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Microwave-assisted domino reactions: function-compatibility, modulation, and greening efforts

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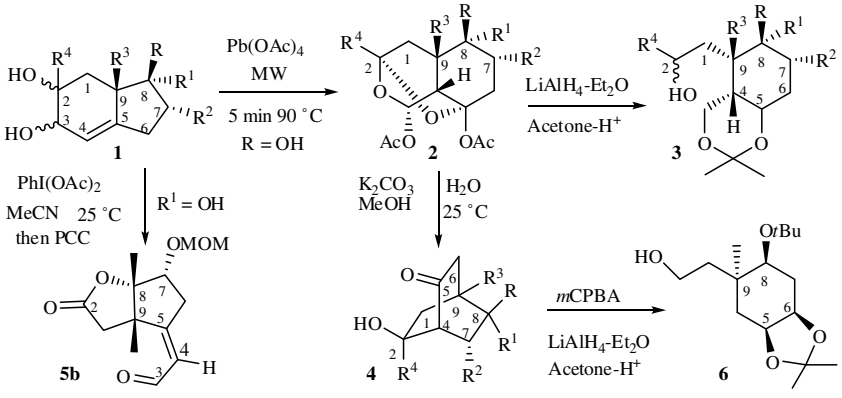
ABSTRACT

Herein we report a microwave-assisted version of a domino protocol, providing ready access to a wide variety of complex oxygen heterocycles. The latter can be converted to stereochemically, well-defined, variously substituted carbocycles, since reaction conditions and the substitution pattern can be tailored to fit a particular type of transformation. Microwave assistance, the influence of solvent, temperature, the function compatibility, and the use of $PhI(OAc)_2$ as a domino promoter are investigated.

1. Introduction

Cyclohexane frameworks containing quaternary centers are present as structural subunits in a wide variety of biologically active natural products. In a preliminary communication,[1] we showed that a variety of cyclohexane derivatives possessing adjacent quaternary carbons can be prepared by a three-step procedure using a $Pb(OAc)_4$ mediated hetero-domino reaction[2] as a key construction step (Scheme 1).[3] The starting hydrindene-diols of type-**1** can be readily assembled and constitute attractive precursors for highly elaborated type-**3** or **6** cyclohexanes, type-**4** bridged bicyclic systems, and type-**5** fused -bicyclic lactones.[4]

Since our early observations, the oxidative cleavage of unsaturated bicyclic diols has been of extensive value in the synthesis of taxol's C-ring,[5] iridal's B-ring,[6] norsesquiterpene spirolactone's B-ring, and their steroid hybrids.[7] The fact that a harsh reagent such as $Pb(OAc)_4$[8] required to induce the domino reaction means that the scope of the method is limited to substrates that lack sensitive functionality. Nevertheless, with various functional and protecting groups at the periphery, the domino process has proven to be highly general with respect to the R^1 and R^2 groups and has shown a wide scope with respect to hydroxyl protecting groups, such as Ac, TMS, TBS, *t*Bu, MOM, and Bn (Scheme 1). An important experimental improvement was that for the oxidative/pericyclic process, $Pb(OAc)_4$ could be replaced by $PhI(OAc)_2$ as the domino promoter, thus decreasing the toxicity of the method.[9] This provided easy access to the stereodefined construction of the adjacent quaternary centers in **8**, a precursor of the norsesquiterpene



Scheme 1.

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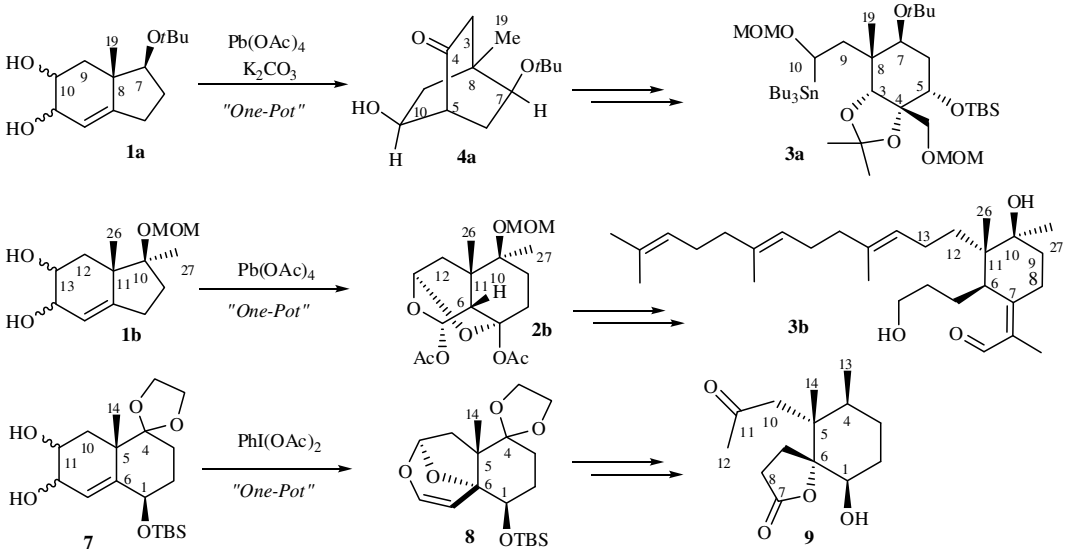


Figure 1. Source of chirality: (*S*)-proline; domino promoters: $Pb(OAc)_4$ or $PhI(OAc)_2$.

spirolactone framework **9**.[3c] Representative examples of a series of these high complexity generating domino reactions and their use in synthetic schemes are presented in Figure 1.[10]

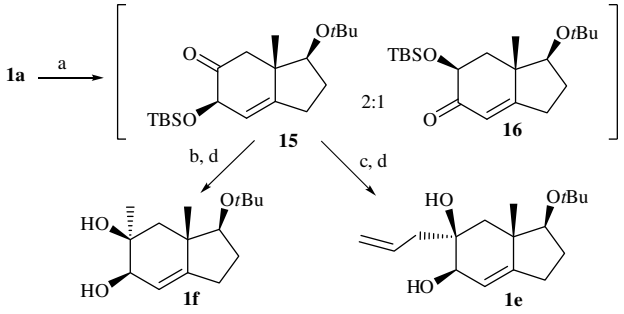
Herein, we report our results broadening further the scope of this domino methodology discovered in our laboratories, namely a microwave-assisted domino version; a modulation by the substituent and the domino promoter as well as secondary reactions of the complex oxygen heterocycles thus obtained.

2. Results and discussion

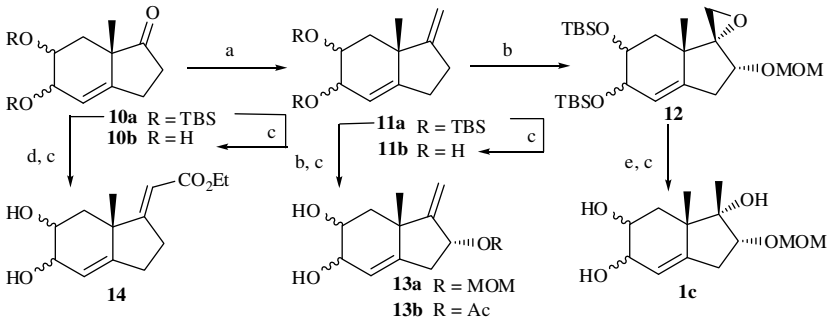
2.1. Preparation of the substrate-diols

Conveniently substituted bicyclic unsaturated diols were obtained using the well-known Robinson annulation procedure.[11] The bicyclic enones thus obtained were further elaborated upon by the appropriate treatment leading to the requisite unsaturated diol probe as a mixture of diastereomeric diols, using methodology based on our previous work.[12]

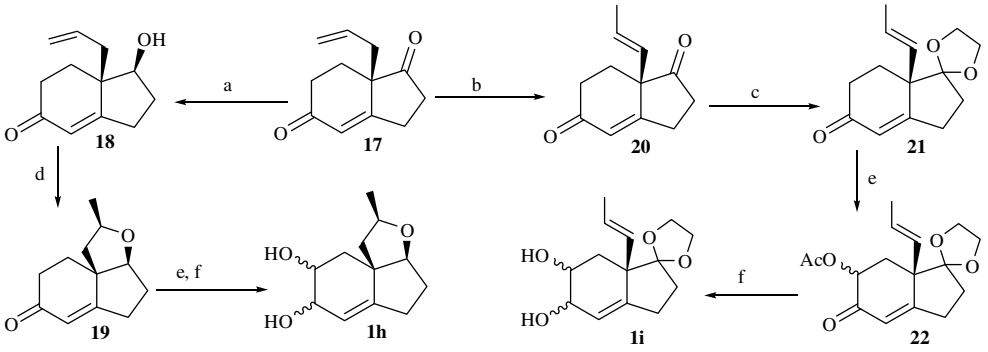
The route began with the conversion of **10**, a known intermediate from our previous work[1] into the two-carbon homologated **14** by the introduction of a conjugated ester functionality at C8[13] using standard HWE conditions (Scheme 2). Wittig olefination of the former afforded the one-carbon homologated **11**, which was transformed to target compound **13**, and also to **1c** via the intermediate epoxide **12**. Once this was achieved, the investigation was extended to include C2 tertiary/C3 secondary probes. Selective monoprotection of **1a** furnished the desired mono-protected **15** along with its silyl-transposed isomer **16**, separable by chromatography (Scheme 3). Efforts to overcome the undesired 1,2-silatropic shift did not produce synthetically useful results. Allyl **1e** and methyl carbinols **1f** were then prepared efficiently by alkylation of **15** with methyl lithium and allylmagnesium bromide leading, respectively, to **1f** and **1e** after desilylation.



Scheme 3. Reagents and conditions: (a) (i) TBSCl, DMF–imidazole, 0–25 °C; (ii) Dess–Martin, py, CH_2Cl_2 (50%); (b) MeLi, THF, −78 °C (79%); (c) AllylMgBr, THF, −78 °C (64%); (d) TBAF, THF, 60 °C (86% for **1e**, 80% for **1f**).



Scheme 2. Reagents and conditions: (a) $MePPh_3Br$, *t*BuOK, PhMe, 25 °C (94%); (b) Ref. 1; (c) TBAF, THF, 60 °C (91% for **14**, 85% for **13a,** and 65% for **1c**); (d) triethyl phosphonoacetate, NaHMDS, THF (90%); (e) $LiAlH_4$, THF, 0 °C, 30 min (99%).



Scheme 4. Reagents and conditions: (a) $NaBH_4$, CH_2Cl_2/EtOH, 0 °C (98%); (b) $RhCl_3{\cdot}3H_2O$, reflux (99%); (c) ethylenglycol, PhH, *p*TsOH, reflux (94%); (d) $BF_3{\cdot}Et_2O$, P_2O_5, H_3PO_4, CH_2Cl_2 (71%); (e) $Pb(OAc)_4$, PhH, 90 °C (55% for **19**, 85% for **22**); (f) $LiAlH_4$, Et_2O, −20 to 0 °C (98% for **1i**, 82% for **1h**).

To increase even further the applicability of the methodology, we prepared the angularly substituted substrates **1h** and **1i** from the known **17**[14] used in our previous work[1] (Scheme 4). Tricyclic enone **19**, the precursor of **1h**, was obtained from **18** using the standard procedure for *t*Bu protection, substituting the external olefin (methylpropene) by the terminal olefin. Target diols **1h** and **1i** were accessed from their corresponding enones via acetoxylation–reduction, as usual.

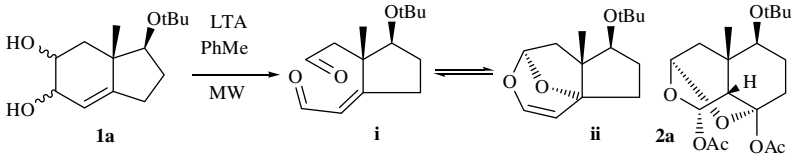
2.2. Domino reactions

In our initial studies, we preferred room temperature to heating since at elevated temperatures the reagent was known to react with unsaturated groups around the diol framework. The domino process under microwave heating was next examined,[15] and was found to be more advantageous compared to conventional heating. While olefins are inert to $Pb(OAc)_4$ at room temperature, they do react sluggishly at reflux temperatures, but no such complications were observed under microwave heating, even at 100 °C. Optimization experiments were carried out on **1a**, since it was available to us in quantity from our synthetic studies on taxoids (Table 1).[5a] To this end, a range of conditions (time and temperature) were tried, all ending in the ring-expanded domino product **2a** in less than 30 min at 60 °C and less than 5 min at 80 °C (Table 1). The reactions were clean and complete, and no side products were observed.

Each substrate-diol thus prepared was reacted in parallel with 2.4 equiv of $Pb(OAc)_4$ in toluene at room temperature (10–15 h) and under microwave heating at 90 °C for 5 min. The broad scope and efficiency of this domino reaction are illustrated by the results summarized in Table 2 (entries 1–10). The process was proven to be highly general with respect to the R groups of various bicyclic unsaturated diols since alkyl, alkenyl, alkyne, acetal containing substrate-diols gave high isolated yields of ring-expanded domino products. The process accommodates free β-hydroxyl groups (entry 2), while it tolerates a wide range of protecting groups. Domino reactions with substrates bearing alkenes (entries 3, 6, 8–10), oxygen-heterocycles (entry 5), ketones (entry 7), and ketals (entries 6 and 7) proceed efficiently to afford the corresponding ring-expanded domino products under either set of conditions (microwave heating, room temperature stirring). The lowest yields were obtained with the diols **1h** and **1i** in the angularly substituted series. The corresponding domino products **2h** and **2i** were isolated in 44% and 60% yields under room temperature stirring, while microwave irradiation gave slightly better yields (71% and 75%, respectively). The substrate-diols **1e** and **1f**, where the peripheral functionality has been switched from the five- to the six-membered ring, furnished the corresponding domino products **2f** and **2h** in ca. 50% isolated yields (entries 3 and 4).

