Iron-Catalyzed Prins-Peterson Reaction for the Direct Synthesis of Δ^4-2,7-disubstituted oxepenes.

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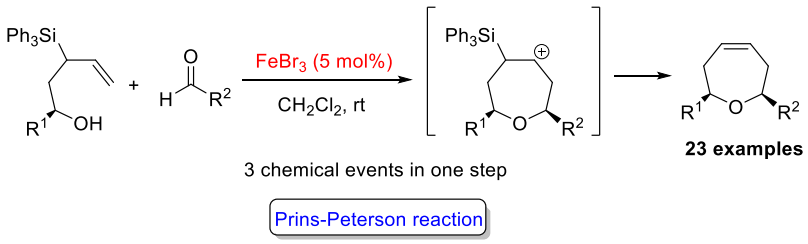


Abstract. A direct iron(III)-catalyzed Prins-Peterson reaction involving α-substituted γ-triphenylsilyl *bis*-homoallylic alcohols and aldehydes is described. Thus *cis*-Δ^4-2,7-disubstituted oxepenes were synthesized in a diastereoselective reaction using sustainable catalytic conditions (3-5 mol%). This highly productive process is the result of a cascade of three chemical events with the concomitant formation of a C-O bond, a C-C bond and a Δ^4 endocyclic double bond, through a Prins cyclization followed by a Peterson-type elimination. This tandem reaction is chemoselective vs the classical Prins cyclization.

Introduction.

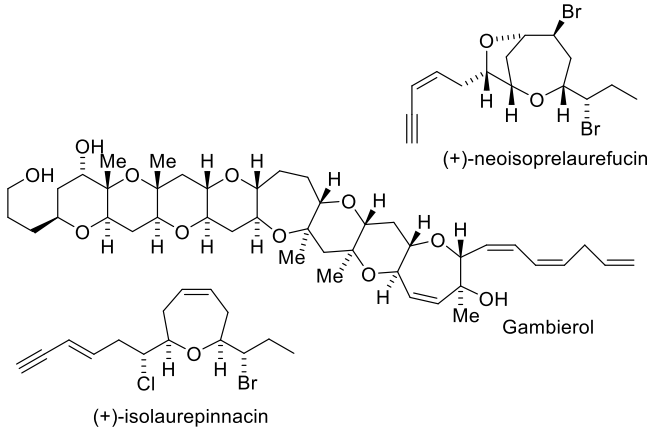
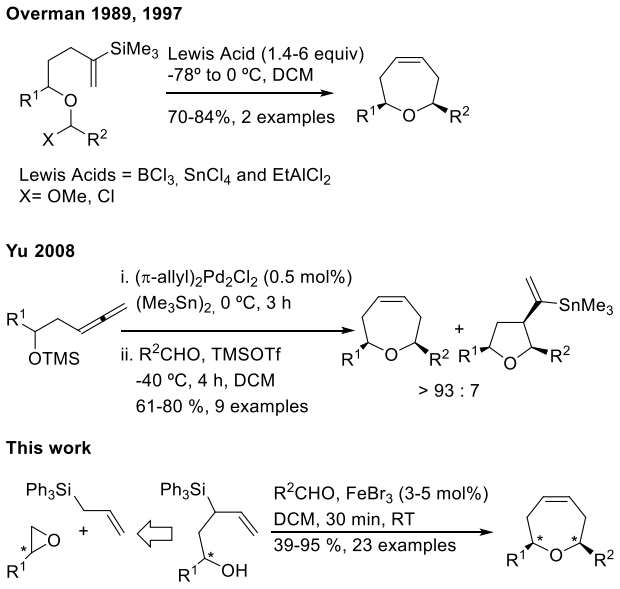


Figure 1. Some representative examples of ladder-ether marine toxins and lauroxepanes.

Oxepenes, unsaturated seven-membered ring oxacycles, are common structural units in the field of organic chemistry. Thus, they can be found in a number of natural products from ladder-ether marine toxins to lauroxanes, nonterpenoid C15-metabolites isolated from the Laurencia species of red algae.[1,2] They can also act as synthetic intermediates in the preparation of more complex structures such as the isoprelaurefucin family (Figure 1).[3-6]

These oxepenes often have useful biological activities,[3] so direct and efficient new methods are still necessary. Several methodologies have been developed toward the synthesis of cyclic ethers based mainly on three different approaches:[4,5] (a) formation of a C-O bond, usually based on the nucleophilic attack of an oxygen functionality; (b) C-C bond formation through a ring-closing metathesis in an acyclic ether, and (c) simultaneous C-O and C-C bond formation around the oxygen of the cyclic ether.[6] Among these processes, those based on the Prins cyclization (c) have been less explored in the synthesis of these unsaturated disubstituted oxacycles (Scheme 1).

Scheme 1. Previous strategies and our method of accessing *cis*-Δ^4-2,7-disubstituted oxepenes.



Several groups have reported the use of this approach. Overman and co-workers obtained unsaturated oxacycles from mixed acetals, and later Yu and co-workers developed a two-step synthesis of oxepenes using palladium catalysis. However, an undesired excess of harsh Lewis acid,[7] as well as highly toxic organotin reagents were used, giving rise to undesired byproducts (Scheme 1).[8]

In 1989, Miginiac et al. described the reaction of ω-silyloxyallyltrimethylsilanes with aldehydes, using stoichiometric amounts of $BF_3{\cdot}OEt_2$ as Lewis acid, which yielded 2-alkyl-monosubstituted oxepenes.[9] This report remained virtually unnoticed until it was rediscovered by Suginome *et al*. (2001) and Panek *et al*. (2009) in order to synthesize monosubstituted oxepene derivatives.[10] Despite its potential as a synthetic tool, to the best of our knowledge, no further attempts towards the synthesis of 2,7-disubstituted oxepenes have been made to date. This encouraged us to design and develop a direct process for the synthesis of disubstituted oxepenes, starting from α-substituted γ-triphenylsilyl *bis*-homoallylic alcohols and aldehydes, using metal sustainable catalysis.

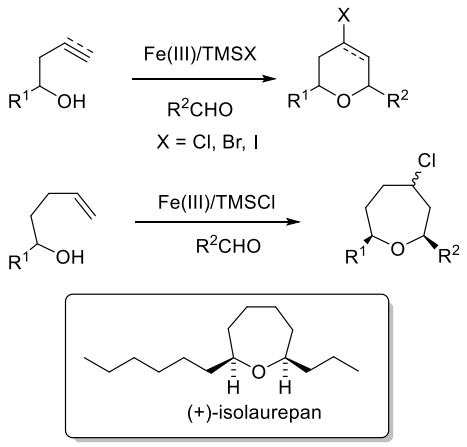
Herein, the first diastereoselective synthesis of *cis*-Δ^4-2,7-disubstituted oxepenes catalyzed by just 3-5 mol% of iron(III) bromide is described. It uses a tandem process that combines a Prins cyclization alongside a Peterson-type elimination (Prins-Peterson reaction, PPR). The low amounts of metal used highlight the efficacy of this catalytic

process. From a formal point of view this reaction could be also considered as an intramolecular Hosomi-Sakurai reaction or a Nokami-type transformation.

Results and discussion.

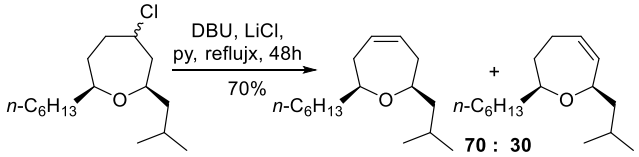
Over the last decade, our research group has developed new methods for the synthesis of oxacycles with six- and seven membered rings, using sustainable metal catalysis based on iron(III) salts (Scheme 2).[11,12] The reaction of *bis*-homoallylic alcohols with aldehydes, catalyzed by iron(III) salts, led directly to 4-chloro-*cis*-2,7-disubstituted-oxepanes with excellent yields. Using this methodology, we performed the shortest total synthesis of (+)-isolaurepan (Scheme 2).[12]

Scheme 2. Synthesis of six- and seven-membered ring oxacycles catalyzed by iron (III) salts.



As a continuation of this previous work, we focused on the synthesis of Δ^4-2,7-disubstituted oxepenes (Figure 1) through elimination of the chlorine at C-4 to obtain the specific intramolecular double-bond (Scheme 3). However, this elimination reaction led to an inseparable mixture of Δ^4- and Δ^3-2,7-disubstituted oxepenes in a ratio 70:30 respectively, of limited use for further synthetic progress.

