was achieved by addition of vinylMgBr (excess, THF, −78 °C, 3 h) in 81% isolated yield. The latter was first oxidized at C2 with IBX (DMSO, 80 °C, 30 min, 91%), then served as a common intermediate for the synthesis of both C2 substituted diol substrates **52** (excess allylMgBr, in THF, −78 °C, 2 h, 84%) and **53** (MeMgBr, THF, −78 °C, 2 h, 81%).

The bis-tertiary 1,2-unsaturated diols **52** and **53** proved to be an exemplary system ultimately giving rise to ring-A modified steroids in (ca. 90%) yields (vide infra).

2.5. Domino reactions

Our initial explorations of reaction conditions for the domino process focused on the oxidative cleavage of unsaturated diols thus obtained using only 1 equiv of $Pb(OAc)_4$ as the domino promoter in toluene (modulation by stoichiometry and solvent). Alternatively, the domino sequence was also activated at room temperature by utilizing the less toxic iodobenzene diacetate as the oxidative cleavage/[4+2] promoter. A parallel series of domino reactions was thus performed using both $Pb(OAc)_4$ and $PhI(OAc)_2$. All things considered (solvent, temperature, stoichiometry), the use of iodobenzene diacetate gave comparable yields of cyclic ene-acetal and was used for all preparative scale experiments. The reaction was exceptionally clean in both cases and yields were comparable; a simple filtration of the reaction crude on silica was enough for obtaining pure compounds. The first compounds tested were the seven monosubstituted diols **7**–**13** whose parent, unsubstituted diols were known to give the domino product. Reactions with substrates, which harbor oxygen substituents or alkene/alkyne, respectively, all proceed smoothly to the half-cascade level. The hitherto unexplored bis-hetero-IMDA option, with two ketone components (both the heterodiene and heterodienophile moieties) has been examined in 20 representative cases. The cyclic ene-acetal (4 + 2 product) of type **III** (Fig. 2) was the sole product formed. The optimized procedure involved addition of iodobenzene diacetate to a solution of the unsaturated diol in acetonitrile (or lead tetraacetate in toluene) and stirring, under inert atmosphere, at room temperature for ca. 24 h. Following TLC control indicating consumption of the starting material, cyclic ene-acetals were isolated after workup and chromatography in good to high yields. The process tolerates a variety of substitution patterns and protecting groups (Table 1, entries 1–31).

As shown in Table 1, a wide range of substrates underwent efficient oxidative/pericyclic (glycol fission/intramolecular bis-hetero Diels–Alder) domino transformation when subjected to iodobenzene diacetate [1.2 equiv of $PhI(OAc)_2$, MeCN, 15–24 h at 25 °C] or lead tetraacetate [1.5 equiv of $Pb(OAc)_4$, PhMe at 25 °C] with high yields. No side products could be detected upon analysis of the reaction crude by high field ^{1}H and ^{13}C NMR. Therefore, the conditions reported above were used as the standard conditions for domino transformations with either oxidant for all the reactions reported. Exposure of the selected diols to the usual domino conditions with $Pb(OAc)_4$ as the oxidant, provided the expected oxidative/pericyclic domino products exclusively in good to high yields. The iodobenzene diacetate induced reaction of all unsaturated diols investigated proceeded uneventfully and provided the expected cyclic ene-acetal as the sole products in comparable (to those obtained with lead tetraacetate) yields. Since the differences in yields were in the range of ±5%, we decided to give the average values in Table 1. It should be noted that entry 9, utilizing diol **15b** as the domino substrate, has not been optimized. The one-pot sequence was successfully employed for the conversion of the steroidal templates **51**–**53** (Table 1, entries 29–31), while preliminary results from competition experiments (Table 1, entries 27 and

Table 1. Reagents and conditions: (A) 1.2 equiv of $PhI(OAc)_2$, in acetonitrile, 15–24 h at 25 °C (B) 1.5 equiv of $Pb(OAc)_4$ in dry PhMe at 25 °C

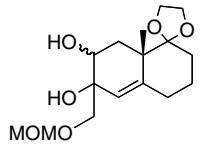
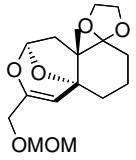
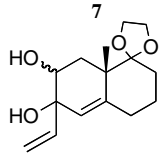
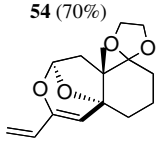
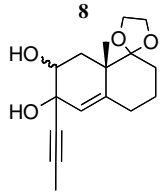
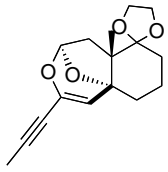
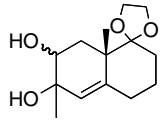
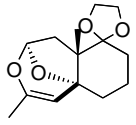
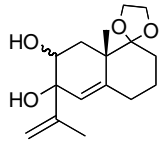
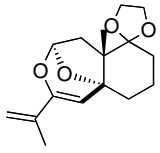
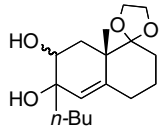
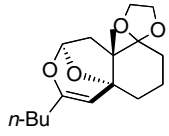
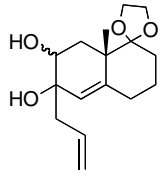
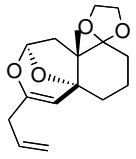
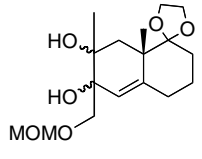
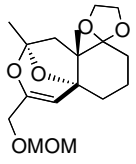
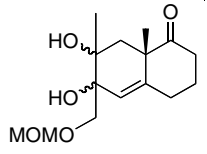
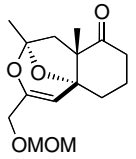
Entry	Starting unsaturated diol	Domino product (% yield)
1	 **7**	 **54** (70%)
2	 **8**	 **55** (99%)
3	 **9**	 **56** (70%)
4	 **10**	 **57** (79%)
5	 **11**	 **58** (67%)
6	 **12**	 **59** (70%)
7	 **13**	 **60** (63%)
8	 **15a**	 **61** (90%)
9	 **15b**	 **62** (46%)

Table 1 (*continued*)

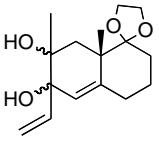
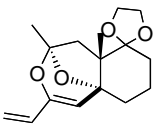
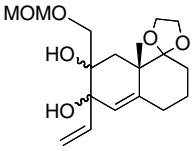
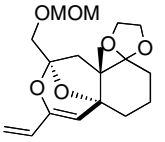
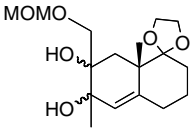
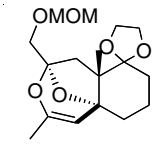
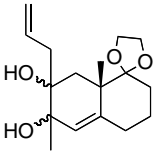
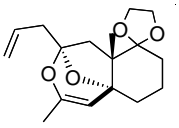
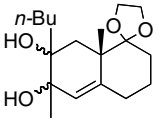
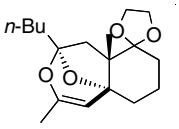
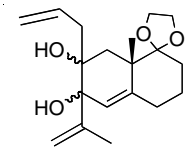
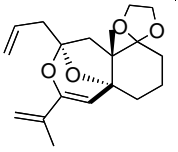
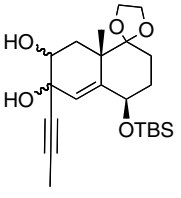
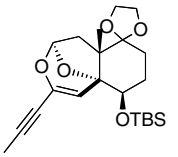
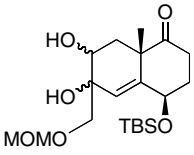
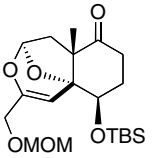
Entry	Starting unsaturated diol	Domino product (% yield)
10	 **17**	 **63** (70%)
11	 **18**	 **64** (96%)
12	 **20**	 **65** (72%)
13	 **21**	 **66** (70%)
14	 **22**	 **67** (78%)
15	 **24**	 **68** (83%)
16	 **28**	 **69** (80%)
17	 **29b**	 **70** (88%)

Table 1 (*continued*)

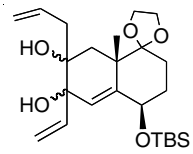
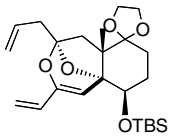
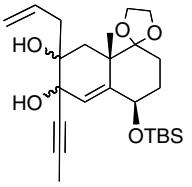
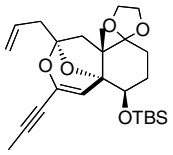
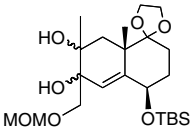
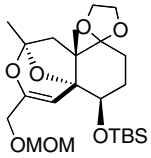
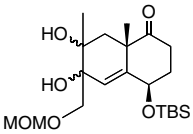
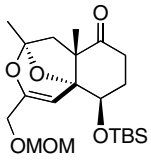
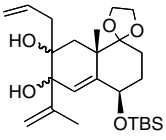
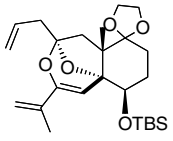
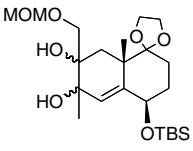
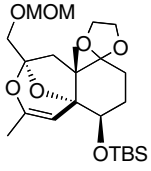
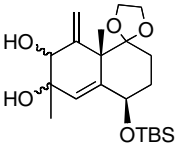
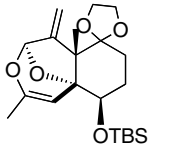
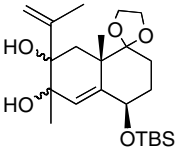
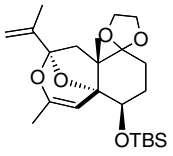
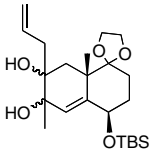
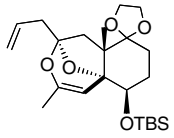
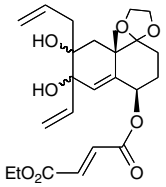
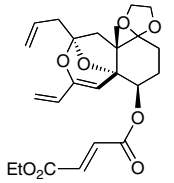
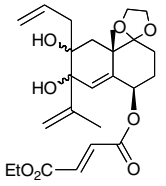
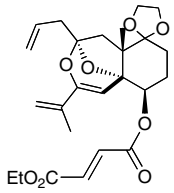
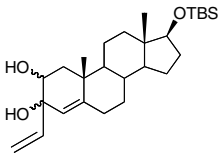
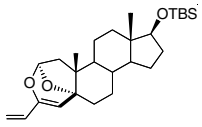
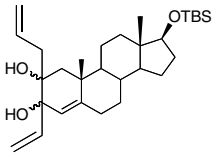
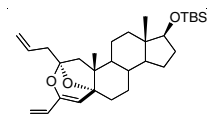
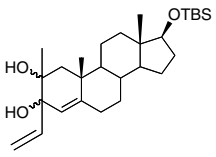
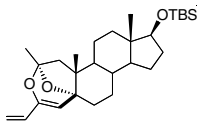
Entry	Starting unsaturated diol	Domino product (% yield)
18	 **33**	 **71** (88%)
19	 **35**	 **72** (86%)
20	 **37**	 **73** (82%)
21	 **5**	 **74** (78%)
22	 **39**	 **75** (83%)
23	 **41**	 **76** (76%)
24	 **43**	 **77** (99%)
25	 **44**	 **78** (99%)

Table 1 (*continued*)

Entry	Starting unsaturated diol	Domino product (% yield)
26	 **45**	 **79** (96%)
27	 **47**	 **80** (83%)
28	 **49**	 **81** (84%)
29	 **51**	 **82** (87%)
30	 **52**	 **83** (82%)
31	 **53**	 **84** (92%)

28) seem consistent with the accepted reactivity pattern based on electron demand.

(*S*)-(+)-Wieland–Miescher ketone **4**, which bears the appropriate absolute configuration at the quaternary centre C5 as required for the target molecule offers enantiomeric purity along with 11 out of the 14 carbons of the C14 sequiterpene skeleton. Application of the domino procedure to bicyclic unsaturated diol **5**, which was readily prepared from **4**, afforded **85**, which we deemed suitable for use in a synthesis of norsesquiterpene spirolactones **1** and **2**, since **5** lends itself well to conversion to cyclic eneacetal **85** (in two steps). This finding provided the opportunity to effect the overall conversion of Wieland–Miescher

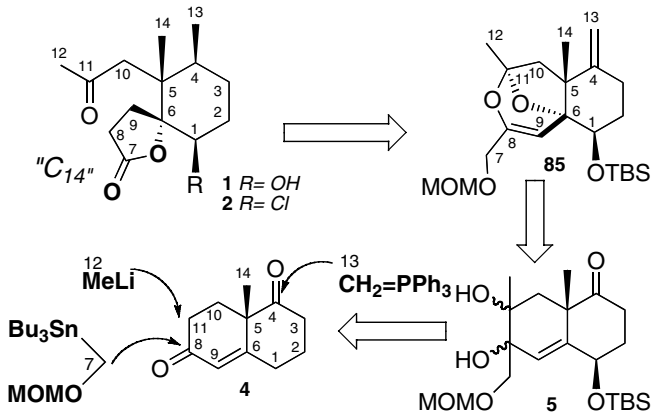


Figure 3. The 14-carbon source and the C–C bonding operations for pathylactone A and napalilactone.

ketone **4** to optically pure bicyclic ene-acetal **85**,[20] with the correct relative and absolute configurations at the quaternary centres C5 and C6. Figure 3 shows in concept the proposed route.

Starting from acetoxy-enone **6**, the missing three carbons were added as follows. Tin-MOM acetal derived nucleophile furnished C7 (**7**, Scheme 1), which following oxidation with IBX allowed for the introduction of C12 via nucleophilic addition using methyllithium (**15a**, Scheme 2). Ketal deprotection furnished the target bis-tertiary diol **5**, which upon subjection to the domino conditions gave **74** (Table 1, entry 21, 78%) while a subsequent Wittig olefination (*t*-BuOK, $MeP^{+}Ph_3,Br^{-}$, THF, 72%) completed the full carbon backbone affording the desired molecule, **85**. This sequence of reactions allowed for a totally stereoselective entry into the norsesquiterpene carbon skeleton, assembled straightforwardly from **4** and which furthermore allows the oxygen functionality to be placed in the appropriate positions. While the final conversion of subunit **85** to pathylactone A must await future efforts, the successful 11-step synthesis of this subunit illustrates the viability of our domino based approach for the synthesis of norsesquiterpene analogues.

In summary, the bis-hetero-intramolecular-Diels–Alder stage of the domino, with ketone components, carried out on diastereomeric mixtures of starting diols, works in high yields offering stereo-cleaning and scope for further selective transformations on the highly functionalized, rigid tricyclic framework (stereo-biasing).

3. Conclusion

The methodology described above has established the feasibility of intramolecular bis-hetero Diels–Alder with both ketone heterodiene/heterodienophile components. Variously substituted unsaturated diols were examined in 20 representative cases in order to document more fully the function compatibility of this domino process. The examples described illustrate the practicality of this approach and also indicate the wide range of substitution that is compatible with the domino process. This is especially noteworthy in cases where the molecule contains either an olefin or an oxygen functionality. The strategic setting of the unsaturated 1,2-diol system in bicyclic precursors allows controlled placement of remote functional groups in the ensuing domino products. This protocol satisfies the Tietze's criteria in that it can be induced by non-toxic reagents, it produces high yields with no byproducts and enantiomeric purity can be introduced at a very early stage. In addition, the reaction proceeds through an intermediate with reactive functionalities available for subsequent modification. Simultaneous or consecutive addition of extra catalysts or reactants, which could in principle create new reaction pathways ending in still higher molecular complexity are currently under investigation and results will be forthcoming. Further transformations allowing access to nor-sesquiterpene spirolactones and their steroidal hybrids will also be reported in due course.

4. Experimental

4.1. General

General experimental details were as previously described.[21] NMR spectra were run in $CDCl_3$ and specific rotations were measured in chloroform, unless otherwise noted. Experimental evidence favouring the structures investigated came from a comprehensive range of ^{1}H and ^{13}C NMR data (1 and 2D experiments) and corroborated by spatial proximity studies using mainly the 1D NOEDIFF technique.[22] For all compounds investigated, multiplicities of ^{13}C resonances were assigned by the SEFT technique.[23] Electron spray mass spectra were obtained in instances where electron impact and chemical ionization failed to produce molecular ions. 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). HR will be added for the high resolution mass measurements (HRESIMS). 'Usual workup' means washing of the organic layer with brine, drying over anhydrous magnesium sulfate and evaporating in vacuo with a rotary evaporator at aspirator pressure. Commercial $Pb(OAc)_4$ was used without purification. The acetic acid content of the latter (introduced in excess of 0.2 equiv.) was mostly removed under vacuum in the reaction vessel. Optical rotations were measured in $CHCl_3$.

4.2. General procedures

4.2.1. General procedure for the nucleophilic addition to enones/hydroxy-ketones using Grignard and organolithium reagents

4.2.1.1. Procedure A. To a solution of enone/hydroxy-ketone (1.0 mmol) in THF was added organolithium or organomagnesium bromide (2.5 mmol), at −78 °C, and the mixture was stirred for 3.5 h under argon. The reaction mixture was poured into satd aq NH_4Cl at 0 °C. This is then extracted with EtOAc, washed with satd aq $NaHCO_3$, worked up as usual and chromatographed on silica gel to give the expected compound.

4.2.1.2. Procedure B. To a magnetically stirred solution of Tin-MOM acetal (2.4 mmol) in dry THF cooled at −78 °C under argon, *n*-BuLi (2.3 mmol) was added and the mixture was stirred at this temperature for 10 min before enone/hydroxy-ketone (1.0 mmol) was added. After stirring for 1 h at −78 °C, the reaction mixture was diluted with Et_2O and quenched with satd aq NH_4Cl. Following usual workup, the expected compound was isolated using SiO_2 column chromatography.

4.2.1.3. Procedure C. To a solution of prop-1-yne (32.0 mmol) in dry THF, at −78 °C, under argon, *n*-BuLi in hexane (9.0 mmol) was added dropwise. The mixture was allowed to warm to −15 °C and stirring was continued at this temperature. After 2 h, HMPA (0.6 mL) was added at −20 °C and the resulting mixture was stirred for 10 min. A solution of enone/hydroxy-ketone (1.0 mmol) in dry THF and HMPA (0.6 mL) was then added at −30 °C and the mixture was left to stir overnight at room temperature. Satd aq NH_4Cl solution and Et_2O were then added and the organic phase was separated. The combined organic phases were washed with water, satd aq $NaHCO_3$ solution, worked up as usual and chromatographed on SiO_2 column chromatography.

4.2.2. General procedure for the preparation of α-ketols. To a solution of IBX (3.0 mmol) in DMSO, at 80 °C, was added tertiary–secondary diol (1.0 mmol) in DMSO and the reaction mixture was stirred at this temperature for 30 min. H_2O was added, the solid obtained was filtered and washed with Et_2O. After removing the solvent under reduced pressure, purification of the crude by SiO_2 chromatography (DCM/acetone, 96:4) gave the expected compound.

4.2.3. General procedure for the lead tetraacetate mediated oxidative cleavage (modulation by stoichiometry). Placed in a flame dried flask, solid unsaturated diols (1.0 mmol) and $Pb(OAc)_4$ (1.2 mmol) were vacuumed and flashed with argon and cooled to 0 °C. Toluene (5 mL) was added, the ice bath removed soon after, and the mixture was stirred at room temperature while monitoring TLC. After TLC analysis indicated consumption of the starting diol and conversion of the intermediate dialdehyde into the cyclic ene-acetal, the reaction mixture was diluted with Et_2O and filtered through Celite. The filtrate was concentrated and purified by SiO_2 chromatography. No side products were produced.

4.2.4. General procedure for $PhI(OAc)_2$ oxidation (modulation by stoichiometry). A dry flask was charged with 1.0 mmol of unsaturated diol and 1.2 mmol of $PhI(OAc)_2$, put under vacuum, flushed with argon and cooled to 0 °C. Acetonitrile (10 mL) was then added and the cooling bath removed soon after. The mixture was stirred at room temperature for 24 h (TLC-monitoring), diluted with dichloromethane, washed with a saturated aqueous solution of $NaHCO_3$ and worked up as usual. The residue was purified by SiO_2 chromatography. No side products were produced.

4.2.5. General procedure for fluoride deprotection. To a magnetically stirred solution of TBS-protected alcohol (1.0 mmol) was added tetrabutylammonium fluoride (2.0 mmol). The reaction was stirred at 60 °C for 23 h. After dilution with EtOAc, workup as usual and chromatography on SiO_2 gave the expected compound.

4.3. Preparation of unsaturated diols 7–13 and their oxidative cleavage

4.3.1. Preparation of 6,7-dihydroxy-6-methoxymethoxymethyl-8a-methyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 7. Nucleophilic addition was carried out on **6** (500 mg, 1.78 mmol) with Tin-MOM acetal (1.56 g, 4.27 mmol) and *n*-BuLi (1.6 M in hexane, 2.6 mL, 4.16 mmol), in dry THF (20 mL) for 1 h using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 1:1) (±)-**7** (429 mg, 76%). An analytical sample was purified on SiO_2 flash chromatography, eluent heptane/EtOAc, 1:1, for characterization purposes.

Compound (±)-**7a**, white solid. Mp: 131–133 °C. IR (film): $\nu = 3437, 2938, 2882, 1439, 1214, 1181, 1145, 1113, 1043, 1020, 950, 873, 772\ cm^{-1}$. ^1H NMR (300 MHz): $\delta = 1.28$ (s, 3H), 1.36 (dd, $J = 9.6$, 14.6 Hz, 1H), 1.71 (m, 4H), 2.04 (m, 1H), 2.29 (m, 1H), 2.29 (dd, $J = 4.6$, 14.6 Hz, 1H), 2.73 (d, $J = 6.0$ Hz, 1H), 2.90 (s, 1H), 3.40 (s, 3H), 3.60 and 3.81 (ABquartet, $J = 10.3$ Hz, 2H), 3.97 (m, 4H), 4.11 (dt, $J = 5.1$, 9.9 Hz, 1H), 4.66 and 4.68 (ABquartet, $J = 6.5$ Hz, 2H), 5.35 (d, $J = 1.6$ Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 23.4$, 25.7, 29.7, 30.7, 35.0, 45.1, 55.6, 64.7, 65.1, 72.2, 72.6, 73.4, 97.2, 113.3, 123.6, 145.3. ESIMS (MeOH): 337.1 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{16}H_{26}O_6Na$ m/z 337.1627, found: 337.1625. Anal. Calcd for $C_{16}H_{26}O_6 \cdot 0.4H_2O$ (314.37): C 59.76, H 8.40. Found: C 59.89, H 8.21.

Compound (±)-**7b**, white solid. Mp: 61–63 °C. IR (film): $\nu = 3440, 2936, 2883, 1440, 1181, 1110, 1034, 951, 929, 872, 754\ cm^{-1}$. ^1H NMR (300 MHz): $\delta = 1.24$ (s, 3H), 1.46 (dd, $J = 10.2$, 14.0, 1H), 1.65 (m, 2H), 1.79 (dd, $J = 4.4$ 13.5, 1H), 2.01 (m, 1H), 2.05 (dd, $J = 4.4$, 14.3, 1H), 2.29 (tdd, $J = 1.9$, 4.9, 13.6, 1H), 2.74 (br s, 1H), 3.02 (br s, 1H), 3.37 (s, 3H), 3.54 and 3.68 (ABquartet, $J = 10.2$, 2H), 3.96 (m, 5H), 4.64 and 4.66 (ABquartet, $J = 6.5$, 2H), 5.32 (d, $J = 1.0$, 1H). ^{13}C NMR (75 MHz): $\delta = 23.5$, 25.5, 30.1, 30.7, 33.7, 44.8, 55.5, 64.6, 65.1, 69.7, 70.0, 74.9, 97.1, 113.4, 121.0, 147.2. ESIMS (MeOH): 337.1 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{16}H_{26}O_6Na$ m/z 337.1627, found: 337.1619. Anal. Calcd for $C_{16}H_{26}O_6$ (314.37): C 61.13, H 8.34. Found: C 61.06, H 8.31.

Oxidative cleavage of **7** (diastereomeric mixture) was achieved using the general procedures affording **54** (15 mg, 70%, Table 1, entry 1) after SiO_2 flash column chromatography (heptane/EtOAc, 2:1 as eluent).

4.3.1.1. 8-Methoxymethoxymethyl-6-methyl-9,12-dioxatricyclo[6.3.1.$0^{0,0}$]dodec-10-en-5-one 54. Colourless oil. IR (film): $\nu = 2940, 2884, 1666, 1461, 1440, 1371, 1260, 1210, 1147, 1109, 1070, 1043, 996, 951, 917, 895, 775\ cm^{-1}$. ^1H NMR (300 MHz): $\delta = 1.27$ (s, 3H), 1.43 (m, 2H), 1.55 (m, 1H), 1.65 (m, 1H), 1.78 (m, 1H), 1.74 (dd, $J = 1.0$, 13.9 Hz, 1H), 1.99 (m, 1H), 2.50 (dd,

$J = 5.8$, 13.8 Hz, 1H), 3.37 (s, 3H), 3.94 (m, 6H), 4.64 and 4.66 (ABquartet, $J = 1.1$ Hz, 2H), 4.88 (s, 1H), 5.66 (d, $J = 5.4$ Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 17.2$, 18.4, 28.6, 28.7, 43.4, 55.4, 57.2, 63.2, 65.3, 66.2, 83.9, 95.6, 100.0, 108.1, 111.1, 146.7.