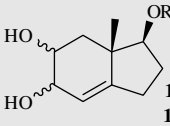
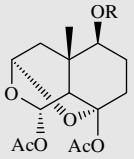
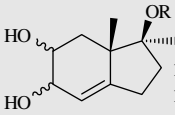
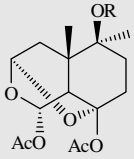
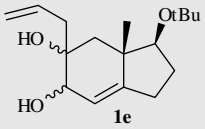
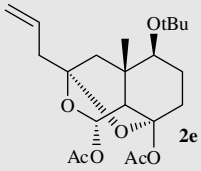
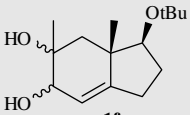
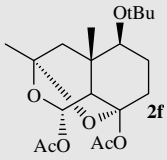
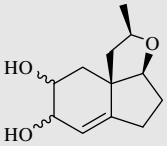
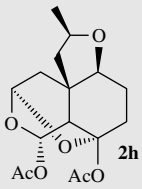
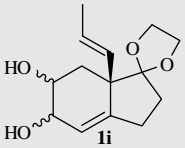
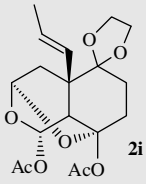
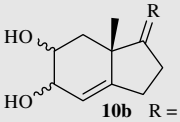
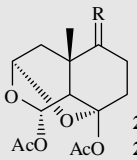
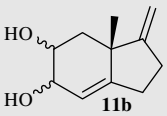
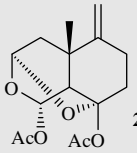
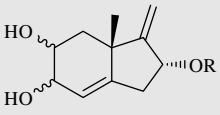
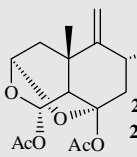
The exocyclic olefin is inert to $Pb(OAc)_4$ at room temperature behaving as a spectator, while it reacts sluggishly at reflux temperatures. However, under microwave heating, even at 100 °C, no such complications were observed. For example, microwave irradiation of **1i**, **10**, **11**, **13,** and **14** resulted in the formation of **2j**, **23–26** with domino yields in the range of 60–84% (entries 6, 8–10), devoid of any side product. In all cases investigated, microwave heating was found to be more desirable compared to both conventional heating (20-fold increase in rate) and room temperature stirring

Table 1
Microwave accelerated domino reactions: experiments to optimize time and temperature



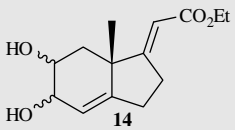
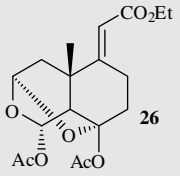
Entry	Time (min)	Temperature (°C)	Yield % (**i** + **ii**/**2a**)
1	5	60	74 (50/50)
2	5	80	83 (0/100)
3	5	90	94 (0/100)
4	15	50	90 (95/5)
5	15	70	91 (2/98)
6	15	90	90 (0/100)
7	30	60	95 (0/100)
8	30	70	90 (0/100)
9	30	90	88 (0/100)

Table 2
Conversion of various hydrindene-diols to ring-expanded domino products

Entry	Substrate	Domino product	Yield (%) A[a] (B)[b]
1	 **1a** R = tBu **1d** R = TBS	 **2a** R = tBu **2d** R = TBS	85 (94) 85 (90)
2	 **1b** R = MOM **1g** R = H	 **2b** R = MOM **2g** R = H	84 (88) 85 (82)
3	 **1e**	 **2e**	59 (45)
4	 **1f**	 **2f**	52 (50)
5	 **1h**	 **2h**	44 (71)
6	 **1i**	 **2i**	60 (75)
7	 **10b** R = O **10c** R = $O(CH_2)_2O$	 **23b** R = O **23c** R = $O(CH_2)_2O$	80 (84) 82 (84)
8	 **11b**	 **24**	80 (84)
9	 **13a** R = Ac **13b** R = MOM	 **25a** R = Ac **25b** R = MOM	60 (77) 86 (82)

(*continued on next page*)

Table 2 (*continued*)

Entry	Substrate	Domino product	Yield (%) A[a] (B)[b]
10	 **14**	 **26**	60 (59)

[a] Method A (conventional): The substrate (1 mmol), $Pb(OAc)_4$ (2.4 mmol) and the solvent (5 mL) were stirred at room temperature (8–12 h, TLC monitoring).
[b] Method B: A mixture of substrate (1 mmol), $Pb(OAc)_4$ (2.4 mmol) in 2 mL of PhMe was microwaved for 5 min at 90 °C.

(over 100-fold increase in rate). The microwave-assisted domino reactions were, in general, very clean, with TLC analysis indicating that only the desired product was present in all experiments; conventional heating at the same temperature (90 °C) gave rise to unidentified side products along with lower yields and thus was abandoned. Table 2 illustrates a wide range of substrates that undergo efficient ring-expanding rearrangement with good to high yields.

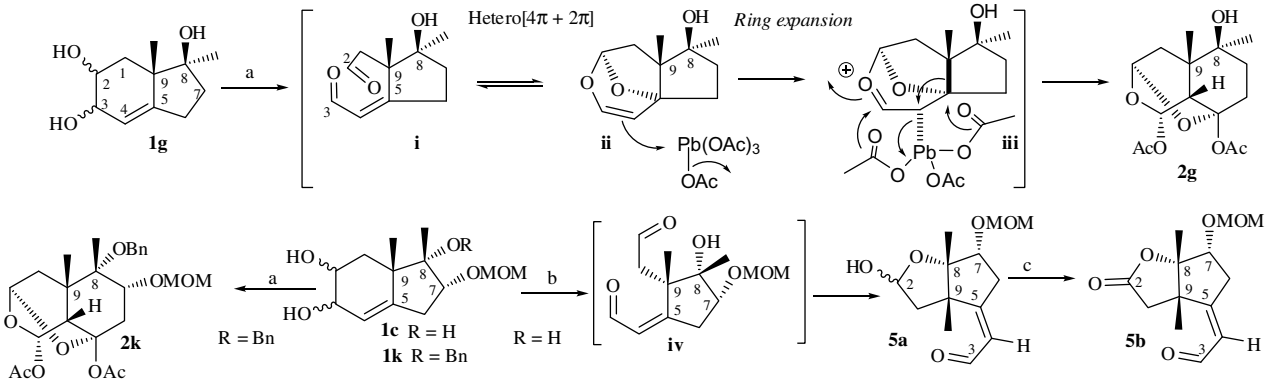
2.3. Modulation by the substituent

The domino substrate **1g** containing a β-hydroxyl group was readily converted into **2g** in 88% isolated yield, suggesting that a free hydroxy group can be included in domino substrates. However, based on the proposed mechanism, we anticipated that with the free-α-OH containing template **1c**, the process could be interrupted half way through leading to the fused-bicyclic lactol **5a** (Scheme 5). Indeed, unlike the free β-hydroxy containing substrate **1g**, the α-hydroxyl group containing substrate **1c** gave lactol **5a** through an interrupted domino process. The oxidative cleavage occurs rapidly, but intramolecular trapping of the resultant hetero[2π] system occurs at the C2 by the free OH, rather than the hetero[4π] system, which leads to the observed lactol **5a**. On the other hand, the β-OH at the C8 position in **1g** is sterically encumbered and does not offer competitive reactivity. Any of the two possible products **2g** or **5a** (both containing adjacent quaternary centers) can be selectively obtained as a single product in these systems via tuning of the C8 configuration (free α- or β-OH). For a ring-expanded domino product, it therefore becomes necessary to temporarily mask the tertiary α-hydroxyl function, for example, as benzyl ethers **1k**–**2k**;[1] when the ring-expansion is in the undesired reaction mode, the tertiary alcohol should remain free. We thus achieved our objective of the stereodefined elaboration of adjacent quaternary centers, by putting in competition a ring-expanding domino process with a fast trap of the in situ formed heterodienophile part of **iv** by the unprotected tertiary hydroxyl group that is left (Scheme 5).

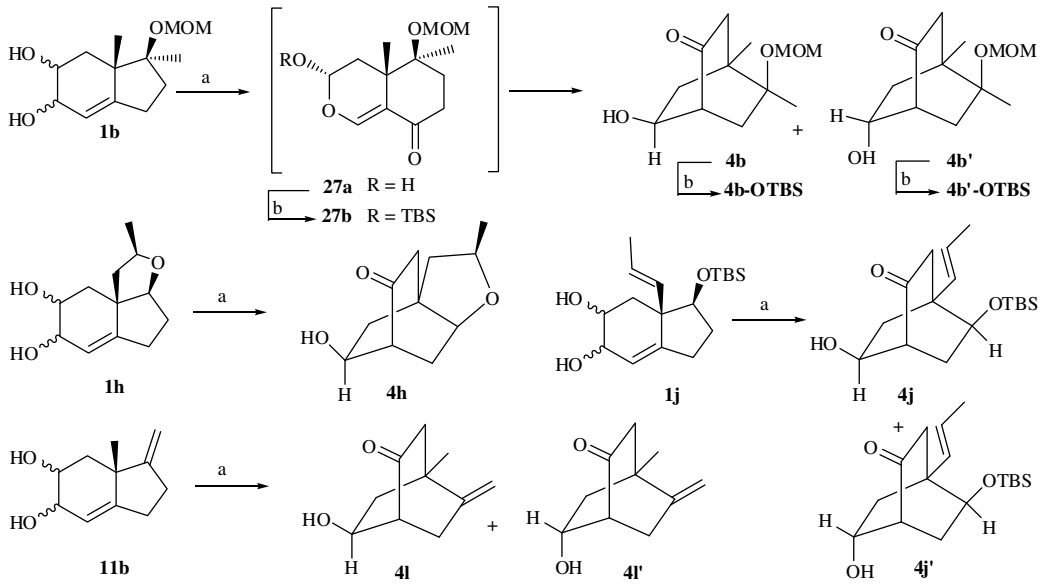
These reactions employ readily available substrates and provide direct access to bis-angularly functionalized fused bicyclic lactones, with the possibility of varying the angular substituents at C8 and C9.

2.4. Ring-expansion/ring system interchange via consecutive hetero-domino transformations

An experimentally appealing means for the synthesis of type-**4** bicyclo[2.2.2]aldols involves the consecutive domino approach that we reported several years ago, where $Pb(OAc)_4$ operates as a multi-task reagent (as an oxidant to effect the oxidative cleavage, and as a Lewis acid to promote the ring-expansion), while solid K_2CO_3 in MeOH–H_2O added a few hours later achieves the fused to bridged ring system interchange, all in one-pot.[4a] A less toxic version of this process, using only one equivalent of $Pb(OAc)_4$, is the three-reagent consecutive hetero-domino reaction initiated by $PhI(OAc)_2$ (oxidative/pericyclic transformation), continued by $Pb(OAc)_4$ (ring expansion), and completed by a mild base (ring system interchange). Some examples of the ring expansion/ring system interchange upon oxidative cleavage of substrate-diols incorporating a mild basic treatment in the same reaction vessel are shown in Scheme 6. By using this one-pot protocol, the bicyclo[2.2.2]octane derivatives **4j/4j′** and **4l/4l′** were obtained directly, a mixture of epimeric aldols from substrate-diols **1j** and **11b,** respectively. Obtained in a single synthetic operation from diol **1h**, the bicyclic aldol **4h** with its challenging array of five asymmetric centers, is a particularly attractive synthetic building block.



Scheme 5. Reagents and conditions: (a) 2.4 equiv $Pb(OAc)_4$ (88% for **2g**, 81% for **2k**); (b) 1.2 equiv $Pb(OAc)_4$, PhMe, 25 °C or 1.2 equiv $PhI(OAc)_2$, MeCN, 25 °C (84%); (c) PCC, CH_2Cl_2, MS 4 Å, 25 °C (85%).



Scheme 6. Reagents and conditions: (a) 2.4 equiv $Pb(OAc)_4$, PhMe, 25 °C then K_2CO_3–MeOH, H_2O, 25 °C, 73% for **4b**/**4b′**, 71% for **4h**, 73% for **4j**/**4j′**, and 72% for **4l/4l′;** (b) TBSCl, DMF–imidazole, 0–25 °C (77%).

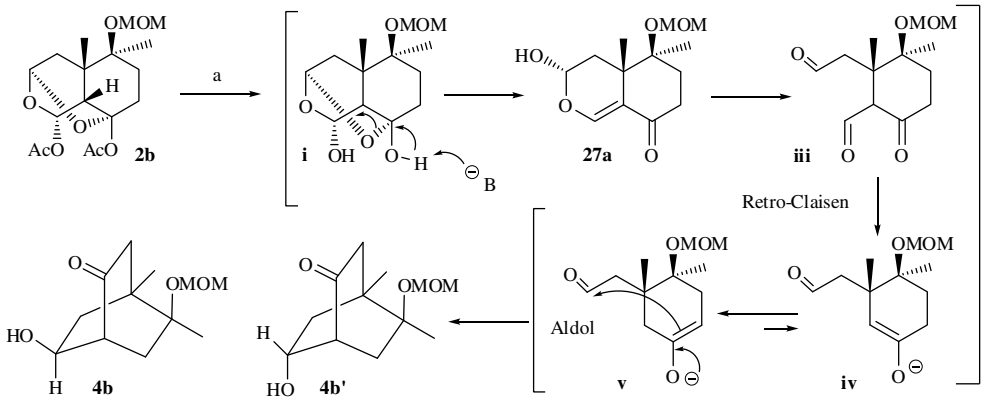


Figure 2. (a) K_2CO_3–MeOH, H_2O, 25 °C.

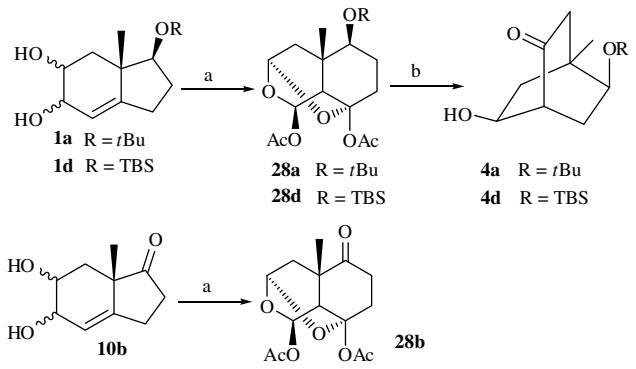
The base-induced rearrangement of **2b**, with a step by step transformation that explains the conversion of the latter into the isolable **27a** and hence into **4b**, is shown in Figure 2.

Following the mechanistic rationale of these consecutive domino reactions, we attempted to stop the process at the step before retro-Claisen deacylation, such as **27a** with the aim of ultimately using it in synthetic projects. At the outset, upon subjection of type-**2b** domino products to mild base treatment we observed the very fast formation of type-**27** intermediates, characterized as their corresponding type-**27b** TBS-ether, or OAc-derivatives, along with an equally fast formation (less than 10 min following base addition) of the type-**4′** kinetic bicyclic aldol. We thus monitored the reaction of **2b** with K_2CO_3–MeOH–H_2O in order to gain control over the final destination (**27a**, **4b′**, **4b**, in the order of their formation), and found that **27a** can be obtained as the major component of a two-component mixture, **27a** and **4b′**, by stopping the process within 5 min. Isolation of the intermediate **27a** (as well as many more in these series) provides substantiation of the proposed mechanism, though the synthetic utility of such an endeavor remains questionable, since ending the process at this point proved impractical due to the difficulties in chromatographic separation of **27** and **4′** in most cases. The present methodology offers easy access to relatively uncommon type-**4** bicyclo[2.2.2]octanone derivatives possessing three differentiable sites (a free hydroxyl group, a *t*Bu-protected hydroxyl, and a carbonyl) on each bridge.