Scheme 3. Elimination reaction of 4-chloro-*cis*-2,7-dialkyl-oxepane.



Aiming to minimize the amount of undesirable Δ^3-oxepene, we next tried different conditions, varying the type of base (*t*-BuOK, MeONa, DBN and $LiClO_4$) and solvents (pyridine and methanol). These neither obtained the Δ^4-2,7-disubstituted oxepenes exclusively nor improved on the results with DBU and LiCl.

We still pursued the synthesis of the only desirable isomer Δ^4-oxepene, and planned a retrosynthetic pathway with dichloride oxepanes as key intermediate compounds (Figure 2). In this case, the *bis*-homoallylic alcohol, necessary for Prins cyclization, should have a chlorine at the allylic position (precursor **3**, Figure 2).

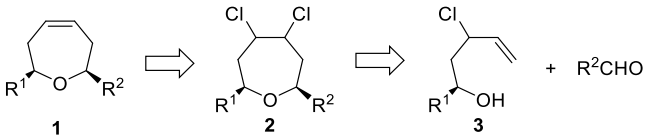
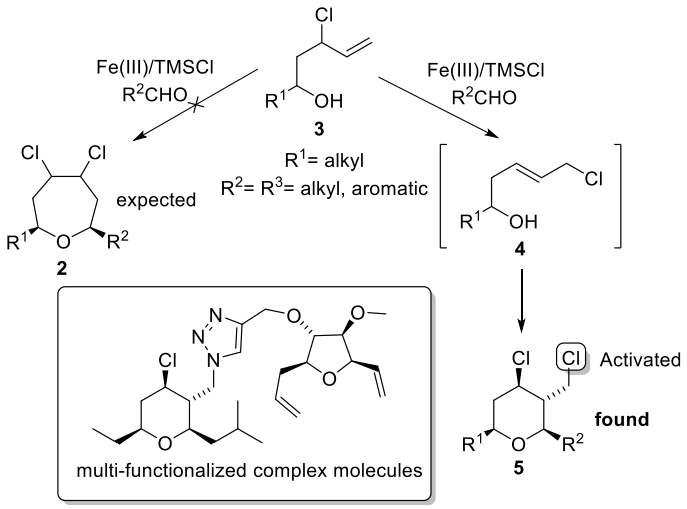


Figure 2. First approach to Δ^4-2,7-disubstituted oxepenes through dichloride oxepanes.

Initially, the alcohol **3** was prepared, to achieve the iron-catalyzed synthesis of the unsaturated disubstituted seven-membered ring oxacycle **2** as precursor to Δ^4–2,7-disubstituted oxepene **1**. However, we obtained a six-membered oxacycle **5** (2,3,4,6-tetrasubstituted tetrahydro-2*H*-pyrans) with four stereogenic centers, three of them generated in one single step, instead of the expected seven-membered ring **2** (Scheme 3). The reaction involves a tandem process via the S_N2' step, generating the intermediate **4**, and a further Prins cyclization reaction without competitive [3,3]-sigmatropic rearrangement. DFT calculations support the in situ S_N2' reaction as a preliminary step of the Prins cyclization.[13] The relative *syn*/*anti* stereochemistry at the chlorine atom in the starting material is irrelevant to the outcome of the subsequent Prins-cyclization reaction. These activated tetrahydro-2*H*-pyran units are easily derivatizable through CuAAC conjugations, in order to generate multi-functionalized complex molecules (Scheme 4).[13]

Scheme 4. Attempt to obtain Δ4-2,7-disubstituted oxepenes. Synthesis of 2,3,4,6-tetrasubstituted tetrahydro-*2H*-pyrans via tandem S_N2'-Prins cyclization.



Despite this unexpected good result, we remained focused on a direct synthesis of oxepenes **1**. The retrosynthetic proposal was then modified, replacing the chlorine at the allylic position with a silyl group. This change opened the way to isolating **6,** avoiding the isomerization in **7**, which led us to the tetrahydropyran ring **5** (Figure 3). This approach is comparable to the original proposal by Miginiac, who used a similar alcohol but primary and silylated, $(TMSO(CH_2)_2CH(TMS)CH=CH_2)$.[9] This led us to synthesize the alcohol **7** and check its reactivity with aldehydes using sustainable metal catalysis.

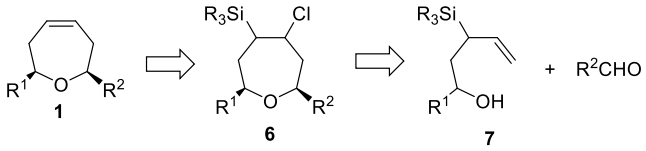
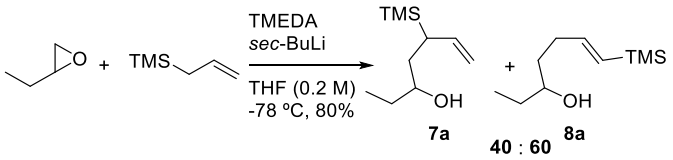


Figure 3. Second approach to Δ^4-2,7-disubstituted oxepenes. Silyl version.

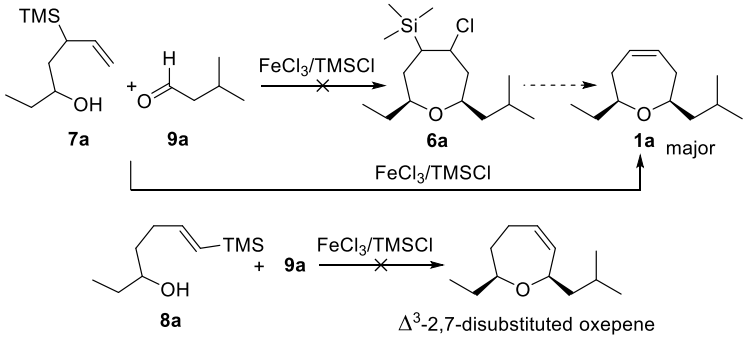
The synthesis of silyl alcohol **7** was obtained in one-step, using the protocol of Schaumann *et al*., which consists in opening an epoxide by the carbanion of the corresponding allyl silyl compound.[14] In our case, we chose a commercial available epoxide (2-ethyloxirane) as starting material. The desired β-silyl unsaturated alcohol **7a** was obtained, as minor compound, the major being the alcohol **8a**, produced by opening the 2-ethyloxirane by means of the rearranged isomer of the trimethylsilyl ylide (Scheme 5).

Scheme 5. Synthesis of β-silyl unsaturated alcohol 7.



Despite the low selectivity of this opening reaction, we next examined the reactivity of 5-(trimethylsilyl)-hept-6-en-3-ol (**7a**) with 3-methyl butanal (**9a**) in the presence of iron salts as catalysts. To our delight, the desired oxepene **1a** was directly obtained without any trace of the oxepane **6a** (Scheme 6). On the other hand, the major silyl alcohol **8a** was inert under the Prins cyclization conditions, so it was not possible to obtain the Δ^3-2,7-disubstituted oxepene isomer (Scheme 6).

Scheme 6. Proof of concept on the synthesis of oxepene 1a.



This highly productive process is the result of a cascade of three chemical events with the concomitant formation of a C-O bond, a C-C bond and a Δ^4 endocyclic double-bond, through a Prins cyclization followed by a Peterson-type elimination.[15] Therefore, this opened up the route to studying the reactivity of this reaction, using different conditions and iron salts (Table 1). As shown in Scheme 6, the iron catalytic system formed from FeX_3 or $Fe(acac)_3$ and trimethylsilyl halides was applied, based on previous work.[11,16] The cyclization works well, with a 51% yield, leading to a *cis*:*trans* mixture (6:1) of 2,7-disubstituted oxepenes (**1a** and **10a**), but with a 22% yield of the tetrasubstituted tetrahydropyran **11a** as side product (Table 1, entry 2). A similar result was obtained using a stoichiometric amount of $FeCl_3$ (Table 1, entry 1). The replacement of $FeCl_3$ with $Fe(acac)_3$, a less hygroscopic species, slightly lowered the overall yield and the amount of side product (Table 1, entry 3).

Next, the reaction was run using only catalytic amounts of $FeCl_3$ (10 mol%, Table 1, entry 4), and surprisingly it was completed quickly with a 72% yield. Iron salts thus effectively catalyzed the reaction, without adding TMSCl as co-catalyst. It also worked with aldehydes bearing other functionalities, although the catalyst load had to be raised to 15 mol% (Table 1, entry 11).