ESIMS (MeOH): 281.1 (6), 313.1 (4), 335.1 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{16}H_{24}O_6Na$ m/z 335.1471, found: 335.1469. Anal. Calcd for $C_{16}H_{24}O_6{\cdot}0.8H_2O$ (312.36): C 58.81, H 7.90. Found: C 58.78, H 7.64.

4.3.2. Preparation of 6,7-dihydroxy-8a-methyl-6-vinyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 8. Nucleophilic addition was carried out on **6** (1.02 g, 4.28 mmol) with vinylmagnesium bromide (1.0 M in THF, 10.7 mL, 10.7 mmol) in dry THF (40 mL) for 3.5 h using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 1:1) **8** (1.14 g, 99%). An analytical sample was purified on SiO_2 flash chromatography, eluent heptane/EtOAc, 1:1, for characterization purposes.

Compound **8a**: White solid. Mp: 107–109 °C. $[\alpha]_D^{20} = -22$ (c 0.56, $CHCl_3$). IR (film): $\nu = 3404$, 2934, 2887, 1749, 1696, 1462, 1439, 1376, 1344, 1220, 1186, 1155, 1112, 1075, 1036, 1012, 945, 919, 836, 776 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 1.24$ (s, 3H), 1.50 (m, 1H), 1.59 (dd, $J = 3.9$, 15.6 Hz, 1H), 1.77 (m, 3H), 2.12 (m, 1H), 2.17 (dd, $J = 5.2$, 15.4 Hz, 1H), 2.34 (tdd, $J = 2.0$, 4.6, 13.6H, 1H), 3.40 (br s, 1H), 3.51 (dddd, $J = 1.2$, 3.7, 5.0, 8.9 Hz, 1H), 4.02 (m, 4H), 4.35 (br s, 1H), 5.18 (dd, $J = 1.7$, 10.5 Hz, 1H), 5.29 (dd, $J = 1.7$, 17.3 Hz, 1H), 5.29 (t, $J = 1.4$ Hz, 1H), 5.83 (dd, $J = 10.5$, 17.3 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 23.0$, 25.5, 29.7, 30.5, 32.9, 43.2, 64.5, 64.7, 69.9, 73.1, 112.2, 115.8, 125.3, 141.1, 142.7.

ESIMS (MeOH): 289.1 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{15}H_{22}O_4Na$ m/z 289.1416, found: 289.1413.

Compound **8b**: Colourless oil. $[\alpha]_D^{20} = +108$ (c 1.0, $CHCl_3$). IR (film): $\nu = 3389$, 2938, 2882, 1664, 1634, 1456, 1438, 1373, 1342, 1182, 1136, 1060, 1013, 943, 914, 870, 729 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 1.32$ (s, 3H), 1.58 (dd, $J = 4.0$, 13.1 Hz, 1H), 1.60 (m, 3H), 1.77 (dd, $J = 4.4$, 13.2 Hz, 1H), 1.99 (d, $J = 12.3$ Hz, 1H), 2.06 (m, 2H), 2.24 (m, 2H), 3.82 (m, 1H), 3.95 (m, 4H), 5.17 (d, $J = 1.7$ Hz, 1H), 5.30 (dd, $J = 1.5$, 10.7 Hz, 1H), 5.41 (dd, $J = 1.5$, 17.4 Hz, 1H), 6.04 (dd, $J = 10.7$, 17.4 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 22.9$, 23.4, 29.8, 30.3, 33.9, 46.1, 65.0, 65.1, 73.1, 76.2, 112.4, 116.4, 124.8, 139.1, 143.6. ESIMS (MeOH): 289.1 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{15}H_{22}O_4Na$ m/z 289.1416, found: 289.1423. Anal. Calcd for $C_{15}H_{22}O_4{\cdot}0.2H_2O$ (266.33): C 66.74, H 8.36. Found: C 66.71, H 8.36.

Compound (**8c**): Colourless oil. $[\alpha]_D^{20} = -68$ (c 1.1, $CHCl_3$). IR (film): $\nu = 3400$, 2938, 2884, 1665, 1634, 1438, 1341, 1214, 1180, 1127, 1054, 1020, 989, 926, 872, 860, 748 666 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 1.22$ (s, 3H), 1.23 (m, 1H), 1.48 (m, 1H), 1.66 (m, 2H), 1.74 (dd, $J = 4.5$, 14.6 Hz, 1H), 1.84 (br s, 1H), 2.07 (m, 1H), 2.18 (dd, $J = 4.8$, 14.3 Hz, 1H), 2.22 (s, 1H), 2.31 (tdd, $J = 1.8$, 4.7, 13.5 Hz, 1H), 3.98 (m, 5H), 5.23 (dd, $J = 1.6$, 3.8 Hz, 1H), 5.30 (d, $J = 1.4$ Hz, 1H), 5.34 (dd, $J = 1.6$, 10.6 Hz, 1H), 5.96 (dd, $J = 10.6$, 17.3 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 23.6$, 25.6, 30.0, 30.5, 35.2, 45.4, 64.6, 65.1, 73.9, 75.8, 113.3, 116.7, 125.0, 138.6, 143.9. ESIMS (MeOH): 289.1 ([M+Na]$^+$, 68), 555.2 ([2M+Na]$^+$, 100). HRESIMS: calcd for $C_{15}H_{22}O_4Na$ m/z 289.1416, found: 289.1405.

Oxidative cleavage of **8** (diastereomeric mixture) was achieved using the general procedures affording **55** (99 mg, 99%, Table 1, entry 2) after SiO_2 flash column chromatography (heptane/EtOAc, 1:1 as eluent).

4.3.2.1. 6-Methyl-10-vinyl-9,12-dioxa-tricyclo[6.3.1.0^{0,0}]-dodec-10-en-5-one 55. Mp: 79–80 °C, $[\alpha]_D = -15$ (c 1.01, $CHCl_3$), IR (film): 2946, 2933, 2874, 1593, 1461, 1433, 1371, 1289, 1262, 1135, 1106, 1067, 1049, 1034, 950, 916, 903, 889, 737 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): 1.26 (3H, s, 1Me), 1.37–1.52 (3H, m), 1.57–1.68 (1H, m), 1.71 (1H, dd, $J = 13.8$, 0.9), 1.82 (1H, dt, $J = 13.4$, 3.6), 1.97–2.06 (1H, m), 2.52 (1H, dd, $J = 13.8$, 5.8), 3.85–4.05 (4H, m), 4.83 (1H, s), 5.08 (1H, ddd, $J = 10.8$, 1.7, 0.7), 5.50 (1H, ddd, $J = 17.2$, 1.7, 0.6), 5.72 (1H, dd, $J = 5.9$, 1.0), 6.01 (1H, dd, $J = 17.3$, 10.9). ^{13}C NMR (75 MHz, $CDCl_3$): 17.3, 18.4, 28.6, 28.8, 43.3, 57.3, 63.2, 65.4, 84.1, 99.8, 110.1, 111.2, 114.0, 131.2, 146.8. ESIMS (MeOH): 287.1 ([M+Na]$^+$, 100). HRESIMS (MeOH) calcd for $C_{15}H_{20}O_4Na$: 287.1259, found: 287.1247. Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 67.93; H, 7.62.

4.3.3. Preparation of 6,7-dihydroxy-8a-methyl-6-prop-1-ynyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 9. Nucleophilic addition was carried out on **6** (1.9 g, 6.73 mmol) with prop-1-yne (12.8 mL, 227.69 mmol), *n*-BuLi (1.6 M in hexane, 40.0 mL, 62.34 mmol) and HMPA (5.9 mL) in dry THF (70 mL) using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 2:1) **9** (1.19 g, 63%).

Compound **9**: orange oil. $[\alpha]_D^{20} = -66$ (c 1.06, $CHCl_3$). IR (film): $\nu = 3410$, 2936, 2878, 2243, 1438, 1374, 1341, 1179, 1133, 1107, 1089, 1058, 910, 732 cm^{-1}. ^{1}H NMR (500 MHz): $\delta = 1.22$ (s, 3H), 1.37 (dd, $J = 11.1$, 14.0 Hz, 1H), 1.46 (m, 1H), 1.62 (m, 1H), 1.68 (m, 1H), 1.74 (dd, $J = 4.4$, 13.5 Hz, 1H), 1.87 (s, 3H), 2.01 (ddt, $J = 1.9$, 4.3, 13.5 Hz, 1H), 2.20 (dd, $J = 14.0$, 14.4 Hz, 1H), 2.27 (tdd, $J = 1.9$, 4.9, 13.6 Hz, 1H), 2.69 (br s, 1H), 3.92 (m, 6H), 5.45 (d, $J = 1.7$ Hz, 1H). ^{13}C NMR (125 MHz): $\delta = 3.8$, 23.4, 25.3, 30.0, 30.3, 35.9, 45.6, 64.6, 65.1, 71.3, 73.6, 78.6, 83.0, 113.1, 124.3, 143.5. ESIMS (MeOH): 301.1 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{16}H_{22}O_4Na$ m/z 301.1416, found: 301.1380.

Oxidative cleavage of **9** (diastereomeric mixture) was achieved using the general procedures affording **56** (18 mg, 70%, Table 1, entry 3) after SiO_2 flash column chromatography (heptane/EtOAc, 4:1 as eluent).

4.3.3.1. 6-Methyl-10-prop-1-ynyl-9,12-dioxa-tricyclo-[6.3.1.0^{0,0}]dodec-10-en-5-one 56. Yellow oil. $[\alpha]_D^{20} = -44$ (c 0.94, $CHCl_3$). IR (film): $\nu = 2950$, 2881, 2238, 1624, 1440, 1359, 1289, 1120, 1109, 1070, 1047, 998, 964, 949, 917, 884 cm^{-1}. ^{1}H NMR (500 MHz): $\delta = 1.27$

(s, 3H), 1.38 (m, 1H), 1.44 (dt, $J = 4.2$, 8.1 Hz, 1H), 1.56 (m, 1H), 1.64 (dtd, $J = 1.5$, 3.3, 13.3 Hz, 1H), 1.79 (m, 1H), 1.78 (dd, $J = 1.3$, 13.9 Hz, 1H), 1.94 (s, 3H), 1.99 (m, 1H), 2.50 (dd, $J = 5.8$, 13.9 Hz, 1H), 3.86 (m, 2H), 3.99 (m, 2H), 5.10 (s, 1H), 5.62 (d, $J = 5.8$ Hz, 1H). ^{13}C NMR (125 MHz): $\delta = 4.0$, 17.1, 18.4, 28.4, 28.8, 43.3, 57.4, 63.2, 65.4, 74.3, 84.2, 85.4, 100.3, 111.0, 114.7, 133.4. ESIMS (MeOH): 299.1 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{16}H_{20}O_4Na$ m/z 299.1259, found 299.1241.

4.3.4. Preparation of 6,7-dihydroxy-6-isopropenyl-8a-methyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 11. Nucleophilic addition was carried out on **6** (500 mg, 2.10 mmol) with isopropenylmagnesium bromide (0.5 M in THF, 12.6 mL, 6.29 mmol) in dry THF (5 mL) for 2 h using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 4:1) **11** (528 mg, 90%).

Compound **11**: White solid. Mp: 124–126 °C. $[\alpha]_D^{20} = +49$ (c 1.16, $CHCl_3$). IR (film): $\nu = 3435$, 2938, 2885, 1679, 1636, 1462, 1453, 1441, 1373, 1343, 1334, 1217, 1185, 1131, 1112, 1060, 1039, 1017, 949, 912, 870 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 1.34$ (s, 3H), 1.58 (dd, $J = 5.8$, 14.9 Hz, 1H), 1.62 (s, 1H), 1.69 (m, 3H), 1.80 (dd, $J = 4.5$, 13.6 Hz, 1H), 1.88 (s, 3H), 2.06 (m, 1H), 2.22 (dd, $J = 3.7$, 14.9 Hz, 1H), 2.29 (br s, 1H), 2.36 (tdd, $J = 1.6$, 5.1, 13.6 Hz, 1H), 3.98 (m, 5H), 4.93 (dd, $J = 0.8$, 1.6 Hz, 1H), 5.11 (t, $J = 1.4$ Hz, 1H), 5.51 (s, 1H). ^{13}C NMR (75 MHz): $\delta = 18.9$, 23.3, 24.4, 29.3, 30.9, 31.6, 43.7, 64.6, 65.0, 70.9, 75.0, 113.6, 114.1, 124.5, 145.2, 147.1. ESIMS (MeOH): 303.1 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{16}H_{24}O_4Na$ m/z 303.1572, found: 303.1573.

Oxidative cleavage of **11** (diastereomeric mixture) was achieved using the general procedures affording **58** (20 mg, 67%, Table 1, entry 5) after SiO_2 flash column chromatography (heptane/Et_2O, 7:3 as eluent).

4.3.4.1. 10-Isopropenyl-6-methyl-9,12-dioxa-tricyclo-[6.3.1.0^{0,0}]dodec-10-en-5-one 58. Colourless oil. $[\alpha]_D^{20} = -16$ (c 0.50, $CHCl_3$). IR (film): $\nu = 2938$, 2876, 1603, 1462, 1441, 1434, 1375, 1363, 1334, 1297, 1278, 1261, 1233, 1202, 1136, 1107, 1062, 1046, 1031, 996, 959, 917, 895, 880 cm^{-1}. ^{1}H NMR (500 MHz): $\delta = 1.27$ (s, 3H), 1.46 (m, 2H), 1.60 (m, 1H), 1.68 (m, 1H), 1.69 (dd, $J = 0.8$, 13.8 Hz, 1H), 1.83 (m, 1H), 1.83 (s, 3H), 2.03 (m, 1H), 2.50 (dd, $J = 5.9$, 13.8 Hz, 1H), 3.88 (m, 2H), 4.02 (m, 2H), 4.92 (s, 1H), 4.95 (ddd, $J = 0.8$, 1.5, 2.1 Hz, 1H), 5.37 (d, $J = 1.5$ Hz, 1H), 5.71 (d, $J = 5.5$ Hz, 1H). ^{13}C NMR (125 MHz): $\delta = 17.5$, 18.5, 18.7, 28.9 (2C), 43.3, 57.3, 63.2, 65.4, 84.0, 99.7, 106.7, 111.3, 112.8, 136.6, 148.0. ESIMS (MeOH + DCM): 597.3 (10), 301.2 ([M+Na]$^+$, 70), 279.2 ([M+H]$^+$, 100), 261.2 (11), 193.1 (13), 149.1 (100). HRESIMS (MeOH + DCM) calcd for $C_{16}H_{22}O_4Na$ m/z 301.1416, found: 301.1407. Anal. Calcd for $C_{16}H_{22}O_4 \cdot 0.3H_2O$ (278.34): C 67.73, H 8.03. Found: C 67.73, H, 7.95.

4.3.5. Preparation of 6-butyl-6,7-dihydroxy-8a-methyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 12. Nucleophilic addition was carried out on **6** (900 mg, 3.78 mmol) with n-BuLi (1.6 M in hexane, 5.7 mL, 9.08 mmol) in dry THF (10 mL) for 1 h using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 1:1) **12** (849 mg, 76%).

Compound **12**: Characterized as a diastereomeric mixture, colourless oil. IR (film): $\nu = 3435$, 2953, 2872, 1680, 1465, 1440, 1376, 1343, 1279, 1217, 1185, 1114, 1090, 1070, 1018, 946, 868 cm^{-1}. ESIMS (MeOH): 320.2 (30), 319.1 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{17}H_{28}O_4Na$ m/z 319.1885, found 319.1877.

Oxidative cleavage of **12** (diastereomeric mixture) was achieved using the general procedures affording **59** (21 mg, 70%, Table 1, entry 6) after SiO_2 flash column chromatography (heptane: Et_2O, 1:1 as eluent).

4.3.5.1. 10-Butyl-6-methyl-9,12-dioxa-tricyclo[6.3.1.0^{0,0}]-dodec-10-en-5-one 59. Colourless oil. $[\alpha]_D^{20} = -29$ (c 1.20, $CHCl_3$). IR (film): $\nu = 2953$, 2933, 2873, 1660, 1460, 1440, 1370, 1259, 1140, 1109, 1070, 1045, 995, 956, 917 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 0.90$ (t, $J = 7.2$ Hz, 3H), 1.26 (s, 3H), 1.23 (m, 1H), 1.34 (m, 2H), 1.43 (m, 3H), 1.62 (m, 2H), 1.67 (dd, $J = 0.9$, 13.6 Hz, 1H), 1.78 (tt, $J = 3.6$, 13.5 Hz, 1H), 1.98 (m, 3H), 2.47 (dd, $J = 5.9$, 13.6 Hz, 1H), 3.87 (m 2H), 4.00 (m 2H), 4.55 (s, 1H), 5.60 (d, $J = 5.5$ Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 13.9$, 17.4, 18.4, 22.3, 28.7, 28.8 (2C), 32.7, 43.5, 57.3, 63.2, 65.4, 83.8, 99.6, 104.5, 111.3, 150.7. ESIMS (MeOH): 317.1 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{17}H_{26}O_4Na$ m/z 317.1729, found: 317.1736. Anal. Calcd for $C_{17}H_{26}O_4$ (294.39): C 69.36, H 8.90. Found: C 69.02, H 8.81.

4.3.6. Preparation of 6-allyl-6,7-dihydroxy-8a-methyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 13. Nucleophilic addition was carried out on **6** (900 mg, 3.78 mmol) with allylmagnesium bromide (1.0 M in THF, 9.1 mL, 9.08 mmol) in dry THF (10 mL) for 1 h using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 1:1 to EtOAc) **13** (1.02 g, 97%).

Compound **13**: Colourless oil. $[\alpha]_D^{20} = +249$ (c 0.27, $CHCl_3$). IR (film): $\nu = 3429$, 2939, 2883, 1661, 1639, 1460, 1437, 1405, 1377, 1343, 1218, 1185, 1108, 1069, 1013, 949, 911, 862 cm^{-1}. ^{1}H NMR (500 MHz): $\delta = 1.25$ (s, 3H), 1.59 (m, 1H), 1.69 (m, 3H), 1.79 (tdd, $J = 1.4$, 4.6, 13.3 Hz, 1H), 2.04 (ddd, $J = 2.4$, 5.5, 14.0 Hz, 1H), 2.11 (ddd, $J = 1.3$, 7.3, 14.6 Hz, 1H), 2.30 (m, 3H), 2.80 (br s, 1H), 3.52 (br s, 1H), 3.58 (m, 1H), 4.00 (m, 4H), 5.08 (dt, $J = 1.6$, 5.8 Hz, 1H), 5.10 (t, $J = 1.5$ Hz, 1H), 5.39 (t, $J = 1.6$ Hz, 1H), 5.88 (dddd, $J = 1.4$, 7.2, 14.5, 16.2 Hz, 1H). ^{13}C NMR (125 MHz): $\delta = 22.9$, 24.7, 29.7, 30.6, 33.4, 43.0, 44.1, 64.8, 64.8, 69.0, 71.2, 112.4, 117.8, 126.6, 133.8, 143.4. ESIMS (MeOH): 303.1 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{16}H_{24}O_4Na$ m/z 303.1572, found: 303.1571. Anal. Calcd for $C_{16}H_{24}O_4 \cdot 0.2H_2O$ (280.36): C 67.68, H 8.66. Found: C67.52, H 8.51.

Oxidative cleavage of **13** (diastereomeric mixture) was achieved using the general procedures affording **60** (25 mg, 63%, Table 1, entry 7) after SiO_2 flash column chromatography (heptane: Et_2O, 1:1 as eluent).

4.3.6.1. 10-Allyl-6-methyl-9,12-dioxa-tricyclo[6.3.1.0^{0,0}]-dodec-10-en-5-one 60. Colourless oil. $[\alpha]_D^{20} = +37$ (c 0.20, $CHCl_3$). IR (film): $\nu = 3077$, 2952, 2880, 1661, 1639, 1460, 1440, 1369, 1336, 1301, 1261, 1166, 1140, 1110, 1070, 1046, 996, 958, 917, 892 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 1.26$ (s, 3H), 1.41 (m, 3H), 1.62 (m, 1H), 1.69 (dd, $J = 1.2$, 13.7 Hz, 1H), 1.81 (m, 1H), 1.97 (m, 1H), 2.48 (dd, $J = 5.8$, 13.7 Hz, 1H), 2.75 (ddd, $J = 1.3$, 2.6, 6.8 Hz, 2H), 3.87 (m, 2H), 3.98 (m, 2H), 4.59 (s, 1H), 5.08 (ddd, $J = 1.3$, 2.8, 10.0 Hz, 1H), 5.11 (ddd, $J = 1.6$, 3.2, 17.1 Hz, 1H), 5.62 (d, $J = 5.6$ Hz, 1H), 5.80 (ddt, $J = 6.8$, 10.1, 16.9 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 17.3$, 18.4, 28.8 (2C), 37.4, 43.4, 57.2, 63.1, 65.3, 83.9, 99.8, 105.3, 111.2, 117.2, 133.6, 148.9. ESIMS (MeOH): 301.1 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{16}H_{22}O_4Na$ m/z 301.1416, found: 301.1411.

4.4. Preparation of bis-tertiary unsaturated diols and their oxidative cleavage

The required α-ketols were obtained by applying the general procedure for the IBX mediated oxidation, while the C2 substitution was effected using the general procedures A, B or C.

4.4.1. Preparation of target molecules 15a, 15b and their oxidative cleavage. Oxidation of **7** (1.63 g, 5.18 mmol) was carried out with IBX (4.35 g, 15.54 mmol) in DMSO (100 mL) for 30 min using the general procedure to give after chromatography (SiO_2, heptane/Et_2O, 2:3) **14** (1.12 g, 70%). An analytical sample was purified on SiO_2 flash chromatography, eluent heptane/Et_2O, 2:3, for characterization purposes.

4.4.1.1. 6-Hydroxy-6-methoxymethoxymethyl-8a-methyl-2,3,4,6,8,8a-hexahydro-naphthalene-1,7-dione 14. Colourless oil. $[\alpha]_D^{20} = -37$ (c 1.37, $CHCl_3$). IR (film): $\nu = 3467$, 2941, 2890, 1724, 1465, 1441, 1379, 1342, 1305, 1213, 1180, 1150, 1114, 1084, 1034, 960, 949, 916 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 1.33$ (s, 3H), 1.53 (m, 2H), 1.76 (m, 2H), 2.13 (m, 1H), 2.33 (ddt, $J = 1.6$, 4.7, 13.5 Hz, 1H), 2.33 (d, $J = 14.9$ Hz, 1H), 2.79 (d, $J = 14.9$ Hz, 1H), 3.31 (s, 3H), 3.59 and 3.66 (ABquartet, $J = 10.4$ Hz, 2H), 3.91 (m, 5H), 4.58 and 4.61 (ABquartet, $J = 6.6$ Hz, 2H), 5.42 (d, $J = 1.9$ Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 24.0$, 24.6, 30.0, 30.4, 42.2, 51.5, 55.6, 64.7, 65.8, 74.1, 76.0, 96.8, 112.6, 122.9, 145.6, 208.0. ESIMS (MeOH): 335.1 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{16}H_{24}O_6Na$ m/z 335.1471, found: 335.1481. Anal. Calcd for $C_{16}H_{24}O_6{\cdot}0.2H_2O$ (321.36): C 60.91, H 7.78. Found: C 60.91, H 7.73.

Nucleophilic addition was carried out on **14** (1.12 g, 3.61 mmol) with MeLi (2.2 M in Et_2O, 6.6 mL, 14.4 mmol) in dry THF (60 mL) for 2.5 h using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 1:1) **15a** (822 mg, 70%).

4.4.1.2. 6,7-Dihydroxy-6-methoxymethoxymethyl-6,8a-dimethyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 15a. Characterized as a diastereomeric mixture, colourless oil. IR (film): $\nu = 3435$, 2936, 2886, 1465, 1441, 1369, 1215, 1169, 1148, 1114, 1062, 1035, 950, 925, 866 cm^{-1}. ESIMS (MeOH): 351.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{17}H_{28}O_6Na$ m/z 351.1784, found: 351.21778. Anal. Calcd for $C_{17}H_{28}O_6$ (328.40): C 62.17, H 8.59, found: C 60.62, H 8.37.

Oxidative cleavage of **15a** (diastereomeric mixture) was achieved using the general procedures affording **61** (40 mg, 90%, Table 1, entry 8) after SiO_2 flash column chromatography (heptane: Et_2O, 1:1 as eluent).

4.4.1.3. 10-Methoxymethoxymethyl-6,8-dimethyl-9,12-dioxa-tricyclo[6.3.1.0^{0,0}]dodec-10-en-5-one 61. Colourless oil. $[\alpha]_D^{20} = -20$ (c 0.45, $CHCl_3$). IR (film): $\nu = 2939$, 2883, 1667, 1460, 1440, 1387, 1345, 1319, 1302, 1264, 1239, 1211, 1194, 1149, 1122, 1050, 989, 948, 921, 896, 848, 823, 767 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 1.24$ (s, 3H), 1.51 (m, 4H), 1.60 (s, 3H), 1.88 (m, 2H), 1.88 (d, $J = 13.9$ Hz, 1H), 2.25 (d, $J = 13.7$ Hz, 1H), 3.37 (s, 3H), 3.95 (m, 6H), 4.64 and 4.67 (ABquartet, $J = 6.9$ Hz, 2H), 4.88 (s, 1H). ^{13}C NMR (75 MHz): $\delta = 17.6$, 18.4, 22.5, 28.8, 28.9, 47.7, 55.4, 58.0, 63.2, 65.2, 66.3, 85.2, 95.5, 107.0, 107.5, 111.9, 148.0. ESIMS (DCM + MeOH): 349.1 ([M+Na]$^+$, 100). HRESIMS (DCM+MeOH) calcd for $C_{17}H_{26}O_6Na$ m/z 349.1627, found: 349.1630. Anal. Calcd for $C_{17}H_{26}O_6{\cdot}0.2H_2O$ (326.38): C 61.73, H 8.03. Found: C 61.69, H 8.09.