2.5. Greening efforts

As the major disadvantage of this methodology concerns the toxicity of $Pb(OAc)_4$, we reinvestigated the version of the domino process using various Rigby oxidants[16] known as efficient glycol fission reagents.[9] All of our attempts to induce **1a**, **1d**, and **10b** to undergo a full-cascade transformation (type-**1** to type-**2**) using $PhI(OAc)_2$, Dess–Martin periodinane, manganic acetate, triphenyl bismuth carbonate, sodium bismuthate, or sodium metaperiodate failed to give any domino product at room temperature. When reaction times were considerably extended at elevated temperatures (70 °C for 48–72 h), $PhI(OAc)_2$[17] did produce a low percentage of ring-expanded product, although the reaction was not clean (presence of PhI). The yields before chromatography were 89%, 85% and 68% for **28a**, **28b**, and **28d**, respectively, dropping to 55%, 22%, and 18% for **28a**, **28b**, and **28d**, respectively, upon silica gel or neutral alumina chromatography. This complication was bypassed by making recourse to in situ basic treatment as an alternative domino procedure (the consecutive domino).[4a] Thus, treatment of substrate-diols **1a** and **1d** with $PhI(OAc)_2$ at 70 °C for 48–72 h gave the corresponding domino products **28a** and

28d, which were converted to **4a** and **4d** by treatment with K_2CO_3–MeOH–H_2O in one-pot (Scheme 7).



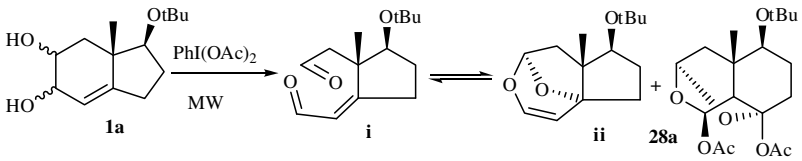
Scheme 7. Reagents and conditions: (a) $PhI(OAc)_2$, MeCN, 70 °C, 40 h; (b) K_2CO_3–MeOH–H_2O, 25 °C.

The use of $PhI(OAc)_2$ in a non-nucleophilic, strongly ionizing solvent,[18] such as 1,1,1,3,3,3-hexafluoropropane-2-ol (HFP), did not help either. In view of the lack of success to achieve acceptable yields in domino products, we again made recourse to microwave-assistance, and optimization experiments were carried out on **1a** (Table 3). The choice of solvent was found to be important in these transformations, with the best results obtained when operating in acetonitrile (1 h at 120 °C gave complete conversion) followed by toluene, while AcOH, CH_2Cl_2, and other domino solvents proved inefficient.

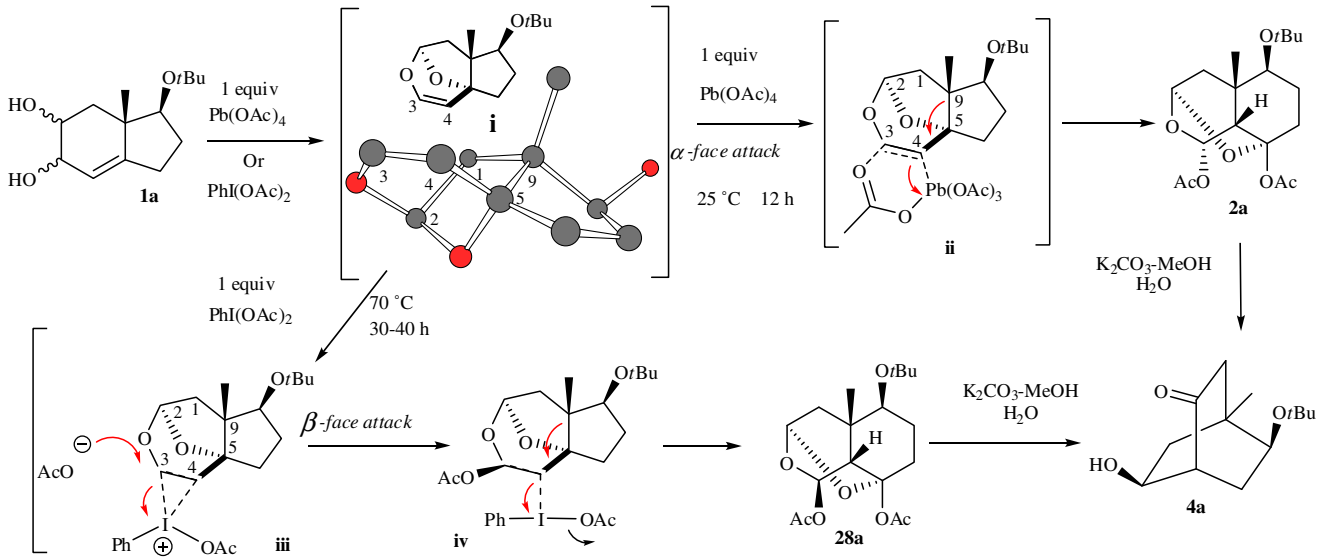
The optimized conditions were then applied to the substrate-diols **1d** and **10b** (Scheme 7), and although the type-**28** domino products could be obtained as approximately 95% pure condition (by inspecting ^1H and ^{13}C NMR of the reaction crudes), they again suffered extensive decomposition when chromatographed (silica gel or neutral alumina). Finally, both $Pb(OAc)_4$-mediated domino product **2a** (whose structure was secured by X-ray analysis)[19] and the bis-acetoxy bis-acetal **28a** obtained upon $PhI(OAc)_2$-mediated ring expansion of the common substrate-diol **1a** provided the same bridged-ring system **4a** in 68% yield upon basic treatment with potassium carbonate (Scheme 8).

This result unequivocally implicates iodonium **iii** formation followed by an S_N2 opening with the reagent's acetate (intermolecular acetate delivery) being responsible for the reversal in facial selectivity at C3, while the $Pb(OAc)_4$-mediated domino product is formed via a [4+2] approach (Scheme 8).[20] The difference in reactivity concerning the ring expansion step can be attributed to

Table 3



Entry	Time (min)	Temperature (°C)	Solvent	(**i** + **ii**/**28a**)
1	15	120	MeCN	83/17
2	60	100	MeCN	58/42
3	60	120	MeCN	0/100
4	120	90	MeCN	50/50
5	120	92	PhMe	70/30



Scheme 8. $Pb(OAc)_4$ and $PhI(OAc)_2$-mediated variants of the domino process: Two closely related reagents and a divergio-convergent pathway from **1a** to **4a**.

higher C–I bond energy compared with the C–Pb in intermediates **iv** and **ii,** respectively.[21] The postulated mechanism accommodates all of the experimental results, and is consistent with the sequence of events proposed in Scheme 8. To summarize, there is no preparative advantage in using $PhI(OAc)_2$, as the overall yield is far inferior to that observed with $Pb(OAc)_4$, underscoring the importance of the former reagent in the success of these domino reactions. Furthermore, the difficulty appeared not only to be associated with production of the type-**28** domino products, but also with their high reactivity, since considerable loss was incurred upon chromatographic purification through a short column of silica or neutral alumina.

3. Conclusion

We have expanded the $Pb(OAc)_4$-mediated domino reactions to variously substituted bicyclic templates useful for the construction of six-membered building blocks embodied in potential synthetic targets. The usefulness of this transformation lies in the ease of its experimental technique and great increase in structural complexity. The tolerance of various substituents on substrate's periphery, including ones that are known to react with the reagent at elevated temperatures, makes this domino process an attractive addition to the synthetic methods, by allowing for the generation of a wide number of heavily substituted six-membered rings in a completely stereoselective manner. Insofar as greening of the process is concerned, while the use of the non-toxic $PhI(OAc)_2$ afforded the ring expanded type-**28** domino compounds, extensive decomposition occurred upon attempted chromatographic separation, which complicated the purification and hence rendered the process less efficient. On the basis of the optimized domino reactions reported here, it appears that microwave-induced organic reaction enhancement techniques can be used conveniently while the green domino protocol did not meet our expectations.

4. Experimental

4.1. General procedures

General experimental details were carried out as previously described.[1] All experiments were run in triplicate, and agreement was generally within less than 10%. Yields are an average of three runs, not optimized. 'Usual work-up' means washing of the organic layer with brine, drying on anhydrous $MgSO_4$, and evaporating in vacuo with a rotary evaporator at aspirator pressure.

4.1.1. Method A (using PhMe, CH_2Cl_2, MeCN, EtOAc as solvent)

A dry flask was charged with unsaturated diols (1.0 mmol) and $Pb(OAc)_4$ (2.4 mmol) vacuumed, flushed with argon and cooled to 0 °C. Solvent (5 mL) was added, the cooling bath removed soon after, and the reaction mixture was stirred for ca. 15 h at room temperature (TLC monitoring). Upon completion, the reaction mixture was diluted with Et_2O, filtered through a pad of Celite and silica gel and flash chromatographed using heptane as eluent, to remove most of the solvent, then heptane–Et_2O, 1:1 as eluent to afford pure domino products.

4.1.2. Method A (using AcOH as solvent)

A dry flask was charged with unsaturated diols (1.0 mmol) and $Pb(OAc)_4$ (2.4 mmol) vacuumed, flushed with argon, and cooled to 0 °C. Acetic acid (5 mL) was added, the cooling bath removed soon after, and the reaction mixture was stirred for 12 h at room temperature. The mixture was diluted with EtOAc and washed carefully with satd $NaHCO_3$ solution till neutral pH, worked up as usual and purified through flash chromatography.

4.1.3. Method B (microwave accelerated domino transformations)

A microwave tube was charged with a solution of a bicyclic unsaturated diol (0.5 mmol) in 2 mL of dry PhMe and $Pb(OAc)_4$ (2.4 mmol) and inserted inside a microwave cavity. The reaction mixture was magnetically stirred for 15 min at 80 °C (100 W) or only 5 min at 90 °C (100 W). The tube was cooled to room temperature, diluted with Et_2O, the suspension filtered over a $MgSO_4$/Celite/SiO_2 path, the filtrate concentrated and purified by flash chromatography.

4.1.4. Typical procedure for two-reagent (two oxidants) domino reactions

To a solution of the selected unsaturated diol (5 mmol) in anhydrous PhMe (50 mL) under an inert atmosphere, $PhI(OAc)_2$ (1.932 g, 6 mmol) was added. Stirring was maintained under argon for 24 h, at which point $Pb(OAc)_4$ (2.660 g, 6 mmol) was added. After an additional 15 h of stirring at room temperature, the reaction mixture was diluted with methylene chloride, washed with saturated sodium bicarbonate, water and brine. The organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified on silica gel.

4.1.5. Typical procedure for consecutive domino reactions

A dry flask was charged with unsaturated diol (1.0 mmol) and $Pb(OAc)_4$ (1.22 g, 2.76 mmol), vacuumed, flushed with argon and then again vacuumed for 1 h. Dry PhMe (14 mL) was then added at −20 °C and stirring continued for 30 min at this temperature for an additional 15 h at 25 °C. Following TLC control indicating the formation of the ring-expanded domino product, K_2CO_3 (1 g) in MeOH–H_2O (22.5 mL, 8:1) was added and after stirring at 25 °C for 7 h, methanol was removed under reduced pressure. The reaction mixture was diluted with methylene chloride, and worked up as usual. The residue was purified on silica gel.

4.1.6. General procedure for fluoride deprotection

To a magnetically stirred solution of TBS-protected alcohol (1.0 mmol) was added tetrabutylammonium fluoride (2.0 mmol, 1M, THF). The reaction mixture was stirred at 60 °C until TLC monitoring showed that no starting material was left (usually ca. 1 h). After dilution with EtOAc, and the usual work-up the residue was purified through flash chromatography.

4.2. Preparation of substrate-diols

4.2.1. Unsaturated diol 1c

Lithium aluminum hydride reduction followed by fluoride deprotection was carried out on **12**[1] of 200 mg (0.41 mmol), using the general procedure (1 h, 60 °C) to give, after chromatography (SiO_2, EtOAc–MeOH, 95:5), 69 mg (65%) of **1c**. One diastereomer was separated for charaterization purposes (see stereochemical abstracts). Colorless oil; $[\alpha]_D^{20} = +18$ (*c* 1.0, $CHCl_3$); IR (film): 3420, 1450, 1371, 1148, 1104, 1038, 915 cm^{-1}; ^1H NMR (300 MHz): δ = 1.10 (s, 3H), 1.18 (s, 3H), 1.60 (dd, *J* = 7.2, 13.8 Hz, 1H), 2.13 (dtd, *J* = 1.1, 5.2, 17.2 Hz, 1H), 2.17 (dd, *J* = 4.5, 14.3 Hz, 1H), 2.91 (dddd, *J* = 1.7, 2.4, 9.7, 17.3 Hz, 1H), 3.38 (s, 3H), 4.0 (ddd, *J* = 4.0, 4.7, 7.2 Hz, 1H), 4.13 (dd, *J* = 5.2, 9.6 Hz, 1H), 4.21 (t, *J* = 4.5 Hz, 1H), 4.66 and 4.71 (ABquartet, *J* = 6.6 Hz, 2H), 5.49 (ddd, *J* = 1.7, 2.3, 4.6 Hz, 1H); ^{13}C NMR (75 MHz): δ = 19.5, 25.2, 31.8, 33.7, 47.7, 55.7, 67.8, 68.8, 80.2, 80.7, 96.0, 118.8, 150.2; ESIMS (MeOH): 281.1 ($[M+Na]^+$, 100); HRESIMS (MeOH) calcd for $C_{13}H_{22}O_5Na$: 281.1365; found 281.1366.

4.2.2. Unsaturated diol 1e

To a stirred solution of **15** (62 mg, 0.18 mmol), in THF (8 mL), at −78 °C, allyl magnesiumbromide (0.72 mL, 1 M in THF) was slowly

added. The solution was stirred for 1 h at −78 °C. Then, the reaction mixture was diluted with Et_2O, and a saturated solution of NH_4Cl was added until pH 7. The aqueous layer was extracted with Et_2O. The organic layer was worked up as usual and chromatographed on silica gel (ethyl acetate/heptane 5:95) to afford 44 mg of **1e-OTBS** (64% and 27% of recovered starting material).