In all cases, the Δ^4-oxepenes were produced with tetrasubstituted desilylated tetrahydropyrans **11** as side product, resulting from a tandem reaction that combines protodesilylation with allylic rearrangment, and a final Prins cyclization (Scheme 7).[17]

Scheme 7. Protodesilylation reaction with allylic rearrangement and Prins cyclization in the synthesis of tetrasubstituted desilylated tetrahydropyran 11a.

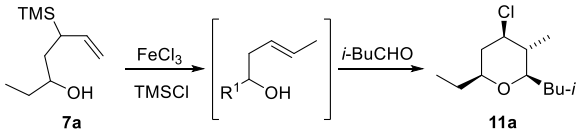
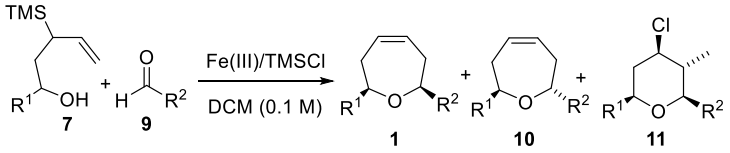


Table 1. First optimization of the Prins-Peterson reaction in the synthesis of Δ^4-2,7-disubstituted oxepenes. Trimethylsilyl option.[a]



Entry	7 (R^1)	9 (R^2)	Fe (III) (mol %)	TMSCl (equiv.)	t (h)	1	10	11
						yield (%)[b]		
1	**7a** Et	**9a** *i*-Bu	$FeCl_3$ (100)	-	0.25	**1a** 42	**10a** 15	**11a** 19
2	Et	*i*-Bu	$FeCl_3$ (10)	1.1	0.5	44	7	22
3	Et	*i*-Bu	$Fe(acac)_3$ (10)	1.1	0.25	43	13	11
4	Et	*i*-Bu	$FeCl_3$ (10)	-	0.25	44	14	14
5	Et	*i*-Bu	$Fe(acac)_3$ (10)	0.1	110	55	13	traces
6	Et	*i*-Bu	$Fe(acac)_3$ (10)	-	NR	NR	NR	NR
7	**7a**	**9b**	$Fe(acac)_3$	1.1	0.15	**1b**	**10b**	**11b**

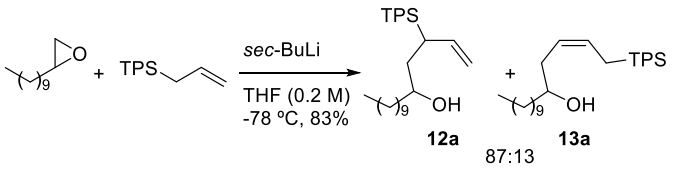
	Et	3-butenyl	(10)			41	12	15
8	Et	3-butenyl	$Fe(acac)_3$ (10)	0.1	18	36	10	traces
9	**7b** *n*-decyl	**9a** *i*-Bu	$FeCl_3$ (15)	-	0.17	**1c** 38	**10c** 16	**11c** 6
10	*n*-decyl	*i*-Bu	$Fe(acac)_3$ (10)	1.1	0.42	46	15	15
11	**7b** n-decyl	**9b** 3-butenyl	$FeCl_3$ (15)	-	0.33	**1d** 45	**10d** 13	**11d** 8

[a] Reaction conditions: **7a-b** (0.5 mmol), **9a-b** (1.0 mmol), Lewis Acid, dry solvent (0.1M), rt, without inert atmosphere. The stereochemistry of the oxepenes and THP **11** was assigned by GOESY experiments (see the Supporting Information).[b] Yields of isolated products after purification by silica-gel column chromatography.

The amount of these tetrahydropyrans **11** depends directly on the amount of acid generated in the reaction medium (Table 1). Reducing the amount of TMSCl also lowered the amount of THPs **11** to trace levels (Table 1, entries 5 and 8). The combination of 10 mol% $Fe(acac)_3$ and 0.1 equiv. of trimethylsilyl halides slowly generates $FeCl_3$ in situ. This fact avoids the protodesilylation of the alcohol **7**, however the reaction time increased up to 18h or 110h, with moderate yields.

At this point, it was clear that a change in the silyl group was necessary, to improve the synthesis of the correct isomer type **7a** and avoid protodesilylation and thus the formation of THP **11**.For this reason, our next focus was the triphenylsilyl (TPS) group, which is more stable and less electrofugal than the TMS group. The desired precursor **12a** was therefore easily prepared from the corresponding epoxide and the lithiated allyltriphenylsilane, using the methodology developed by Schaumann et al. (Scheme 8).[14]

Scheme 8. Synthesis of 3-(triphenylsilyl)pentadec-1-en-5-ol (12a).

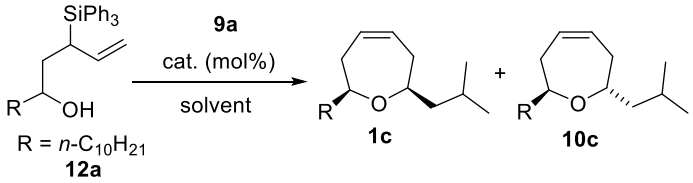


In this case, we used an epoxide with a long side-chain to generate **12a**, a less volatile alcohol than **7a**. This epoxide opening worked really well with excellent yield (95%), leading to the desired **12a** as a major compound in a ratio **12a**:**13a**, 87:13. According to the results described above (Table 1), we checked the reactivity of **12a** using

only substoichiometric amounts of Lewis acids to avoid the formation of THPs **11**, thus favouring the exclusive formation of 2,7-disubstituted oxepenes.

The reactivity of 3-(triphenylsilyl)pentadec-1-en-5-ol (**12a**) was first examined with 3-methyl butanal (**9a**) in the presence of iron salts as catalysts (Table 2). First, different amounts of iron(III) chloride were evaluated using dry methylene chloride (DCM) as solvent (entries 1-4). The cyclization proceeded satisfactorily, affording exclusively the desired Δ^4-2,7-disubstituted oxepene in good yield, without the presence of the THPs **11**. In all cases, the major compound was the *cis* isomer, the *cis*:*trans* ratio being practically constant around 4:1. Replacing iron(III) chloride with iron(III) bromide under otherwise identical reaction conditions improved the yield (entries 5-6), whereas the *cis*:*trans* ratio remained the same. Although different catalysts were used (entries 1, 6, 13-15), the best result was obtained with 5 mol% of $FeBr_3$, and dry DCM as solvent at room temperature (entry 6). The results of $InBr_3$ are comparable with those of $FeBr_3$, but with longer reaction time than with iron (entry 14). The use of other solvents led to worse results (entries 7-10). Decreasing the amount of $FeBr_3$ below 5 mol% increased the reaction time, while inducing a decrease in the reaction yields, which was more evident when 1 mol% was used (entries 11 and 12). Applying lower temperature (0 ºC) did not affect the diastereomeric ratio.

Table 2. Optimization of Prins-Peterson reaction in the synthesis of Δ^4-2,7-disubstituted oxepenes. Triphenylsilyl option.[a]



Entry	cat. (mol %)	solvent	t (h)	yield (%)[b]	**1c:10c**
1	$FeCl_3$ (15)	DCM	0.25	86	83:17
2	$FeCl_3$ (10)	DCM	0.25	75	82:18
3	$FeCl_3$ (7)	DCM	23	80	82:18
4[c]	$FeCl_3$ (5)	DCM	23	63	80:20
5	$FeBr_3$ (7)	DCM	0.5	88	82:18
6	$FeBr_3$ (5)	DCM	0.5	95	82:18

7	$FeBr_3$ (5)	DCE	0.5	90	82:18
8	$FeBr_3$ (5)	$CHCl_3$	1.5	76	83:17
9	$FeBr_3$ (5)	THF	1.5	NR	NR
10	$FeBr_3$ (5)	C_6H_6	1.5	74	77:23
11	$FeBr_3$ (3)	DCM	2	76	83:17
12[d]	$FeBr_3$ (1)	DCM	22	58	81:19
13[e]	$InCl_3$ (5)	DCM	17	69	72:28
14	$InBr_3$ (5)	DCM	1.5	90	82:18
15	$Fe(OTf)_3$ (5)	DCM	1.5	72	67:33
16	$Fe(acac)_3$ (5)	DCM	1.5	NR	NR

[a] Reaction conditions: **12a** (0.5 mmol), **9a** (1.0 mmol), LA, dry solvent (0.1 M), rt, without inert atmosphere.[b] Yield of isolated product. [c] 75% conversion.[d] 69% conversion.[e] 77% conversion. NR = no reaction.