Ketal deprotection of **15a** (HCl 4 N, THF, 5 °C) afforded the desired **15b** (63%) as a diastereomeric mixture, which was taken as such for the next operation.

Oxidative cleavage of **15b** (diastereomeric mixture) was achieved using the general procedures affording **62** (12 mg, 46%, Table 1, entry 9) after SiO_2 flash column chromatography (heptane: Et_2O, 1:1 as eluent).

4.4.1.4. 10-Methoxymethoxymethyl-6,8-dimethyl-9,12-dioxa-tricyclo[6.3.1.0^{0,0}]dodec-10-en-5-one 62. Colourless oil. $[\alpha]_D^{20} = -7$ (c 0.35, $CHCl_3$). IR (film): $\nu = 2938$, 1711, 1671, 1442, 1390, 1315, 1206, 1189, 1150, 1120, 1047, 1013, 954, 920, 853 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 1.25$ (s, 3H), 1.52 (s, 3H), 1.89 (m, 2H), 1.90 (d, $J = 13.9$ Hz, 1H), 2.06 (m, 2H), 2.33 (m, 1H), 2.49 (ddd, $J = 6.0$, 13.6, 14.2 Hz, 1H), 3.09 (d, $J = 13.9$ Hz, 1H), 3.37 (s, 3H), 3.92 (dd, $J = 0.9$, 2.8 Hz, 2H), 4.65 (s, 2H), 4.97 (s, 1H). ^{13}C NMR (75 MHz): $\delta = 18.3$, 20.5, 23.8, 28.7, 37.2, 46.8, 55.4, 64.9, 65.9, 86.4, 95.7, 104.1, 105.8, 149.0, 213.1. ESIMS (DCM+MeOH): 305.1 ([M+Na]$^+$, 100). HRESIMS (DCM+MeOH) calcd for $C_{15}H_{22}O_5Na$ m/z 305.1365, found: 305.1373. Anal. Calcd for $C_{15}H_{22}O_5$ (282.33): C 63.81, H 7.85, found C 63.41, H 8.01.

4.4.2. Preparation of target molecules 17 and 18 and their oxidative cleavage. Oxidation of **8** (85 mg, 0.32 mmol) was carried out with IBX (268 mg, 0.96 mmol) in DMSO (3 mL) for 30 min using the general procedure to give after chromatography (SiO_2, DCM/acetone, 96:4) **16** (68 mg, 81%). An analytical sample was purified on SiO_2 flash chromatography, eluent DCM/acetone, 96:4, for characterization purposes.

4.4.2.1. 6-Hydroxy-8a-methyl-6-vinyl-2,3,4,6,8,8a-hexahydro-naphthalene-1,7-dione 16a. White solid. Mp: 67–

68 °C. $[\alpha]_D^{20} = -164$ (*c* 1.07, $CHCl_3$). IR (film): $\nu = 3414$, 2933, 2888, 1721, 1393, 1300, 1181, 1149, 1109, 1080, 1065, 1047, 921, 861, 741 cm^{-1}. ^1H NMR (300 MHz): $\delta = 1.32$ (s, 3H), 1.52 (m, 2H), 1.77 (m, 2H), 2.17 (m, 1H), 2.31 (tdd, $J = 1.5$, 4.7, 13.2 Hz, 1H), 2.34 (d, $J = 14.8$ Hz, 1H), 2.65 (d, $J = 14.8$ Hz, 1H), 3.99 (m, 5H), 5.25 (dd, $J = 1.0$, 10.2 Hz, 1H), 5.40 (s, 1H), 5.43 (dd, $J = 1.1$, 17.0 Hz, 1H), 5.85 (dd, $J = 10.2$, 17.0 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 24.1$, 24.3, 30.0, 30.3, 40.7, 51.5, 65.6, 65.8, 77.6, 112.6, 116.8, 123.9, 140.7, 144.0, 208.1. ESIMS (MeOH): 287.1 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{15}H_{20}O_4Na$ *m/z* 287.1259, found: 287.1270. Anal. Calcd for $C_{15}H_{20}O_4 \cdot 0.1H_2O$ (264.32): C 67.70, H 7.65. Found: C 67.67, H 7.36.

Compound **16b**: White solid. Mp: 67–69 °C. $[\alpha]_D^{20} = +167$ (*c* 0.92, $CHCl_3$). IR (film): $\nu = 3481$, 2939, 2887, 1720, 1461, 1438, 1377, 1344, 1268, 1216, 1185, 1154, 1123, 1067, 1017, 939 cm^{-1}. ^1H NMR (300 MHz): $\delta = 1.20$ (d, $J = 0.8$ Hz, 3H), 1.67 (m, 5H), 2.16 (d, $J = 12.3$ Hz, 1H), 2.34 (m, 2H), 3.36 (dt, $J = 0.8$, 12.3 Hz, 1H), 3.94 (m, 4H), 5.26 (dd, $J = 0.9$, 10.3 Hz, 1H), 5.29 (dd, $J = 1.0$, 2.6 Hz, 1H), 5.56 (dd, $J = 0.9$, 17.1 Hz, 1H), 5.90 (dd, $J = 10.3$, 17.1 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 22.3$, 22.6, 29.1, 30.0, 40.4, 51.5, 64.8, 65.1, 78.2, 111.6, 117.1, 124.2, 139.7, 143.9, 210.2. ESIMS (MeOH): 287.1 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{15}H_{20}O_4Na$ *m/z* 287.1259, found: 287.1264.

Nucleophilic addition was carried out on **16** (15 mg, 0.06 mmol) with MeLi (1.6 M in Et_2O, 0.2 mL, 0.28 mmol) in dry THF (2 mL) for 3 h using the general procedure to give after chromatography (SiO_2, DCM/acetone, 95:5) **17** (9 mg, 56%).

4.4.2.2. 6,7-Dihydroxy-7,8a-dimethyl-6-vinyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 17. White solid. Mp: 109–111 °C. $[\alpha]_D^{20} = +180$ (*c* 0.56, $CHCl_3$). IR (film): $\nu =$ 3456, 2931, 2883, 1440, 1371, 1342, 1157, 1116, 1063, 1019, 951, 918, 878, 865, 840, 753, 724 cm^{-1}. ^1H NMR (600 MHz): $\delta = 1.17$ (s, 3H), 1.44 (s, 3H), 1.52 (d, $J = 14.6$ Hz, 1H), 1.56 (m, 1H), 1.62 (m, 1H), 1.70 (dtd, $J = 2.3$, 4.7, 12.2 Hz, 1H), 1.86 (td, $J = 13.7$, 4.6 Hz, 1H), 2.04 (ddd, $J = 1.9$, 3.9, 6.3 Hz, 1H), 2.07 (s, 1H), 2.08 (d, $J = 14.8$ Hz, 1H), 2.31 (tdd, $J = 1.7$, 5.3, 13.8 Hz, 1H), 2.50 (s, 1H), 3.94 (m, 4H), 5.11 (d, $J = 1.6$ Hz, 1H), 5.12 (dd, $J = 1.7$, 10.7 Hz, 1H), 5.42 (dd, $J = 1.7$, 17.3 Hz, 1H), 5.89 (dd, $J = 10.7$, 17.3 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 23.2$, 23.8, 24.8, 29.3, 30.6, 37.9, 44.4, 64.8, 65.0, 73.7, 77.2, 113.4, 114.4, 125.5, 140.4, 142.3. ESIMS (MeOH): 295.2 (9), 303.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{16}H_{24}O_4Na$ *m/z* 303.1572, found: 303.1590.

Oxidative cleavage of **17** (diastereomeric mixture) was achieved using the general procedures affording **63** (6 mg, 70%, Table 1, entry 10) after SiO_2 flash column chromatography (heptane/EtOAc, 6:1 as eluent).

4.4.2.3. 6,8-Dimethyl-10-vinyl-9,12-dioxa-tricyclo[6.3.1.$0^{0,0}$]-dodec-10-en-5-one 63. Colourless oil. $[\alpha]_D^{20} = +2$ (*c* 0.54, $CHCl_3$). IR (film): $\nu = 2938$, 2879, 1595, 1440, 1385, 1350, 1237, 1211, 1193, 1130, 1052, 1038, 979, 946, 920, 861, 780 cm^{-1}. ^1H NMR (500 MHz): $\delta = 1.22$ (s, 3H), 1.44 (m, 2H), 1.54 (m, 1H), 1.63 (s, 3H), 1.66 (td, $J = 1.6$, 3.4 Hz, 1H), 1.84 (d, $J = 13.7$ Hz, 1H), 1.91 (dt, $J = 3.6$, 13.4 Hz, 1H), 1.97 (dtd, $J = 1.8$, 4.0, 14.6 Hz, 1H), 2.26 (d, $J = 13.7$ Hz, 1H), 3.89 (m, 2H), 4.01 (m, 2H), 4.82 (s, 1H), 5.07 (dd, $J = 1.1$, 10.9 Hz, 1H), 5.51 (dd, $J = 1.2$, 17.2 Hz, 1H), 6.02 (dd, $J = 10.9$, 17.2 Hz, 1H). ^{13}C NMR (125 MHz): $\delta = 17.7$, 18.4, 22.7, 28.8, 29.0, 47.8, 58.0, 63.3, 65.2, 85.4, 106.7, 109.6, 111.9, 113.8, 131.4, 148.0. ESIMS (MeOH): 301.1 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{16}H_{22}O_4Na$ *m/z* 301.1416, found: 301.1427.

Starting from **16**, the target bis-tertiary diol **18** was synthesized analogously. Nucleophilic addition was carried out on **16** (50 mg, 0.19 mmol) with Tin-MOM acetal (248 mg, 0.68 mmol) and *n*-BuLi (1.6 M in hexane, 0.35 mL, 0.57 mmol), in dry THF (4 mL) for 1 h at −78 °C, and 2.5 h at 0 °C using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 1:1) **18** (39 mg, 61%) and **16** (13 mg, 27%).

4.4.2.4. 6,7-Dihydroxy-7-methoxymethoxymethyl-8a-methyl-6-vinyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 18. Colourless oil. $[\alpha]_D^{20} = -63$ (*c* 1.05, $CHCl_3$). IR (film): $\nu = 3368$, 2936, 2888, 1463, 1438, 1409, 1345, 1331, 1111, 1040, 992, 926, 880, 864 cm^{-1}. ^1H NMR (300 MHz): $\delta = 1.27$ (s, 3H), 1.46 (d, $J = 16.1$ Hz, 1H), 1.55 (m, 1H), 1.77 (m, 3H), 2.11 (ddt, $J = 2.0$, 4.3, 13.3 Hz, 1H), 2.34 (tdd, $J = 1.8$, 4.4, 13.2 Hz, 1H), 2.39 (d, $J = 16.2$ Hz, 1H), 3.36 (s, 3H), 3.48 (dd, $J = 0.7$, 10.3 Hz, 1H), 3.65 (d, $J = 10.3$ Hz, 1H), 3.72 (br s, 1H), 4.04 (m, 4H), 4.63 and 4.66 (ABquartet, $J = 6.4$ Hz, 2H), 5.11 (dd, $J = 1.8$, 10.6 Hz, 1H), 5.18 (d, $J = 1.8$ Hz, 1H), 5.30 (dd, $J = 1.8$, 17.2 Hz, 1H), 5.51 (br s, 1H), 5.75 (dd, $J = 10.6$, 17.1 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 23.1$, 27.0, 30.0, 30.4, 35.5, 43.1, 55.4, 64.7, 64.8, 71.5, 72.5, 75.8, 97.1, 112.7, 114.8, 127.7, 138.9, 140.2. ESIMS (MeOH): 363.1 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{18}H_{28}O_6Na$ *m/z* 363.1784, found: 363.1789.

Oxidative cleavage of **18** (diastereomeric mixture) was achieved using the general procedures affording **64** (18 mg, 96%, Table 1, entry 11) after SiO_2 flash column chromatography (heptane/EtOAc, 1:1 as eluent).

4.4.2.5. 8-Methoxymethoxymethyl-6-methyl-10-vinyl-9,12-dioxa-tricyclo[6.3.1.$0^{0,0}$]dodec-10-en-5-one 64. Colourless oil. $[\alpha]_D^{20} = -10$ (*c* 1.24, $CHCl_3$). IR (film): $\nu = 2939$, 2882, 1594, 1458, 1440, 1349, 1301, 1142, 1117, 1090, 1053, 941, 919 781 cm^{-1}. ^1H NMR (300 MHz): $\delta = 1.24$ (s, 3H), 1.47 (m, 3H), 1.65 (m, 1H), 1.79 (d, $J = 13.9$ Hz, 1H), 1.88 (dt, $J = 3.5$, 13.6 Hz, 1H), 2.01 (m, 1H), 2.35 (d, $J = 13.8$ Hz, 1H), 3.42 (s, 3H), 3.93 (m, 6H), 4.76 (s, 2H), 4.85 (s, 1H), 5.08 (dd, $J = 1.4$, 10.8 Hz, 1H), 5.52 (dd, $J = 1.5$, 17.2 Hz, 1H), 6.02 (dd, $J = 10.8$, 17.2 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 17.5$, 18.3, 28.7, 29.0, 44.8, 55.2, 57.3, 63.2, 65.1, 68.2, 85.6, 96.7, 106.7, 109.7, 111.7, 114.1, 131.1, 147.9. ESIMS (MeOH): 361.1 ($[M+Na]^+$, 100), 377.1 ($[M+K]^+$, 90). HRESIMS: calcd for $C_{18}H_{26}O_6Na$ *m/z* 361.1627, found: 361.1635.

4.4.3. Preparation of target molecules 20, 21, 22. Oxidation of **10** (500 mg, 1.97 mmol) was carried out with IBX (1.65 g, 5.91 mmol) in DMSO (50 mL) for 30 min using the general procedure to give after chromatography (SiO_2, heptane/Et_2O, 2:3) **19** (346 mg, 70%). An analytical sample was purified on SiO_2 flash chromatography, eluent heptane/Et_2O, 2:3, for characterization purposes.

4.4.3.1. 6-Hydroxy-6,8a-dimethyl-2,3,4,6,7,8a-hexahydro-naphthalene-1,7-dione 19. Colourless oil. $[\alpha]_D^{20} = -11$ (*c* 0.74, $CHCl_3$). IR (film): $\nu = 3479$, 2971, 2939, 2886, 1719, 1457, 1437, 1378, 1272, 1216, 1187, 1153, 1128, 1065, 1036, 1017, 950, 937, 863 cm^{-1}. ^1H NMR (300 MHz): $\delta = 1.18$ (d, $J = 0.8$ Hz, 3H), 1.46 (s, 3H), 1.59 (m, 4H), 2.18 (m, 2H), 2.20 (d, $J = 12.6$ Hz, 1H), 3.27 (dd, $J = 0.8$, 12.5 Hz, 1H), 3.57 (br s, 1H), 3.93 (m, 4H), 5.41 (d, $J = 1.7$ Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 22.0$, 22.4, 28.4, 28.8, 29.6, 40.7, 51.1, 64.6, 64.9, 73.7, 111.4, 126.3, 141.7, 212.9. ESIMS (MeOH): 277.1 (35), 275.1 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{14}H_{20}O_4Na$ *m*/*z* 275.1259, found: 275.1244. Anal. Calcd for $C_{14}H_{20}O_4 \cdot 0.5H_2O$ (252.31): C 64.35, H 8.10. Found: C 64.31, H 7.72.

Nucleophilic addition was carried out on **19** (60 mg, 0.24 mmol) with Tin-MOM acetal (208 mg, 0.57 mmol) and *n*-BuLi (1.6 M in hexane, 0.4 mL, 0.56 mmol), in dry THF (4 mL) for 2 h using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 7:3 to 3:7) **20** (33 mg, 72%).

4.4.3.2. 6,7-Dihydroxy-7-methoxymethoxymethyl-6,8a-dimethyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 20. Characterized as a diastereomeric mixture, colourless oil. IR (film): $\nu = 3399$, 2936, 2890, 1726, 1667, 1463, 1440, 1374, 1356, 1332, 1215, 1149, 1113, 1075, 1043, 952, 927, 916, 878, 863 cm^{-1}. ESIMS (MeOH+DCM): 351.1 ($[M+Na]^+$, 100). HRESIMS (MeOH+DCM) calcd for $C_{17}H_{28}O_6Na$ *m*/*z* 351.1784, found: 351.1783. Anal. Calcd for $C_{17}H_{28}O_6$ (328.40): C 62.17, H 8.59. Found: C 61.89, H 8.67.

Oxidative cleavage of **20** (diastereomeric mixture) was achieved using the general procedures affording **65** (13 mg, 72%, Table 1, entry 12) after SiO_2 flash column chromatography (heptane/EtOAc, 7:3).

4.4.3.3. 8-Methoxymethoxymethyl-6,10-dimethyl-9,12-dioxa-tricyclo[6.3.1.$0^{0,0}$]dodec-10-en-5-one 65. Colourless oil. $[\alpha]_D^{20} = -24$ (*c* 0.45, $CHCl_3$). IR (film): $\nu = 2937$, 2879, 1665, 1459, 1439, 1377, 1325, 1302, 1239, 1188, 1140, 1114, 1090, 1047, 1031, 1018, 941, 917, 873, 755, 677 cm^{-1}. ^1H NMR (500 MHz): $\delta = 1.24$ (s, 3H), 1.36 (tdd, $J = 1.3$, 4.7, 15.0 Hz, 1H), 1.43 (td, $J = 3.7$, 13.5 Hz, 1H), 1.50 (m, 1H), 1.62 (dtd, $J = 1.6$, 3.4, 13.2 Hz, 1H), 1.75 (s, 3H), 1.81 (d, $J = 13.7$ Hz, 1H), 1.88 (tt, $J = 3.5$, 13.6 Hz, 1H), 1.95 (ddt, $J = 2.0$, 3.9, 14.7 Hz, 1H), 2.32 (d, $J = 13.7$ Hz, 1H), 3.40 (s, 3H), 3.80 and 3.83 (ABquartet, $J = 10.5$ Hz, 2H), 3.88 (m, 2H), 3.97 (m, 2H), 4.58 (s, 1H), 4.72 and 4.74 (ABquartet, $J = 6.5$ Hz, 2H). ^{13}C NMR (125 MHz): $\delta = 17.5$, 18.3, 19.1, 28.8, 29.1, 45.0, 55.3, 57.4, 63.3, 65.1, 68.6, 85.3, 96.7, 104.7, 106.3, 111.9, 148.4. ESIMS (MeOH): 349.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{17}H_{26}O_6Na$ *m*/*z* 349.1627, found: 349.1614. Anal. Calcd for $C_{17}H_{26}O_6$ (326.38): C 62.56, H 8.03. Found: C, 62.73, H 8.12.

Starting from **19**, the target bis-tertiary diol **21** was synthesized analogously. Nucleophilic addition was carried out on **19** (58 mg, 0.23 mmol) with allylmagnesium bromide (1.0 M in THF, 0.9 mL, 0.92 mmol) in dry THF (1 mL) for 2 h using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 2:1) **21** (55 mg, 81%).

4.4.3.4. 7-Allyl-6,7-dihydroxy-6,8a-dimethyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 21. Colourless oil. $[\alpha]_D^{20} = +10$ (*c* 0.45, $CHCl_3$). IR (film): $\nu = 3468$, 2937, 2884, 1638, 1467, 1440, 1376, 1344, 1276, 1187, 1159, 1121, 1068, 1018, 996, 948, 917, 892, 868, 840 cm^{-1}. ^1H NMR (500 MHz): $\delta = 1.27$ (s, 3H), 1.39 (s, 3H), 1.49 (m, 1H), 1.61 (m, 1H), 1.58 (d, $J = 13.6$ Hz, 1H), 1.68 (dtd, $J = 2.1$, 4.7, 12.1 Hz, 1H), 1.84 (td, $J = 4.6$, 13.7 Hz, 1H), 2.00 (m, 1H), 1.99 (d, $J = 14.5$ Hz, 1H), 2.13 (s, 1H), 2.23 (dd, $J = 6.7$, 13.9 Hz, 1H), 2.28 (tdd, $J = 1.5$, 5.3, 13.8 Hz, 1H), 2.49 (s, 1H), 2.56 (dd, $J = 8.5$, 13.8 Hz, 1H), 3.94 (m, 4H), 5.19 (ddd, $J = 1.6$, 3.7, 17.1 Hz, 1H), 5.23 (ddd, $J = 1.0$, 2.2, 10.1 Hz, 1H), 5.27 (d, $J = 1.4$ Hz, 1H), 6.04 (dddd, $J = 6.7$, 8.5, 10.0, 16.9 Hz, 1H). ^{13}C NMR (125 MHz): $\delta = 23.1$, 23.7, 24.9, 29.1, 30.3, 36.1, 41.2, 44.3, 64.8, 65.0, 73.2, 74.7, 113.4, 119.5, 128.3, 134.3, 140.4. ESIMS (MeOH): 317.1 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{17}H_{26}O_4Na$ *m*/*z* 317.1729, found: 317.1738. Anal. Calcd for $C_{17}H_{26}O_4 \cdot 0.4H_2O$ (294.39): C 67.70, H 8.96. Found: C 67.85, H 8.81.

Oxidative cleavage of **21** (diastereomeric mixture) was achieved using the general procedures affording **66** (7 mg, 70%, Table 1, entry 13) after SiO_2 flash column chromatography (heptane/EtOAc, 1:1 as eluent).

4.4.3.5. 8-Allyl-6,10-dimethyl-9,12-dioxa-tricyclo[6.3.1.$0^{0,0}$]-dodec-10-en-5-one 66. Colourless oil. $[\alpha]_D^{20} = +56$ (*c* 0.40, $CHCl_3$). IR (film): $\nu = 2952$, 2886, 2360, 2341, 1704, 1685, 1666, 1611, 1457, 1444, 1353, 1337, 1280, 1190, 1144, 1081, 1070, 1050, 1039, 970, 951 cm^{-1}. ^1H NMR (300 MHz): $\delta = 1.21$ (s, 3H), 1.36 (m, 2H), 1.51 (m, 1H), 1.62 (m, 1H), 1.71 (s, 3H), 1.72 (d, $J = 13.7$ Hz, 1H), 1.81 (m, 1H), 1.92 (m, 1H), 2.24 (d, $J = 13.7$ Hz, 1H), 2.58 (ddt, $J = 1.2$, 7.9, 14.1 Hz, 1H), 2.68 (ddt, $J = 1.6$, 6.2, 14.1 Hz, 1H), 3.88 (m, 4H), 4.55 (s, 1H), 5.12 (m, 2H), 5.97 (dddd, $J = 6.3$, 7.9, 10.2, 17.2 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 17.7$, 18.3, 19.1, 28.9, 29.1, 41.0, 46.2, 57.4, 63.2, 65.1, 85.0, 104.6, 107.1, 112.0, 117.5, 133.3, 148.3. ESIMS (MeOH): 293.2 ($[M+H]^+$, 100), 585.3 ($[2M+H]^+$, 30). HRESIMS (MeOH+DCM) calcd for $C_{17}H_{25}O_4$ *m*/*z* 293.1753, found: 213.1753. Anal. Calcd for $C_{17}H_{24}O_4 \cdot 0.5H_2O$ (292.37): C 67.75, H 8.36. Found: C 67.61, H 8.31.

Starting from **19**, the target bis-tertiary diol **22** was synthesized analogously. Nucleophilic addition was carried out on **19** (23 mg, 0.09 mmol) with *n*-BuLi (1.6 M in hexane, 0.45 mL, 0.72 mmol) in dry THF (2 mL) for 3 h using the

general procedure to give after chromatography (SiO_2, heptane/EtOAc, 5:1) **22** (21 mg, 75%).

4.4.3.6. 7-Butyl-6,7-dihydroxy-6,8a-dimethyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 22. White solid. Mp: 105–106 °C. $[\alpha]_D^{20} = +28$ (c 0.69, $CHCl_3$). IR (film): $\nu =$ 3466, 2953, 2871, 1467, 1440, 1376, 1275, 1207, 1188, 1160, 1121, 1065, 1035, 1018, 949, 936, 892, 867, 841 cm^{-1}. ^1H NMR (500 MHz): $\delta = 0.94$ (t, $J = 7.2$ Hz, 3H), 1.24 (s, 3H), 1.36 (m, 2H), 1.40 (s, 3H), 1.42 (m, 3H), 1.51 (dt, $J = 13.8$, 4.6 Hz, 1H), 1.61 (m, 1H), 1.65 (d $J = 14.7$ Hz, 1H), 1.71 (m, 1H), 1.77 (ddd, $J = 15.7$, 10.8, 5.2 Hz, 1H), 1.83 (td, $J = 13.7$, 4.6 Hz, 1H), 1.87 (s, 1H), 1.89 (d, $J = 15.0$ Hz, 1H), 2.00 (dd, $J = 4.5$, 13.7 Hz, 1H), 2.28 (tdd, $J = 1.4$, 5.2, 13.8 Hz, 1H), 2.36 (br s, 1H), 3.94 (m, 4H), 5.27 (d, $J = 1.4$ Hz, 1H). ^{13}C NMR (125 MHz): $\delta = 14.2$, 23.2, 23.6, 24.0, 25.0, 25.5, 29.2, 30.3, 35.4, 35.9, 44.1, 64.8, 65.0, 73.7, 75.5, 113.5, 128.7, 140.3. ESIMS (MeOH): 333.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{18}H_{30}O_4Na$ m/z 333.2042, found: 333.2034. Anal. Calcd for $C_{18}H_{30}O_4$ (310.43): C 69.64, H 9.74, found: C 69.42, H 9.73.