Fluoride deprotection was carried out on 26 mg (0.07 mmol) of **1e-OTBS**, using the general procedure (2 h, 60 °C) to give, after chromatography (SiO_2, EtOAc–heptane, 1:5), 16 mg (86%) of **1e**. One diastereomer was separated for charaterization purposes (see stereochemical abstracts). Colorless solid; mp: 94.0–95.0 °C; $[\alpha]_D^{20} = -7$ (*c* 0.25, $CHCl_3$); IR (film): ν = 3204, 1462, 1390, 1362, 1196, 1089 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.14 (s, 9H), 1.15 (s, 3H), 1.35 (d, *J* = 14.2 Hz, 1H), 1.66 (tdd, *J* = 6.2, 8.7, 12.7 Hz, 1H), 1.92 (dddd, *J* = 4.0, 8.2, 9.6, 18.4 Hz, 1H), 1.95 (d, *J* = 14.2 Hz, 1H), 2.07 (m, 1H), 2.25 (dd, *J* = 7.2, 13.4 Hz, 1H), 2.37 (dd, *J* = 7.8, 13.5 Hz, 1H), 2.51 (td, *J* = 3.0, 13.6 Hz, 1H), 3.34 (t, *J* = 8.6 Hz, 1H), 4.02 (s, 1H), 5.14 (dd, *J* = 2.0, 11.0 Hz, 1H), 5.18 (d, *J* = 2.9 Hz, 1H), 5.25 (s, 1H), 5.95 (ddt, *J* = 7.2, 10.4, 17.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 18.5, 26.4, 28.8 (3C), 30.1, 43.3, 43.7, 45.8, 71.6, 71.9, 72.6, 80.9, 119.1, 119.2, 133.9, 148.8; ESIMS (MeOH): 303.1 ([M+Na]$^+$, 100); HRESIMS: calcd for $C_{17}H_{28}O_3Na$ *m*/*z* 303.1936, found 303.1939.

4.2.3. Unsaturated diol 1f

To a stirred solution of **15** (105 mg, 0.3 mmol), in THF (10 mL), at −78 °C, methyl lithium (0.6 mL, 1.6 M in Et_2O) was slowly added. The solution was stirred for 1 h at −78 °C. Then the reaction mixture was diluted with Et_2O, and a saturated solution of NH_4Cl was added until pH 7. The aqueous layer was extracted with Et_2O. The organic layer was worked up as usual and chromatographed on silica gel (EtOAc–heptane 1:9) to afford 87 mg of **1f-OTBS** (79%).

Fluoride deprotection was carried out on 39 mg (0.11 mmol) of **1f-OTBS**, using the general procedure (2 h, 60 °C) to give after chromatography (SiO_2, EtOAc–heptane, 1:5) 22 mg (80%) of **1f**. One diastereomer was separated for charaterization purposes (see stereochemical abstracts). Colorless solid; mp: 94.5–95.5 °C; $[\alpha]_D^{20} = -11$ (*c* 0.7, $CHCl_3$); IR (film): ν = 3395, 1455, 1362, 1195, 1090, 1075, 1020, 882 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.15 (s, 9H), 1.26 (s, 3H), 1.45 and 1.92 (ABquartet, *J* = 14.4 Hz, 2H), 1.65 (tdd, *J* = 6.1, 8.8, 13.0 Hz, 1H), 1.82–1.95 (m, 1H), 2.06 (dd, *J* = 6.2, 16.0 Hz, 1H), 2.52 (t, *J* = 14.5 Hz, 1H), 3.36 (t, *J* = 8.6 Hz, 1H), 3.92 (s, 1H), 5.29 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.0, 26.5, 28.2, 28.9 (3C), 30.2, 43.6, 45.4, 70.8, 72.5, 73.0, 80.3, 119.4, 149.0; ESIMS (MeOH): 277.1 ([M+Na]$^+$, 100); HRESIMS: calcd for $C_{15}H_{26}O_3Na$ *m*/*z* 277.1780, found 277.1770; Anal. Calcd for $C_{15}H_{26}O_3$ (254.37): C, 70.83; H, 10.30. Found: C, 71.01; H, 10.28.

4.2.4. Unsaturated diol 1h

4.2.4.1. Bicyclic enone 19. The enantiomeric excess for **17**, used as the starting material, was determined through reduction to the alcohol **18** and formation of the corresponding (*S*)-2-acetoxypropionyl ester by reaction with (*S*)-2-acetoxypropionyl chloride in the presence of triethylamine and DMAP in dry CH_2Cl_2 at 0 °C under an inert atmosphere. The ^1H NMR spectrum of the diastereomeric lactates thus formed displayed a 9.1:1 ratio of doublets at δ 4.74 and 4.80 ppm, and methyl doublets at δ 1.35 and 1.32 ppm indicating that hydrindene-dione **17** was formed in 81% ee. To a stirred solution of **18** (910 mg, 4.73 mmol) in dry CH_2Cl_2 (5.8 mL) at −78 °C were added 0.11 mL of H_3PO_4 (prepared by dissolving 480 mg of P_2O_5 in 1.32 mL of 84% H_3PO_4) and 0.23 mL of boron trifluoride etherate. The mixture was stirred for 1.5 h at −78 °C and then for 2 days at 25 °C. The mixture was then poured into 7 mL of 2 M NH_4OH solution and the product was extracted with CH_2Cl_2, the solvent was evaporated under reduced pressure to give after chromatography (EtOAc–heptane, 1:9) 21% of starting material recovered and 646 mg (71%) of **19**. Yellow oil; $[\alpha]_D^{20} = +163$ (*c* 1.8, $CHCl_3$); IR (film): ν = 1669, 1445, 1385, 1353, 1213, 1167, 1106, 1053, 961, 908, 871, 850 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.19 (dd, *J* = 1.5, 5.9 Hz, 3H), 1.22 (dd, *J* = 4.5, 12.2 Hz, 1H), 1.54 (tdd, *J* = 1.1, 6.7, 13.4 Hz, 1H), 1.73 (tdd, *J* = 1.5, 5.8, 12.9 Hz, 1H), 1.89 (dd, *J* = 8.1, 13.7 Hz, 1H), 2.01 (ddd, *J* = 2.3, 4.8, 13.0 Hz, 1H), 2.16 (dd, *J* = 4.2, 12.3 Hz, 1H), 2.23 (dd, *J* = 6.8, 15.0 Hz, 1H), 2.30–2.44 (m, 2H), 2.61–2.70 (m, 1H), 3.79–3.85 (m, 1H), 3.97 (d, *J* = 5.7 Hz, 1H), 5.66 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.7, 30.4, 31.3, 32.8, 35.5, 44.9, 53.7, 75.6, 88.9, 121.0, 174.8, 199.3; ESIMS (MeOH): 215.1 ([M+Na]$^+$, 55); HRESIMS: calcd for $C_{12}H_{16}O_2Na$ *m*/*z* 215.1048; found 215.1015.

4.2.4.2. Diol 1h. A dry three-necked flask, equipped with a Dean-Stark apparatus, was charged with $Pb(OAc)_4$ (12.5 g, 28.2 mmol) and then vacuumed, and flushed with argon. Dry benzene (57 mL) and **19** (922 mg, 4.7 mmol) were added and the reaction mixture was heated at 90 °C (oil bath temperature should not exceed 100 °C) for 4 days. After cooling, a large volume of Et_2O was added, and the mixture was stirred for an additional hour, filtered, and the filtrate worked up as usual. Chromatography on silica with heptane–Et_2O 1:1 as eluent afforded 624 mg (55%) of the corresponding acetoxyenone **19** as a mixture of diastereoisomers, which were directly used in the next step. To a stirred suspension of $LiAlH_4$ (133 mg, 3.51 mmol) in anhydrous Et_2O (3 mL), cooled to nearly 0 °C, was added dropwise a solution of acetoxyenone (220 mg, 0.88 mmol) in anhydrous Et_2O (2 mL). After stirring at this temperature for 30–40 min (TLC monitoring) the mixture was diluted with Et_2O and treated with a small amount of 6 N NaOH solution (for each 1 g of $LiAlH_4$, 1 mL of water, 1 mL of 6 N NaOH, and 3 mL more water were added). The organic layer was worked up as usual to give, after silica gel chromatography (EtOAc–heptane, 4:1), 82% (150 mg) of the desired diols **1h**. One diastereomer was separated for charaterization purposes (see stereochemical abstracts). Yellow oil; $[\alpha]_D^{20} = +34$ (*c* 0.5, $CHCl_3$); IR (film): ν = 3400, 2962, 2924, 1434, 1384, 1278, 1172, 1103, 1046, 1028, 995, 970, 946 cm^{-1}; ^1H NMR (300 MHz): δ = 1.24 (d, *J* = 5.9 Hz, 3H), 1.29–1.33 (m, 1H), 1.48 (ddd, *J* = 1.3, 2.5, 11.3 Hz, 1H), 1.52–1.56 (m, 1H), 1.78 (dd, *J* = 7.6, 13.4 Hz, 1H), 2.03 (ddd, *J* = 7.0, 14.0 Hz, 1H), 2.32 (dd, *J* = 3.9, 14.0 Hz, 1H), 2.44–2.56 (m, 1H), 2.62 (dd, *J* = 4.1, 12.5 Hz, 1H), 3.87 (ddd, *J* = 4.1, 5.9, 11.0 Hz, 1H), 3.94 (d, *J* = 6.3 Hz, 1H), 4.10 (m, 1H), 4.22 (m, 1H), 5.27 (t, *J* = 1.4 Hz, 1H); ^{13}C NMR (75 MHz): δ = 19.5, 29.6, 31.3, 37.4, 47.5, 49.7, 67.8, 68.6, 75.3, 89.7, 117.4, 150.1; ESIMS (MeOH): 233.1 ([M+Na]$^+$, 56); HRESIMS: calcd for $C_{12}H_{18}O_3Na$ *m*/*z* 233.1254, found 233.1159.

4.2.5. Unsaturated diol 1i

4.2.5.1. Ketal 21. Hydrindene-dione **20** (1.5 g, 7.8 mmol) was dissolved in ethylene glycol (37.5 mL). Molecular sieves (4 Å) and *p*-TsOH (1.35 mg, 7.8 mmol, 1 equiv) were then added and the reaction mixture was stirred at 25 °C for 45 min. The reaction mixture was poured carefully into a mixture of ice and saturated aqueous $NaHCO_3$. This solution was extracted with EtOAc. The organic layer was worked up as usual to give 1.7 g (94%) of the desired ketal **21**: colorless oil; $[\alpha]_D^{20} = +27$ (*c* 1.0, $CHCl_3$); IR (film): ν = 1663, 1419, 1336, 1315, 1266, 1223, 1198, 1171, 1037, 972, 931, 897, 770 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.62 (ddd, *J* = 2.0, 4.9, 12.3 Hz, 1H), 1.70 (dd, *J* = 1.4, 6.4 Hz, 3H), 1.77 (ddd, *J* = 2.3, 8.3, 12.9 Hz, 1H), 2.02 (dt, *J* = 10.5, 12.5 Hz, 1H), 2.20–2.39 (m, 3H), 2.46–2.59 (m, 2H), 3.95–3.99 (m, 4H), 5.37 (dq, *J* = 6.4, 15.7 Hz, 1H), 5.60 (dq, *J* = 1.7, 15.7 Hz, 1H), 5.96 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 18.0, 25.7, 26.5, 31.6, 32.8, 54.8, 64.7, 65.7, 117.0, 125.1, 127.6, 129.7, 170.1, 199.5; ESIMS (MeOH): 257.1 ([M+H]$^+$, 65); HRESIMS: calcd for $C_{14}H_{19}O_3$ *m*/*z* 235.1312, found 235.1334;

Anal. Calcd for $C_{14}H_{18}O_3$ (234.13): C, 71.77; H, 7.74. Found: C, 71.65; H, 7.94.

4.2.5.2. Acetoxyenones 22. A dry three-necked flask equipped with a Dean-Stark apparatus was charged with **21** (300 mg, 1.2 mmol) and $Pb(OAc)_4$ (2.27 g, 5.12 mmol, 4 equiv) vacuumed, flushed with argon before dry benzene (15 mL) was added, and the reaction mixture was heated at 90 °C (oil bath temperature should not exceed 100 °C) for 4 days. After cooling, a large volume of Et_2O was added, and the reaction mixture stirred for an additional hour, filtered, the filtrate was worked up as usual, and purified by chromatography on silica with CH_2Cl_2–Et_2O, 30:1 as eluent affording 298 mg (85%) of a mixture of **22α** and **22β** (1/1) as white solids. Compound **22α**: Mp: 112–113 °C; $[\alpha]_D^{20} = +59$ (*c* 1.0, $CHCl_3$); IR (film): ν = 1746, 1683, 1445, 1372, 1310, 1235, 1208, 1151, 1069, 1045, 976, 948, 902 cm^{-1}; ^1H NMR (500 MHz): δ = 1.72 (dd, *J* = 1.5, 6.4 Hz, 3H), 1.78 (ddd, *J* = 2.1, 8.7, 13.1 Hz, 1H), 1.92 (dd, *J* = 5.3, 11.6 Hz, 1H), 2.02–2.09 (m, 1H), 2.13 (s, 3H), 2.37 (dd, *J* = 11.7, 13.3 Hz, 1H), 2.46–2.53 (m, 1H), 2.56–2.63 (m, 1H), 3.91–3.99 (m, 4H), 5.35 (dd, *J* = 5.3, 13.4 Hz, 1H), 5.44 (dq, *J* = 6.4, 15.7 Hz, 1H), 5.70 (dq, *J* = 1.5, 15.7 Hz, 1H), 6.01 (t, *J* = 1.8 Hz, 1H); ^{13}C NMR (125 MHz): δ = 18.0, 20.8, 26.5, 31.6, 32.1, 55.9, 64.7, 65.8, 71.1, 116.6, 123.9, 128.0, 129.5, 170.0, 170.1, 193.1; ESIMS (MeOH): 315.1 ([M+Na]$^+$, 100); HRESIMS: calcd for $C_{16}H_{20}O_5Na$ *m/z* 315.1208, found 315.1198; Anal. Calcd for for $C_{16}H_{20}O_5$ (292.13): C, 65.74; H, 6.90. Found: C, 65.26; H, 7.04.