Related to our methodology, Panek and co-workers have studied the reactivity of vinyl and crotyl silanes in the synthesis of dihydropyrans through [4+2] annulation. They concluded that the stereochemical course of the annulation was determined by relative stereochemical arrangement (*syn* or *anti*) of the silicon with the silyl ether and the adjacent α groups to this silyl ether.[18] However, we synthesized a seven membered ring oxacycle and the relative stereochemistry of the silicon with the hydroxy group (*syn* or *anti*), with one carbon more between them, has no influence in the *cis*:*trans* diastereoselectivity of the corresponding oxepene.[19] In fact, the treatment of two different *syn*/*anti* mixtures of **12a** (50:50 and 71:29) led to the same oxepenes *cis*:*trans* ratio 4:1.[20]

Encouraged by our initial results, we decided to study a series of alkenols **12** and aldehydes **9** to determine the scope of our direct Prins Peterson type reaction (PPR). We examinated the PPR starting with alkenols bearing a non-functionalized side chain and finishing with more functionalized chain (bearing double bond or an aromatic group). As shown in Table 3, a range of aldehydes could be efficiently used to generate the corresponding oxepenes **1a-1t**. First, we used alkenols with a large side chain. The reaction worked well with aliphatic and aromatic aldehydes.[21] Interestingly, good results with aldehydes bearing double bonds such as **1d** and **1e** were observed leading to

oxepenes with endocyclic and exocyclic olefins. The case of **1e** is particularly notorious due to the difficulty of incorporating acrolein under iron(III) catalyst.[12] In the case of aromatic aldehydes, we observed a decrease on the reaction yields when oxygenated substituents were present (NO_2, OMe). In the case of NO_2 substituent, we only observed *cis* oxepene, problably due to steric factors in the oxocarbenium ion C (Scheme 13). Furthermore, to show the synthetic applicability of this cyclization, the reaction of **12a** and **9a** was carried out in a 3 mmol scale, and oxepene **1c** was isolated in 87% yield.

Next, we moved to alkenols with a functionality at the side chain (entries 11-14). The reactions worked really well both with isovaleraldehyde (entry 11) and with functionalized aldehydes (entries 12 and 14). Although with moderate yield, the PPR also worked with a heteroaromatic aldehyde such as furan-3-carbaldehyde (entry 13). Moreover, the relative *cis* configuration of the two stereocenters in the final oxepene ring as well as Δ^4-double bond were confirmed by X-ray diffraction analysis of **1s** (Table 3, entry 17) (Figure 4).[22] This method permitted the access to oxepenes with both side chains functionalized.

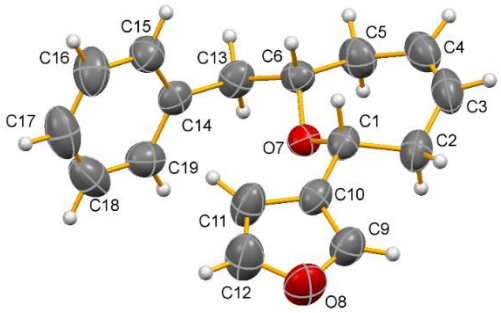


Figure 4. ORTEP plot of *cis*-2-benzyl-7-(furan-3-yl)-Δ^4 oxepene **1s**.

Last, we used alkenols with aromatic ring at the side chain. The yields of the reaction were almost identical than those described above, but with a better ratio *cis*:*trans* (entries 15-18). In these cases the ratio of *cis* isomer increased untill 90% approximately or even higher (entries 16 and 18). The participation of the aromatic ring in the oxocarbenium ion intermediate **C** (Scheme 13), could be the responsible of this *cis* isomer increase.

Our next challenges was to check the reactivity of several ketones in this PPR cyclization, where we never got positive results in our previous experiences with the Prins cyclization and iron(III) salts as catalyts.[16]

Table 3. Substrate scope for direct synthesis of Δ^4-2,7-disubstituted oxepenes.[a]

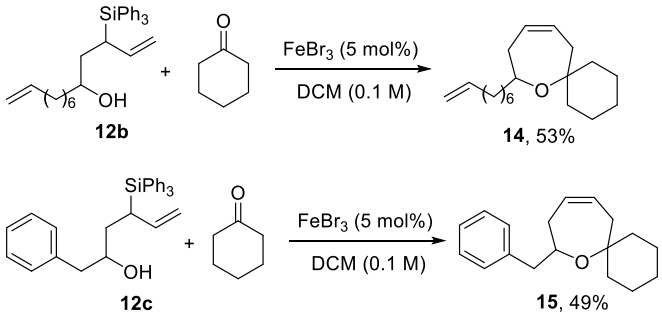
Entry	12 (R^1)	9 (R^2)	yield[b] (%)	1:10[c]	
1	**12a,** *n*-decyl	**9a**	95	**1c:10c**	82:18
2	*n*-decyl	**9b**	78	**1d:10d**	83:17
3	*n*-decyl	**9e**, ethenyl	71	**1e:10e**	80:20
4	*n*-decyl	**9f**, Cy	81	**1f:10f**	85:15
5	*n*-decyl	**9g**, Ph	54	**1g:10g**	76:24
6	*n*-decyl	**9h**, *p*-MeO-Ph	42	**1h:10h**	90:10
7	*n*-decyl	**9i**, *p*-NO_2-Ph	39	**1i:10i**	100:0
8	*n*-decyl	**9j**, *p*-F-Ph	76	**1j:10j**	83:17
9	*n*-decyl	**9k**, *p*-Me-Ph	72	**1k:10k**	83:17
10	*n*-decyl	**9l**, Bn	87	**1l:10l**	91:9
11	**12b**, 7-octenyl	**9a**	88	**1m:10m**	81:19
12	7-octenyl	**9e**	86	**1n:10n**	82:18
13	7-octenyl	**9o**, furan-3-yl	55	**1o:10o**	82:18
14	7-octenyl	**9p**, 3-benzoate-propyl	83	**1p:10p**	84:16
15	**12c**, Bn	**9a**	88	**1q:10q**	87:13
16	Bn	**9e**	84	**1r:10r**	92:8
17[d]	Bn	**9o**	42	**1s:10s**	90:10
18	Bn	**9p**	80	**1t:10t**	94:6

[a] Reaction conditions: **12a-c** (0.5 mmol), **9a-l** (1.0 mmol), $FeBr_3$ (5 mol%), dry solvent (0.1M), rt, without inert atmosphere. The stereochemistry of the oxepenes was assigned by GOESY experiments (see the Supporting Information). [b] Yields of isolated products are given.[c] Ratio *cis:trans* (**1:10**) are given.[d] 74% conversion.

As Scheme 9 shows, the reaction incorporated the cyclohexanone backbone with moderate yields (14 and 15, Scheme 9). This is a noteworthy result because, as commented above, all the other ketones were unreactive in the Prins cyclization catalyzed

by iron(III) salts. We checked acyclic (methyl phenyl ketone, acetone and ethyl methyl ketone) and cyclic ketones unsuccessfully. We therefore tried other cyclic ketones varying the size of the ring, but without positive results.[23] Neither was any incorporation detected using cyclohexane bearing two ketones, such as 5,5-dimethylcyclohexane-1,3-dione. At this stage, we decided to check the reactivity of our alkenols **12b** (R^1 = 7-octenyl) and **12c** (R^1 = Bn) with cyclopentanone (non-reactive with iron(III)salts) and another Lewis acid that has favored the reaction of ketones in the Prins cyclization, $BF_3{\cdot}OEt_2$. Used in 30 mol% with DCM (0.1M) as solvent, it did not even show traces of the corresponding oxepene.

Scheme 9. Prins-Peterson type reaction with cyclohexanone.