Oxidative cleavage of **22** (diastereomeric mixture) was achieved using the general procedures affording **67** (10 mg, 78%, Table 1, entry 14) after SiO_2 flash column chromatography (heptane/EtOAc, 2:1 as eluent).

4.4.3.7. 8-Butyl-6,10-dimethyl-9,12-dioxa-tricyclo[6.3.1.$0^{0,0}$]-dodec-10-en-5-one 67. Yellow oil. $[\alpha]_D^{20} = -7$ (c 0.51, $CHCl_3$). IR (film): $\nu = 2952$, 2930, 2874, 1666, 1459, 1439, 1377, 1328, 1231, 1220, 1186, 1133, 1120, 1051, 1033, 1017, 994, 943, 920, 898, 753, 677 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.92$ (t, $J = 7.1$ Hz, 3H), 1.22 (s, 3H), 1.35 (m, 5H), 1.56 (m, 4H), 1.71 (d, $J = 1.1$ Hz, 3H), 1.76 (d, $J = 13.5$ Hz, 1H), 1.88 (m, 3H), 2.21 (d, $J = 13.5$ Hz, 1H), 3.94 (m, 4H), 4.53 (d, $J = 1.0$ Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 13.9$, 17.7, 18.3, 19.0, 23.0, 25.6, 28.8, 28.9, 36.0, 46.7, 57.2, 63.1, 65.0, 84.6, 104.3, 107.9, 112.0, 148.2. ESIMS (MeOH): 331.1 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{18}H_{28}O_4Na$ m/z 331.1885, found: 331.1884. Anal. Calcd for $C_{18}H_{28}O_4$ (308.41): C 70.10, H 9.15. Found: C 69.65, H 9.21.

4.4.4. Preparation of target diol 24. Oxidation of **11** (170 mg, 0.61 mmol) was carried out with IBX (512 mg, 1.83 mmol) in DMSO (10 mL) for 30 min using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 7:3) **23** (99 mg, 80%). An analytical sample was purified on SiO_2 flash chromatography, eluent heptane/EtOAc, 7:3, for characterization purposes.

4.4.4.1. 6-Hydroxy-6-isopropenyl-8a-methyl-2,3,4,6,8,8a-hexahydro-naphthalene-1,7-dione 23. Colourless oil. $[\alpha]_D^{20} = +265$ (c 0.93, $CHCl_3$). IR (film): $\nu = 3476$, 2939, 2879, 1715, 1437, 1377, 1268, 1216, 1186, 1122, 1065, 1017, 942, 911, 772 cm^{-1}. ^1H NMR (300 MHz): $\delta = 1.19$ (d, $J = 0.6$ Hz, 3H), 1.25 (m, 1H), 1.69 (dd, $J = 0.9$, 1.5 Hz, 3H), 1.74 (m, 3H), 2.05 (d, $J = 11.9$ Hz, 1H), 2.25 (m, 2H), 3.42 (dd, $J = 0.5$, 11.9 Hz, 1H), 3.90 (m, 5H), 5.10 (t, $J = 1.4$ Hz, 1H), 5.35 (s, 1H), 5.35 (t, $J = 1.3$ Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 17.6$, 22.5 (2C), 29.4, 30.2, 39.6, 51.7, 64.9, 65.2, 79.9, 111.7, 116.0, 124.4, 144.2, 146.1, 211.4. ESIMS (MeOH): 301.1 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{16}H_{22}O_4Na$ m/z 301.1416, found: 301.1433.

Nucleophilic addition was carried out on **23** (55 mg, 0.12 mmol) with allylmagnesium bromide (1.0 M in Et_2O, 0.3 mL, 0.30 mmol) in dry THF (7 mL) at −78 °C for 4 h for 3 h at room temperature using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 9:1) **24** (35 mg, 53%).

4.4.4.2. 7-Allyl-4-(*tert*-butyl-dimethyl-silanyloxy)-6,7-dihydroxy-6-isopropenyl-8a-methyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 24. Colourless oil. $[\alpha]_D^{20} = -99$ (c 1.55, $CHCl_3$). IR (film): $\nu = 3482$, 3352, 3074, 2936, 2895, 1637, 1438, 1347, 1244, 1169, 1146, 1134, 1108, 1084, 1058, 1019, 950, 909, 666, 631, 613, 535 cm^{-1}. ^1H NMR (300 MHz): $\delta = 1.26$ (s, 3H), 1.44 (d, $J = 16.3$ Hz, 1H), 1.55 (m, 1H), 1.69 (m, 2H), 1.78 (m, 2H), 1.84 (s, 3H), 2.07 (m, 1H), 2.16 (d, $J = 16.3$ Hz, 1H), 2.34 (tdd, $J = 1.7$, 4.4, 13.6 Hz, 1H), 2.60 (dd, $J = 5.1$, 14.0 Hz, 1H), 4.00 (m, 5H), 5.00 (m, 4H), 5.20 (d, $J = 2.0$ Hz, 1H), 5.64 (br s, 1H), 5.93 (m, 1H). ^{13}C NMR (75 MHz): $\delta = 21.3$, 23.3, 26.2, 30.4 (2C), 36.8, 40.7, 43.1, 64.7, 64.8, 72.4, 77.8, 112.9, 114.9, 117.1, 129.4, 135.1, 139.0, 146.2. ESIMS (MeOH): 343.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{19}H_{28}O_4Na$ m/z 343.1885, found: 343.1855. Anal. Calcd for $C_{19}H_{28}O_4 \cdot 0.3H_2O$ (320.42): C 70.04, H 8.85. Found: C 70.15, H 8.41.

Oxidative cleavage of **24** (diastereomeric mixture) was achieved using the general procedures affording **68** (10 mg, 83%, Table 1, entry 15) after SiO_2 flash column chromatography (heptane/EtOAc, 10:1 as eluent).

4.4.4.3. 8-Allyl-10-isopropenyl-6-methyl-9,12-dioxa-tricyclo[6.3.1.$0^{0,0}$]dodec-10-en-5-one 68. White solid. Mp: 46–48 °C. $[\alpha]_D^{20} = +1$ (c 0.44, $CHCl_3$). IR (film): $\nu = 3075$, 2952, 2879, 1642, 1602, 1459, 1440, 1347, 1302, 1277, 1224, 1190, 1134, 1088, 1052, 998, 956, 920, 902 cm^{-1}. ^1H NMR (300 MHz): $\delta = 1.23$ (s, 3H), 1.45 (m, 3H), 1.65 (m, 1H), 1.71 (d, $J = 13.8$ Hz, 1H), 1.83 (dd, $J = 0.8$, 1.4 Hz, 3H), 1.99 (m, 2H), 2.28 (d, $J = 13.7$ Hz, 1H), 2.63 (ddt, $J = 1.2$, 7.9, 14.0 Hz, 1H), 2.75 (ddt, $J = 1.5$, 6.3, 14.0 Hz, 1H), 3.96 (m, 4H), 4.89 (s, 1H), 4.93 (m, 1H), 5.14 (m, 2H), 5.39 (dt, $J = 0.7$, 2.3 Hz, 1H), 6.01 (dddd, $J = 6.3$, 7.9, 10.1, 16.5 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 17.7$, 18.3, 18.5, 29.1 (2C), 40.9, 45.8, 57.4, 63.1, 65.0, 84.9, 106.0, 107.0, 111.8, 112.5, 117.5, 133.1, 136.5, 148.9. ESIMS (MeOH): 341.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{19}H_{26}O_4Na$ m/z 341.1729, found: 341.1740.

4.5. Preparation and domino reactions of the allylically substituted substrates 27–31, their bis-tertiary analogues and their oxidative cleavage

The allylically functionalized bicyclic unsaturated diols **26b** was synthesized from **6** by way of the intermediate dienol acetate species **25a** (DMAP, pyridine, acetic anhydride, 100 °C, 24 h, 70%), using published procedures (cf. Ref. 20). Installation of the allylic hydroxy group was then

carried out using methyltrioxorhenium (30% H_2O_2, pyridine, DCM, 75%) and its protection was performed with TBSCl-imidazole (DMF, 60 °C, 84%).

4.5.1. Preparation of the key precursor 26b. To a stirred solution of **6** (5.00 g, 17.83 mmol) and DMAP (1.19 g, 9.80 mmol) in dry pyridine (35 mL), acetic anhydride (27 mL, 0.25 mmol) was added, under argon, at 0 °C. The reaction mixture was allowed to reach room temperature, then heated at 100 °C for 24 h, after which the solvent was removed under reduced pressure. Purification of the crude by silica gel chromatography (heptane/Et_2O, 7:1) gave **25a** (4.01 g, 70%) along with unreacted SM (1.00 g, 20%).

Compound **25a**: Colourless oil. $[\alpha]_D^{20} = -46$ (*c* 1.61, $CHCl_3$). IR (film): $\nu = 2958$, 2882, 1759, 1738, 1428, 1365, 1232, 1203, 1188, 1147, 1121, 1084, 1040, 1011, 952, 905, 886, 751, 732 cm^{-1}. ^1H NMR (300 MHz): $\delta = 1.30$ (s, 3H), 1.66 (dddd, $J = 0.9$, 2.9, 5.7, 13.6 Hz, 1H), 1.92 (d, $J = 10.8$ Hz, 1H), 1.98 (m, 1H), 2.00 (d, $J = 6.4$ Hz, 1H), 2.06 (s, 3H), 2.09 (s, 3H), 2.36 (m, 2H), 3.96 (m, 4H), 5.54 (t, $J = 3.8$ Hz, 1H), 5.71 (ddt, $J = 1.3$, 6.5, 10.3 Hz, 1H), 5.88 (s, 1H). ^{13}C NMR (75 MHz): $\delta = 20.7$, 21.0, 23.0, 24.4, 25.5, 32.4, 42.0, 65.0, 65.2, 67.7, 111.4, 120.4, 125.1, 136.6, 143.3, 168.9, 170.5. ESIMS (MeOH): 345.2 ($[M+Na]^+$, 10), 285.1 (100), 159.1 (3). HRESIMS: calcd for $C_{17}H_{22}O_6Na$ *m/z* 345.1314, found: 345.1313. Anal. Calcd for $C_{17}H_{22}O_6 \cdot 0.2H_2O$ (322.35): C 62.64, H 6.93. Found: C 62.72, H 6.92.

To a stirred solution of **25a** (4.00 g, 12.41 mmol) in 12 mL of DCM, pyridine (0.12 mL, 1.49 mmol), 30% H_2O_2 (3.5 mL, 31.02 mmol) and $MeReO_3$ (15 mg, 0.06 mmol) were added and the reaction mixture was stirred under argon at room temperature for 24 h. Dilution with DCM, washings with satd aq $Na_2S_2O_3$ and usual workup gave, after silica gel chromatography (heptane/EtOAc, 3:1 to 1:1), **26a** (2.76 g, 75%).

Compound **26a**: White solid. Mp: 116–118 °C. $[\alpha]_D^{20} = +11$ (*c* 0.87, $CHCl_3$). IR (film): $\nu = 3444$, 2973, 2891, 1751, 1725, 1693, 1674, 1375, 1250, 1206, 1113, 1072, 1056, 1024, 990, 951, 876, 738, 687 cm^{-1}. ^1H NMR (300 MHz): $\delta = 1.58$ (dt, $J = 3.5$, 13.5 Hz, 1H), 1.69 (d, $J = 0.9$ Hz, 3H), 1.87 (dd, $J = 5.4$, 12.2 Hz, 1H), 1.93 (m, 2H), 2.06 (br s, 1H), 2.17 (s, 3H), 2.28 (ddd, $J = 7.9$, 7.9, 13.5 Hz, 1H), 2.43 (ddd, $J = 0.9$, 12.2, 14.4 Hz, 1H), 3.96 (m, 4H), 4.34 (dd, $J = 2.8$, 5.5 Hz, 1H), 5.52 (dd, $J = 5.4$, 14.4 Hz, 1H), 5.90 (s, 1H). ^{13}C NMR (75 MHz): $\delta = 20.8$, 22.8, 24.5, 28.7, 33.9, 46.2, 64.9, 65.2, 71.1, 71.5, 111.7, 126.0, 165.5, 170.2, 194.2. ESIMS (MeOH): 319.1 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{15}H_{20}O_6Na$ *m/z* 319.1158, found: 319.1163. Anal. Calcd for $C_{15}H_{20}O_6 \cdot 0.2H_2O$ (296.32): C 60.07, H 6.86. Found: C 59.98, H 6.86.

Compound **26a** (7.20 g, 24.30 mmol) was added to a solution of imidazole (8.27 g, 121.49 mmol) and TBSCl (14.65 g, 97.19 mmol) in DMF (45 mL), at 60 °C, and stirring was continued for 3.5 h. After cooling, the mixture was diluted with Et_2O, washed with HCl 1 N, satd aq $NaHCO_3$ and worked up as usual. SiO_2 flash chromatography (heptane/Et_2O, 2:1) of the residue gave **26b** (8.45 g, 84%).

Compound **26b**: White solid. Mp: 132–135 °C. $[\alpha]_D^{20} = +6$ (*c* 0.82, $CHCl_3$). IR (film): $\nu = 2952$, 2927, 2887, 2856, 1743, 1690, 1470, 1378, 1361, 1237, 1216, 1071, 1035, 1011, 952, 917, 832, 772 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.03$ (s, 3H), 0.07 (s, 3H), 0.87 (s, 9H), 1.56 (m, 1H), 1.66 (s, 3H), 1.83 (m, 2H), 1.85 (dd, $J = 5.5$, 12.2 Hz, 1H), 2.18 (s, 3H), 2.28 (td, $J = 4.3$, 13.5 Hz, 1H), 2.43 (ddd, $J = 0.9$, 12.2, 14.4 Hz, 1H), 3.95 (m, 4H), 4.25 (t, $J = 2.5$ Hz, 1H), 5.55 (dd, $J = 5.4$, 14.4 Hz, 1H), 5.82 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.1$, −4.7, 17.8, 20.8, 22.9, 24.6, 25.5 (3C), 30.3, 34.1, 46.5, 64.9, 65.2, 71.5, 71.7, 111.7, 125.2, 165.3, 170.1, 194.4. ESIMS (MeOH): 433.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{21}H_{34}O_6NaSi$ *m/z* 433.2022, found: 433.2018. Anal. Calcd for $C_{21}H_{34}O_6Si$ (410.58): C 61.43, H 8.35. Found: C 61.44, H 8.38.

4.5.2. Preparation of target diol 33. Nucleophilic addition was carried out on **26b** (3.17 g, 7.72 mmol) with vinylmagnesium bromide (1.0 M in THF, 46.3 mL, 46.32 mmol) in dry THF (40 mL) for 3 h using the general procedure to give after chromatography (heptane/EtOAc, 3:1) **27** (2.57 g, 84%).

4.5.2.1. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6,7-dihydroxy-8a-methyl-6-vinyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 27. White solid. Mp: 105–107 °C. $[\alpha]_D^{20} = -72$ (*c* 0.91, $CHCl_3$). IR (film): $\nu = 3407$, 2956, 2931, 2885, 2857, 1254, 1065, 1003, 926, 836, 773 cm^{-1}. ^1H NMR (500 MHz): $\delta = 0.04$ (s, 3H), 0.06 (s, 3H), 0.88 (s, 9H), 1.15 (dd, $J = 12.0$, 14.1 Hz, 1H), 1.37 (s, 3H), 1.50 (ddd, $J = 5.3$, 9.3, 14.0 Hz, 1H), 1.73 (m, 3H), 2.09 (s, 1H), 2.15 (td, $J = 5.2$, 13.4 Hz, 1H), 2.15 (dd, $J = 4.9$, 14.2 Hz, 1H), 3.98 (m, 5H), 4.25 (t, $J = 2.9$ Hz, 1H), 5.33 (s, 1H), 5.36 (dd, $J = 1.5$, 8.6 Hz, 1H), 5.42 (s, 1H), 5.95 (dd, $J = 10.8$, 17.2 Hz, 1H). ^{13}C NMR (125 MHz): $\delta = -5.0$, −4.5, 18.0, 25.3, 25.8 (3C), 28.2, 32.1, 36.3, 45.4, 65.0, 64.6, 73.7, 74.1, 76.1, 113.5, 117.3, 128.6, 138.0, 144.0. ESIMS (MeOH): 419.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{21}H_{36}O_5NaSi$ *m/z* 419.2230, found: 419.2227. Anal. Calcd for $C_{21}H_{36}O_5Si \cdot 0.05$ heptane (396.59): C 63.85, H 9.24. Found: C 63.99, H 9.06.

Oxidation of **27** (2.30 g, 5.80 mmol) was carried out with IBX (4.88 g, 17.41 mmol) in DMSO (40 mL) for 30 min using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 6:1) **32** (2.18 g, 95%). An analytical sample was purified on SiO_2 flash chromatography, eluent heptane/EtOAc, 6:1, for characterization purposes.

4.5.2.2. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6-hydroxy-8a-methyl-6-vinyl-2,3,4,6,8,8a-hexahydro-naphthalene-1,7-dione 32. White solid. Mp: 92–94 °C. $[\alpha]_D^{20} = -124$ (*c* 1.42, $CHCl_3$). IR (film): $\nu = 3476$, 2954, 2928, 2886, 2856, 1725, 1470, 1361, 1252, 1113, 1064, 1002, 922, 833, 774 cm^{-1}. ^1H NMR (500 MHz): $\delta = 0.08$ (s, 6H), 0.90 (s, 9H), 1.48 (dt, $J = 3.5$, 13.7 Hz, 1H), 1.49 (s, 3H), 1.72 (m, 2H), 2.12 (dt, $J = 9.6$, 13.6 Hz, 1H), 2.33 and 2.63

(ABquartet, $J = 14.9$ Hz, 2H), 3.82 (ddd, $J = 5.8$, 6.9, 7.8 Hz, 1H), 3.92 (m, 2H), 4.04 (m, 2H), 4.35 (t, $J = 2.7$ Hz, 1H), 5.28 (dd, $J = 0.9$, 10.3 Hz, 1H), 5.45 (dd, $J = 0.9$, 17.1 Hz, 1H), 5.51 (s, 1H), 5.83 (dd, $J = 10.3$, 17.1 Hz, 1H). ^{13}C NMR (125 MHz): $\delta = -5.1$, −4.5, 18.0, 25.2, 25.8 (3C), 26.8, 32.5, 40.9, 51.3, 64.6, 65.6, 74.0, 77.4, 112.7, 117.0, 126.9, 140.2, 144.3, 207.9. ESIMS (MeOH): 417.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{21}H_{34}O_5NaSi$ m/z 417.2073, found: 417.2083. Anal. Calcd for $C_{21}H_{34}O_5Si{\cdot}0.5H_2O$ (394.58): C 62.50, H 8.74. Found: C 62.81, H 8.29.

Nucleophilic addition was carried out on **32** (850 mg, 2.16 mmol) with allylmagnesium bromide (1.0 M in THF, 17.20 mL, 17.20 mmol) in dry THF (15 mL) for 1 h 45 min using the general procedure to give after chromatography (heptane/EtOAc, 6:1) **33** (726 mg, 77%).

4.5.2.3. 7-Allyl-4-(*tert*-butyl-dimethyl-silanyloxy)-6,7-dihydroxy-8a-methyl-6-vinyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 33. Yellow oil. $[\alpha]_D^{20} = -85$ (c 1.18, $CHCl_3$). IR (film): $\nu = 3384$, 2953, 2928, 2889, 2856, 1471, 1435, 1409, 1360, 1253, 1201, 1107, 1067, 1003, 922, 834, 774 cm^{-1}. ^{1}H NMR (500 MHz): $\delta = 0.03$ (s, 3H), 0.06 (s, 3H), 0.87 (s, 9H), 1.29 (d, $J = 16.3$ Hz, 1H), 1.39 (s, 3H), 1.55 (m, 2H), 1.72 (ddt, $J = 2.8$, 4.7, 13.8 Hz, 1H), 1.78 (tdd, $J = 3.0$, 4.2, 13.6 Hz, 1H), 1.94 (dd, $J = 8.7$, 13.9 Hz, 1H), 2.20 (d, $J = 16.3$ Hz, 1H), 2.61 (ddt, $J = 1.7$, 5.6, 14.2 Hz, 1H), 3.61 (s, 1H), 4.03 (m, 4H), 4.26 (t, $J = 2.6$ Hz, 1H), 5.05 (m, 2H), 5.18 (dd, $J = 1.7$, 10.7 Hz, 1H), 5.28 (d, $J = 1.9$, 1H), 5.33 (dd, $J = 1.7$, 17.3 Hz, 1H), 5.37 (s, 1H), 5.79 (dd, $J = 10.6$, 17.2 Hz, 1H), 5.93 (dddd, $J = 5.6$, 8.6, 10.2, 17.0 Hz, 1H). ^{13}C NMR (125 MHz): $\delta = -5.1$, −4.5, 18.0, 25.5, 25.7 (3C), 29.5, 31.8, 38.2, 40.0, 43.2, 64.8 (2C), 72.5, 73.4, 76.5, 113.2, 115.7, 117.0, 131.9, 135.0, 138.8, 141.0. ESIMS (MeOH): 459.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{24}H_{40}O_5NaSi$ m/z 459.2543, found: 459.2521. Anal. Calcd for $C_{24}H_{40}O_5Si$ (436.66): C 66.01, H 9.23. Found: C 67.26, H 9.07.

Oxidative cleavage of **33** (diastereomeric mixture) was achieved using the general procedures affording **71** (12 mg, 88%, Table 1, entry 18) after SiO_2 flash column chromatography (heptane/EtOAc, 6:1 as eluent).

4.5.2.4. 8-Allyl-2-(*tert*-butyl-dimethyl-silanyloxy)-6-methyl-10-vinyl-9,12-dioxa-tricyclo[6.3.1.0^{0,0}]dodec-10-en-5-one 71. Colourless oil. $[\alpha]_D^{20} = -4$ (c 1.23, $CHCl_3$). IR (film): $\nu = 2951$, 2927, 2856, 1595, 1462, 1363, 1257, 1207, 1088, 996, 948, 906, 834, 774 cm^{-1}. ^{1}H NMR (500 MHz): $\delta = 0.07$ (s, 3H), 0.10 (s, 3H), 0.92 (s, 9H), 1.30 (s, 3H), 1.44 (m, 1H), 1.59 (ddd, $J = 3.1$, 6.2, 13.8 Hz, 1H), 1.68 (d, $J = 13.7$ Hz, 1H), 1.95 (ddd, $J = 3.4$, 12.5, 14.2 Hz, 1H), 2.09 (m, 1H), 2.28 (d, $J = 13.7$ Hz, 1H), 2.64 (ddt, $J = 1.2$, 8.0, 14.0 Hz, 1H), 2.72 (ddt, $J = 1.5$, 6.3, 14.0 Hz, 1H), 3.96 (m, 5H), 5.07 (dd, $J = 2.1$, 10.8 Hz, 1H), 5.11 (ddt, $J = 1.2$, 2.4, 10.3 Hz, 1H), 5.15 (ddd, $J = 1.5$, 3.6, 17.2 Hz, 1H), 5.33 (s, 1H), 5.51 (dd, $J = 1.6$, 17.2 Hz, 1H), 5.99 (m, 2H), 6.05 (dd, $J = 10.8$, 17.2 Hz, 1H). ^{13}C NMR (125 MHz): $\delta = -5.0$, −4.4, 18.0, 18.3, 23.8, 25.8 (3C), 26.9, 40.9, 46.5, 58.1, 63.3, 65.1, 68.5, 85.8, 107.2, 107.5, 111.9, 113.6, 117.7, 131.6, 133.1, 148.1. ESIMS (MeOH): 457 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{24}H_{38}O_5NaSi$ m/z 457.2386, found: 457.2383.

Fluoride deprotection was carried out on **33** (580 mg, 1.33 mmol) for 19.5 h using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 6:1) **46** (429 mg, 99%).