4.2.5.3. Diol 1i. To a magnetically stirred suspension of $LiAlH_4$ (83 mg, 2.18 mmol, 4 equiv) in 1.5 mL of anhydrous Et_2O, cooled to nearly 0 °C, was added dropwise a solution of acetoxyenones **22** (160 mg, 0.54 mmol) in anhydrous Et_2O (1.5 mL). After stirring at this temperature for 30–40 min (TLC monitoring) the mixture was diluted with Et_2O and treated with a small amount of 6 M NaOH solution (for each 1 g of $LiAlH_4$, 1 mL of water, 1 mL of 6 M NaOH, and 3 mL more water were added). The organic layer was worked up as usual to give, after silica gel chromatography (EtOAc–heptane, 4:1), 120 mg (98%) of the desired diols **1i**. One diastereomer was separated for charaterization purposes (see stereochemical abstracts). Yellow oil; $[\alpha]_D^{20} = -61$ (*c* 1.8, $CHCl_3$); IR (film): ν = 3403, 1441, 1306, 1252, 1155, 1035, 959, 914 cm^{-1}; ^1H NMR (500 MHz): δ = 1.69 (m, 1H), 1.71 (dd, *J* = 1.4, 6.4 Hz, 3H), 1.88–1.97 (m, 2H), 2.05 (dd, *J* = 3.0, 13.9 Hz, 1H), 2.28 (ddd, *J* = 8.0, 9.5, 16.8 Hz, 1H), 2.45 (ddd, *J* = 2.5, 11.9, 16.8 Hz, 1H), 3.92 (m, 4H), 4.01 (dd, *J* = 4.3, 8.5 Hz, 1H), 4.16 (d, *J* = 2.9 Hz, 1H), 5.57 (dq, *J* = 6.4, 15.8 Hz, 1H), 5.66 (s, 1H), 5.86 (dd, *J* = 1.4, 15.8 Hz, 1H); ^{13}C NMR (125 MHz): δ = 18.0, 25.5, 31.3, 31.4, 51.4, 64.5, 65.6, 68.6, 68.9, 117.1, 124.1, 126.4, 136.9, 143.0; ESIMS (MeOH): 275.1 ([M+Na]$^+$, 100). HRESIMS: calcd for $C_{14}H_{20}O_4Na$ *m/z* 275.1259, found 275.1244.

4.2.6. Unsaturated diol 11b

Fluoride deprotection was carried out on 286 mg (0.69 mmol) of known **11a**,[1] using the general procedure (1 h, 60 °C) to give after chromatography (SiO_2, heptane–EtOAc, 3:2) 100 mg (81%) of **11b**. Colorless oil; $[\alpha]_D^{20} = +22$ (*c* 1.3, $CHCl_3$); IR (film): ν = 3386, 1710, 1650, 1457, 1263, 1115, 1051, 879 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): 1.35 (s, 3H), 1.86 (dd, *J* = 3.2, 14.3 Hz, 1H), 2.35–2.75 (m, 5H), 3.95 (m, 1H), 4.25 (m, 1H), 4.80 (m, 2H), 5.45 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 28.0, 29.0, 37.4 (2C), 43.8, 68.0, 68.5, 103.0, 117.2, 151.3, 159.0; ESIMS (MeOH): 203.2 ([M+Na]$^+$, 100); HRESIMS: calcd for $C_{11}H_{16}O_2Na$ *m/z* 203.2387; found 203.2384.

4.2.7. Unsaturated diol 13a

Starting from **11a**, following allylic hydroxylation and MOM-protection,[1] fluoride deprotection was carried out on 260 mg (0.55 mmol), using the general procedure (1 h, 60 °C) to give after chromatography (SiO_2, heptane–EtOAc, 1:1) 110 mg (85%) of **13a**. Colorless oil; $[\alpha]_D^{20} = -34$ (*c* 1.0, $CHCl_3$); IR (film): ν = 3363, 1736, 1427, 1373, 1244, 1047, 918 cm^{-1}; ^1H NMR (300 MHz): δ = 1.19 (s, 3H), 1.70 (t, *J* = 12.4 Hz, 1H), 2.03–2.09 (m, 1H), 2.06 (s, 3H), 2.21 (d, *J* = 16.7 Hz, 1H), 2.92 (ddt, d, *J* = 2.4, 8.3, 16.8 Hz, 1H), 3.93 (ddd, *J* = 3.7, 7.4, 12.4 Hz, 1H), 4.13 (ddd, *J* = 3.7, 7.4, 12.4 Hz, 1H), 5.00 (d, *J* = 1.8 Hz, 1H), 5.12 (d, *J* = 1.8 Hz, 1H), 5.34 (m, 1H), 5.70 (ddd, *J* = 2.0, 3.9, 8.3 Hz, 1H); ^{13}C NMR (75 MHz): δ = 21.2, 27.6, 36.1, 41.2, 46.2, 72.2, 73.9, 75.1, 108.1, 120.1, 146.6, 157.5, 170.9; ESIMS (MeOH): 261.1 ([M+Na]$^+$, 100); HRESIMS: calcd for $C_{13}H_{18}O_4Na$ *m/z* 261.1066, found 261.1103.

4.2.8. Unsaturated diols 13b

Starting from **11a**, following allylic hydroxylation and acetyl-protection,[1] fluoride deprotection was carried out on 40 mg (0.08 mmol), using the general procedure (1 h, 60 °C) to give after chromatography (SiO_2, heptane–EtOAc, 1:1) 16 mg (88%) of **13b**. One diastereomer was separated for charaterization purposes (see stereochemical abstracts): yellow oil; $[\alpha]_D^{20} = -36$ (*c* 1.1, $CHCl_3$); IR (film): ν = 3381, 1658, 1450, 1147, 1093, 1043, 915 cm^{-1}; ^1H NMR (500 MHz): δ = 1.18 (s, 3H), 1.71 (td, *J* = 4.6, 12.2 Hz, 1H), 2.05 (dt, *J* = 3.8, 12.2 Hz, 1H), 2.30 (d, *J* = 15.8 Hz, 1H), 2.70 (br s, 1H), 2.76 (ddt, *J* = 2.5, 7.6, 15.7 Hz, 1H), 3.38 (s, 3H), 3.94 (ddd, *J* = 4.2, 7.8, 11.4 Hz, 1H), 4.13 (m, 1H), 4.66 (m, 1H), 4.66 and 4.69 (ABquartet, *J* = 6.8 Hz, 2H), 5.03 (d, *J* = 1.8 Hz, 1H), 5.16 (d, *J* = 1.8 Hz, 1H), 5.35 (d, *J* = 2.5 Hz, 1H); ^{13}C NMR (125 MHz): δ = 27.8, 36.3, 41.4, 45.8, 55.4, 72.4, 75.2, 76.3, 94.8, 108.3, 120.0, 147.7, 159.0; ESIMS (MeOH): 263.1 ([M+Na]$^+$, 100); HRESIMS: calcd for $C_{13}H_{20}O_4Na$ *m/z* 263.1259, found 263.1290.

4.2.9. Unsaturated diol 14

Fluoride deprotection was carried out on 209 mg (0.43 mmol) of **10a**, using the general procedure (1 h, 60 °C) to give after chromatography (SiO_2, heptane–EtOAc, 1:1) 98 mg (91%) of **14**. One diastereomer was separated for charaterization purposes (see stereochemical abstracts). Colorless oil; $[\alpha]_D^{20} = -8$ (*c* 1.2, $CHCl_3$); IR (film): ν = 3417, 1707, 1648, 1370, 1347, 1221, 1181, 1150, 1034, 859 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.27 (t, *J* = 7.1 Hz, 3H), 1.32 (s, 3H), 1.74 (dd, *J* = 2.8, 14.0 Hz, 1H), 2.25 (dd, *J* = 5.3, 14.1 Hz, 1H), 2.29 (ddd, *J* = 2.0, 9.4, 14.7 Hz, 1H), 2.37 (br s, 1H), 2.57–2.62 (m, 1H), 2.85 (dtd, *J* = 2.6, 9.1, 19.9 Hz, 1H), 3.03 (ddt, *J* = 2.4, 10.5, 19.9 Hz, 1H), 4.06 (br s, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 4.21 (br s, 1H), 5.38 (td, *J* = 0.9, 2.2 Hz, 1H), 5.61 (t, *J* = 2.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.4, 28.4, 28.9, 29.8, 37.6, 45.5, 59.7, 67.8, 68.4, 110.2, 118.3, 149.0, 167.1, 174.0; ESIMS (MeOH): 275.1 ([M+Na]$^+$, 100); HRESIMS: calcd for $C_{14}H_{20}O_4Na$ *m/z* 275.1259, found 275.1237.

4.3. Domino products

4.3.1. Domino product 2e

Oxidative cleavage of diols **1e** (16 mg, 0.06 mmol) was achieved using the general procedure (method A) affording after 15 h of stirring at room temperature 14 mg (59%) of **2e** (SiO_2 flash chromatography, heptane–Et_2O 1:1 as eluent). Method B on 20.0 mg (0.07 mmol) afforded 13 mg (45%) of **2e**. Colorless oil; $[\alpha]_D^{20} = -28$ (*c* 0.5, $CHCl_3$); IR (film): ν = 1736, 1367, 1224, 1072, 1021 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.18 (s, 9H), 1.27 (s, 3H), 1.51 (d, *J* = 14.1 Hz, 1H), 1.60 (m, 2H), 1.70 (d, *J* = 14.1 Hz, 1H), 1.84 (tdd, *J* = 2.2, 4.7, 13.5 Hz, 1H), 2.09 (s, 3H), 2.10 (s, 3H), 2.50 (t, *J* = 7.2 Hz, 2H), 2.73 (td, *J* = 4.7, 12.9 Hz, 1H), 3.15 (s, 1H), 3.24 (s, 1H), 5.09 (dd, *J* = 1.8, 5.0 Hz, 1H), 5.14 (s, 1H), 5.85 (m, 1H), 6.44 (d, *J* = 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.4, 22.7, 25.6, 25.9, 28.7, 28.9 (3C), 36.7, 36.8, 42.0, 42.5, 72.9, 73.6, 91.5, 99.3, 104.7, 118.7, 132.0, 169.79 (2C); ESIMS (MeOH): 419.2 ([M+Na]$^+$,

100); HRESIMS: calcd for $C_{21}H_{32}O_7Na$ *m/z* 419.2046, found 419.2044; Anal. Calcd for $C_{21}H_{32}O_7$ (396.47): C, 63.62; H, 8.14. Found: C, 63.52; H, 8.32.

4.3.2. Domino product 2f

Oxidative cleavage of diols **1f** (30 mg, 0.12 mmol) was achieved using the general procedure (method A) affording after 15 h of stirring at room temperature 23 mg (52%) of **2f** (SiO_2 flash chromatography, heptane–Et_2O 1:2 as eluent). Method B on 30.0 mg (0.12 mmol) afforded 22 mg (50%) of **2f**. Colorless solid; mp: 94.5–95.5 °C; $[\alpha]_D^{20} = -34$ (*c* 0.9, $CHCl_3$); IR (film): ν = 1735, 1462, 1368, 1255, 1208, 1021, 1003 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.20 (s, 9H), 1.27 (s, 3H), 1.44 (d, *J* = 11.4 Hz, 1H), 1.46 (s, 3H), 1.58 (ddd, *J* = 2.2, 4.4, 12.8 Hz, 1H), 1.64 (d, *J* = 11.4 Hz, 1H), 1.70–1.74 (m, 1H), 1.88 (ddd, *J* = 2.2, 4.6, 12.8 Hz, 1H), 2.09 (s, 3H), 2.10 (s, 3H), 2.72 (td, *J* = 4.7, 13.0 Hz, 1H), 3.14 (d, *J* = 0.7 Hz, 1H), 3.24 (s, 1H), 6.42 (d, *J* = 0.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.4, 22.7, 24.7, 25.5, 25.9, 28.6, 28.9 (3C), 36.3, 37.0, 44.4, 72.8, 73.6, 91.4, 98.3, 104.8, 169.5, 169.9; ESIMS (MeOH): 393.1 ($[M+Na]^+$, 100); HRESIMS: calcd for $C_{19}H_{30}O_7Na$ *m/z* 393.1889, found 393.1867; Anal. Calcd for $C_{19}H_{30}O_7$ (370.44): C, 61.60; H, 8.16. Found: C, 61.82; H, 8.36.

4.3.3. Domino product 2g

Oxidative cleavage of diols **1g** (2.3 g, 11.6 mmol) was achieved using the general procedure (method A) affording after 19 h of stirring at room temperature 3.01 g (85%) of **2g** (SiO_2 flash chromatography, heptane–Et_2O 1:1 as eluent). Method B on 50.0 mg (0.25 mmol) afforded 65 mg (82%) of **2g**. Colorless solid; mp: 129.0–130.0 °C; $[\alpha]_D^{20} = -44$ (*c* 1.0, $CHCl_3$); IR (film): ν = 3547, 1734, 1370, 1254, 1107, 1061, 1022, 979, 937 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.20 (s, 3H), 1.31 (s, 3H), 1.53 (ddd, *J* = 2.0, 5.1, 14.4 Hz, 1H), 1.61 (dd, *J* = 1.5, 14.3 Hz, 1H), 1.69 (ddd, *J* = 1.9, 5.1, 13.2 Hz, 1H), 1.77 (dd, *J* = 2.6, 14.3 Hz, 1H), 1.90 (ddd, *J* = 5.1, 13.3, 14.3 Hz, 1H), 2.09 (s, 3H), 2.10 (s, 3H), 2.67 (dt, *J* = 5.1, 13.3 Hz, 1H), 3.23 (s, 1H), 5.29 (s, 1H), 6.49 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 20.3, 21.3, 22.6, 24.6, 29.2, 33.5, 37.0, 38.8, 39.3, 72.6, 91.2, 92.7, 103.8, 169.5, 169.8; ESIMS (MeOH): 337.1 ($[M+Na]^+$, 100); HRESIMS: calcd for $C_{15}H_{22}O_7Na$ *m/z* 337.1263, found 337.1263; Anal. Calcd for $C_{15}H_{22}O_7$ (314.33): C, 57.32; H, 7.05. Found: C, 57.47; H, 7.11.