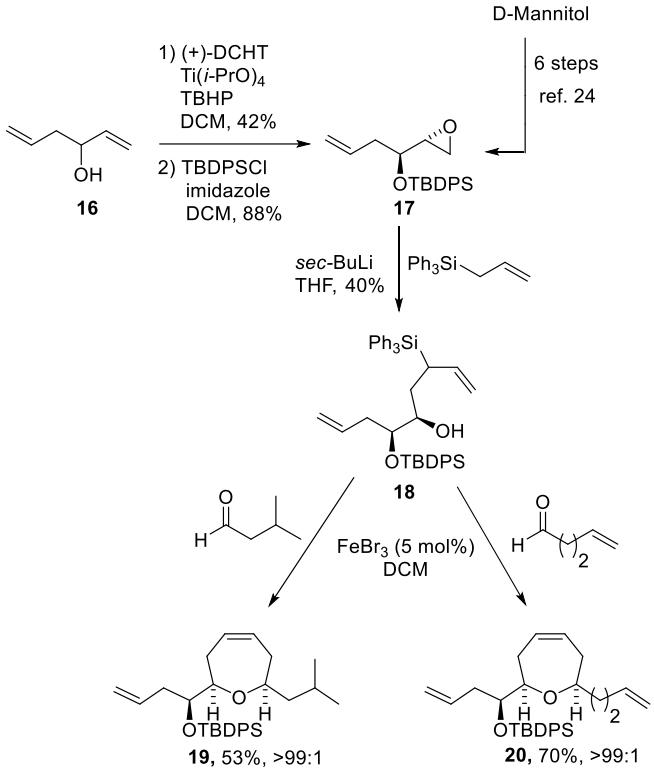


After this result, we moved on to improve the *cis*:*trans* diastereoselectivity. It is clear that the side-chains at R^1 and R^2 influence the ring-closing selectivity (entries 6, 7, 10, 16-18, Table 3). In most cases, the *cis*:*trans* diastereoselectivity was around 4:1, however this ratio change favored the *cis* isomer in some types of chain (entries 6, 7, 10, 16-18, Table 3). Inspired by this, we proceeded to explore the influence of a bulky group in the α- position to the hydroxyl moiety. A suitable group should have (a) adequate bulkiness to drive the process exclusively towards the *cis* oxepene, and (b) versatility to be converted into another functional group. The *tert*-butyldiphenyl silyl ether (OTBDPS) protecting group (**18**, Scheme 10) was an ideal candidate.

We focused our attention on the preparation of a model compound that could also serve as an intermediate to check our method in the synthesis of (+)-isolaurepinnacin. Thus, the desired alcohol **18** was synthesized starting from epoxide **17**, which can be obtained from *D*-mannitol[24] or in a two-step sequence from the commercially available allylic alcohol **16**, followed by further protection of the hydroxyl group (see Supporting Information).[6j,25,26] The regioselective ring-opening of epoxide **17** with allyl triphenyl silane under Schaumann´s conditions afforded the desired alcohol **18** in 40% yield.[14] We

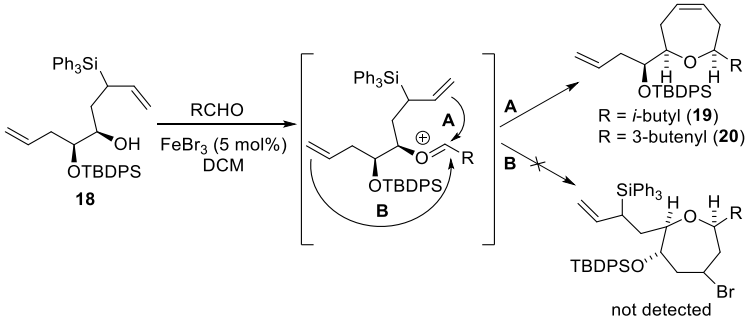
tested its reactivity toward simple aldehydes such as isobutyraldehyde and 4-pentenal. In both cases, oxepenes **19** and **20** were obtained with good yields and complete *cis* diastereoselectivity (Scheme 10).

Scheme 10. Synthesis of *cis*-2,7-disubstituted oxepenes.



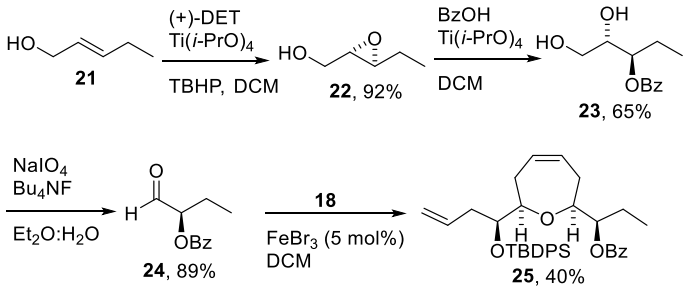
It is important to highlight the chemoselectivity of this process. The alcohol **18** bears two double-bonds in a suitable position to lead to an oxepane ring, however the reaction only proceeded through the double-bond attack **A**, leading to oxepenes **19** and **20**. The bromo-oxepane, resulting from double-bond attack **B**, was not formed or even detected by NMR (Scheme 11).

Scheme 11. Chemoselectivity in the Prins Peterson-type reaction of alcohol 18.



Our attention next became focused on the potential use of an aldehyde bearing a α-protected hydroxyl group (**24**, Scheme 12). This aldehyde **24** was obtained in three steps from commercially available allylic alcohol **21**. Katsuki-Sharpless asymmetric epoxidation generated the epoxy alcohol **22**, which was regioselectively opened under acidic conditions to proceed to the desired 1,2-diol **23** and further periodate cleavage of the diol in 89% yield (Scheme 12).[27] The Prins-Peterson type (PPR) reaction catalyzed by iron(III) bromide between the alcohol **18** and aldehyde **24** produced the oxepene **25** in 40% yield in one single step. A C-O bond, a C-C and an endocyclic olefin were generated in a regioselective manner in the course of the catalytic process. As in the case of oxepenes **19** and **20**, the cyclization occurred with complete *cis* diastereoselectivity. This substrate has the two hydroxyl moieties orthogonally protected, allowing us future transformations onto much more complex structures.

Scheme 12. PPR with aldehydes bearing a α-protected hydroxyl group.



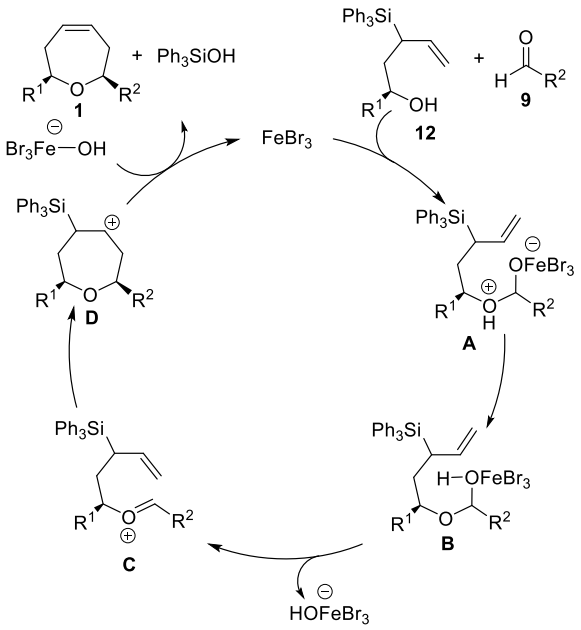
With this type of aldehyde, we will be able to prepare more complex substrates such as **25**, which would allow us to generate a wide variety of structures with important implications in Diverted Total Synthesis (DTS) Strategies.[28]

Regarding the reaction mechanism of PPR (Scheme 13), we propose that the attack of alcohol **12** on aldehyde **9** is previously activated by the iron(III) bromide, to form the zwitterionic species **A**.

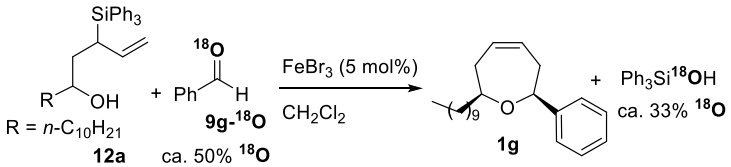
This intermediate leads to the mixed acetal **B** and the oxocarbenium ion **C**, which is intramolecularly trapped by the olefin moiety to give rise to a carbocation **D**, already stabilized by the presence of the silyl group (β-effect).[29] Further attack by Br_3Fe-OH generated under the reaction conditions produces the Δ^4-2,7-disubstituted oxepene and triphenylsilanol. The double bond would be formed via a direct elimination or an induced Peterson-type elimination, in either case regenerating the catalytic species $FeBr_3$. To more strongly verify the generation of Br_3Fe-OH and its involvement in the final elimination

step, an isotopic labeling experiment was performed. As shown in Scheme 14, the ^{18}O-labeled aldehyde **9e** was used under the standard conditions, and the silanol product was analyzed by ESI-MS. It was found that ^{18}O-labeled Ph_3SiOH was formed with ca. 33% ^{18}O-labeled. This result indicated that the oxygen atom of the aldehyde is involved in the elimination step. This data supports the last stage of the proposed mechanism.