4.5.2.5. 7-Allyl-4,6,7-trihydroxy-8a-methyl-6-vinyl-3,4,6,-7,8,8a-hexahydro-2*H*-naphthalen-1-one 46. Colourless oil. $[\alpha]_D^{20} = -112$ (c 1.24, $CHCl_3$). IR (film): $\nu = 3381$, 2968, 2937, 2891, 1436, 1410, 1335, 1205, 1140, 1105, 1067, 1051, 1022, 999, 962, 917, 893, 873, 735 cm^{-1}. ^{1}H NMR (500 MHz): $\delta = 1.31$ (d, $J = 16.4$ Hz, 1H), 1.42 (s, 3H), 1.57 (ddd, $J = 2.6$, 4.5, 13.8 Hz, 1H), 1.76 (br s, 1H), 1.83 (dt, $J = 3.8$, 13.8 Hz, 1H), 1.88 (ddd, $J = 2.4$, 4.7, 14.2 Hz, 1H), 1.92 (ddd, $J = 0.7$, 8.6, 14.2 Hz, 1H), 2.19 (td, $J = 4.6$, 13.8 Hz, 1H), 2.23 (d, $J = 16.4$ Hz, 1H), 2.58 (ddt, $J = 1.8$, 5.5, 14.3 Hz, 1H), 3.61 (s, 1H), 4.04 (m, 4H), 4.33 (t, $J = 2.8$ Hz, 1H), 5.02 (dd, $J = 1.9$, 17.1 Hz, 1H), 5.05 (dd, $J = 1.6$, 10.7 Hz, 1H), 5.17 (dd, $J = 1.6$, 10.7 Hz, 1H), 5.21 (d, $J = 1.6$ Hz, 1H), 5.35 (dd, $J = 1.6$, 17.2 Hz, 1H), 5.47 (s, 1H), 5.76 (dd, $J = 10.7$, 17.2 Hz, 1H), 5.91 (dddd, $J = 5.5$, 8.6, 10.3, 17.2 Hz, 1H). ^{13}C NMR (125 MHz): $\delta = 25.3$, 29.6, 29.9, 38.1, 39.8, 43.0, 64.8, 72.5, 72.9, 76.4, 112.9, 115.4, 117.1, 133.3, 134.7, 138.5, 141.2. ESIMS (MeOH): 345.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{18}H_{26}O_5Na$ m/z 345.1678, found 345.1668. Anal. Calcd for $C_{18}H_{26}O_5{\cdot}0.2H_2O$ (322.40): C 66.32, H 8.16. Found: C 66.34, H 8.13.

To a stirred solution of **46** (170 mg, 0.53 mmol) and fumaric acid monoester (198 mg, 1.37 mmol) in dry DCM (5 mL), under argon, at 0 °C, were added DCC (282 mg, 1.37 mmol) and DMAP (52 mg, 0.42 mmol). The reaction mixture was stirred at room temperature for 20 h. DCM was added and the reaction mixture was filtered. The organic layer was washed with aqueous AcOH (5%), then usual workup and chromatography on SiO_2 gave (heptane/EtOAc, 2:1) **47** (208.2 mg, 88%).

4.5.2.6. But-2-enedioic acid 6-allyl-6,7-dihydroxy-4a-methyl-4-oxo-7-vinyl-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-yl ester ethyl ester 47. Yellow oil. $[\alpha]_D^{20} = -85$ (c 1.31, $CHCl_3$). IR (film): $\nu = 3378$, 2977, 2940, 2898, 1715, 1257, 1152, 1107, 1064, 1023, 977, 929, 734, 701 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 1.30$ (td, $J = 1.2$, 7.1 Hz, 3H), 1.31 (s, 3H), 1.66 (dt, $J = 3.6$, 13.9 Hz, 1H), 1.96 (m, 4H), 2.09 (td, $J = 4.5$, 13.8 Hz, 1H), 2.23 (d, $J = 16.4$ Hz, 1H), 2.60 (ddd, $J = 1.4$, 5.5, 14.2 Hz, 1H), 3.62 (s, 1H), 4.03 (m, 4H), 4.24 (q, $J = 7.1$ Hz, 2H), 5.04 (m, 2H), 5.15 (dt, $J = 1.5$, 10.7 Hz, 1H), 5.20 (s, 1H), 5.25 (dt, $J = 1.5$, 17.3 Hz, 1H), 5.44 (t, $J = 3.1$ Hz, 1H), 5.70 (s, 1H), 5.73 (m, 1H), 5.91 (ddddd, $J = 1.1$, 5.4, 8.7, 10.0, 15.5 Hz, 1H), 6.78 (dd, $J = 1.2$, 15.9 Hz, 1H), 6.82 (dd, $J = 1.2$, 16.0 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = 14.0$, 25.8, 28.0, 28.6, 37.8, 39.8, 42.9, 61.3, 64.9 (2C), 72.4, 75.7, 76.4, 112.2, 116.3, 117.2, 133.6, 133.8, 134.6, 135.9, 137.1, 138.1, 163.8, 164.9. ESIMS (MeOH): 471.2 ([M+Na]$^+$, 100). HRESIMS (MeOH) calcd for $C_{24}H_{32}O_8Na$ m/z 471.1995, found: 471.1996. Anal. Calcd for $C_{24}H_{32}O_8{\cdot}0.36$ DCM (448.51): C 61.07, H 6.88. Found: C 61.01, H 7.02.

Oxidative cleavage of **47** (diastereomeric mixture) was achieved using the general procedures affording **80** (55 mg, 83%, Table 1, entry 27) after SiO_2 flash column chromatography (heptane/Et_2O, 2:1 as eluent).

4.5.2.7. But-2-enedioic acid 8-allyl-6-methyl-5-oxo-10-vinyl-9,12-dioxa-tricyclo[6.3.1.$0^{0,0}$]dodec-10-en-5-one 80. Colourless oil. $[\alpha]_D^{20} = -5$ (*c* 1.24 $CHCl_3$). IR (film): $\nu = 2981, 2951, 2884, 1722, 1438, 1367, 1294, 1258, 1206, 1152, 1046, 975, 668\ cm^{-1}$. ^1H NMR (300 MHz): $\delta = 1.33$ (t, $J = 7.1$ Hz, 3H), 1.34 (s, 3H), 1.53 (dt, $J = 3.9$, 7.0 Hz, 1H), 1.73 and 2.33 (ABquartet, $J = 13.8$ Hz, 2H), 1.79 (m, 2H), 2.20 (m, 1H), 2.64 (ddt, $J = 1.2$, 7.9, 14.0 Hz, 1H), 2.74 (ddt, $J = 1.5$, 6.3, 14.1 Hz, 1H), 3.95 (m, 4H), 4.28 (q, $J = 7.1$ Hz, 2H), 4.98 (s, 1H), 5.10 (m, 3H), 5.19 (t, $J = 2.6$ Hz, 1H), 5.53 (dd, $J = 1.6$, 17.1 Hz, 1H), 5.98 (m, 1H), 6.00 (dd, $J = 10.9$, 17.2 Hz, 1H), 6.84 and 6.90 (ABquartet, $J = 15.8$ Hz, 2H). ^{13}C NMR (75 MHz): $\delta = 14.1$, 17.9, 23.8, 24.2, 40.7, 46.3, 58.3, 61.5, 63.3, 65.2, 71.4, 84.1, 104.7, 107.8, 111.2, 114.6, 117.9, 131.1, 132.7, 133.2, 134.3, 148.8, 163.6, 164.8. ESIMS (MeOH): 469.1 ($[M+Na]^+$, 100). HRESIMS (MeOH) calcd for $C_{24}H_{30}O_8Na$ *m*/*z* 469.1838, found: 469.1843. Anal. Calcd for $C_{24}H_{30}O_8 \cdot 0.44$ DCM (446.49): C 60.67, H 6.43. Found: C 60.66, H 7.27.

4.5.3. Preparation of target diol 35. Nucleophilic addition was carried out on **26b** (540 mg, 1.32 mmol) with prop-1-yne (2.4 mL, 42.10 mmol), *n*-BuLi (1.6 M in hexane, 7.2 mL, 11.5 mmol) and HMPA (1.2 mL) in dry THF (11 mL) using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 2:1) **28** (473 mg, 88%).

4.5.3.1. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6,7-dihydroxy-8a-methyl-6-prop-1-ynyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 28. Yellow oil. $[\alpha]_D^{20} = -6$ (*c* 1.40, $CHCl_3$). IR (film): $\nu = 3406, 2953, 2928, 2884, 2856, 2238, 1471, 1360, 1253, 1204, 1109, 1066, 1036, 1003, 835, 774\ cm^{-1}$. ^1H NMR (500 MHz): $\delta = 0.04$ (s, 3H), 0.06 (s, 3H), 0.86 (s, 9H), 1.38 (s, 3H), 1.41 (dd, $J = 2.4$, 13.8 Hz, 1H), 1.49 (dt, $J = 3.4$, 13.8 Hz, 1H), 1.61 (br s, 1H), 1.72 (m, 2H), 1.86 (s, 3H), 2.09 (dd, $J = 4.6$, 14.0 Hz, 1H), 2.16 (dt, $J = 9.4$, 13.5 Hz, 1H), 2.45 (br s, 1H), 3.97 (m, 5H), 4.22 (t, $J = 2.5$ Hz, 1H), 5.69 (s, 1H). ^{13}C NMR (125 MHz): $\delta = -5.1$, −4.4, 3.8, 18.0, 25.5, 25.8 (3C), 28.2, 32.1, 33.7, 45.1, 64.7, 65.1, 67.2, 72.3, 73.6, 80.3, 81.9, 113.7, 126.3, 146.2. ESIMS (MeOH): 431.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{22}H_{36}O_5NaSi$ *m*/*z* 431.2230, found: 431.2251.

Oxidative cleavage of **28** (diastereomeric mixture) was achieved using the general procedures affording **69** (24 mg, 86%, Table 1, entry 16) after SiO_2 flash column chromatography (heptane/EtOAc, 5:1 as eluent).

4.5.3.2. 2-(*tert*-Butyl-dimethyl-silanyloxy)-6-methyl-10-prop-1-ynyl-9,12-dioxa-tricyclo[6.3.1.$0^{0,0}$]dodec-10-en-5-one 69. Yellow oil. $[\alpha]_D^{20} = -38$ (*c* 1.23, $CHCl_3$). IR (film): $\nu = 2954, 2929, 2884, 2858, 2446, 1623, 1256, 1084, 951, 905, 840\ cm^{-1}$. ^1H NMR (500 MHz): $\delta = 0.08$ (s, 3H), 0.12 (s, 3H), 0.92 (s, 9H), 1.34 (s, 3H), 1.44 (dt, $J = 2.1$, 6.4 Hz, 1H), 1.61 (ddd, $J = 2.8$, 3.0, 13.3 Hz, 1H), 1.73 (dd, $J = 1.2$, 13.8 Hz, 1H), 1.91 (dd, $J = 3.0$, 14.0 Hz, 1H), 1.96 (s, 3H), 2.00 (dt, $J = 2.7$, 13.8 Hz, 1H), 2.49 (dd, $J = 5.9$, 13.8 Hz, 1H), 3.94 (m, 5H), 5.57 (s, 1H), 5.59 (dd, $J = 1.3$, 5.9 Hz, 1H). ^{13}C NMR (125 MHz): $\delta = -5.0$, −4.5, 4.1, 17.7, 18.0, 23.5, 25.8 (3C), 26.9, 43.6, 58.2, 63.2, 65.3, 68.2, 74.5, 84.5, 85.2, 100.3, 111.1, 112.1, 133.7. ESIMS (MeOH): 429.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{22}H_{34}O_5NaSi$ *m*/*z* 429.2073, found: 429.2061. Anal. Calcd for $C_{22}H_{34}O_5Si \cdot 0.85H_2O$ (406.59): C 62.63, H 8.59. Found: C 62.92, H 8.59.

Oxidation of **28** (305 mg, 0.75 mmol) was carried out with IBX (627 mg, 2.24 mmol) in DMSO (2 mL) for 30 min using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 6:1) **34** (249 mg, 92%). An analytical sample was purified on SiO_2 flash chromatography, eluent heptane/EtOAc, 6:1, for characterization purposes.

4.5.3.3. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6-hydroxy-8a-methyl-6-prop-1-ynyl-2,3,4,6,8,8a-hexahydro-naphthalene-1,7-dione 34a. White solid. Mp: 69–72 °C. $[\alpha]_D^{20} = -114$ (*c* 1.19, $CHCl_3$). IR (film): $\nu = 3474, 2951, 2928, 2887, 2856, 1734, 1471, 1360, 1253, 1118, 1069, 1003, 913, 856, 774\ cm^{-1}$. ^1H NMR (500 MHz): $\delta = 0.10$ (2s, 6H), 0.90 (s, 9H), 1.47 (m, 1H), 1.52 (s, 3H), 1.71 (m, 2H), 1.84 (s, 3H), 2.11 (ddd, $J = 6.2$, 12.2, 13.7 Hz, 1H), 2.67 and 2.72 (ABquartet, $J = 14.7$ Hz, 2H), 3.83 (m, 2H), 3.92 (m, 1H), 4.04 (m, 2H), 4.29 (t, $J = 2.7$ Hz, 1H), 5.66 (s, 1H). ^{13}C NMR (125 MHz): $\delta = -5.1$, −4.4, 3.7, 18.0, 25.4, 25.8 (3C), 26.6, 32.2, 40.8, 51.2, 64.6, 65.6, 68.6, 73.5, 78.7, 82.9, 112.7, 127.4, 142.9, 204.4. ESIMS (MeOH): 429.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{22}H_{34}O_5NaSi$ *m*/*z* 429.2073, found: 429.2071.

Compound **34b**: Colourless oil. $[\alpha]_D^{20} = +129$ (*c* 1.11, $CHCl_3$). IR (film): $\nu = 3482, 2951, 2928, 2886, 2856, 1732, 1471, 1360, 1255, 1109, 1081, 1061, 1011, 950, 833, 774\ cm^{-1}$. ^1H NMR (500 MHz): $\delta = -0.02$ (s, 3H), 0.05 (s, 3H), 0.83 (s, 9H), 1.33 (s, 3H), 1.54 (dt, $J = 3.2$, 13.3 Hz, 1H), 1.74 (ddd, $J = 3.1$, 6.3, 13.7 Hz, 1H), 1.84 (s, 3H), 1.92 (m, 1H), 2.15 (dd, $J = 3.8$, 13.6 Hz, 1H), 2.19 (d, $J = 11.6$ Hz, 1H), 3.59 (d, $J = 11.6$ Hz, 1H), 3.97 (m, 5H), 4.22 (t, $J = 2.4$ Hz, 1H), 5.62 (s, 1H). ^{13}C NMR (125 MHz): $\delta = -5.2$, −4.4, 4.0, 17.9, 24.5, 24.8, 25.7 (3C), 30.9, 41.7, 50.9, 65.3, 64.9, 69.6, 71.6, 78.1, 83.0, 111.7, 128.2, 143.7, 206.6. ESIMS (MeOH): 429.2 ($[M+Na]^+$, 100), 835.5 ($[2M+Na]^+$, 15). HRESIMS: calcd for $C_{22}H_{34}O_5NaSi$ *m*/*z* 429.2073, found: 429.2103.

Nucleophilic addition was carried out on **34** (30 mg, 0.07 mmol) with allylmagnesium bromide (1.0 M in THF, 0.6 mL, 0.59 mmol) in dry THF (1 mL) for 3 h using the general procedure to give after chromatography (heptane/EtOAc, 5:1) **35** (28 mg, 86%).

4.5.3.4. 7-Allyl-4-(*tert*-butyl-dimethyl-silanyloxy)-6,7-dihydroxy-8a-methyl-6-prop-1-ynyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 35. Yellow oil. $[\alpha]_D^{20} = -84$ (*c* 1.48, $CHCl_3$). IR (film): $\nu = 3378, 2953, 2926, 2891, 2855, 1360, 1253, 1201, 1108, 1069, 1011, 910, 834, 774\ cm^{-1}$.

^{1}H NMR (500 MHz): $\delta = 0.06$ (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 1.39 (s, 3H), 1.53 (dt, $J = 3.4$, 13.6 Hz, 1H), 1.58 (d, $J = 16.1$ Hz, 1H), 1.73 (m, 2H), 1.83 (s, 3H), 2.17 (dd, $J = 11.8$, 13.5 Hz, 1H), 2.21 (d, $J = 16.1$ Hz, 1H), 2.38 (dd, $J = 8.7$, 14.2 Hz, 1H), 2.73 (ddt, $J = 1.7$, 5.7, 14.3 Hz, 1H), 3.97 (m, 2H), 4.07 (m, 2H), 4.22 (t, $J = 2.6$ Hz, 1H), 5.10 (m, 2H), 5.59 (s, 1H), 5.94 (dddd, $J = 5.7$, 8.7, 10.2, 17.0 Hz, 1H). ^{13}C NMR (125 MHz): $\delta = -5.2$, -4.3, 3.7, 18.0, 25.4, 25.8 (3C), 28.7, 31.7, 38.4, 40.2, 43.4, 64.8 (2C), 70.6, 73.1 (2C), 78.6, 82.9, 113.1, 117.3, 131.9, 134.9, 140.0. ESIMS (MeOH): 471.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{25}H_{40}O_5NaSi$ m/z 471.2543, found: 471.2557.

Oxidative cleavage of **35** (diastereomeric mixture) was achieved using the general procedures affording **72** (12 mg, 86%, Table 1, entry 19) after SiO_2 flash column chromatography (heptane/EtOAc, 4:1 as eluent).

4.5.3.5. 8-Allyl-2-(*tert*-butyl-dimethyl-silanyloxy)-6-methyl-10-prop-1-ynyl-9,12-dioxa-tricyclo[6.3.1.0^{0,0}]dodec-10-en-5-one 72. Colourless oil. $[\alpha]_D^{20} = -17$ (c 1.29, $CHCl_3$). IR (film): $\nu = 2954$, 2929, 2883, 2856, 1623, 1462, 1435, 1362, 1313, 1255, 1221, 1116, 1086, 1076, 1034, 984, 953, 912, 834, 784, 772, 692 cm^{-1}. ^{1}H NMR (500 MHz): $\delta = 0.07$ (s, 3H), 0.11 (s, 3H), 0.92 (s, 9H), 1.31 (s, 3H), 1.41 (dt, $J = 3.4$, 13.0 Hz, 1H), 1.58 (ddd, $J = 13.9$, 6.5, 3.2 Hz, 1H), 1.77 (d, $J = 13.8$ Hz, 1H), 1.92 (td, $J = 3.0$, 13.8 Hz, 1H), 1.96 (s, 3H), 2.07 (tt, $J = 2.8$, 13.9 Hz, 1H), 2.27 (d, $J = 13.8$ Hz, 1H), 2.60 (ddt, $J = 2.2$, 7.9, 14.2 Hz, 1H), 2.67 (ddt, $J = 1.7$, 6.3, 14.2 Hz, 1H), 3.89 (m, 4H), 3.99 (m, 1H), 5.12 (m, 2H), 5.58 (s, 1H), 5.96 (dddd, $J = 6.2$, 7.9, 10.2, 17.2 Hz, 1H). ^{13}C NMR (125 MHz): $\delta = -5.2$, -4.7, 4.0, 17.8, 17.9, 23.6, 25.6 (3C), 26.6, 40.5, 46.3, 58.1, 63.0, 64.8, 68.1, 74.5, 84.7, 85.6, 108.1, 111.56 (2C), 117.6, 132.7, 134.6. ESIMS (MeOH): 469.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{25}H_{38}O_5NaSi$ m/z 469.2386, found: 469.2369.

4.5.4. Preparation of target diols 37 and 5. Nucleophilic addition was carried out on **26b** (6.00 g, 14.61 mmol) with (19.20 g, 52.61 mmol) and n-BuLi (1.6 M in hexane, 32.0 mL, 51.14 mmol), in dry THF (100 mL) for 1 h using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 3:2 to EtOAc) **29a** (5.81 g, 90%). An analytical sample was purified on SiO_2 flash chromatography, eluent heptane/EtOAc, 3:2, for characterization purposes.

4.5.4.1. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6,7-dihydroxy-6-methoxymethoxymethyl-8a-methyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 29a. White solid. Mp: 73–75 °C. $[\alpha]_D^{20} = -10$ (c 1.59, $CHCl_3$). IR (film): $\nu = 3422$, 2928, 2883, 2856, 1470, 1403, 1360, 1252, 1204, 1148, 1116, 1071, 1045, 1013, 947, 915, 835, 774 cm^{-1}. ^{1}H NMR (800 MHz): $\delta = 0.00$ (s, 3H), 0.05 (s, 3H), 0.86 (s, 9H), 1.42 (s, 3H), 1.53 (m, 2H), 1.62 (br s, 1H), 1.69 (ddt, $J = 2.7$, 4.1, 13.7 Hz, 1H), 1.79 (tdd, $J = 3.3$, 4.1, 13.8 Hz, 1H), 2.17 (dd, $J = 6.3$, 8.0 Hz, 1H), 2.21 (m, 1H), 3.19 (br s, 1H), 3.38 (s, 3H), 3.53 and 3.57 (ABquartet, $J = 10.2$ Hz, 2H), 3.83 (br s, 1H), 3.99 (m, 4H), 4.18 (t, $J = 2.8$ Hz, 1H), 4.67 (s, 2H), 5.49 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.2$, -4.6, 17.8, 24.9, 25.6 (3C), 26.7, 31.3, 33.7, 44.1, 55.3, 64.7, 64.8, 67.8, 70.9, 72.7, 73.2, 96.9, 112.4, 127.2, 145.5. ESIMS (MeOH): 467.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{22}H_{40}O_7NaSi$ m/z 467.2441, found: 467.2441. Anal. Calcd for $C_{22}H_{40}O_7Si$ (444.63): C 59.43, H 9.07. Found: C 59.33, H 9.03.

A mixture of PPTS (91 mg, 0.36 mmol) and **29a** (800 mg, 1.80 mmol) in acetone containing 10% of water was refluxed for 21 h. After evaporation, the residue was diluted with water and EtOAc. The aqueous phase was extracted with EtOAc. The combined organic fractions were worked up as usual to afford after chromatography on SiO_2 (heptane/EtOAc, 4:1 to 1:2) **29b** (458 mg, 64%).

4.5.4.2. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6,7-dihydroxy-6-methoxymethoxymethyl-8a-methyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 29b. Colourless oil. $[\alpha]_D^{20} = -6$ (c 0.5, $CHCl_3$). IR (film): $\nu = 3414$, 2951, 2928, 2885, 2856, 1711, 1659, 1463, 1360, 1252, 1149, 1113, 1042, 992, 832, 774 669 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 0.05$ (s, 3H), 0.10 (s, 3H), 0.89 (s, 9H), 1.48 (s, 3H), 1.94 (m, 4H), 2.22 (dddd, $J = 2.8$, 2.9, 4.3, 14.9 Hz, 1H), 2.65 (d, $J = 6.0$ Hz, 1H), 3.01 (s, 1H), 3.11 (ddd, $J = 5.8$, 6.2, 14.5 Hz, 1H), 3.39 (s, 3H), 3.60 (s, 2H), 3.91 (ddd, $J = 3.8$, 6.0, 12.1 Hz, 1H), 4.36 (dd, $J = 2.8$, 2.9 Hz, 1H), 4.66 and 4.69 (ABquartet, $J = 6.5$ Hz, 2H), 5.54 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.0$, -4.4, 18.1, 25.8 (3C), 27.5, 32.2, 32.6, 35.2, 51.2, 55.6, 68.2, 69.9, 72.6, 74.2, 97.1, 125.9, 146.4, 212.4. ESIMS (MeOH): 424.2 (62), 423.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{20}H_{36}O_6NaSi$ m/z 423.2179, found: 423.2191. Anal. Calcd for $C_{20}H_{36}O_6Si$ (400.58): C 59.97, H 9.06. Found: C 59.75, H 8.85.

Oxidative cleavage of **29b** (diastereomeric mixture) was achieved using the general procedures affording **70** (35 mg, 88%, Table 1, entry 17) after SiO_2 flash column chromatography (heptane/Et_2O, 9:1 as eluent).

4.5.4.3. 2-(*tert*-Butyl-dimethyl-silanyloxy)-10-methoxymethoxymethyl-6-methyl-9,12-dioxa-tricyclo[6.3.1.0^{0,0}]dodec-10-en-5-one 70. Colourless oil. $[\alpha]_D^{20} = -39$ (c 1.50, $CHCl_3$). IR (film): $\nu = 2954$, 2932, 2886, 2857, 1714, 1672, 1472, 1463, 1444, 1371, 1308, 1259, 1197, 1151, 1102, 1084, 1057, 1005, 986, 954, 932, 898, 836 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 0.13$ (s, 3H), 0.15 (s, 3H), 0.95 (s, 9H), 1.36 (s, 3H), 1.76 (dd, $J = 1.1$, 14.2 Hz, 1H), 1.92 (m, 1H), 2.16 (m, 1H), 2.22 (ddd, $J = 2.3$, 3.9, 13.9 Hz, 1H), 2.95 (m, 1H), 3.27 (dd, $J = 5.9$, 14.2 Hz, 1H), 3.38 (s, 3H), 3.92 (dd, $J = 0.5$, 12.9 Hz, 1H), 3.98 (dd, $J = 0.9$, 12.9 Hz, 1H), 4.09 (t, $J = 2.4$ Hz, 1H), 4.66 (s, 2H), 5.40 (s, 1H), 5.59 (dd, $J = 1.1$, 5.9 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = -5.0$, -4.5, 18.0, 19.2, 25.7 (3C), 28.8, 31.8, 43.8, 55.4, 64.6, 66.0, 68.6, 85.2, 95.7, 99.0, 102.4, 148.0, 213.4. ESIMS (MeOH): 461.2 (5), 423.2 (9), 422.2 (71), 421.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{20}H_{34}O_6NaSi$ m/z 421.2022, found: 421.2025. Anal. Calcd for $C_{20}H_{34}O_6Si\cdot 0.3$ heptane (398.57): C 61.93, H 9.12. Found: C 61.81, H 8.71.