4.3.4. Domino product 2h

Oxidative cleavage of diols **1h** (54 mg, 0.26 mmol) was achieved using the general procedure (method A) affording after 15 h of stirring at room temperature 37 mg (44%) of **2h** (SiO_2 flash chromatography, heptane–EtOAc 4:1 as eluent). Method B on 20.0 mg (0.09 mmol) afforded 22 mg (71%) of **2h**. Colorless oil; $[\alpha]_D^{20} = -29$ (*c* 1.0, $CHCl_3$); IR (film): ν = 1731, 1445, 1370, 1260, 1236, 1221, 1181, 1127, 1076, 1042, 1020, 960, 933, 882 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.34 (d, *J* = 6.3 Hz, 3H), 1.72–1.78 (m, 2H), 1.90–1.98 (m, 2H), 2.00–2.06 (m, 3H), 2.10 (s, 3H), 2.10 (s, 3H), 2.60 (td, *J* = 5.4, 13.1 Hz, 1H), 2.98 (s, 1H), 3.44 (dd, *J* = 1.6, 3.5 Hz, 1H), 4.18 (m, 1H), 5.34 (d, *J* = 2.9 Hz, 1H), 6.28 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.2, 22.3, 22.6 (2C), 28.3, 35.9, 37.9, 42.1, 42.8, 73.1, 81.4, 91.6, 93.5, 103.7, 169.4, 169.5; ESIMS (MeOH): 349.1 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{16}H_{22}O_7Na$ *m/z* 349.1263; found 349.1252.

4.3.5. Domino product 2i

Oxidative cleavage of diols **1i** (35 mg, 0.14 mmol) was achieved using the general procedure (method A) affording after 5 h of stirring at room temperature 31 mg (60%) of **2i** (SiO_2 flash chromatography, heptane–EtOAc 3:1 as eluent). Method B on 30.0 mg (0.12 mmol) afforded 33 mg (75%) of **2i**. Colorless oil; $[\alpha]_D^{20} = -28$ (*c* 1.4, $CHCl_3$); IR (film): ν = 1736, 1444, 1368, 1254, 1224, 1193, 1160, 1083, 1026, 994, 960 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.64 (ddd, *J* = 2.0, 4.8, 13.7 Hz, 1H), 1.74 (dd, *J* = 1.5, 6.3 Hz, 3H), 1.82 (ddd, *J* = 2.0, 5.0, 13.1 Hz, 1H), 1.98 (td, *J* = 5.3, 13.7 Hz, 1H), 2.07 (s, 3H), 2.10 (s, 3H), 2.08–2.13 (m, 2H), 2.60 (td, *J* = 4.8, 13.3 Hz, 1H), 3.29 (s, 1H), 3.86–3.93 (m, 4H), 5.33 (t, *J* = 6.4, 15.8 Hz, 1H), 5.46 (dd, *J* = 1.5, 15.8 Hz, 1H), 5.67 (dq, *J* = 6.4, 15.8 Hz, 1H), 6.18 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 17.4, 20.2, 21.5, 28.3, 29.7, 34.7, 37.2, 43.7, 64.7, 64.8, 90.4, 91.6, 102.1, 109.4, 128.2, 129.7, 168.2, 168.4; ESIMS (MeOH): 391.1 ($[M+Na]^+$, 100); HRESIMS: calcd for $C_{18}H_{24}O_8Na$ *m/z* 391.1369, found 361.1373.

4.3.6. Domino product 23b

Oxidative cleavage of diols **10b** (180 mg, 0.98 mmol) was achieved using the general procedure (method A) affording after 20 h of stirring at room temperature 233 mg (80%) of **23b** (SiO_2 flash chromatography, heptane–Et_2O 1:1 as eluent). Method B on 30.0 mg (0.16 mmol) afforded 42 mg (84%) of **23b**. Colorless solid; mp: 110–120 °C; $[\alpha]_D^{20} = +2$ (*c* 0.6, $CHCl_3$); IR (film): ν = 1740, 1448, 1371, 1251, 1073, 1029, 977 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): 1.29 (d, *J* = 14.6 Hz, 1H), 1.38 (s, 3H), 1.8 (dd, *J* = 1.2, 14.7 Hz, 1H), 2.05 (dd, *J* = 3.0, 14.0 Hz, 1H), 2.11 (s, 3H), 2.14 (s, 3H), 2.47 (ddd, *J* = 2.7, 5.5, 14.0 Hz, 1H), 2.69–2.95 (m, 2H), 3.17 (s, 1H), 5.43 (d, *J* = 2.6 Hz, 1H), 6.41 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.8, 21.0, 22.2, 31.8, 33.8, 39.9, 40.2, 43.0, 90.0, 91.9, 102.1, 169.1, 169.5, 208.4; ESIMS (MeOH): 321.2 ($[M+Na]^+$, 100); HRESIMS calcd for $C_{14}H_{18}O_7Na$ *m/z* 321.0950, found 321.0949; Anal. Calcd for $C_{14}H_{18}O_7$ (298.29): C, 56.37; H, 6.08. Found: C, 56.76; H, 6.21.

4.3.7. Domino product 23c

Oxidative cleavage of diols **10c** (230 mg, 1.00 mmol) was achieved using the general procedure (method A) affording after 20 h of stirring at room temperature 280 mg (82%) of **23c** (SiO_2 flash chromatography, heptane–Et_2O 1:1 as eluent). Method B on 20.0 mg (0.09 mmol) afforded 25 mg (84%) of **23c**. Colorless solid; mp: 110–120 °C; $[\alpha]_D^{20} = -40$ (*c* 1.0, $CHCl_3$,); IR (film): ν = 1736, 1445, 1370, 1261, 1223, 1078, 1039, 1007, 950 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): 1.18 (s, 3H), 1.66 (dd, *J* = 1.5, 14.7 Hz, 1H), 1.67 (ddd, *J* = 2.1, 5.2, 13.5 Hz, 1H), 1.78 (ddd, *J* = 2.0, 5.0, 13.0 Hz, 1H), 1.91 (td, *J* = 5.0, 13.5 Hz, 1H), 2.09 (s, 3H), 2.10 (s, 3H), 2.13 (dd, *J* = 2.7, 14.7 Hz, 1H), 2.56 (td, *J* = 5.0, 13.0 Hz, 1H), 3.14 (d, *J* = 1.2 Hz, 1H), 3.90–4.07 (m, 4H), 5.32 (dd, *J* = 1.3, 2.7 Hz, 1H), 6.43 (d, *J* = 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 19.3, 21.2, 22.5, 27.9, 30.5, 38.8, 38.9, 39.2, 65.4, 65.5, 90.6, 92.6, 103.1, 110.1, 169.2, 169.6; ESIMS (MeOH): 365.1 ($[M+Na]^+$, 100); HRESIMS calcd for $C_{16}H_{22}O_8Na$ *m/z* 365.1212, found 365.1215; Anal. Calcd for $C_{16}H_{22}O_8$ (342.34): C, 56.13; H, 6.48. Found: C, 56.41; H, 6.51.

4.3.8. Domino product 24

Oxidative cleavage of diols **11b** (245 mg, 1.36 mmol) was achieved using the general procedure (method A) affording after 20 h of stirring at room temperature 325 mg (82%) of **24** (SiO_2 flash chromatography, heptane–Et_2O 1:1 as eluent). Method B on 25.0 mg (0.14 mmol) afforded 34 mg (84%) of **24**. Colorless solid; mp: 110–115 °C; $[\alpha]_D^{20} = -28$ (*c* 1.5, $CHCl_3$); IR (film): ν = 1730, 1380, 1200, 1080, 950 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.45 (s, 3H), 1.70 (dd, *J* = 1.4, 14.3 Hz, 1H), 1.86–1.90 (m, 1H), 1.95 (dd, *J* = 2.7, 14.3 Hz, 1H), 2.09 (s, 6H), 2.18–2.38 (m, 2H), 4.47 (tdt, *J* = 1.6, 5.2, 12.3 Hz, 1H), 2.79 (d, *J* = 1.2 Hz, 1H), 4.87 (br s, 1H), 4.90 (br s, 1H), 5.36 (dd, *J* = 1.4, 2.7 Hz, 1H), 6.54 (d, *J* = 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.2, 22.5, 23.6, 29.5, 34.2, 35.6, 41.0, 41.5, 90.7, 92.2, 103.8, 109.8, 149.8, 169.5, 169.6; ESIMS (MeOH): 319.2 ($[M+Na]^+$, 100); HRESIMS: calcd for $C_{15}H_{20}O_6Na$ *m/z* 319.1157; found 319.1155; Anal. Calcd for $C_{15}H_{20}O_6$ (296.32): C, 60.80; H, 6.80. Found: C, 60.57; H, 6.74.

4.3.9. Domino product 25a

Oxidative cleavage of diols **13a** (50 mg, 0.21 mmol) was achieved using the general procedure (method A) affording after 20 h of stirring at room temperature 44 mg (56%) of **25a** (SiO_2 flash chromatography, heptane–EtOAc 3:1 as eluent). Method B on 10 mg (0.04 mmol) afforded 10 mg (67%) of **25a**. Colorless oil; $[\alpha]_D^{20} = -9$ (*c* 1.0, $CHCl_3$); IR (film): ν = 1732, 1434, 1369, 1240, 1167, 1131, 1072, 1027, 968 cm^{-1}; ^1H NMR (300 MHz): δ = 1.49 (s, 3H), 1.74 (dd, *J* = 1.2, 14.0 Hz, 1H), 2.03 (s, 3H), 2.10 (s, 6H), 2.22 (dd, *J* = 2.8, 14.8 Hz, 1H), 2.55 (dd, *J* = 2.8, 14.0 Hz, 1H), 2.75 (dd, *J* = 5.8, 14.8 Hz, 1H), 2.90 (s, 1H), 5.28 (s, 1H), 5.31 (s, 1H), 5.33 (dd, *J* = 1.0, 2.8 Hz, 1H), 5.60 (dd, *J* = 2.8, 5.6 Hz, 1H), 6.56 (d, *J* = 0.8 Hz, 1H); ^{13}C NMR (75 MHz): δ = 21.2, 21.4, 22.4, 24.8, 35.1, 38.6, 40.5, 41.2, 73.1, 90.6, 92.4, 102.6, 117.2, 147.1, 169.5, 169.8, 169.9; ESIMS (MeOH): 377.1 ($[M+Na]^+$, 100); HRESIMS: calcd for $C_{17}H_{22}O_8Na$ *m/z* 377.1212, found 377.1198.

4.3.10. Domino product 25b

Oxidative cleavage of diols **13b** (50 mg, 0.21 mmol) was achieved using the general procedure (method A) affording after 20 h of stirring at room temperature 64 mg (86%) of **25b** (SiO_2 flash chromatography, heptane–EtOAc 3:1 as eluent). Method B on 24 mg (0.10 mmol) afforded 29 mg (82%) of **25b**. Yellow oil; $[\alpha]_D^{20} = +14$ (*c* 0.5, $CHCl_3$); IR (film): ν = 1730, 1369, 1248, 1229, 1213, 1168, 1075, 1022, 972 cm^{-1}; ^1H NMR (500 MHz): δ = 1.47 (s, 3H), 1.66 (d, *J* = 13.8 Hz, 1H), 2.10 (s, 3H), 2.11 (s, 3H), 2.22 (dd, *J* = 2.8, 14.3 Hz, 1H), 2.56 (dd, *J* = 2.6, 13.8 Hz, 1H), 2.75 (dd, *J* = 6.0, 14.3 Hz, 1H), 2.89 (s, 1H), 3.35 (s, 3H), 4.37 (dd, *J* = 2.9, 6.1 Hz, 1H), 4.55 and 4.66 (ABquartet, *J* = 6.8 Hz, 2H), 5.18 (s, 1H), 5.27 (s, 1H), 5.31 (dd, *J* = 1.2, 2.8 Hz, 1H), 6.55 (d, *J* = 1.0 Hz, 1H); ^{13}C NMR (125 MHz): δ = 21.2, 22.5, 25.1, 34.8, 39.6, 40.8 (2C), 55.4, 74.3, 90.7, 92.5, 93.0, 103.0, 115.9, 147.5, 169.5, 169.8; Anal. Calcd for $C_{17}H_{24}O_8$ (356.14): C, 57.30; H, 6.79. Found: C, 57.91; H, 7.01.

4.3.11. Domino product 26

Oxidative cleavage of diols **14** (24 mg, 0.09 mmol) was achieved using the general procedure (method A) affording after 19 h of stirring at room temperature 21 mg (60%) of **26** (SiO_2 flash chromatography, heptane–EtOAc 1:1 as eluent). Method B on 12 mg (0.05 mmol) afforded 11 mg (59%) of **26**. Colorless solid; mp: 102–103 °C; $[\alpha]_D^{20} = +36$ (*c* 0.7, $CHCl_3$); IR (film): ν = 1732, 1711, 1640, 1368, 1245, 1182, 1071, 1027 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.30 (t, *J* = 7.1 Hz, 3H), 1.48 (s, 3H), 1.74 (dd, *J* = 1.3, 14.4 Hz, 1H), 1.95 (dd, *J* = 2.7, 7.4 Hz, 1H), 2.04 (dd, *J* = 2.7, 14.5 Hz, 1H), 2.10 (s, 3H), 2.11 (s, 3H), 2.31–2.39 (m, 2H), 2.91 (d, *J* = 0.9 Hz, 1H), 3.91–3.99 (m, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 5.40 (dd, *J* = 1.3, 2.6 Hz, 1H), 5.88 (s, 1H), 6.56 (d, *J* = 1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 14.3, 21.3, 22.1, 22.5, 23.7, 33.4, 37.6, 41.1, 41.4, 60.2, 90.6, 92.1, 103.1, 115.4, 160.8, 166.6, 169.6 (2C); ESIMS (MeOH): 391.1 ($[M+Na]^+$, 100); HRESIMS: calcd for $C_{18}H_{24}O_8Na$ *m/z* 391.1369, found 391.1356.

4.4. Consecutive-domino products 4

4.4.1. Bicyclic aldols 4b-OTBS, 4b′-OTBS, and intermediate 27b

To a stirred solution of **2b** (1 g, 2.79 mmol) in an 8:1 mixture of methanol (4 mL) and water (0.5 mL), chilled at 0 °C was added potassium carbonate (1.92 mg, 13.95 mmol, 5 equiv). The resulting mixture was stirred at 25 °C for 40 min. After removing the solvents without heating, dilution with EtOAc, and washing with brine until neutral pH, the organic layers were dried over magnesium sulfate, concentrated under reduced pressure, and the residue was filtered over silica (heptane–EtOAc, 1:1) affording 570 mg (90%) of a mixture of three products. The crude product (555 mg, 2.43 mmol) was directly protected with *tert*-butyldimethylsilyl chloride (1.17 g, 7.77 mmol) in the presence of imidazole (1.05 g, 15.55 mmol) in DMF (12 mL) at 0 °C. The reaction mixture was stirred for 36 h, then diluted with hexane, worked up as usual, and purified (SiO_2 flash chromatography, heptane–EtOAc, 2:1) to give **4b-TBS** (353 mg, 37%), **4b′-TBS** (181 mg, 19%), and **27b** (237 mg, 23%). By interrupting the ring system interchange after only five min stirring, **27b** can be obtained as the major constituent of a two-component (**27a** and **4b′**) mixture.