Scheme 13. Proposed mechanism.



Scheme 14. The Prins Peterson-type reaction with ^{18}O-labeled aldehyde.



In summary, we have developed a highly efficient, stereoselective and direct synthesis of Δ^4-2,7-disubstituted oxepenes via a low catalyst loading process (LCL) with iron(III)-bromide. This highly productive process is the result of a cascade of three chemical events with the concomitant formation of a C-O bond, a C-C bond and a Δ^4 endocyclic double bond. A bulky substituent at the α-position with respect to the hydroxyl group of the bis-homoallylic alcohol drives the Prins cyclization toward the exclusive formation of the cis-oxepene. The silyl substrate favored elimination rather than trapping of the carbocation with a nucleophile such as halide.. Approaches to (+)-isolaurepinnacin

and (+)-neoisoprelaurefucin are under development and the results will be reported in due course.

Experimental Section

General remarks. NMR spectra were recorded on a Bruker Avance instrument. ^{1}H-NMR spectra were recorded at 400, 500 and 600 MHz, and ^{13}C-NMR were recorded at 100, 125 and 150 MHz, VTU 298.0 °K. Chemical shifts were reported in parts per million. The residual solvent peak was used as an internal reference ($CDCl_3$: δ_H 7.26, δ_C 77.0). Dept 90, Dept 135, 2D-COSY and HSQC were used to confirm the NMR peak assignments.

Optical rotations were measured on a Perkin-Elmer 343 polarimeter by using a Na lamp. HRMS-TOF was used for HRMS measurements and performed on a Micromass Autospec spectrometer by addition of CHO_2H (10% in water).

Silica gel ready-foils were used for analytical thin-layer chromatography. They were developed with 254 nm UV light and spraying with a solution of phosphomolybdic acid solution (20 wt. % in ethanol) and heating. Column chromatography was performed using silica gel (0.015-0.04 mm) and Chromatotron chromatography with 1, 2 and 4 mm silica gel disks, both using *n*-hexane/EtOAc solvent systems. All reagents were obtained from commercial sources, without further purification.

General procedure for the preparation of *bis*-homoallylsilyl alcohols (12). This procedure is based on the work published by Schaumann *et al.*[14] The reagent *sec*-butyllithium (1.2-2.5 eq.) was added to a well-stirred solution of allyltriphenylsilane (1.2-2.5 eq.) in dry tetrahydrofuran (THF) (0.08-0.2 M), previously cooled to -78 ºC under inert atmosphere. Then the system was allowed to reach -50 ºC and this temperature was maintained for 2 hours. After that, the system was cooled again to -78 ºC and the corresponding epoxide (1.0 eq.) was added dropwise, dissolved in a small amount of dry THF. The reaction was stirred at -78 ºC until analysis via TLC showed complete formation of product. Quenched by addition of a mixture of *n*-hexane/ethyl ether/saturated aqueous NH_4Cl (2:2:1), the volume of this mixture being 25 times the equivalents of allyltriphenylsilane used and extracted with ethyl ether. The combined organic layers were dried over anhydrous magnesium sulfate, filtered and the solvent was removed under reduced pressure. This crude reaction mixture was purified by flash silica gel column chromatography (*n*-hexane/EtOAc: 95/5 solvent system).

General procedure for the synthesis of Δ^4-2,7-disubstituted oxepenes (1 and 10). To a well-stirred and open-air solution of *bis*-homoallylsilyl alcohol **12** (1.0 eq.) in dry dichloromethane (DCM) (0.1 M) at room temperature, were added the corresponding aldehyde (2.0 eq.) and the $FeBr_3$ (3 – 5mol%). The reaction is monitored by TLC and, once complete, the process is quenched by addition of the same amount of water as DCM. The aqueous phases were separated and washed with DCM. The combined organic layers were dried over anhydrous magnesium sulfate, filtered and the solvent was removed under reduced pressure. This crude reaction mixture was purified by flash silica gel column chromatography (*n*-hexane/EtOAc: 95/5 solvent systems) in order to obtain the *cis*:*trans* mixture of the oxepenes. The final separation of the two isomers was made using the chromatotron (*n*-hexane/EtOAc: 98/2 solvent system).

General procedure for alcohol tosylation. To a well-stirred solution of the alcohol (1.0 eq.) in dry dichloromethane (DCM) (0.1 M) at 0 ºC, trimethylamine (Et_3N) (3.5 eq.) was added dropwise, and *p*-toluensulfonyl chloride (TsCl) (2.5 eq.) portionwise. The system reached room temperature slowly under stirring overnight. Once the reaction was completed, it was quenched by addition of aqueous saturated $CuSO_4$ with vigorous stirring. The solution was extracted with 3 x DCM and the combined organic layer was dried over $MgSO_4$. Organic solvent was removed under reduced pressure. The crude reaction mixture was purified by flash silica gel column chromatography (*n*-hexane/EtOAc solvent systems).

General procedure for Sharpless epoxidation of an allylic alcohol. Following the procedure developed by Sharpless *et al.*,[26] MS (4Å) was added into a round bottom flask equipped with an addition funnel with pressure-equalization arm. To activate MS, the system was flamed under vacuum and cooled under nitrogen. Next, DCM and $Ti(i\text{-}OPr)_4$ were added and the mixture was cooled to -20 ºC (this temperature was maintained through the whole process). After 5 minutes, (+)- or (-)-diethyltartrate (DET) was added and the mixture stirred another 5 minutes. Then the allylic alcohol was added, and the mixture was stirred 20 minutes. Finally, the *tert*-butylhydroperoxide (TBHP) was added dropwise and the flask placed in the freezer overnight at -20 ºC. Once the reaction was complete (checked by TLC), the suspension was filtered through a pad of celite® and then, 15% aqueous tartaric acid was added and stirred 30 min. Next, the mixture was separated and the organic phase concentrated under reduced pressure. The crude was dissolved in Et_2O and cooled to 0 ºC. Aqueous 15% NaCl was added and stirred only 1 minute. The organic phase was separated and extracted with 2 x Et_2O and 2 x EtOAc,

dried over $MgSO_4$ and concentrated under reduced pressure. The crude reaction mixture was purified by flash silica gel column chromatography (*n*-hexane/EtOAc solvent systems).

5-(trimethylsilyl)hept-6-en-3-ol (7a). Following the general procedure for *bis*-homoallylsilyl alcohol formation, 1,2-epoxybutane (11.0 mmol, 1.0 eq.) was added to a solution of allyltrimethylsilane (10.0 mmol, 1.1 eq.), TMEDA (10.0 mmol, 1.0 eq.) and *sec*-butyllithium (11.0 mmol, 1.1 eq.) in dry THF (0.2 M) to obtain 0.655 g of the product (32% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.63 (dt, *J* = 10.1 & 16.9 Hz, 1H), 4.94-4.90 (dd, *J* = 1.8 and 10.3 Hz, 1H), 4.89-4.85 (ddd, *J* = 0.9, 1.9 and 17.0 Hz, 1H), 3.56 (m, 1H), 1.84 (ddd, *J* = 2.8, 9.8 and 12.5 Hz, 1H), 1.61-1.37 (m, 5H), 0.94 (t, *J* = 7.5 Hz, 3H), -0.02 (s, 9H) ppm; ^{13}C{^{1}H}-NMR ($CDCl_3$, 150 MHz) δ 139.8 (CH), 112.5 (CH_2), 71.4 (CH), 35.3 (CH_2), 30.7 (CH), 30.5 (CH_2), 10.2 (CH_3), -3.5 (3xCH_3). HRMS (ESI$^+$): m/z $[M+Na]^+$ Calcd for $C_{10}H_{22}OSiNa$: 209.1338; Found: 209.1334.