Oxidation of **29a** (1.69 g, 3.80 mmol) was carried out with IBX (3.19 g, 11.40 mmol) in DMSO (10 mL) for 30 min using the general procedure to give after chromatography

(SiO_2, heptane/Et_2O, 9:1 to 1:1) **36** (1.69 g, 99%). An analytical sample was purified on SiO_2 flash chromatography, eluent heptane/Et_2O, 9:1 to 1:1, for characterization purposes.

4.5.4.4. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6-hydroxy-6-methoxymethoxymethyl-8a-methyl-2,3,4,6,8,8a-hexahydro-2*H*-naphthalene-1,7-dione 36. Colourless oil. $[\alpha]_D^{20} = -31$ (*c* 0.65, $CHCl_3$). IR (film): $\nu = 3452$, 2956, 2930, 2888, 2857, 1727, 1471, 1460, 1361, 1253, 1217, 1204, 1150, 1114, 1069, 1041, 1010, 948, 935, 917, 836, 774, 677 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.05$ (s, 3H), 0.07 (s, 3H), 0.88 (s, 9H), 1.48 (dt, $J = 3.4$, 13.8 Hz, 1H), 1.51 (s, 3H), 1.74 (m, 2H), 2.12 (dt, $J = 9.3$, 13.5 Hz, 1H), 2.30 (d, $J = 15.1$ Hz, 1H), 2.79 (d, $J = 15.1$ Hz, 1H), 3.33 (s, 3H), 3.63 and 3.71 (ABquartet, $J = 10.4$ Hz, 2H), 3.92 (m, 5H), 4.30 (t, $J = 2.6$ Hz, 1H), 4.59 and 4.63 (ABquartet, $J = 6.6$ Hz, 2H), 5.53 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.0$, -4.5, 18.1, 25.4, 25.8 (3C), 27.2, 32.3, 42.5, 51.3, 55.6, 64.7, 65.6, 73.9 (2C), 75.7, 96.9, 112.8, 125.9, 145.9, 207.7. ESIMS (MeOH): 466.2 (4), 465.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{22}H_{38}O_7NaSi$ *m*/*z* 465.2285, found: 465.2276. Anal. Calcd for $C_{22}H_{38}O_7Si$·0.1 heptane (442.62): C 60.23, H 8.82. Found: C 60.31, H 8.72.

Nucleophilic addition was carried out on **36** (3.84 g, 8.68 mmol) with MeLi (1.6 M in Et_2O, 21.7 mL, 34.72 mmol) in dry THF (70 mL) at -50 °C for 4 h using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 7:3) **37** (2.74 g, 69%) and **36** (720 mg, 19%).

4.5.4.5. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6,7-dihydroxy-6-methoxymethoxymethyl-7,8a-dimethyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 37. Colourless oil. $[\alpha]_D^{20} = -39$ (*c* 1.25, $CHCl_3$). IR (film): $\nu = 3398$, 2934, 2888, 2857, 1462, 1364, 1254, 1204, 1145, 1118, 1070, 1041, 1010, 951, 920, 873, 837, 775, 674 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.01$ (s, 3H), 0.05 (s, 3H), 0.85 (s, 9H), 1.17 (s, 3H), 1.39 (s, 3H), 1.55 (dt, $J = 3.7$, 13.6 Hz, 1H), 1.63 (d, $J = 16.0$ Hz, 1H), 1.72 (td, $J = 2.9$, 5.4 Hz, 1H), 1.79 (dt, $J = 3.7$, 13.6 Hz, 1H), 2.18 (m, 1H), 2.14 (d, $J = 16.0$ Hz, 1H), 3.34 (s, 3H), 3.51 (s, 2H), 3.54 (s, 1H), 4.03 (m, 4H), 4.24 (t, $J = 2.6$ Hz, 1H), 4.59 and 4.61 (ABquartet, $J = 6.5$ Hz, 2H), 5.19 (s, 1H), 5.53 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.1$, -4.6, 18.0, 23.1, 25.1, 25.7 (3C), 29.4, 31.8, 42.0, 43.2, 55.4, 64.5, 64.7, 70.1, 71.9, 73.5, 73.6, 97.1, 113.2, 131.3, 142.0. ESIMS (MeOH): 482.3 (4), 481.3 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{23}H_{42}O_7NaSi$ *m*/*z* 481.2598, found: 481.2598. Anal. Calcd for $C_{23}H_{42}O_7Si$ (458.66): C 60.23, H 9.23. Found: C 60.21, H 9.26.

Oxidative cleavage of **37** (diastereomeric mixture) was achieved using the general procedures affording **73** (9 mg, 82%, Table 1, entry 20) after SiO_2 flash column chromatography (heptane/EtOAc, 4:1 as eluent).

4.5.4.6. 2-(*tert*-Butyl-dimethyl-silanyloxy)-10-methoxy-methoxymethyl-6,8-dimethyl-9,12-dioxa-tricyclo[6.3.1.$0^{0,0}$]-dodec-10-en-5-one 73. Colourless oil. $[\alpha]_D^{20} = -10$ (*c* 0.36, $CHCl_3$). IR (film): $\nu = 2929$, 2883, 2856, 1257, 1203, 1150, 1106, 1078, 1042, 1018, 1002, 983, 918, 831, 801, 771 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.07$ (s, 3H), 0.09 (s, 3H), 0.92 (s, 9H), 1.32 (s, 3H), 1.44 (dt, $J = 2.7$, 6.1 Hz, 1H), 1.58 (s, 3H), 1.59 (m, 2H), 1.84 (d, $J = 13.6$ Hz, 1H), 2.02 (m, 1H), 2.24 (d, $J = 13.6$ Hz, 1H), 3.37 (s, 3H), 3.95 (m, 7H), 4.65 and 4.68 (ABquartet, $J = 6.6$ Hz, 2H), 5.39 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.1$, -4.5, 18.0, 18.2, 22.4, 23.7, 25.7 (3C), 26.9, 48.0, 55.3, 58.6, 63.2, 65.0, 66.4, 68.4, 85.7, 95.6, 104.7, 107.2, 111.9, 148.4. ESIMS (MeOH): 479.5 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{23}H_{40}O_7NaSi$ *m*/*z* 479.2441, found: 479.2437.

A mixture of PPTS (17 mg, 0.07 mmol) and **37** (155 mg, 0.34 mmol) in acetone containing 10% of water was refluxed for 28 h. After evaporation, the residue was diluted with water and EtOAc. The aqueous phase was extracted with EtOAc. The combined organic fractions were worked up as usual to afford after chromatography on SiO_2 (heptane/EtOAc, 4:1 to 1:2) **5** (97 mg, 69%).

4.5.4.7. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6,7-dihydroxy-6-methoxymethyl-7,8a-dimethyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 5. Colourless oil. $[\alpha]_D^{20} = -34$ (*c* 0.40, $CHCl_3$). IR (film): $\nu = 3469$, 2956, 2930, 2888, 2857, 1713, 1664, 1470, 1463, 1361, 1254, 1151, 1116, 1070, 1038, 1005, 995, 906, 876, 836, 776 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.07$ (s, 3H, MeSi), 0.11 (s, 3H, MeSi), 0.90 (s, 9H, *t*-Bu), 1.25 (s, 3H, H10), 1.46 (s, 3H, H9), 1.54 (d, $J = 14.9$ Hz, 1H, H8), 1.99 (m, 2H, H3), 2.24 (dt, $J = 4.6$, 14.7 Hz, 1H, H2), 2.29 (s, 1H, OH), 2.70 (d, $J = 14.9$ Hz, 1H, H8′), 3.01 (ddd, $J = 6.1$, 12.2, 14.7 Hz, 1H, H2′), 3.17 (s, 1H, OH), 3.36 (s, 3H, H13), 3.51 and 3.55 (ABquartet, $J = 10.0$ Hz, 2H, H11), 4.47 (t, $J = 3.6$ Hz, 1H, H4), 4.62 and 4.65 (ABquartet, $J = 6.5$ Hz, 2H, H12), 5.51 (s, 1H, H5). ^{13}C NMR (75 MHz): $\delta = -5.0$, -4.5, 18.1, 23.9, 25.8 (3C), 29.0, 33.5, 34.1, 41.3, 50.5, 55.5, 71.5, 71.6, 73.2, 73.7, 97.1, 129.3, 142.2, 214.2. ESIMS (MeOH): 481.3 (29), 438.2 (10), 437.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{21}H_{38}O_6NaSi$ *m*/*z* 437.2335, found: 437.2356. Anal. Calcd for $C_{21}H_{38}O_6Si$ (414.61): C 60.83, H 9.24. Found: C 60.87, H 9.44.

Oxidative cleavage of **5** (diastereomeric mixture) was achieved using the general procedures affording **74** (1.61 g, 78%, Table 1, entry 21) after SiO_2 flash column chromatography (heptane/Et_2O, 9:1 as eluent).

4.5.4.8. 2-(*tert*-Butyl-dimethyl-silanyloxy)-10-methoxy-methoxymethyl-6,8-dimethyl-9,12-dioxa-tricyclo[6.3.1.$0^{0,0}$]-dodec-10-en-5-one 74. Colourless oil. $[\alpha]_D^{20} = -12$ (*c* 1.55, $CHCl_3$). IR (film): $\nu = 2956$, 2931, 2885, 2856, 1712, 1672, 1461, 1443, 1390, 1360, 1255, 1150, 1115, 1083, 1049, 983, 832, 774, 723 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.12$ (s, 3H), 0.14 (s, 3H), 0.95 (s, 9H), 1.32 (s, 3H), 1.49 (s, 3H), 1.87 (d, $J = 14.0$ Hz, 1H), 1.91 (m, 1H), 2.15 (m, 1H), 2.25 (ddd, $J = 2.3$, 3.9, 14.0 Hz, 1H), 1.91 (m, 1H), 3.05 (d, $J = 13.9$ Hz, 1H), 3.37 (s, 3H), 3.91 (dd, $J = 0.6$, 13.0 Hz, 1H), 3.97 (dd, $J = 0.9$, 3.0 Hz, 1H,), 4.05 (t, $J = 2.2$ Hz, 1H), 4.64 and 4.66 (ABquartet, $J = 6.6$ Hz, 2H), 5.40 (s, 1H). ^{13}C NMR (75 MHz):

$\delta = -5.0, -4.5, 18.0, 19.2, 23.8, 25.8$ (3C), 28.9, 31.8, 47.6, 55.3, 65.3, 66.0, 68.7, 86.7, 95.7, 101.6, 106.0, 149.4, 213.5. ESIMS (MeOH): 453.2 (100), 435.2 ($[M+Na]^+$, 98). HRESIMS: calcd for $C_{21}H_{36}O_6NaSi$ m/z 435.2179, found: 435.2189. Anal. Calcd for $C_{21}H_{36}O_6Si{\cdot}0.2H_2O$ (412.59): C 60.60, H 8.82. Found: C 60.62, H 8.87.

4.5.5. Preparation of target diol 39. Nucleophilic addition was carried out on **26b** (712 mg, 1.73 mmol) with isopropenylmagnesium bromide (0.5 M in THF, 17.3 mL, 8.65 mmol) in dry THF (5 mL) for 2 h using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 6:1) **30** (712 mg, 78%).

4.5.5.1. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6,7-dihydroxy-6-isopropenyl-8a-methyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 30. White solid. Mp: 131–133 °C. $[\alpha]_D^{20} = -19$ (c 0.71, $CHCl_3$). IR (film): $\nu = 3394$, 2929, 2886, 2857, 1471, 1360, 1253, 1202, 1108, 1071, 1004, 948, 910, 835, 756, 668 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.04$ (s, 3H), 0.06 (s, 3H), 0.87 (s, 9H), 1.25 (d, $J = 0.7$ Hz, 1H), 1.39 (s, 3H), 1.54 (dt, $J = 3.8$, 6.0 Hz, 1H), 1.55 (m, 1H), 1.74 (m, 2H), 1.80 (dd, $J = 0.8$, 1.4 Hz, 3H), 2.12 (dd, $J = 5.8$, 15.1 Hz, 1H), 2.21 (td, $J = 4.8$, 13.3 Hz, 1H), 3.39 (br s, 1H), 3.72 (m, 1H), 4.01 (m, 4H), 4.24 (t, $J = 2.6$ Hz, 1H), 4.98 (t, $J = 1.6$ Hz, 1H), 5.05 (dd, $J = 0.9$, 1.9 Hz, 1H), 5.44 (d, $J = 0.7$ Hz, 1H). ^{13}C NMR (75 MHz): $\delta = -5.0, -4.6$, 17.9, 18.4, 25.1, 25.7 (3C), 27.5, 31.6, 33.5, 43.2, 64.7 (2C), 67.6, 73.5, 75.0, 112.6, 114.4, 130.0, 143.3, 146.7. ESIMS (MeOH): ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{22}H_{38}NaO_5Si$ m/z 433.2386, found: 433.2384. Anal. Calcd for $C_{22}H_{38}O_5Si{\cdot}0.2H_2O$ (410.62): C 63.79, H 9.34. Found: C 63.81, H 9.21.

Oxidation of **30** (210 mg, 0.51 mmol) was carried out with IBX (430 mg, 1.53 mmol) in DMSO (3 mL) for 30 min using the general procedure to give after chromatography (SiO_2, heptane/Et_2O, 2:1) **38** (196 mg, 94%). An analytical sample was purified on SiO_2 flash chromatography, eluent heptane/Et_2O, 2:1, for characterization purposes.

4.5.5.2. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6-hydroxy-6-isopropenyl-8a-methyl-2,3,4,6,8,8a-hexahydro-2*H*-naphthalene-1,7-dione 38a. White solid. Mp: 106 °C. $[\alpha]_D^{20} = -131$ (c 1.05, $CHCl_3$). IR (film): $\nu = 3476$, 2955, 2929, 2888, 2857, 1723, 1471, 1370, 1303, 1252, 1125, 1111, 1069, 1011, 938, 911, 835, 774, 681 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.00$ (s, 3H), 0.05 (s, 3H), 0.84 (s, 9H), 1.36 (d, $J = 0.7$ Hz, 3H), 1.52 (dt, $J = 3.3$, 13.2 Hz, 1H), 1.68 (dd, $J = 0.8$, 1.5 Hz, 3H), 1.75 (ddt, $J = 2.8$, 4.1, 13.7, Hz, 1H), 1.86 (tdd, $J = 3.1$, 4.0, 13.6 Hz, 1H), 1.98 (d, $J = 11.6$ Hz, 1H), 2.18 (td, $J = 4.0$, 13.4 Hz, 1H), 3.44 (dd, $J = 0.8$, 11.6 Hz, 1H), 3.92 (m, 5H), 4.30 (t, $J = 2.6$ Hz, 1H), 5.06 (t, $J = 1.2$ Hz, 1H), 5.19 (t, $J = 0.9$ Hz, 1H), 5.51 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.3, -4.5$, 17.4, 17.8, 24.5, 24.9, 25.6 (3C), 31.2, 40.6, 51.1, 64.7, 65.1, 71.8, 79.7, 111.8, 115.8, 128.8, 144.6, 145.9, 211.3. ESIMS (MeOH): 431.1 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{22}H_{36}O_5NaSi$ m/z 431.2230, found: 431.2219. Anal. Calcd for $C_{22}H_{36}O_5Si$ (408.60): C 64.67, H 8.88. Found: C 64.66, H 8.99.

Compound **38b**: Colourless oil. $[\alpha]_D^{20} = -117$ (c 0.67, $CHCl_3$). IR (film): $\nu = 3476$, 2955, 2928, 2888, 2857, 1723, 1471, 1370, 1345, 1303, 1252, 1183, 1125, 1111, 1069, 1011, 938, 911, 835, 774, 681 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.09$ (s, 6H), 0.90 (s, 9H), 1.46 (s, 3H), 1.67 (dd, $J = 0.8$, 1.5 Hz, 3H), 1.73 (m, 3H), 2.12 (m, 1H), 2.36 (d, $J = 14.6$ Hz, 1H), 2.55 (d, $J = 14.6$ Hz, 1H), 3.95 (m, 5H), 4.38 (t, $J = 2.7$ Hz, 1H), 5.09 (t, $J = 1.3$ Hz, 1H), 5.24 (t, $J = 1.0$ Hz, 1H), 5.58 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.2, -4.7$, 17.2, 17.9, 25.4, 25.6 (3C), 26.2, 32.2, 40.1, 51.2, 64.4, 65.5, 73.8, 79.0, 112.7, 115.1, 127.3, 144.2, 146.7, 208.7. ESIMS (MeOH): 431.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{22}H_{36}O_5NaSi$ m/z 431.2230, found: 431.2215. Anal. Calcd for $C_{22}H_{36}O_5Si$ (408.60): C 64.67, H 8.88. Found: C 64.54, H 8.86.

Nucleophilic addition was carried out on **38** (106 mg, 0.26 mmol) with allylmagnesium bromide (1.0 M in Et_2O, 2.1 mL, 2.07 mmol) in dry THF (9 mL) for 1.5 h using the general procedure to give after chromatography (SiO_2, heptane/Et_2O, 5:1) **39** (86 mg, 74%).

4.5.5.3. 7-Allyl-4-(*tert*-Butyl-dimethyl-silanyloxy)-6,7-dihydroxy-6-isopropenyl-8a-methyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 39. White solid. Mp: 112–114 °C. $[\alpha]_D^{20} = +37$ (c 1.26, $CHCl_3$). IR (film): $\nu = 3533$, 2928, 2856, 1461, 1344, 1253, 1221, 1127, 1069, 1036, 1003, 917, 835, 773, 759, 696 cm^{-1}. ^1H NMR (600 MHz): $\delta = 0.03$ (s, 3H), 0.05 (s, 3H), 0.86 (s, 9H), 1.46 (d, $J = 14.4$ Hz, 1H), 1.47 (m, 1H), 1.56 (s, 3H), 1.71 (ddd, $J = 2.7$, 7.0, 13.6 Hz, 1H), 1.78 (tdd, $J = 3.4$, 4.1, 13.7 Hz, 1H), 1.86 (d, $J = 0.6$ Hz, 3H), 2.05 (dd, $J = 6.7$, 13.6 Hz, 1H), 2.16 (d, $J = 12.1$ Hz, 1H), 2.18 (s, 1H), 2.29 (td, $J = 4.2$, 13.5 Hz, 1H), 2.47 (dd, $J = 8.3$, 13.6 Hz, 1H), 3.24 (s, 1H), 3.91 (m, 4H), 4.17 (t, $J = 2.9$ Hz, 1H), 5.04 (t, $J = 1.6$ Hz, 1H), 5.15 (ddd, $J = 1.6$, 3.7, 17.1 Hz, 1H), 5.21 (s, 1H), 5.23 (d, $J = 2.3$ Hz, 1H), 5.30 (d, $J = 1.9$ Hz, 1H), 5.96 (dddd, $J = 6.7$, 8.3, 10.1, 17.0 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = -5.1, -4.2$, 18.0, 21.1, 25.1, 25.8 (3C), 26.3, 31.7, 35.8, 41.8, 43.5, 64.6, 64.9, 73.4, 74.6, 77.3, 113.7, 116.1, 120.1, 130.8, 134.0, 141.0, 146.3. ESIMS (MeOH): 473.3 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{25}H_{42}O_5NaSi$ m/z 473.2643, found: 473.2715. Anal. Calcd for $C_{25}H_{42}O_5Si{\cdot}0.5H_2O$ (450.68): C 65.32, H 9.43. Found: C 65.41, H 9.24.

Oxidative cleavage of **39** (diastereomeric mixture) was achieved using the general procedures affording **75** (30 mg, 83%, Table 1, entry 22) after SiO_2 flash column chromatography (heptane/Et_2O, 5:1 as eluent).

4.5.5.4. 8-Allyl-2-(*tert*-butyl-dimethyl-silanyloxy)-10-isopropenyl-6-methyl-9,12-dioxa-tricyclo[6.3.1.$0^{0.0}$]-dodec-10-en-5-one 75. Yellow oil. $[\alpha]_D^{20} = -6$ (c 1.59, $CHCl_3$). IR (film): $\nu = 3077$, 2955, 2930, 2884, 2858, 1643, 1604, 1442, 1462, 1438, 1350, 1297, 1257, 1204, 1167, 1130, 1104, 1083, 1049, 1003, 961, 899, 837, 773, 756, 696 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.07$ (s, 3H), 0.11 (s, 3H), 0.93 (s, 9H), 1.30 (s, 3H), 1.42 (dt, $J = 3.1$, 12.9 Hz, 1H), 1.60 (m, 1H), 1.66 (d, $J = 13.7$ Hz, 1H), 1.84 (s, 3H), 2.03 (m, 2H), 2.26 (d, $J = 13.7$ Hz, 1H), 2.67 (qdt, $J = 1.3$, 7.9,

13.9 Hz, 2H), 3.92 (m, 4H), 4.01 (dd, $J = 4.3$, 6.8 Hz, 1H), 4.93 (s, 1H), 5.13 (m, 2H), 5.39 (d, $J = 2.0$ Hz, 1H), 5.48 (s, 1H), 5.99 (dddd, $J = 6.3$, 7.9, 10.1, 16.7 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = -7.9$, -6.3, 18.0, 18.4, 18.7, 23.8, 25.7 (3C), 26.9, 41.0, 46.3, 58.1, 63.2, 65.0, 68.6, 85.6, 103.8, 107.3, 111.9, 112.4, 117.6, 133.1, 136.8, 149.2. ESIMS (MeOH): 471.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{25}H_{40}O_5NaSi$ m/z 471.2543, found: 471.2543. Anal. Calcd for $C_{25}H_{40}O_5Si\cdot 0.3$ heptane (448.67): C 67.99, H 9.43. Found: C 67.96, H 9.33.

Fluoride deprotection was carried out on **39** (570 mg, 1.26 mmol) for 22h40 using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 6:1) **48** (358 mg, 84%).

4.5.5.5. 7-Allyl-4,6,7-trihydroxy-6-isopropenyl-8a-methyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 48. Characterized as a diastereomeric mixture, white solid. Mp: 122–124 °C. IR (film): $\nu = 3349$, 2971, 2930, 2892, 1434, 1365, 1335, 1206, 1137, 1102, 1064, 1019, 963, 910, 752 cm^{-1}. ESIMS (MeOH): 359.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{19}H_{28}O_5Na$ m/z 359.1834, found 359.1811. Anal. Calcd for $C_{19}H_{28}O_5$ (336.42): C 67.83, H 8.39. Found: C 67.99, H 8.75.

To a stirred solution of **48** (49 mg, 0.14 mmol) and fumaric acid monoester (54 mg, 0.38 mmol) in dry DCM (1 mL), under argon, at 0 °C, were added DCC (78 mg, 0.38 mmol) and DMAP (14 mg, 0.12 mmol). The reaction mixture was stirred at room temperature for 19 h. DCM was added and the reaction mixture was filtered. The organic layer was washed with aqueous AcOH (5%), then usual workup and chromatography on SiO_2 gave (heptane/EtOAc, 6:1) **49** (2.18 g, 95%).

4.5.5.6. But-2-enedioic acid 6-allyl-6,7-dihydroxy-7-isopropenyl-4a-methyl-4-oxo-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-yl ester ethyl ester 49. A major component (unidentified) of a diastereomeric mixture after chromatography is described; yellow oil. IR (film): $\nu = 3483$, 3345, 2977, 2896, 1715, 1639, 1435, 1367, 1292, 1256, 1150, 1104, 1064, 1022, 976, 910, 754 cm^{-1}. ^{1}H NMR (500 MHz): $\delta = 1.32$ (t, $J = 7.1$ Hz, 3H), 1.36 (s, 3H), 1.45 (d, $J = 16.3$ Hz, 1H), 1.67 (ddd, $J = 2.7$, 4.2, 13.9 Hz, 1H), 1.83 (m, 1H), 1.83 (s, 3H), 1.92 (m, 1H), 1.99 (ddt, $J = 2.5$, 4.7, 14.5 Hz, 1H), 2.13 (td, $J = 13.9$, 4.5 Hz, 1H), 2.24 (d, $J = 16.4$ Hz, 1H), 2.60 (ddt, $J = 1.8$, 5.3, 14.0 Hz, 1H), 4.05 (m, 4H), 4.26 (qd, $J = 1.4$, 7.4 Hz, 2H), 5.08 (m, 5H), 5.44 (t, $J = 2.6$ Hz, 1H), 5.51 (s, 1H), 5.71 (s, 1H), 5.92 (dddd, $J = 5.7$, 10.7, 14.2, 15.3 Hz, 1H), 6.80 and 6.83 (ABquartet, $J = 15.9$ Hz, 2H). ^{13}C NMR (125 MHz): $\delta = 14.1$, 21.1, 26.1, 28.0, 28.1, 37.1, 40.5, 42.6, 61.4, 64.9 (2C), 72.6, 76.2, 77.7, 112.4, 115.8, 117.4, 133.7, 133.9, 134.7, 134.8, 138.2, 144.9, 163.9, 165.0. ESIMS (MeOH): 485.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{25}H_{34}O_8Na$ m/z 485.2151, found 485.2131.

Oxidative cleavage of **49** (diastereomeric mixture) was achieved using the general procedures affording **81** (27 mg, 84%, Table 1, entry 28) after SiO_2 flash column chromatography (heptane/EtOAc, 5:1 as eluent).