4.4.1.1. Bicyclic aldol 4b-OTBS. Colorless solid; mp: 58.0 °C; $[\alpha]_D^{20} = +2$ (*c* 1.4, $CHCl_3$); IR (film): ν = 1732, 1462, 1361, 1256, 1108, 1064, 1030, 920, 886, 836, 777 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ = 0.00 (s, 3H), 0.01 (s, 3H), 0.83 (s, 9H), 0.95 (s, 3H), 1.20 (s, 3H), 1.30 (d, *J* = 14.6 Hz, 1H), 1.40 (d, *J* = 14.7 Hz, 1H), 1.95 (d, *J* = 18.0 Hz, 1H), 2.07 (ddd, *J* = 3.0, 8.2, 14.6 Hz, 1H), 2.21 (dd, *J* = 4.4, 14.7 Hz, 1H), 2.37 (t, *J* = 4.5 Hz, 1H), 2.65 (dd, *J* = 2.9, 18.0 Hz, 1H), 3.28 (s, 3H), 4.01 (dd, *J* = 4.2, 8.2 Hz, 1H), 4.63 and 4.68 (ABquartet, *J* = 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = −4.8, −4.7, 17.9, 20.2, 20.9, 25.7 (3C), 36.5, 40.6, 41.3, 45.9, 51.3, 55.3, 69.2, 76.9, 90.9, 214.0; ESIMS (MeOH): 365.2 ($[M+Na]^+$, 100); HRESIMS: calcd for $C_{18}H_{34}O_4NaSi$ *m/z* 365.2124, found 365.2125.

4.4.1.2. Bicyclic aldol 4b′-OTBS. Yellow oil; $[\alpha]_D^{20} = +5$ (*c* 1.4, $CHCl_3$); IR (film): ν = 1726, 1462, 1377, 1251, 1154, 1120, 1069, 1032, 975, 917, 835 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ = 0.01 (s, 3H), 0.03 (s, 3H), 0.87 (s, 9H), 0.96 (s, 3H), 1.38 (s, 3H), 1.57–1.63 (m, 1H), 1.66 (d, *J* = 18.7 Hz, 1H), 1.80 (dd, *J* = 9.2, 14.6 Hz, 1H), 1.98 (dd, *J* = 3.0, 14.4 Hz, 1H), 2.21 (dd, *J* = 2.0, 14.4 Hz, 1H), 2.34 (dd, *J* = 2.7, 5.6 Hz, 1H), 2.73 (dd, *J* = 3.5, 18.7 Hz, 1H), 3.31 (s, 3H), 4.05 (td, *J* = 3.2, 9.3 Hz, 1H), 4.70 (s, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = −4.8 (2C), 18.0, 20.0, 20.5, 25.7 (3C), 32.6, 40.9, 42.4, 45.9, 53.1, 55.2, 65.6, 77.7, 90.8, 215.6; ESIMS (MeOH): 365.2 ($[M+Na]^+$, 100); HRESIMS: calcd for $C_{18}H_{34}O_4NaSi$ *m/z* 365.2124, found 365.2125; Anal. Calcd for $C_{18}H_{34}O_4Si$ (342.22): C, 63.11; H, 10.00. Found: C, 63.03; H, 10.01.

4.4.1.3. Intermediate 27b. Yellow oil; $[\alpha]_D^{20} = +57$ (*c* 2.0, $CHCl_3$); IR (film): ν = 1679, 1589, 1253, 1189, 1134, 1092, 1034, 917, 840, 782 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ = 0.15 (s, 3H), 0.16 (s, 3H), 0.92 (s, 9H), 1.27 (s, 3H), 1.36 (s, 3H), 1.79–1.86 (m, 2H), 1.98–2.03 (m, 1H), 2.23–2.36 (m, 2H), 2.47–2.53 (m, 1H), 3.38 (s, 3H), 4.71 and 4.81 (ABquartet, 7.5 Hz, 2H), 5.34 (dd, *J* = 3.3, 8.6 Hz, 1H), 7.30 (s, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = −5.2, −4.3, 17.9, 19.4, 24.6, 25.6 (3C), 29.8, 35.6, 36.3, 40.6, 55.3, 77.8, 91.0, 95.1, 119.1, 152.1, 197.9; ESIMS (MeOH): 393.2 ($[M+Na]^+$, 100). HRESIMS: calcd for $C_{19}H_{34}O_5SiNa$ *m/z* 393.2073, found 393.2062.

4.4.2. Bicyclic aldol product 4h

Using the general procedure for consecutive domino reactions, **1h** (21 mg, 0.10 mmol) was treated sequentially with $Pb(OAc)_4$ (domino promoter) and an 8:1 mixture of methanol-water, potassium carbonate (base). For the ring system interchange (following formation of the ring-expanded domino product **2h**), the reaction mixture was stirred at room temperature for 62 h.

After removing the solvents without heating, dilution with EtOAc, and the usual work-up, the residue was purified by flash chromatography (heptane–EtOAc, 1:1) affording 14 mg (71%) of **4h**. Colorless oil; $[\alpha]_D^{20} = 26$ (*c* 0.8, $CHCl_3$); mp: 137–138 °C; IR (film): ν = 3414, 1712, 1452, 1367, 1300, 1230, 1124, 1080, 999, 890, cm^{-1}; ^1H NMR (500 MHz): δ = 1.23 (d, *J* = 6.3 Hz, 3H), 1.53 (dd, *J* = 5.0, 13.5 Hz, 1H), 1.68 (m, 1H), 1.85 (dd, *J* = 9.4, 12.7 Hz 1H), 1.97 (dd, *J* = 1.3, 18.4 Hz, 1H), 2.05 (ddd, *J* = 2.0, 9.3, 12.7 Hz, 1H), 2.15 (ddd, *J* = 4.2, 9.5, 14.0 Hz, 1H), 2.23 (br s, 1H), 2.31 (m,

1H), 2.52 (dd, J = 3.0, 18.5 Hz, 1H), 3.60 (ddd, J = 1.6, 6.2, 9.3 Hz, 1H), 4.12 (m, 1H), 4.26 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 22.4, 25.3, 40.3, 41.5, 44.1, 46.0, 51.9, 68.9, 76.0, 78.1, 213.1; HRESIMS: calcd for $C_{11}H_{16}O_3Na$ m/z 219.0997, found 219.0972; Anal. Calcd for $C_{11}H_{16}O_3$ (196.10): C, 67.32; H, 8.22. Found: C, 67.02; H, 8.11.

4.4.3. Bicyclic aldol products 4j and 4j′

Using the general procedure for consecutive domino reactions **1j** (310 mg, 0.95 mmol) was treated sequentially with $Pb(OAc)_4$ (domino promoter) and an 8:1 mixture of methanol-water, potassium carbonate (base). For the ring system interchange (following formation of the ring-expanded domino product **2j**), the reaction mixture was stirred at room temperature for 29 h.

After removing the solvents without heating, dilution with EtOAc, and usual work-up, SiO_2 chromatography (heptane–EtOAc, 1:1) afforded **4j** (119 mg, 40%) and **4j′** (98 mg, 33%). **4j**. colorless oil; $[\alpha]_D^{20} = +24$ (c 1.0, $CHCl_3$); IR (film): ν = 3421, 1721, 1471, 1360, 1251, 1093, 1056, 1004, 970, 891, 836, 774 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = −0.02 (s, 3H), 0.00 (s, 3H), 0.83 (s, 9H), 1.53 (dd, J = 2.0, 14.9 Hz, 1H), 1.64 (ddd, J = 2.0, 3.9, 14.6 Hz, 1H), 1.67 (d, J = 4.8 Hz, 3H), 1.99 (ddd, J = 3.0, 8.7, 14.8 Hz, 1H), 2.06 (d, J = 18.5 Hz, 1H), 2.08 (ddd, J = 2.7, 8.8, 14.1 Hz, 1H), 2.46 (qt, J = 1.7, 3.7 Hz, 1H), 2.72 (dd, J = 2.9, 18.6 Hz, 1H), 3.6 (d, J = 8.6 Hz, 1H), 3.78 (d, J = 8.6 Hz, 1H), 4.17 (ddd, J = 2.0, 4.1, 8.9 Hz, 1H), 5.34–5.37 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = −4.9, −4.4, 17.9, 18.1, 25.6 (3C), 33.8, 38.4, 41.4, 42.4, 51.0, 68.4, 70.6, 123.9, 134.7, 214.0; ESIMS (MeOH): 333.1 ([M+Na]$^+$, 100); HRESIMS: calcd for $C_{17}H_{30}O_3SiNa$ m/z 333.1862, found: 333.1841; Anal. Calcd for $C_{17}H_{30}O_3Si$ (310.5): C, 65.76; H, 9.74. Found: C, 65.71; H, 9.88.

Compound 4j′: Colorless oil; $[\alpha]_D^{20} = +38$ (c 1.8, $CHCl_3$); IR (film): ν = 3416, 1714, 1471, 1462, 1390, 1306, 1250, 1220, 1161, 1089, 1074, 1022, 971, 887, 773 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = −0.03 (s, 3H), −0.01 (s, 3H), 0.83 (s, 9H), 1.53 (d, J = 14.7 Hz, 1H), 1.64 (br d, J = 14.4 Hz, 1H), 1.67 (d, J = 4.6 Hz, 3H), 1.98 (ddd, J = 2.7, 8.8, 14.7 Hz, 1H), 2.06 (d, J = 18.5 Hz, 1H), 2.08 (ddd, J = 2.5, 8.4, 15.1 Hz, 1H), 2.46 (dt, J = 2.4, 4.0 Hz, 1H), 2.71 (dd, J = 2.9, 18.5 Hz, 1H), 3.6 (d, J = 8.4 Hz, 1H), 4.17 (ddd, J = 1.8, 4.0, 8.9 Hz, 1H), 5.32–5.39 (m, 2H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = −4.9, −4.4, 17.9, 18.2, 25.6 (3C), 30.2, 39.4, 40.8, 42.9, 52.2, 64.9, 70.9, 123.8, 134.8, 214.5; ESIMS (MeOH): 333.1 ([M+Na]$^+$, 100); HRESIMS: calcd for $C_{17}H_{30}O_3SiNa$ m/z 333.1862, found: 333.1865; Anal. Calcd for $C_{17}H_{30}O_3Si$ (310.5): C, 65.76; H, 9.74. Found: C, 65.71; H, 9.88.

4.4.4. Bicyclic aldol products 4l and 4l′

Using the general procedure for consecutive domino reactions **11b** (199 mg, 1.1 mmol) was treated sequentially with $Pb(OAc)_4$ (domino promoter) and an 8:1 mixture of methanol-water, potassium carbonate (base). For the ring system interchange (following formation of the ring-expanded domino product **24**), the reaction mixture was stirred at room temperature for 7 h.

After removing the solvents without heating, dilution with EtOAc, and usual work-up, SiO_2 chromatography (heptane–EtOAc, 4:1) afforded **4l** (94 mg, 51%) and **4l′** (37 mg, 21%).

Compound 4l: Colorless solid; M.p: 107–110 °C; $[\alpha]_D^{20} = +19$ (c 0.8, $CHCl_3$); IR (film): ν = 3453, 1713, 1396, 1218, 1120, 1072, 1040, 887 cm^{-1}; ^{1}H NMR (300 MHz): δ = 1.13 (s, 3H), 1.53 (dd, J = 3.0, 14.0 Hz, 1H), 2.05 (m, 1H), 2.07 (d, J = 3.0, 19.0 Hz, 1H), 2.28 (d, J = 19.0 Hz, 1H), 2.51 (m, 2H), 2.60 (q, J = 3.2 Hz, 1H), 2.67 (br s, OH, 1H), 4.24 (dt, J = 8.7, 3.6 Hz, 1H), 4.78 (t, J = 2.0 Hz, 1H), 4.89 (t, J = 2.4 Hz, 1H); ^{13}C NMR (75 MHz): δ = 22.6, 29.4, 38.0, 43.1, 49.9, 52.3, 68.8, 106.2, 148.4, 212.0; HRESIMS (MeOH) calcd for $C_{10}H_{14}O_2Na$: 189.0891; found 189.0885; Anal. Calcd for $C_{10}H_{14}O_2$ C, 72.26; H, 8.49. Found: C, 71.09; H, 8.43.

Compound 4l′. Colorless oil; $[\alpha]_D^{20} = +10$ (c 0.5, $CHCl_3$); IR (film): ν = 3453, 1713, 1396, 1182, 887 cm^{-1}; ^{1}H NMR (300 MHz): δ = 1.14 (s, 3H), 1.49 (dt, J = 14.2, 3.0 Hz, 1H), 1.99–2.16 (m, 3H), 2.48 (m, 1H), 2.61 (q, J = 3.0, 1H), 3.03 (dq, J = 2.5, 17.5 Hz, 1H), 4.24 (ddd, J= 1.3, 3.3, 9.5 Hz, 1H), 4.84 (t, J = 2.2 Hz, 1H), 4.92 (t, J = 2.5, 1H); ^{13}C NMR (75 MHz): δ = 21.6, 24.8, 37.5, 43.7, 48.3, 51.7, 64.5, 104.8, 148.1, 212.7; HRESIMS (MeOH) calcd for $C_{10}H_{14}O_2Na$: 189.0891; found 189.0888.

4.5. Lactone 5b

Oxidative cleavage of diols **1c** (100 mg, 0.39 mmol) was achieved either using the general procedure (method A, 1.2 equiv. of $Pb(OAc)_4$ affording after 20 min of stirring at 25 °C, 84 mg (84%) of **5a** (SiO_2 flash chromatography, heptane–EtOAc 1:4 as eluent). Comparable yields (82%) were obtained using the green counterpart ($PhI(OAc)_2$ in MeCN at 25 °C). The crude bicyclic lactol **5a** thus obtained (anomeric mixture) was converted to its corresponding lactone **5b** upon treatment with PCC (540 mg, 2.52 mmol) in CH_2Cl_2 (5 mL). After 1 h the reaction was diluted with Et_2O and filtered over a florisil pad. The filtrate was evaporated and purified by silica gel flash chromatography (heptane–EtOAc, 1:2) affording 70 mg (85%) of the lactone **5b**. Yellow oil; $[\alpha]_D^{20} = -101$ (c 0.5, $CHCl_3$); IR (film): ν = 1773, 1729, 1673, 1387, 1149, 1119, 1038, 1000, 943 cm^{-1}; ^{1}H NMR (300 MHz): δ = 1.45 (s, 3H), 1.46 (s, 3H), 2.76 (ddd, J = 1.8, 5.2, 17.9 Hz, 1H), 2.80 and 3.06 (ABquartet, 17.9 Hz, 2H), 2.92 (ddd, J = 2.2, 5.4, 17.8 Hz, 1H), 3.38 (s, 3H), 4.03 (t, J = 5.3 Hz, 1H), 4.66 and 4.72 (ABquartet, 6.8 Hz, 2H), 6.05 (td, J = 2.0, 6.9 Hz, 1H), 9.95 (d, J = 7.0 Hz, 1H); ^{13}C NMR (75 MHz): δ = 18.7, 23.6, 40.2, 44.1, 49.8, 55.8, 79.3, 94.1, 96.3, 125.7, 169.4, 174.1, 188.8; ESIMS (MeOH): 277.1 ([M+Na]$^+$, 100); HRESIMS (MeOH) calcd for $C_{13}H_{18}O_5Na$: 277.1052; found 277.1064.