3-(triphenylsilyl)pentadec-1-en-5-ol (12a). Following the general procedure for *bis*-homoallylsilyl alcohol formation, 1,2-epoxydodecane (8.14 mmol, 1.0 eq.) was added to a solution of allyltriphenylsilane (9.77 mmol, 1.2 eq.) and sec-butyllithium (9.77 mmol, 1.2 eq.) in dry THF (0.2 M) to obtain 2.82 g of the product (72% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) (mixture *syn*/*anti* (41:59)) δ 7.60-7.55 (dt, *J* = 1.5 & 8.0 Hz, 12H), 7.44-7.38 (m, 6H), 7.38-7.32 (m, 12H), 5.94-5.83 (m, 1H), 5.80-5.68 (m, 1H), 5.04-4.93 (m, 4H), 3.76-3.61 (m, 2H), 2.96 (m, 1H), 2.61 (m, 1H), 1.87 (ddd, *J* = 2.5 & 6.1 & 14.0 Hz, 1H), 1.79-1.69 (m, 2H), 1.67-1.63 (m, 1H), 1.63-1.58 (m, 1H), 1.41-1.18 (m, 36H), 0.90-0.85 (m, 6H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 150 MHz) (mixture *syn*/*anti* (41:59)) δ 139.6 (CH), 138.6 (CH), 136.2 (6 x CH), 136.1 (6 x CH), 133.8 (3 x C), 133.6 (3xC), 129.5 (3 x CH), 129.4 (3 x CH), 127.8 (6 x CH), 127.x7 (6 x CH), 115.2 (CH_2), 114.9 (CH2), 73.2 (CH), 69.7 (CH), 38.0 (CH_2), 37.1 (CH_2), 36.7 (CH_2), 36.2 (CH_2), 31.9 (2xCH_2), 30.9 (CH), 29.6 (8 x CH_2), 29.3 (2xCH_2), 27.9 (CH), 25.9 (CH_2), 25.3 (CH_2), 22.7 (2xCH_2), 14.1 (2xCH_3). HRMS (ESI+): m/z $[M+Na]^+$ Calcd for $C_{33}H_{44}OSiNa$: 507.3059; Found: 507.3050.

3-(triphenylsilyl)trideca-1,12-dien-5-ol (12b). Following the general procedure for *bis*-homoallylsilyl alcohol formation, 1,2-epoxy-9-decene (6.5 mmol, 1.0 eq.) was added to a solution of allyltriphenylsilane (7.8 mmol, 1.2 eq.) and *sec*-butyllithium (7.8 mmol, 1.2 eq.) in dry THF (0.2 M) to obtain 1.72 g of the product (70% yield, 83% conversion). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) (mixture *syn*/*anti* (41:59)) δ 7.57 (brddd, *J* =

1.5, 8.0 & 8.0 Hz, 12H), 7.44-7.32 (m, 18H), 5.95-5.64 (m, 4H), 5.03-4.90 (m, 8H), 3.68 (m, 2H), 2.95 (m, 1H), 2.61 (m, 1H), 2.03 (m, 4H), 1.86 (ddd, *J* = 2.5, 6.2 & 14.1 Hz, 1H), 1.79-1.68 (m, 2H), 1.68-1.57 (m, 2H), 1.47 (m, 1H), 1.43-1.19 (m, 20H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 150 MHz) (mixture *syn*/*anti* (41:59)) δ 139.6 (CH), 139.2 (CH), 139.1 (CH), 138.5 (CH), 136.2 (6xCH), 136.1 (6xCH), 133.8 (3xC), 133.6 (3xC), 129.6 (3xCH), 129.4 (3xCH), 127.8 (6xCH), 127.8 (6xCH), 115.2 ($2xCH_2$), 115.0 ($2xCH_2$), 114.1 ($4xCH_2$), 73.2 (CH), 69.7 (CH), 37.9 (CH_2), 37.1 (CH_2), 36.7 (CH_2), 36.2 (CH_2), 33.8 (CH_2), 33.7 (CH_2), 30.9 (CH), 29.4 ($2xCH_2$), 29.1 (CH_2), 29.0 (CH_2), 28.8 (CH_2), 28.8 (CH_2), 27.8 (CH), 25.8 (CH_2), 25.2 (CH_2). HRMS (ESI+): m/z $[M+Na]^+$ Calcd for $C_{31}H_{38}OSiNa$: 477.2590; Found: 477.2592.

1-phenyl-4-(triphenylsilyl)hex-5-en-2-ol (12c). Following the general procedure for *bis*-homoallylsilyl alcohol formation, (2,3-epoxypropyl)benzene, (8.5 mmol, 1.0 eq.), synthesized by epoxidation of allylbenzene with *m*-CPBA, was added to a solution of allyltriphenylsilane (8.5 mmol, 1.0 eq.) and *sec*-butyllithium (8.5 mmol, 1.0 eq.) in dry THF (0.2 M) to obtain 1.35 g of the product (two steps: 44% yield, 82% conversion). Colorless oil. ^{1}H-NMR ($CDCl_3$, 600 MHz) (mixture *syn*/*anti* (41:59)) δ 7.60-7.53 (m, 12H), 7.41 (m, 6H), 7.36 (m, 12H), 7.28 (m, 4H), 7.21 (m, 2H), 7.15 (m, 4H), 5.89 (m, 1H), 5.71 (m, 1H), 5.06-4.88 (m, 4H), 3.91 (m, 2H), 2.99 (brt, *J* = 10.3 Hz, 1H), 2.89 (dd, *J* = 4.0 & 13.7 Hz, 1H), 2.72-2.64 (m, 2H), 2.64-2.58 (dd, *J* = 8.9 & 13.7 Hz, 1H), 2.54 (dd, *J* = 8.5 & 13.6 Hz, 1H), 1.95 (ddd, *J* = 2.6, 6.8 & 14.0 Hz, 1H), 1.91-1.82 (m, 2H), 1.74 (m, 1H), 1.69 (m, 1H), 1.53 (m, 1H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 150 MHz) (mixture *syn*/*anti* (41:59)) δ 139.3 (CH), 138.8 (C), 138.6 (C), 138.3 (CH), 136.2 (6xCH), 136.1 (6xCH), 133.8 (3xC), 133.4 (3xC), 129.5 (3xCH), 129.4 (3xCH), 129.3 (2xCH), 129.3 (2xCH), 128.5 (2xCH), 128.5 (2xCH), 127.8 (6xCH), 127.8 (6xCH), 126.4 (CH), 126.3 (CH), 115.3 (CH_2), 115.1 (CH_2), 73.6 (CH), 70.4 (CH), 44.5 (CH_2), 42.6 (CH_2), 36.3 (CH_2), 36.2 (CH_2), 30.5 (CH), 237.8 (CH). HRMS (ESI+): m/z $[M+Na]^+$ Calcd for $C_{30}H_{30}OSiNa$: 457.1964; Found: 457.1959.

4-benzoyloxybutanal (9p): A solution of 4-(benzoyloxy)-1-butanol (synthesized following procedure reported in literature) (10.3 mmol, 1.0 equiv) in dry DCM (2.06 M) was added in one portion at r.t to a stirred suspension of pyridinium chlorochromate (PCC) (15.5 mmol, 1.5 equiv) and Celite (3.30 g), in the same solvent (27 mL). The resulting reaction mixture was kept at r.t for 1.5 h then diluted with anhydrous Et_2O and filtered. The solvents were evaporated under reduced pressure and the crude residue was

purified by column chromatography on silica gel to give the aldehyde **9p** as a colorless oil (1.64 g, 83% yield). Spectral data was consistent with the known aldehyde.[30]

(*S*)-1-((*R*)-oxiran-2-yl)but-3-en-1-ol: this compound was synthesized following the procedure used by Sharpless *et al*.[26] Spectral data was consistent with the known product.[25] $[\alpha]_D^{25}$ = +26.5 (*c* = 1.0, DCM).