4.5.5.7. But-2-enedioic acid 8-allyl-10-isopropenyl-6-methyl-5-oxo-9,12-dioxa-tricyclo[6.3.1.0^{0,0}]dodec-10-en-5-one 81. Colourless oil. $[\alpha]_D^{20} = -33$ (c 1.17, $CHCl_3$). IR (film): $\nu = 2956$, 2925, 1722, 1644, 1603, 1440, 1293, 1257, 1151, 1132, 1046, 975, 904, 800 cm^{-1}. ^{1}H NMR (500 MHz): $\delta = 1.33$ (t, $J = 5.9$ Hz, 3H), 1.35 (s, 3H), 1.52 (dt, $J = 3.0$, 13.5 Hz, 1H), 1.72 (d, $J = 13.8$ Hz, 1H), 1.76 (dd, $J = 2.2$, 12.9 Hz, 1H), 1.80 (s, 3H), 1.85 (ddd, $J = 3.1$, 3.2, 14.8 Hz, 1H), 2.21 (tt, $J = 3.0$, 14.5 Hz, 1H), 2.32 (d, $J = 13.7$ Hz, 1H), 2.64 (dd, $J = 8.0$, 14.0 Hz, 1H), 2.73 (dd, $J = 6.2$, 14.0 Hz, 1H), 3.97 (m, 4H), 4.28 (qd, $J = 1.5$, 7.1 Hz, 2H), 4.95 (s, 1H), 5.07 (s, 1H), 5.12 (dd, $J = 2.2$, 10.2, 1H), 5.16 (dd, $J = 2.0$, 17.2 Hz, 1H), 5.20 (t, $J = 2.7$, 1H), 5.41 (s, 1H), 5.98 (m, 1H), 6.87 and 6.91 (ABquartet, $J = 15.8$ Hz, 2H). ^{13}C NMR (125 MHz): $\delta = 14.1$, 18.0, 18.6, 23.8, 24.3, 40.8, 46.2, 58.3, 61.5, 63.3, 65.2, 71.6, 83.9, 101.0, 107.6, 111.2, 113.2, 117.9, 132.8, 133.3, 134.3, 136.5, 150.1, 163.7, 164.9. ESIMS (MeOH): 483.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{25}H_{32}O_8Na$ m/z 483.1995, found: 483.1952.

4.5.6. Preparation of target diols 41, 43, 44 and 45. Nucleophilic addition was carried out on **26b** (731 mg, 1.78 mmol) with MeLi (2.2 M in Et_2O, 4.1 mL, 8.9 mmol) in dry THF (12 mL) for 1 h using the general procedure to give after chromatography (SiO_2, DCM/acetone, 9:1) **31** (685 mg, 99%). An analytical sample was purified on SiO_2 flash chromatography, eluent DCM/acetone, 9:1, for characterization purposes.

4.5.6.1. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6,7-dihydroxy-6,8a-dimethyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 31a. Colourless oil. $[\alpha]_D^{20} = -34$ (c 1.05, $CHCl_3$). IR (film): $\nu = 3489$, 2961, 2856, 1720, 1650, 1464, 1361, 1255, 1206, 1139, 1104, 1067, 1005, 951, 836, 775, 755 cm^{-1}. ^{1}H NMR (800 MHz): $\delta = 0.03$ (s, 3H), 0.06 (s, 3H), 0.86 (s, 9H), 1.29 (s, 3H), 1.36 (dd, $J = 10.0$, 14.2 Hz, 1H), 1.41 (s, 3H), 1.48 (ddd, $J = 2.5$, 4.4, 13.5 Hz, 1H), 1.68 (m, 2H), 1.84 (br s, 1H), 1.99 (br s, 1H), 2.13 (dd, $J = 4.3$, 14.2 Hz, 1H), 2.17 (td, $J = 4.6$, 13.6 Hz, 1H), 3.75 (dd, $J = 3.9$, 9.7 Hz, 1H), 3.91 (m, 1H), 3.95 (m, 1H), 4.01 (m, 2H), 4.17 (t, $J = 2.9$ Hz, 1H), 5.50 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.3$, -4.6, 17.8, 25.3, 25.6 (3C), 26.2, 28.6, 31.9, 35.4, 44.6, 64.5, 64.9, 69.1, 71.9, 73.6, 113.4, 129.3, 145.0. ESIMS (MeOH): 407.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{20}H_{36}O_5NaSi$ m/z 407.2230, found: 407.2244.

Compound **31b**: White solid. Mp: 36–37 °C. $[\alpha]_D^{20} = -5$ (c 1.02, $CHCl_3$). IR (film): $\nu = 3306$, 2926, 2856, 1470, 1360, 1353, 1250, 1203, 1139, 1070, 1032, 1009, 947, 915, 865, 832, 772 748 cm^{-1}. ^{1}H NMR (800 MHz): $\delta = 0.01$ (s, 3H), 0.06 (s, 3H), 0.86 (s, 9H), 1.24 (s, 3H), 1.40 (s, 3H), 1.54 (ddd, $J = 2.5$, 4.3, 13.6 Hz, 1H), 1.58 (dd, $J = 3.6$, 15.3 Hz, 1H), 1.70 (ddt, $J = 2.7$, 4.6, 13.6 Hz, 1H), 1.76 (dddd, $J = 3.1$, 4.1, 13.6, 13.6 Hz, 1H), 2.17 (dd, $J = 5.5$, 15.3 Hz, 1H), 2.18 (ddd, $J = 5.1$, 12.1, 15.3 Hz, 1H), 3.11 (br s, 1H), 3.52 (dddd, $J = 1.4$, 3.6, 5.3, 9.1 Hz, 1H), 4.01 (m, 5H), 4.18 (t, $J = 2.8$ Hz, 1H), 5.53 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.1$, -4.3, 18.0, 25.0, 25.2, 25.8 (3C), 28.3, 31.7, 34.6, 43.2, 64.7, 64.8, 69.8, 71.3, 73.5, 112.6, 132.3, 141.7. ESIMS (MeOH): 407.2 ([M+Na]$^+$, 100).

HRESIMS: calcd for $C_{20}H_{36}O_5NaSi$ *m/z* 407.2230, found: 407.2234. Anal. Calcd for $C_{20}H_{36}O_5Si$ (384.58): C 62.46; H 9.44. Found: C 62.51, H 9.41.

Compound **31c**: White solid. Mp: 70–71 °C. $[\alpha]_D^{20} = -38$ (*c* 1.05, $CHCl_3$). IR (film): $\nu = 3489$, 2960, 2926, 2854, 1462, 1448, 1360, 1254, 1205, 1137, 1103, 1065, 1052, 1038, 1003, 950, 931, 918, 833, 773 cm^{-1}. ^1H NMR (800 MHz): $\delta = 0.02$ (s, 3H), 0.05 (s, 3H), 0.87 (s, 9H), 1.16 (dd, $J = 11.5$, 14.2 Hz, 1H), 1.23 (s, 3H), 1.36 (s, 3H), 1.49 (ddd, $J = 4.1$, 7.7, 10.2 Hz, 1H), 1.69 (m, 2H), 1.92 (br s, 2H), 2.13 (ddd, $J = 7.2$, 11.0, 13.6 Hz, 1H), 2.19 (dd, $J = 5.0$, 14.3 Hz, 1H), 3.89 (dd, $J = 5.0$, 11.5 Hz, 1H), 3.93 (m, 1H), 4.02 (m, 3H), 4.18 (t, $J = 2.8$ Hz, 1H), 5.53 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.1$, −4.4, 18.0, 21.1, 25.2, 25.8 (3C), 28.5, 32.1, 36.3, 45.0, 64.6, 65.0, 72.6, 73.6, 74.1, 113.5, 131.8, 142.3. ESIMS (MeOH): 407.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{20}H_{36}O_5NaSi$ *m/z* 407.2230, found: 407.2213. Anal. Calcd for $C_{20}H_{36}O_5Si$ (384.58): C 62.46, H 9.94. Found: C 62.21, H 9.34.

Oxidation of **31** (163 mg, 0.42 mmol) was carried out with IBX (353 mg, 1.26 mmol) in DMSO (2 mL) for 30 min using the general procedure to give after chromatography (SiO_2, heptane/Et_2O, 1:1) **40** (152 mg, 93%). An analytical sample was purified on SiO_2 flash chromatography, eluent heptane/Et_2O, 1:1, for characterization purposes.

4.5.6.2. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6-hydroxy-6,8a-dimethyl-2,3,4,6,8,8a-hexahydro-naphthalene-1,7-dione 40a. White solid. Mp: 70–71 °C. $[\alpha]_D^{20} = +43$ (*c* 1.03, $CHCl_3$). IR (film): $\nu = 3493$, 2954, 2928, 2886, 2856, 1722, 1471, 1359, 1254, 1138, 1072, 1013, 835, 774 cm^{-1}. ^1H NMR (300 MHz): $\delta = -0.01$ (s, 3H), 0.05 (s, 3H), 0.84 (s, 9H), 1.36 (s, 3H), 1.44 (s, 3H), 1.53 (dt, $J = 3.3$, 13.3 Hz, 1H), 1.73 (ddt, $J = 2.8$, 4.3, 13.7 Hz, 1H), 1.85 (tdd, $J = 3.0$, 4.0, 13.5 Hz, 1H), 2.14 (d, $J = 12.2$ Hz, 1H), 2.18 (td, $J = 4.3$, 13.4 Hz, 1H), 3.31 (d, $J = 12.2$, 0.8 Hz, 1H), 3.53 (br s, 1H), 3.93 (m, 2H), 4.01 (m, 2H), 4.20 (t, $J = 2.7$ Hz, 1H), 5.56 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.2$, −4.3, 17.9, 24.4, 25.2, 25.7 (3C), 28.5, 31.1, 42.2, 51.1, 64.8, 65.2, 71.9, 74.0, 111.8, 131.1, 142.6, 213.4. ESIMS (MeOH): 405.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{20}H_{34}O_5SiNa$ *m/z* 405.2073, found: 405.2055. Anal. Calcd for $C_{20}H_{34}O_5Si$ (382.57): C 62.79, H 8.96. Found: C 62.78, H 8.89.

Compound **40b**: White solid. Mp: 72–73 °C. $[\alpha]_D^{20} = -14$ (*c* 1.16, $CHCl_3$). IR (film): $\nu = 3421$, 2954, 2928, 2886, 2856, 1724, 1471, 1361, 1252, 1072, 1010, 835, 773 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.06$ (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 1.44 (s, 3H), 1.48 (dd, $J = 3$;4, 13.5 Hz, 1H), 1.49 (s, 3H), 1.73 (m, 2H), 2.12 (dt, $J = 9.3$, 13.6 Hz, 1H), 2.26 (d, $J = 15.0$ Hz, 1H), 2.78 (d, $J = 15.0$ Hz, 1H), 3.42 (br s, 1H), 3.88 (m, 2H), 4.04 (m, 2H), 4.28 (t, $J = 2.8$ Hz, 1H), 5.63 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.1$, −4.5, 18.0, 25.4, 25.8 (3C), 26.9, 28.5, 32.3, 41.9, 50.9, 64.7, 65.5, 72.7, 73.7, 112.7, 129.9, 142.7, 210.7. ESIMS (MeOH): 405.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{20}H_{34}O_5NaSi$ *m/z* 405.2073, found: 405.2062. Anal. Calcd for $C_{20}H_{34}O_5Si{\cdot}0.7H_2O$ (382.57): C 60.79, H 9.03. Found: C 60.81, H 8.97.

Nucleophilic addition was carried out on **40** (50 mg, 0.19 mmol) with Tin-MOM acetal (209 mg, 0.57 mmol) and *n*-BuLi (1.6 M in hexane, 0.3 mL, 0.48 mmol), in dry THF (1 mL) for 7 h at 0 °C using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 10:1) **41** (38 mg, 52%), **42** (6 mg, 10%) and SM (23 mg, 37%).

4.5.6.3. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6,7-dihydroxy-7-methoxymethoxymethyl-6,8a-dimethyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 41. Characterized as a diastereomeric mixture, yellow oil. IR (film): $\nu = 3406$, 2927, 2855, 1462, 1360, 1253, 1200, 1147, 1115, 1076, 1039, 1012, 835, 774 cm^{-1}. ESIMS (MeOH): 481.3 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{23}H_{42}O_7NaSi$ *m/z* 481.2598, found 481.2609. Anal. Calcd for $C_{23}H_{42}O_7Si{\cdot}0.1$ heptane (458.66): C 60.74, H 9.38. Found: C 60.85, H 9.25.

4.5.6.4. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6-hydroxy-6,8a-dimethyl-8-methylene-2,3,4,6,8,8a-hexahydro-naphthalene-1,7-dione 42. White solid. Mp: 37–38 °C. $[\alpha]_D^{20} = -80$ (*c* 1.02, $CHCl_3$). IR (film): $\nu = 3497$, 2956, 2928, 2893, 2857, 1703, 1609, 1471, 1360, 1252, 1084, 1041, 1010, 948, 907, 836, 773, 678 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.06$ (s, 3H), 0.09 (s, 3H), 0.89 (s, 9H), 1.35 (s, 3H), 1.39 (dt, $J = 3.4$, 13.5 Hz, 1H), 1.69 (s, 3H), 1.75 (m, 1H), 1.81 (tdd, $J = 3.1$, 4.3, 13.7 Hz, 1H), 2.19 (td, $J = 5.1$, 13.4 Hz, 1H), 3.60 (br s, 1H), 3.77 (m, 2H), 3.92 (m, 2H), 4.28 (t, $J = 2.8$ Hz, 1H), 5.66 (d, $J = 1.5$ Hz, 1H), 5.78 (s, 1H), 5.96 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.1$, −4.4, 18.0, 24.3, 25.8 (3C), 26.5, 29.4, 31.8, 52.2, 65.3, 65.8, 72.7, 73.8, 113.2, 123.6, 130.3, 140.2, 147.4, 204.0. ESIMS (MeOH): 417.1 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{21}H_{34}O_5NaSi$ *m/z* 417.2073, found: 417.2047. Anal. Calcd for $C_{21}H_{34}O_5Si$ (394.58): C 63.92, H 8.68. Found: C 64.08, H 8.57.

Oxidative cleavage of **41** (diastereomeric mixture) was achieved using the general procedures affording **76** (15 mg, 73%, Table 1, entry 23) after SiO_2 flash column chromatography (heptane/EtOAc, 4:1 as eluent).

4.5.6.5. 2-(*tert*-Butyl-dimethyl-silanyloxy)-8-methoxymethoxymethyl-6,10-dimethyl-9,12-dioxa-tricyclo[6.3.1.$0^{0,0}$]-dodec-10-en-5-one 76. Yellow oil. $[\alpha]_D^{20} = -3$ (*c* 0.73, $CHCl_3$). IR (film): $\nu = 2954$, 2930, 2884, 2856, 1666, 1462, 1439, 1360, 1256, 1208, 1079, 1052, 945, 835, 777 cm^{-1}. ^1H NMR (500 MHz): $\delta = 0.06$ (s, 3H), 0.09 (s, 3H), 0.91 (s, 9H), 1.32 (s, 3H), 1.36 (dt, $J = 3.8$, 13.7 Hz, 1H), 1.55 (ddd, $J = 3.1$ 6.5, 9.2 Hz, 1H), 1.69 (d, $J = 13.8$ Hz, 1H), 1.77 (s, 3H), 1.93 (dt, $J = 2.9$, 13.5 Hz, 1H), 2.07 (tt, $J = 2.6$, 13.9 Hz, 1H), 2.28 (d, $J = 13.6$ Hz, 1H), 3.40 (s, 3H), 3.78 and 3.81 (ABquartet, $J = 10.5$ Hz, 2H), 3.94 (m, 5H), 4.71 and 4.73 (ABquartet, $J = 6.5$ Hz, 2H), 5.09 (d, $J = 1.21$ Hz, 1H). ^{13}C NMR (125 MHz): $\delta = -5.0$, −4.5, 18.1 (2C), 19.4, 23.7, 25.8 (3C), 26.8, 45.3, 55.2, 58.0, 63.3, 65.0, 68.4, 68.6, 85.6, 96.7, 102.1, 106.5, 111.9, 148.6. ESIMS (MeOH): 479.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{23}H_{40}O_7NaSi$ *m/z* 479.2441, found: 479.2444.

Diol **43** was obtained in 65% yield from its corresponding enone **42** by a Luche reduction ($NaBH_4$–$CeCl_3$, 0 °C,

30 min) and used as a crude diastereomeric mixture for the oxidative cleavage.

$CeCl_3{\cdot}7H_2O$ (24 mg, 0.06 mmol) was added to a solution of **42** (23 mg, 0.06 mmol) in DCM (1 mL) and EtOH (1 mL) at 0 °C. After 5 min, $NaBH_4$ (2 mg, 0.06 mmol) was added, the mixture was stirred for 15 min at 0 °C and then quenched by careful addition of brine followed by dilution with Et_2O. After being allowed to warm to room temperature, the organic layer was separated and the aqueous layer was extracted with Et_2O. The combined organic fractions were worked up as usual to afford after chromatography (SiO_2, heptane/EtOAc, 1:1) **43** (15 mg, 65%).

4.5.6.6. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6,7-dihydroxy-6,8a-dimethyl-8-methylene-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 43. Colourless oil. $[\alpha]_D^{20} = -41$ (*c* 0.61, $CHCl_3$). IR (film): $\nu = 3504$, 2952, 2926, 2890, 2852, 1701, 1613, 1469, 1462, 1359, 1249, 1201, 1172, 1107, 1079, 1041, 1014, 1004, 948, 920, 907, 851, 833, 811, 771, 698, 679 cm^{-1}. ^1H NMR (800 MHz): $\delta = 0.02$ (s, 3H), 0.07 (s, 3H), 0.87 (s, 9H), 1.09 (s, 3H), 1.42 (dddd, $J = 0.5$, 2.7, 4.1, 13.5 Hz, 1H), 1.57 (s, 3H), 1.72 (ddt, $J = 2.7$, 4.2, 13.7 Hz, 1H), 1.80 (tdd, $J = 3.2$, 4.3, 13.9 Hz, 1H), 2.01 (br s, 1H), 2.07 (br s, 1H), 2.22 (td, $J = 4.1$, 13.8 Hz, 1H), 3.81 (m, 2H), 3.92 (m, 2H), 4.24 (t, $J = 3.0$ Hz, 1H), 4.35 (t, $J = 2.3$ Hz, 1H), 5.33 (dd, $J = 1.3$, 2.3 Hz, 1H), 5.44 (dd, $J = 1.2$, 2.3 Hz, 1H), 5.69 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.1$, −4.4, 18.0, 21.3, 25.0, 25.8 (3C), 27.2, 31.8, 49.9, 65.1, 65.7, 72.7, 73.4, 77.8, 110.9, 113.2, 132.7, 140.7, 148.9. ESIMS (MeOH): 419.5 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{21}H_{36}O_5NaSi$ *m*/*z* 419.2230, found: 419.2226.

Oxidative cleavage of **43** (diastereomeric mixture) was achieved using the general procedures affording **77** (12 mg, 99%, Table 1, entry 24) after SiO_2 flash column chromatography (heptane/EtOAc, 2:1 as eluent).

4.5.6.7. 2-(*tert*-Butyl-dimethyl-silanyloxy)-6,10-dimethyl-7-methylene-9,12-dioxa-tricyclo-[6.3.1.$0^{0,0}$]dodec-10-en-5-one 77. White solid. Mp: 129–130 °C. $[\alpha]_D^{20} = -40$ (*c* 1.08, $CHCl_3$). IR (film): $\nu = 2952$, 2927, 2883, 2854, 1662, 1470, 1461, 1366, 1283, 1253, 1199, 1082, 1021, 1001, 974, 951, 927, 905, 831, 812, 771, 722, 672 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.08$ (s, 3H), 0.10 (s, 3H), 0.92 (s, 9H), 1.34 (s, 3H), 1.39 (m, 1H), 1.63 (ddd, $J = 2.8$, 5.8, 12.9 Hz, 1H), 1.71 (d, $J = 0.9$ Hz, 3H), 2.06 (m, 2H), 3.82 (m, 5H), 5.04 (d, $J = 0.9$ Hz, 1H), 5.09 (d, $J = 1.3$ Hz, 1H), 5.32 (d, $J = 0.8$ Hz, 1H), 5.77 (t, $J = 1.2$ Hz, 1H). ^{13}C NMR (75 MHz): $\delta = -5.1$, −4.5, 16.4, 18.0, 19.4, 25.4, 25.7 (3C), 26.9, 60.5, 63.9, 65.7, 68.6, 85.0, 99.8, 102.7, 109.4, 111.7, 148.5, 156.7. ESIMS (MeOH): 417.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{21}H_{34}O_5NaSi$ *m*/*z* 417.2073, found: 417.2063. Anal. Calcd for $C_{21}H_{34}O_5Si$ (394.58): C 63.92, H 8.69. Found: C 64.15, H 8.89.

Starting from **40**, the target bis-tertiary diol **44** was synthesized analogously. Nucleophilic addition was carried out on **40** (151 mg, 0.39 mmol) with isopropenylmagnesium bromide (0.5 M in THF, 3.9 mL, 1.97 mmol) in dry THF (4 mL) at −78 °C for 2 h, then for 3.5 h at 0 °C using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 6:1) **44** (52 mg, 30%) and SM (92 mg, 61%).

4.5.6.8. 4-(*tert*-Butyl-dimethyl-silanyloxy)-6,7-dihydroxy-7-isopropenyl-6,8a-dimethyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 44. Colourless oil. $[\alpha]_D^{20} = -30$ (*c* 0.86, $CHCl_3$). IR (film): $\nu = 3380$, 2952, 2928, 2891, 2856, 1636, 1470, 1462, 1433, 1360, 1251, 1200, 1097, 1074, 1009, 909, 834, 773 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.03$ (s, 3H), 0.06 (s, 3H), 0.87 (s, 9H), 1.13 (d, $J = 0.9$ Hz, 3H), 1.43 (s, 3H), 1.56 (dt, $J = 0.9$, 13.4 Hz, 1H), 1.73 (m, 2H), 1.86 (d, $J = 16.0$ Hz, 1H), 1.95 (dd, $J = 0.7$, 1.5 Hz, 3H), 2.15 (ddd, $J = 5.7$, 12.3, 13.5 Hz, 1H), 2.17 (d, $J = 16.0$ Hz, 1H), 3.45 (d, $J = 0.8$ Hz, 1H), 4.02 (m, 4H), 4.23 (t, $J = 2.7$ Hz, 1H), 4.89 (dd, $J = 0.8$, 1.4 Hz, 1H), 4.98 (t, $J = 1.4$ Hz, 1H), 5.37 (s, 1H), 5.50 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.1$, −4.3, 18.0, 21.9, 23.8, 25.1, 25.8 (3C), 30.3, 31.8, 38.8, 43.2, 64.5, 64.6, 73.1, 73.2, 74.4, 112.2, 113.0, 135.2, 136.6, 148.3. ESIMS (MeOH): 447.3 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{23}H_{40}O_5NaSi$ *m*/*z* 447.2543, found: 447.2557.

Oxidative cleavage of **44** (diastereomeric mixture) was achieved using the general procedures affording **78** (9 mg, 99%, Table 1, entry 25) after SiO_2 flash column chromatography (heptane/EtOAc, 3:1 as eluent).

4.5.6.9. 2-(*tert*-Butyl-dimethyl-silanyloxy)-6,10-dimethyl-8-isopropenyl-9,12-dioxa-tricyclo[6.3.1.$0^{0,0}$]-dodec-10-en-5-one 78. Colourless oil. $[\alpha]_D^{20} = +1$ (*c* 0.98, $CHCl_3$). IR (film): $\nu = 2953$, 2926, 2855, 1667, 1461, 1375, 1361, 1316, 1257, 1207, 1141, 1093, 1072, 1030, 1017, 948, 904, 834, 797 cm^{-1}. ^1H NMR (300 MHz, C_6D_6): $\delta = -0.03$ (s, 3H), 0.06 (s, 3H), 0.29 (s, 3H), 0.96 (s, 9H), 1.34 (m, 1H), 1.56 (ddd, $J = 3.1$, 6.4, 13.5 Hz, 1H), 1.65 (s, 3H), 1.73 (d, $J = 1.0$ Hz, 3H), 2.07 (d, $J = 13.3$ Hz, 1H), 2.10 (m, 1H), 2.41 (tdd, $J = 2.4$, 3.1, 13.8 Hz, 1H), 2.56 (d, $J = 13.3$ Hz, 1H), 3.43 (m, 4H), 4.10 (t, $J = 2.5$ Hz, 1H), 5.05 (dd, $J = 1.6$, 2.1 Hz, 1H), 5.30 (d, $J = 1.1$ Hz, 1H), 5.68 (dd, $J = 1.0$, 2.2 Hz, 1H). ^{13}C NMR (125 MHz, C_6D_6): $\delta = -5.0$, −4.5, 1.4, 18.2, 18.8, 19.6, 24.4, 26.0 (3C), 27.5, 48.2, 58.6, 63.1, 65.0, 69.6, 85.8, 101.9, 107.7, 111.9, 112.0, 143.2, 149.1. ESIMS (MeOH): 445.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{23}H_{38}O_5SiNa$ *m*/*z* 445.2386, found: 445.2434.