4.6. Type-28 'green' domino products

4.6.1. Domino product 28a

A dry flask was charged with unsaturated diols **1a** (500 mg, 2.08 mmol) and $PhI(OAc)_2$ (3.35 g, 10.4 mmol, 5 equiv), vacuumed and flashed with argon. Dry CH_3CN (10 mL) was added and the reaction mixture was stirred at 70 °C for 48 h under argon. After cooling, dilution with Et_2O and washing with a saturated solution of $Na_2S_2O_3$, usual work-up gave **28a** as a colorless oil. Note: The yield is 55% after column chromatography over silica gel using EtOAc–heptane 1:4 as eluent. Without chromatography, the NMR of the crude showed the presence of the desired product, which is contaminated with iodobenzene, which can be removed under vacuum by heating at 30–35 °C for 2 days (89%). Compound **28a**. Colorless oil; $[\alpha]_D^{20} = +40$ (c 1.5, $CHCl_3$); IR (film): ν = 1754, 1739, 1367, 1219, 1181, 1101, 1044, 1022, 1005, 965, 944 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.19 (s, 9H), 1.39 (s, 3H), 1.71 (ddt, J = 2.7, 4.3, 14.3 Hz, 1H), 1.76 (dd, J = 2.4, 4.3 Hz, 2H), 1.87 (tdd, J = 2.3, 4.8, 12.9 Hz, 1H), 2.06 (s, 3H), 2.10 (s, 3H), 2.28 (td, J = 4.4, 12.9 Hz, 1H), 2.35 (ddd, J = 2.6, 4.6, 12.9 Hz, 1H), 2.69 (d, J = 2.3 Hz, 1H), 3.12 (t, J = 2.3 Hz, 1H), 5.33 (t, J = 2.4 Hz, 1H), 6.50 (d, J = 2.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.5, 22.3, 25.4, 27.0, 29.0 (4C), 34.7, 38.7, 39.7, 73.5, 74.7, 90.9, 93.3, 104.7, 169.1, 169.5; ESIMS (MeOH): 379.2 ([M+Na]$^+$, 100); HRESIMS: calcd for $C_{18}H_{28}O_7Na$ m/z 379.1733, found 379.1722.

4.6.2. Domino product 28b

Proceeding as above, diols **10b** (250 mg, 1.37 mmol) and $PhI(OAc)_2$ (2.2 g, 6.86 mmol, 5 equiv) in dry CH_3CN (7 mL) afforded **28b** as a colorless oil. Note: The yield is 22% after column chromatography over silica gel using EtOAc–heptane 1:2 as eluent. Without chromatography, the NMR of the crude showed the presence of the desired product, which was contaminated with iodobenzene;

this can be removed later under vacuum by heating at 30–35 °C for 2 days (85%). Compound **28b**. Colorless oil; $[\alpha]_D^{20} = +17$ (*c* 1.2, $CHCl_3$); IR (film): ν = 1731, 1715, 1450, 1368, 1325, 1170, 1105, 1083, 1062, 1019, 996 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.47 (s, 3H), 1.93 (d, *J* = 14.2 Hz, 1H), 2.11 (s, 3H), 2.12 (s, 3H), 2.30 (dd, *J* = 3.3, 14.2 Hz, 1H), 2.51 (m, 1H), 2.61 (dd, *J* = 12.9, 4.2 Hz, 1H), 2.63–2.70 (m, 1H), 2.73 (dd, *J* = 5.3, 13.0 Hz, 1H), 3.03 (dd, *J* = 0.9, 3.0 Hz, 1H), 5.40 (d, *J* = 3.3 Hz, 1H), 6.40 (d, *J* = 3.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.3, 22.0, 22.8, 32.0, 34.5, 40.0, 41.5, 42.3, 90.0, 93.1, 102.9, 169.1, 169.4, 211.1; ESIMS (MeOH): 321.1 ($[M+Na]^+$, 100); HRESIMS: calcd for $C_{14}H_{18}O_7Na$ *m*/*z* 321.0950, found 321.0947.

4.6.3. Domino product 28d

Proceeding as above, diols **1d** (100 mg, 0.33 mmol) and $PhI(OAc)_2$ (531 mg, 1.65 mmol, 5 equiv) in dry CH_3CN (2 mL) afforded **28d** as a colorless oil. Note: The yield is 18% after column chromatography over silica gel using EtOAc–heptane 1:2 as eluent. Without chromatography, the NMR of the crude showed the presence of the desired product, which is contaminated with iodobenzene; this can be removed later under vacuum by heating at 30–35 °C for 2 days (68%). Compound **28d**. Colorless oil; $[\alpha]_D^{20} = +3$ (*c* 1.5, $CHCl_3$); IR (film): ν = 1754, 1737, 1462, 1366, 1247, 1220, 1182, 1082, 1004, 964, 945, 834, 774 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz): δ = 0.06 (s, 6H), 0.92 (s, 9H), 1.39 (s, 3H), 1.57–1.63 (m, 1H), 1.74 (d, *J* = 2.2 Hz, 2H), 1.92–1.99 (m, 1H), 2.07 (s, 3H), 2.10 (s, 3H), 2.25–2.35 (m, 2H), 2.74 (d, *J* = 2.5 Hz, 1H), 3.28 (t, *J* = 2.5 Hz, 1H), 5.32 (t, *J* = 2.2 Hz, 1H), 6.47 (d, *J* = 2.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ = −4.8, −4.4, 18.0, 21.4, 22.2, 25.8 (3C), 26.7, 26.8, 28.9, 35.1, 38.3, 39.3, 76.1, 90.6, 93.1, 104.6, 169.2, 169.4; ESIMS (MeOH): 437.2 ($[M+Na]^+$, 100); HRESIMS: calcd for $C_{20}H_{34}O_7SiNa$ *m*/*z* 437.1971, found 437.1968.

References

1. Corbu, A.; Gauron, G.; Castro, J. M.; Dakir, M.; Arseniyadis, S. *Org. Lett.* **2007**, *9*, 4745–4748.
2. (a) Tietze, L. F.; Beifuss, U. *Angew. Chem., Int. Ed.* **1993**, *32*, 131–163; (b) Tietze, L. F. *Chem. Rev.* **1996**, *96*, 115–136; (c) *Domino Reactions in Organic Synthesis*; Tietze, L. F., Brasche, G., Gericke, K. M., Eds.; Wiley-VCH: Weinheim, Germany, 2006. ISBN:3-527-29060-5.
3. The probe used is an unsaturated bicyclic 1,2-diol having a variable substitution pattern. Advantages are the very rapid increase in molecular complexity and its modular character. (a) Safir, I.; Castellote, I.; Porcel, S.; Kaoudi, T.; Birlirakis, N.; Toupet, L.; Arseniyadis, S. *Chem. Eur. J.* **2006**, *12*, 7337–7344; (b) Elkhayat, Z.; Safir, I.; Retailleau, P.; Arseniyadis, S. *Org. Lett.* **2007**, *9*, 4841–4844; (c) Chanu, A.; Castellote, I.; Commeureuc, A.; Safir, I.; Arseniyadis, S. *Tetrahedron: Asymmetry* **2006**, *17*, 2565–2591; (d) Öztürk, C.; Topal, K.; Aviyente, V.; Tüzün, N.; Sanchez, E.; Arseniyadis, S. *J. Org. Chem.* **2005**, *70*, 7080–7086.
4. (a) Finet, L.; Candela Lena, J. I.; Kaoudi, T.; Birlirakis, N.; Arseniyadis, S. *Chem. Eur. J.* **2003**, *9*, 3813–3820; (b) Ozturk, C.; Topal, K.; Avijente, V.; Tuzun, N.; Sanchez, E.; Arseniyadis, S. *J. Org. Chem.* **2005**, *70*, 7080–7086; (c) Safir, I.; Castellote, I.; Porcel, S.; Kaoudi, T.; Birlirakis, N.; Toupet, L.; Arseniyadis, S. *Chem. -Eur. J.* **2006**, *12*, 7337–7344.
5. (a) Martín Hernando, J. I.; Rico Ferreira, M.; Candela Lena, J. I.; Birlirakis, N.; Arseniyadis, S. *Tetrahedron: Asymmetry* **2000**, *11*, 951–973; (b) Finet, L.; Dakir, M.; Chiaroni, A.; Arseniyadis, S. *Eur. J. Org. Chem.* **2007**, 342–350.
6. Corbu, A.; Aquino, M.; Pratap, T. V.; Retailleau, P.; Arseniyadis, S. *Org. Lett.* **2008**, *10*, 1787–1790.
7. (a) Chanu, A.; Safir, I.; Basak, R.; Chiaroni, A.; Arseniyadis, S. *Org. Lett.* **2007**, *9*, 1351–1354; (b) Chanu, A.; Safir, I.; Basak, R.; Chiaroni, A.; Arseniyadis, S. *Eur. J. Org. Chem.* **2007**, 4305–4312.
8. Articles dealing with specific aspects of organo lead chemistry: (a) Criegee, R. In *Oxidation in Organic Chemistry*; Wiberg, K. B., Ed.; Academic Press: New York, 1965; pp 277–366. Part A; (b) Rubottom, G. M. In *Oxidation in Organic Chemistry*; Trahanovsky, W. H., Ed.; Academic Press: London, 1982; Vol. D, Chapter 1 (c) Moloney, M. G. *Main Group Metal Chem.* **2001**, *24*, 653–660; (d) Moloney, M.; Nettleton, E.; Smithies, K. *Tetrahedron Lett.* **2002**, *43*, 907–909.
9. Candela Lena, J. I.; Sánchez Fernández, E.; Ramani, A.; Birlirakis, N.; Barrero, A. F.; Arseniyadis, S. *Eur. J. Org. Chem.* **2005**, 683–700; The domino process is operative over a wide range of solvents Sesenoglu, Ö.; Candela Lena, J. I.; Altinel, E.; Birlirakis, N.; Arseniyadis, S. *Tetrahedron: Asymmetry* **2005**, *15*, 995–1015.
10. Taxoid numbering for **3a**, Marner's Iridal numbering for **3b** and norsesquiterpenespirolactone numbering for **9** is used.
11. Rapson, W. S.; Robinson, R. *J. Chem. Soc.* **1935**, 1285;; Hajos, Z. G.; Parrish, D. R. *J. Org. Chem.* **1973**, *38*, 3239–3243; Eder, U.; Sauer, G.; Wiechert, R. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 496–497; Gutzwiller, J.; Buchschacher, P.; Fürst, A. *Synthesis* **1977**, 167.
12. It should be noted that all domino reactions are performed on crude diastereomeric mixtures; we only show the stereopure target diols for characterization purposes, by separating various amounts of stereopure compounds using the eluent indicated in Section 4.
13. Beilstein numbering is given for the compounds in Section 4, while an easier to follow, though an arbitrary numbering illustrated in Scheme 1 is used in the text.
14. Adler, M. E.; Yumagulova, S. A.; Torosyan, S. A.; Miftakhov, M. S. *Russ. J. Org. Chem.* **1994**, *30*, 1006–1007; For $RhCl_3$ catalyzed double bond migration we adapted the method of Hanselmann, R.; Benn, M. *Synth. Commun.* **1996**, *26*, 945–961.
15. For reviews on the use of microwaves in organic synthesis see: (a) de la Hoz, A.; Diaz-Ortis, A.; Moreno, A.; Langa, F. *Eur. J. Org. Chem.* **2000**, 3659–3673; (b) Kappe, C. O.; Stadler, A. *Microwaves in Organic and Medicinal Chemistry*; Wiley-VCH: Weinheim, 2005; (c) Kappe, C. O.; Dallinger, D. *Drug Discovery* **2006**, *5*, 51–63.
16. Rigby, W. *J. Chem. Soc.* **1950**, *1907*. Rigby has defined the efficiency of such reagents as oxidants 'which concern elements which (a) can reasonably be envisaged as capable of forming a preliminary cyclic compound with the glycol, and (b) exist in two stable oxidation states which are two valency units apart, the lower representing a substance which is not an oxidizing agent under ordinary conditions (Pb(II), Bi(III) or which no longer fulfills condition (a) (the IO_3-ion)'.
17. Hypervalent iodine reagents frequently imitate the transformations mediated by Hg^{2+}, Tl^{3+}, Pb^{4+}, and Pd^{2+} but without the toxic and environmental issues: (a) Moriarty, R. M.; Vaid, R. K. *Synthesis* **1990**, 431–447; (b) Varvoglis, A. *Tetrahedron* **1997**, *53*, 1179–1255; (c) Ladziata, U.; Zhdankin, V. *ARKIVOC* **2006**, *ix*, 26–58.
18. De Mico, A.; Margarita, R.; Mariani, A.; Piancatelli, G. *J. Chem. Soc., Chem. Commun.* **1997**, 1237–1238.
19. Arseniyadis, S.; Brondi Alves, R.; Pereira de Freitas, R.; Muñoz-Dorado, M.; Yashunsky, D. V.; Potier, P.; Toupet, L. *Heterocycles* **1997**, *46*, 727–764; Arseniyadis, S.; Yashunsky, D. V.; Pereira de Freitas, R.; Muñoz-Dorado, M.; Potier, P.; Toupet, L. *Tetrahedron* **1996**, *52*, 12443–12458.
20. By analogy to the higher homologue series, see Ref. 4b.
21. The energy of C–I bond (2 Å) in $PhI(OAc)_2$ is given as 55 kcal/mol, while the C–Pb bond (2.29 Å) was calculated as 31 kcal/mol Varvoglis, A. *Tetrahedron* **1997**, *53*, 1179–1255.