Starting from **40**, the target bis-tertiary diol **45** was synthesized analogously. Nucleophilic addition was carried out on **40** (50 mg, 0.13 mmol) with allylmagnesium bromide (1.0 M in Et_2O, 0.7 mL, 0.65 mmol) in dry THF (1 mL) for 3 h at 0 °C using the general procedure to give after chromatography (SiO_2, heptane/Et_2O, 1:1) **45** (36 mg, 65%) and SM (11.3 mg, 23%).

4.5.6.10. 7-Allyl-4-(*tert*-butyl-dimethyl-silanyloxy)-6,7-dihydroxy-6,8a-dimethyl-3,4,6,7,8,8a-hexahydro-2*H*-naphthalen-1-one 45. Colourless oil. $[\alpha]_D^{20} = -35$ (*c* 1.20, $CHCl_3$). IR (film): $\nu = 3396$, 2928, 2888, 2855, 1638, 1470, 1434, 1360, 1250, 1200, 1106, 1072, 1057, 1002, 909, 832, 772 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.02$ (s, 3H), 0.06 (s, 3H), 0.87 (s, 9H), 1.18 (s, 3H), 1.30 (d, $J = 16.3$ Hz, 1H), 1.36 (s, 3H), 1.53 (dt, $J = 3.5$, 13.5 Hz,

1H), 1.70 (ddt, $J = 2.7, 5.5, 7.9$ Hz, 1H), 1.78 (ddd, $J = 2.9, 4.2, 13.7$ Hz, 1H), 2.02 (dd, $J = 8.6, 14.3$ z, 1H), 2.15 (ddd, $J = 2.9, 4.1, 13.6$ Hz, 1H), 2.24 (d, $J = 16.4$ Hz, 1H), 2.65 (ddt, $J = 1.7, 5.5, 14.1$ Hz, 1H), 3.40 (s, 1H), 4.03 (m, 4H), 4.20 (t, $J = 2.6$ Hz, 1H), 5.05 (d, $J = 1.5$ Hz, 1H), 5.07 (br s, 1H), 5.11 (s, 1H), 5.52 (s, 1H), 5.97 (dddd, $J = 5.5, 8.6, 11.5, 14.1$ Hz, 1H). ^{13}C NMR (75 MHz): $\delta = -5.1, -4.3, 18.0, 23.1, 25.4, 25.8$ (3C), 29.7, 31.8, 38.8, 39.4, 43.1, 64.8, 72.5, 72.6, 73.4, 113.1, 117.0, 135.0, 135.1, 139.5. ESIMS (MeOH): 447.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{23}H_{40}O_5NaSi$ m/z 447.2543, found: 447.2545.

Oxidative cleavage of **45** (diastereomeric mixture) was achieved using the general procedures affording **79** (16 mg, 96%, Table 1, entry 26) after SiO_2 flash column chromatography (heptane/EtOAc, 3:1 as eluent).

4.5.6.11. 2-(*tert*-Butyl-dimethyl-silanyloxy)-6,10-dimethyl-8-propyl-9,12-dioxa-tricyclo[6.3.1.0^{0,0}]-dodec-10-en-5-one 79. Colourless oil. $[\alpha]_D^{20} = -6$ (c 0.80, $CHCl_3$). IR (film): $\nu = 2953, 2925, 2854, 1666, 1461, 1436, 1363, 1257, 1206, 1085, 1017, 1004, 947, 904, 833, 797, 756, 699$ cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): $\delta = -0.05$ (s, 3H), 0.05 (s, 3H), 0.95 (s, 9H), 1.19 (m, 1H), 1.53 (ddd, $J = 3.2, 6.5, 13.7$ Hz, 1H), 1.63 (s, 3H), 1.73 (d, $J = 1.1$ Hz, 3H), 1.91 (d, $J = 13.3$ Hz, 1H), 2.08 (ddd, $J = 3.1, 12.9, 14.1$ Hz, 1H), 2.40 (dddd, $J = 2.4, 3.2, 13.9, 13.9$ Hz, 1H), 2.41 (d, $J = 13.3$ Hz, 1H), 2.86 (ddt, $J = 1.2, 8.0, 14.1$ Hz, 1H), 2.99 (ddt, $J = 1.6, 6.2, 14.1$ Hz, 1H), 3.62 (m, 4H), 4.06 (t, $J = 2.7$ Hz, 1H), 5.14 (dddd, $J = 1.3, 1.3, 2.4, 10.2$ Hz, 1H), 5.21 (ddd, $J = 1.5, 3.8, 17.2$ Hz, 1H), 5.29 (dd, $J = 1.1, 2.2$ Hz, 1H), 6.30 (dddd, $J = 6.2, 8.0, 10.2, 17.2$ Hz, 1H). ^{13}C NMR (75 MHz, C_6D_6): $\delta = -5.0, -4.4, 18.2, 18.8, 19.5, 24.2, 26.0$ (3C), 27.3, 41.5, 47.5, 58.7, 63.1, 65.0, 69.5, 85.7, 102.1, 107.8, 112.2, 117.4, 134.1, 149.2. ESIMS (MeOH): 445.2 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{23}H_{38}O_5SiNa$ m/z 445.2386, found: 445.2381.

4.6. Preparation and domino reactions of the allylically substituted substrate 51, his bis-tertiary analogues and their oxidative cleavage

Nucleophilic addition was carried out on **50** (120 mg, 0.26 mmol) by adding vinylmagnesium bromide (1.0 M in THF, 1.6 mL, 1.56 mmol) in dry THF (2 mL) for 3 h using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 2:1) **51** (93 mg, 81%). A major component (unidentified) of a diastereomeric mixture after chromatography is described.

4.6.1. 13-(*tert*-Butyl-dimethyl-silanyloxy)-10-methyl-3-vinyl-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthrene-2,3-diol 51. White solid. Mp: 61–63 °C. IR (film): $\nu = 3408, 2956, 2929, 2854, 1471, 1462, 1388, 1360, 1249, 1139, 1089, 911, 886, 834, 774, 668$ cm^{-1}. ^{1}H NMR (300 MHz): $\delta = -0.01$ (s, 3H), -0.05 (s, 3H), 0.72 (s, 3H), 0.87 (s, 9H), 0.89 (m, 2H), 1.16 (s, 3H), 1.26 (m, 2H), 1.40 (m, 3H), 1.54 (m, 4H), 1.80 (m, 5H), 2.05 (ddd, $J = 2.4, 4.0, 13.0$ Hz, 1H), 2.28 (dtd, $J = 1.4, 4.5, 13.3$ Hz, 1H), 2.42 (br s, 1H), 3.53 (t, $J = 8.2$ Hz, 1H), 3.70 (br s, 1H), 5.10 (s, 1H), 5.18 (dd, $J = 1.5, 10.5$ Hz, 1H), 5.30 (dd, $J = 1.5, 17.3$ Hz, 1H), 5.86 (dd, $J = 10.5, 17.3$ Hz, 1H). ^{13}C NMR (75 MHz): $\delta = -4.8, -4.5, 11.4, 18.1, 21.3, 21.8, 23.5, 25.8$ (3C), 30.9, 32.1 (2C), 33.7, 35.9, 37.0, 38.1, 43.4, 50.3, 53.9, 70.6, 73.2, 81.7, 115.3, 119.9, 142.5, 150.3. ESIMS (MeOH): 469.3 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{27}H_{46}O_3NaSi$ m/z 469.3114, found: 469.3103. Anal. Calcd for $C_{27}H_{46}O_3Si{\cdot}0.25H_2O$ (446.74): C 71.87, H 10.39. Found: C 71.88, H 10.22.

Oxidative cleavage of **51** (diastereomeric mixture) was achieved using the general procedures affording **82** (17 mg, 87%, Table 1, entry 29) after SiO_2 flash column chromatography (heptane/Et_2O, 4:1 as eluent).

Compound **82**: White solid. Mp: 91–93 °C. $[\alpha]_D^{20} = +30$ (c 1.37, $CHCl_3$). IR (film): $\nu = 2951, 2927, 2855, 1596, 1462, 1376, 1249, 1147, 1087, 1024, 967, 938, 907, 883, 832, 774, 732, 669$ cm^{-1}. ^{1}H NMR (300 MHz): $\delta = 0.00$ (2s, 6H), 0.70 (s, 3H), 0.87 (s, 9H), 0.91 (m, 2H), 1.03 (s, 3H), 1.19 (m, 4H), 1.36 (m, 2H), 1.47 (m, 2H), 1.58 (m, 2H), 1.75 (dt, $J = 3.3, 12.2$ Hz, 1H), 1.81 (dd, $J = 0.8, 14.0$ Hz, 1H), 1.89 (ddd, $J = 3.9, 6.8, 9.3$ Hz, 1H), 1.99 (m, 1H), 2.20 (dd, $J = 5.9, 13.9$, 1H), 3.56 (dd, $J = 7.8, 8.7$ Hz, 1H), 4.81 (s, 1H), 5.06 (dd, $J = 1.6, 10.8$ Hz, 1H), 5.47 (dd, $J = 1.6, 17.2$ Hz, 1H), 5.69 (d, $J = 5.5$ Hz, 1H), 6.01 (dd, $J = 10.9, 17.2$ Hz, 1H). ^{13}C NMR (75 MHz): $\delta = -4.8, -4.6, 11.4, 14.2, 18.1, 21.5, 23.5, 25.7, 25.9$ (3C), 28.8, 31.1, 35.2, 37.3, 43.2, 47.5, 47.7, 50.2, 53.6, 81.7, 84.5, 99.3, 110.8, 113.6, 131.2, 147.2. ESIMS (MeOH): 444.3 ([M+Na]$^+$, 100). HRESIMS (MeOH) calcd for $C_{27}H_{44}O_3NaSi$ m/z 467.2957 found: 467.2940. Anal. Calcd for $C_{27}H_{44}O_3Si{\cdot}0.35$ heptane (444.72): C 73.72, H 10.42. Found: C 73.73, H 10.41.

Oxidation of **51** (1.58 g, 3.53 mmol) was carried out with IBX (2.97 g, 10.59 mmol) in DMSO (12 mL) for 30 min using the general procedure to give after chromatography (SiO_2, heptane/Et_2O, 4:1) the corresponding **C2-keto** derivative (1.43 g, 91%) as a colourless oil. A major component (unidentified) of a diastereomeric mixture after chromatography is described.

4.6.2. 13-(*tert*-Butyl-dimethyl-silanyloxy)-3-hydroxy-10-methyl-3-vinyl-1,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-cyclopenta[*a*]phenanthren-2-one C2-keto-51. IR (film): $\nu = 3484, 2951, 2929, 2853, 1721, 1471, 1462, 1253, 1139, 1086, 886, 836, 775$ cm^{-1}. ^{1}H NMR (300 MHz): $\delta = -0.01$ (s, 6H, 2MeSi), 0.71 (s, 3H, H18), 0.86 (s, 9H, *t*-Bu), 0.95 (m, 3H, H9 + H12 + H14), 1.03 (s, 3H, H19), 1.24 (m, 2H, H15 + H16), 1.42 (m, 3H, H8 + 2H11), 1.57 (m, 1H, H15′), 1.77 (m, 3H, 2H7 + H12′), 1.88 (m, 1H, H16′), 2.22 (m, 2H, H6), 2.40 (dd, $J = 1.5, 12.1$ Hz, 1H, H1), 2.69 (d, $J = 12.1$ Hz, 1H, H1′), 3.54 (t, $J = 8.2$ Hz, 1H, H17), 3.89 (s, 1H, OH), 5.21 (s, 1H, H4), 5.26 (ddd, $J = 1.3, 2.3, 10.2$ Hz, 1H, H21), 5.44 (ddd, $J = 1.7, 10.7, 17.1$ Hz, 1H, H21′), 5.85 (ddd, $J = 1.8, 10.2, 17.1$ Hz, 1H20). ^{13}C NMR (75 MHz): $\delta = -5.2$ (MeSi), -4.8 (MeSi), 11.3 (C18), 18.0 (Cq-TBS), 19.7 (C19), 20.9 (C11), 23.4 (C15), 25.8 (3C, *t*-Bu), 30.8 (C16), 31.3 (C6), 32.2 (C7), 35.5 (C8), 36.8 (C12), 44.2 (C13), 46.8 (C10), 48.0 (C1), 50.2 (C14), 55.0 (C9), 78.2 (C3), 81.6 (C17), 117.1 (C21), 121.9 (C4), 140.1 (C20),

147.5 (C5), 210.4 (C2). ESIMS (MeOH): 467.3 ([M+Na]$^+$, 100). HRESIMS (MeOH) calcd for $C_{27}H_{44}O_3NaSi$ *m/z* 467.2957, found: 467.2969. Anal. Calcd for $C_{27}H_{44}O_3Si{\cdot}0.9H_2O$ (444.72): C 70.36, H 10,02. Found: C 70.11, H 9.63.

Nucleophilic addition was carried out on the C2-keto derivative thus obtained (89 mg, 0.20 mmol) with allylmagnesium bromide (1.0 M in THF, 1.6 mL, 1.6 mmol) in dry THF (2 mL) for 2 h using the general procedure to give after chromatography (SiO_2, heptane/EtOAc, 3:1) **52** (82 mg, 84%).

4.6.3. 2-Allyl-13-(*tert*-butyl-dimethyl-silanyloxy)-10-methyl-3-vinyl-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthrene-2,3-diol 52. A major component (unidentified) of a diastereomeric mixture after chromatography, obtained as a colourless oil, is described. IR (film): $\nu = 3466$, 2951, 2929, 2853, 1471, 1439, 1372, 1361, 1250, 1139, 1091, 1022, 993, 910, 887, 836, 774, 668 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = -0.01$ (s, 3H), 0.00 (s, 3H), 0.72 (s, 3H), 0.87 (s, 9H), 1.06 (m, 2H), 1.21 (s, 3H), 1.29 (m, 3H), 1.39 (d, $J = 14.6$ Hz, 1H), 1.52 (m, 4H), 1.81 (d, $J = 14.4$ Hz, 1H), 1.82 (m, 4H), 2.06 (m, 2H), 1.27 (s, 1H), 1.27 (m, 1H), 2.46 (dd, $J = 7.8$, 13.9 Hz, 1H), 2.65 (s, 1H), 3.53 (dd, $J = 7.7$, 8.7 Hz, 1H), 4.96 (d, $J = 1.2$ Hz, 1H), 5.15 (dd, $J = 1.7$, 10.5 Hz, 1H), 5.14 (m, 2H), 5.27 (dd, $J = 1.7$, 17.2 Hz, 1H), 5.86 (dd, $J = 10.5$, 17.2 Hz, 1H), 5.97 (ddt, $J = 2.6$, 7.5, 17.3 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = -4.8$, -4.5, 11.4, 18.1, 20.9, 21.0, 23.5, 25.9 (3C), 30.9, 31.9, 33.2, 35.6, 37.1, 37.5, 41.7, 43.3, 44.2, 50.3, 56.8, 74.0, 77.5, 81.7, 115.2, 119.3, 122.3, 134.1, 140.6, 146.5. ESIMS (MeOH): 509.4 ([M+Na]$^+$, 100). HRESIMS (MeOH) calcd for $C_{30}H_{50}O_3NaSi$ *m/z* 509.3427, found: 507.3448. Anal. Calcd for $C_{30}H_{50}O_3Si{\cdot}0.6H_2O$ (486.80): C 72.41, H 10.37. Found: C 72.44, H 10.41.

Oxidative cleavage of **52** (diastereomeric mixture) was achieved using the general procedures affording **83** (14 mg, 82%, Table 1, entry 30) after SiO_2 flash column chromatography (heptane/Et_2O, 4:1 as eluent).

Compound **83**: Colourless oil. $[\alpha]_D^{20} = +32$ (*c* 1.70, $CHCl_3$). IR (film): $\nu = 2954$, 2928, 1596, 1472, 1394, 1377, 1250, 1127, 1087, 1066, 909, 885, 834, 775, 668 cm^{-1}. ^{1}H NMR (500 MHz): $\delta = 0.00$ (s, 3H), 0.01 (s, 3H), 0.70 (s, 3H), 0.88 (s, 9H), 0.96 (m, 2H), 0.99 (s, 3H), 1.17 (m, 3H), 1.30 (m, 4H), 1.43 (m, 1H), 1.57 (m, 2H), 1.75 (dt, $J = 2.6$, 11.9 Hz, 1H), 1.81 and 2.03 (ABquartet, $J = 13.8$ Hz, 2H), 1.88 (ddd, $J = 4.6$, 8.7, 14.7 Hz, 1H), 1.95 (m, 1H), 2.59 (d, $J = 14.6$ Hz, 1H), 2.64 (d, $J = 14.8$ Hz, 1H), 3.56 (t, $J = 8.3$ Hz, 1H), 4.82 (s, 1H), 5.05 (d, $J = 10.8$ Hz, 1H), 5.17 (m, 2H), 5.48 (d, $J = 17.2$ Hz, 1H), 5.94 (ddt, $J = 7.8$, 10.2, 17.4 Hz, 1H), 6.02 (dd, $J = 10.8$, 17.2 Hz, 1H). ^{13}C NMR (125 MHz): $\delta = -4.8$, -4.5, 11.4, 14.5, 18.1, 21.3, 23.5, 25.7, 25.9 (3C), 29.0, 31.1, 35.2, 37.4, 42.3, 43.5, 46.7, 49.1, 50.3, 53.1, 81.7, 84.5, 106.5, 110.3, 113.5, 118.5, 131.3, 132.6, 147.3. ESIMS (MeOH): 507.3 ([M+Na]$^+$, 100). HRESIMS (MeOH) calcd for $C_{30}H_{48}O_3NaSi$ *m/z* 507.3270, found: 507.3259. Anal. Calcd for $C_{30}H_{48}O_3Si{\cdot}0.7$ DCM (484.79): C 70.99, H 9.59. Found: C 70.64, H 9.97.

Starting from **C2-keto** derivative, the target bis-tertiary diol **53** was synthesized analogously. Nucleophilic addition was carried out on the C2-keto derivative obtained from **51** (100 mg, 0.23 mmol) with MeMgBr (1.4 M in toluene, 1.29 mL, 1.8 mmol) in dry THF (2 mL) at 0 °C for 2 h using the general procedure to give after chromatography (heptane/EtOAc, 7:1) **53** (76 mg, 74%) and SM (9 mg, 9%).

4.6.4. 13-(*tert*-Butyl-dimethyl-silanyloxy)-2,10-dimethyl-3-vinyl-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthrene-2,3-diol 53. A major component (unidentified) of a diastereomeric mixture after chromatography, obtained as a yellow oil, is described. IR (film): $\nu = 3439$, 2953, 2928, 2853, 1471, 1463, 1373, 1250, 1138, 1088, 911, 887, 836, 775, 668 cm^{-1}. ^{1}H NMR (300 MHz): $\delta = -0.01$ (2s, 6H), 0.72 (s, 3H), 0.87 (s, 9H), 0.91 (m, 2H), 1.15 (s, 3H), 1.23 (s, 3H), 1.29 (m, 3H), 1.49 (m, 4H), 1.50 (d, $J = 14.1$ Hz, 1H), 1.75 (d, $J = 14.5$ Hz, Hz, 1H), 1.82 (m, 4H), 2.09 (m, 2H), 2.26 (td, $J = 4.1$, 13.6 Hz, 1H), 2.63 (s, 1H), 3.53 (t, $J = 8.2$ Hz, 1H), 5.01 (s, 1H), 5.13 (dd, $J = 1.2$, 10.5 Hz, 1H), 5.25 (dd, $J = 1.3$, 17.3 Hz, 1H), 5.87 (dd, $J = 10.5$, 17.3 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = -4.8$, -4.5, 11.4, 18.1, 21.0, 21.2, 23.5, 24.3, 25.9 (3C), 30.9, 32.0, 33.3, 35.6, 37.0, 37.6, 43.3, 46.6, 50.3, 56.6, 73.3, 76.5, 81.7, 115.3, 122.2, 140.9, 147.0. ESIMS (MeOH): 483.3 ([M+Na]$^+$, 100). HRESIMS (MeOH) calcd for $C_{28}H_{48}O_3NaSi$ *m/z* 483.3270, found: 481.3282. Anal. Calcd for $C_{28}H_{48}O_3Si$ (460.76): C 72.42; H 10.51. Found: C 72.31, H 10.33.

Oxidative cleavage of **53** (diastereomeric mixture) was achieved using the general procedures affording **84** (44 mg, 92%, Table 1, entry 31) after SiO_2 flash column chromatography (heptane/Et_2O, 4:1 as eluent).

Compound **84**: Colourless oil. $[\alpha]_D^{20} = +40$ (*c* 1.73 $CHCl_3$). IR (film): $\nu = 2956$, 2927, 2873, 2858, 1597, 1473, 1388, 1349, 1254, 1199, 1140, 1088, 1029, 913, 858, 836, 775, 670 cm^{-1}. ^{1}H NMR (300 MHz,): $\delta = 0.00$ (s, 3H), 0.01 (s, 3H), 0.70 (s, 3H), 0.88 (s, 9H), 0.98 (m, 2H), 1.00 (s, 3H), 1.15 (m, 2H), 1.29 (m, 4H), 1.45 (m, 3H), 1.57 (m, 1H), 1.59 (s, 3H), 1.75 (dt, $J = 3.2$, 12.2 Hz, 1H), 1.88 (ddd, $J = 4.6$, 9.1, 15.0 Hz, 1H), 1.92 (dd, $J = 2.2$, 2.9 Hz, 1H), 1.95 (s, 2H), 3.56 (t, $J = 8.3$ Hz, 1H), 4.81 (s, 1H), 5.05 (d, $J = 1.4$, 10.8 Hz, 1H), 5.48 (dd, $J = 1.4$, 17.2 Hz, 1H), 6.02 (dd, $J = 10.8$, 17.2 Hz, 1H). ^{13}C NMR (75 MHz): $\delta = -4.8$, -4.5, 11.4, 14.5, 18.1, 21.5, 23.5, 25.1, 25.6, 25.9 (3C), 28.9, 31.0, 35.2, 37.4, 43.5, 47.3, 50.2, 51.7, 53.5, 81.7, 84.5, 105.5, 110.1, 113.5, 131.4, 147.5. ESIMS (MeOH): 481.3 ([M+Na]$^+$, 100). HRESIMS (MeOH) calcd for $C_{28}H_{46}O_3NaSi$ *m/z* 481.3114, found: 481.3143. Anal. Calcd for $C_{28}H_{46}O_3Si{\cdot}0.9H_2O$ (458.75): C 70.81, H 10.14. Found: C 70.81, H 9.99.

4.7. Preparation of *tert*-Butyl-(10-methoxymethoxymethyl-6,8-dimethyl-5-methylene-9,12-dioxa-tricyclo[6.3.1.0^{0,0}]-dodec-10-en-2-yloxy)-dimethyl-silane 85

A solution of potassium *tert*-butoxide (115 mg, 1.02 mmol) and methyl triphenylphosphonium bromide (377 mg, 1.05 mmol) in 6 mL of dry THF was stirred under argon at room temperature. The resulting bright yellow solution

was stirred for 1 h, cooled to 0 °C before ketone **74** (70 mg, 0.17 mmol) was added in dry THF (4 mL). The ice bath was removed and the solution was stirred at room temperature for 17 h. After dilution with heptane and filtration, purification of the crude by silica gel chromatography (heptane/Et_2O, 95:5) gave **85** (50 mg, 72%).

Compound **85**: Colourless oil. $[\alpha]_D^{20} = -33$ (c 0.55, $CHCl_3$). IR (film): $\nu = 2930$, 2886, 2858, 1667, 1639, 1450, 1390, 1257, 1209, 1150, 1101, 1088, 1059, 996, 836 cm^{-1}. ^1H NMR (300 MHz): $\delta = 0.08$ (s, 3H), 0.10 (s, 3H), 0.93 (s, 9H), 1.29 (s, 3H), 1.54 (s, 3H), 1.66 (m, 1H), 1.84 (tddd, $J = 1.2$, 2.5, 3.7, 13.8 Hz, 1H), 2.03 (dt, $J = 3.2$, 13.6 Hz, 1H), 2.10 (dd, $J = 1.2$, 14.0 Hz, 1H), 2.60 (d, $J = 13.9$ Hz, 1H), 2.61 (m, 1H), 3.38 (s, 3H), 3.96 (dd, $J = 12.7$, 16.5 Hz, 2H), 3.98 (m, 1H), 4.67 (s, 2H), 4.70 (s, 1H), 4.83 (s, 1H), 5.40 (s, 1H). ^{13}C NMR (75 MHz): $\delta = -5.1$, -4.5, 18.0, 22.4, 24.4, 25.8 (3C), 26.5, 29.7, 50.3, 55.3, 57.5, 66.3, 69.5, 84.8, 95.6, 104.2, 105.8, 107.8, 148.5, 152.9. ESIMS (MeOH): 433.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{22}H_{38}O_5NaSi$ m/z 433.2386, found: 433.2384.

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References

1. Tietze proposed the following definition: 'a domino reaction is a process involving two or more bond-forming transformations (usually C–C bonds), which take place under the same reaction conditions without adding additional reagents and catalysts, and in which the subsequent reactions result as a consequence of the functionality formed in the previous step.' Tietze, L. F.; Beifuss, U. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 131–163; Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115–136; Tietze, L. F.; Modi, A. *Med. Res. Rev.* **2000**, *20*, 304–322; Tietze, L. F.; Haunert, F. In *Stimulating Concepts in Chemistry*; Shibasaki, M., Stoddart, J. F., Vogtle, F., Eds.; Wiley-VCH: Weinheim, 2000; pp 39–64.
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