***tert*-butyl(((*S*)-1-((*R*)-oxiran-2-yl)but-3-en-1-yl)oxy)diphenylsilane (17):** to a solution of the previous epoxyalcohol (0.45 g, 4.0 mmol) in dry DCM (0.1 M), was added imidazole (0.69 g, 10.0 mmol, 2.5 eq.) and the mixture was stirred until totally dissolved. Then, the mixture was cooled to 0 ºC and TBDPSCl (2.65 mL, 10.0 mmol, 2.5 eq.) was added dropwise (solved in 3 mL of DCM). The mixture was allowed to reach r.t. slowly and stirred overnight. The quenching was performed by addition of water. Then the mixture was extracted with 3 x DCM, dried over $MgSO_4$ and concentrated under reduced pressure. The reaction mixture was purified by flash silica gel column chromatography (*n*-hexane/EtOAc: 95/5 solvent system) to obtain 1.24 g of the product (88% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.69 (bdd, *J* = 6.7 & 9.1 *Hz*, 4H), 7.47-7.34 (m, 6H), 5.88 (m, 1H), 5.05 (m, 2H), 3.48 (q, *J* = 5.6 *Hz*, 1H), 2.91 (ddd, *J* = 2.9, 3.6 & 6.1 *Hz*, 1H), 2.46 (dd, *J* = 4.0 & 5.1 *Hz*, 1H), 2.35 (m, 2H), 2.15 (dd, *J* = 2.6 & 5.2 *Hz*, 1H), 1.06 (s, 9H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 100 MHz) δ 135.9 (4 x CH), 133.8 (C), 133.75 (CH), 133.7 (C), 129.8 (CH), 129.7 (CH), 127.6 (2 x CH), 127.5 (2 x CH), 117.6 (CH_2), 72.8 (CH), 53.9 (CH), 46.2 (CH_2), 39.8 (CH_2), 26.9 (3 x CH_3), 19.4 (C). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{22}H_{28}O_2SiNa$: 375.1756; Found: 375.1743. $[\alpha]_D^{26}$ = +32.2 (*c* = 1.33, $CHCl_3$).

Benzaldehyde-^{18}O (9g-^{18}O): this compound was synthesized following the procedure by Carlsen and Ystenes.[31] Spectral data was consistent with the known product.[31] The crude reaction mixture was used without further purification. HRMS (ESI^+): *m/z* $[C_7H_5{}^{16}O{}^{18}O]^+$: Calcd for 123.0330; Found:123.0332. MS analysis revealed an 50% ^{18}O isotope incorporation.

(5*R*,6*S*)-6-((*tert*-butyldiphenylsilyl)oxy)-3-(triphenylsilyl)nona-1,8-dien-5-ol (18). Following the general procedure above for the preparation of *bis*-homoallylsilyl alcohol, 0.6 g (1.7 mmol, 1.0 eq.) of the epoxide **17** was added to a solution of allyltriphenylsilane (1.3 g, 4.25 mmol, 2.5 eq.) and *sec*-butyllithium 1.4 M in cyclohexane (3.04 mL, 4.25 mmol) in 21 mL of dry THF (0.08 M). The crude of the reaction mixture was purified by flash silica gel column chromatography (*n*-hexane/EtOAc: 95/5 solvent system) to give

0.27 g of the product (40% yield, 61% conversion). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.68-7.46 (m, 10H), 7.45-7.23 (m, 15H), 5.56 (m, 2H), 4.94-4.82 (m, 4H), 3.75 (m, 1H), 3.64 (bd, *J* = 10.2 *Hz*, 1H), 2.89 (t, *J* = 10.7 *Hz*, 1H), 2.19-1.98 (m, 2H), 1.89-1.79 (m, 1H), 1.61-1.49 (m, 2H), 0.99 (m, 9H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 100 MHz) δ 137.9 (CH), 136.2 (6 x CH), 136.0 (CH), 135.9 (CH), 135.8 (CH), 134.5 (CH), 134.0 (2 x C), 129.8 (CH), 129.7 (CH), 129.5 (CH), 129.4 (3 x CH), 127.9 (CH), 127.8 (CH), 127.7 (6 x CH), 127.6 (CH), 127.5 (CH), 117.0 (CH_2), 115.2 (CH_2), 76.4 (CH), 71.6 (CH), 37.3 (CH_2), 30.7 (CH_2), 27.2 (CH), 27.0 (3 x CH_3), 19.4 (C). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{43}H_{48}O_2Si_2Na$: 675.3091; Found: 675.3091. $[\alpha]_D^{25}$ = +1.27 (*c* = 2.0, $CHCl_3$).

((2*S*,3*S*)-3-ethyloxiran-2-yl)methanol (22). Following the general procedure for Sharpless epoxidation, (+)-DET (2.1 g, 1.75 mL, 10.1 mmol, 0.35 eq.), 2-penten-1-ol, 95 % (**21**) (2.5 g, 3.1 mL, 29.0 mmol, 1.0 eq.) and TBHP 5.06 M in isooctane (10.3 mL, 1.8 eq.), were added to a suspension of MS (4Å) and Ti(*i*-OPr)$_4$ (2.5 g, 2.6 mL, 0.3 eq.) in 145 mL of dry DCM (0.2 M). The crude reaction mixture was purified by flash silica gel column chromatography (*n*-hexane/EtOAc: 40/60 solvent system) to obtain 2.73 g of the product **22** (92 % yield). Colorless oil. Spectral data was consistent with the known product.[6] HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_5H_{10}O_2Na$: 125.0578; Found: 125.0582. $[\alpha]_D^{25}$ = -27.5 (*c* = 1.0, EtOH, Reference.[32] $[\alpha]_D^{22}$ = -31.1 (*c* = 0.56, EtOH)).

(2*S*,3*R*)-1,2-dihydroxypentan-3-yl benzoate (23). To a solution of Ti(*i*-OPr$_4$) (3.04 mL, 10.3 mmol, 1.5 eq.) and the epoxyalcohol **22** (0.7 g, 6.85 mmol, 1.0 eq.) in 137 mL of dry DCM (0.05 M), was added benzoic acid (1.51 g, 12.3 mmol, 1.85 eq.). Once the reaction was completed (monitored by TLC), aqueous 15% tartaric acid was added. Then the mixture was extracted with 3 x DCM and 2 x EtOAc, dried over $MgSO_4$ and concentrated under reduced pressure. The reaction mixture was purified by flash silica gel column chromatography (*n*-hexane/EtOAc: 40/60 solvent system) to obtain 1.0 g of the diol **23** (65% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.05 (d, *J* = 1.3 *Hz*, 2H), 7.59 (tt, *J* = 1.3 & 7.4 *Hz*, 1H), 7.46 (t, *J* = 7.7 *Hz*, 2H), 5.03 (ddd, *J* = 3.5, 6.8 & 8.7 *Hz*, 1H), 3.74 (ddd, *J* = 3.1, 4.7 & 7.7 *Hz*, 1H), 3.71 (dd, *J* = 3.0 & 14.5 *Hz*, 1H), 3.62(dd, *J* = 4.6 & 11.8 *Hz*, 1H), 3.01-2.28 (bs, 2H), 2.03-1.91 (dtd, *J* = 3.5, 7.5 & 21.9 *Hz*, 1H), 1.90-1.76 (sex, *J* = 7.3 & 8.7 *Hz*, 1H), 1.01 (t, *J* = 7.4 *Hz*, 3H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 100 MHz) δ 167.4 (C), 133.4 (CH), 129.8 (2 x CH), 128.5 (2 x CH), 76.1 (CH), 72.8 (CH), 62.5 (CH_2), 23.9 (CH_2), 9.8 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{12}H_{16}O_4Na$: 247.0946; Found: 247.0947. $[\alpha]_D^{25}$ = +3.1 (*c* = 1.07, EtOH).

(*R*)-1-oxobutan-2-yl benzoate (24). To a solution of diol **23** (0.22 g, 1.0 mmol) in diethyl ether (0.27 M) was added a solution of $NaIO_4$ (0.27 g, 1.26 mmol) and Bu_4NF (26 μL, 0.026 mmol) in H_2O (0.45 M). Stirred at RT and monitored by TLC. The reaction mixture was quenched by diluting with diethyl ether and water. Next, it was extracted with 3 x Et_2O and dried over $MgSO_4$, followed by concentration under reduced pressure, giving 0.172 g of the crude product (89% yield). Spectral data were consistent with the known compound,[33] so our product was later used without further purification.

***cis*-Δ⁴-2-ethyl-7-isobutyloxepene (1a).** Following the general procedure above, isovaleraldehyde (1.08 mmol, 2.0 eq.) and $FeCl_3$ (0.054 mmol, 0.10 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **7a** (0.54 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 43.0 mg of the product (44% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.74 (d, *J* = 3.8 *Hz*, 1H), 5.73 (d, *J* = 3.3 *Hz*, 1H), 3.39 (ddt, *J* = 1.6 *Hz*, 3.6 & 9.8 *Hz*, 1H), 3.20 (m, 1H), 2.18 (m, 4H), 1.89 (m, 1H), 1.56 (m, 2H), 1.44 (m, 1H), 1.10 (m, 1H), 0.96 (t, *J* = 7.4 *Hz*, 3H), 0.90 (d, *J* = 6.8 *Hz*, 3H), 0.88 (d, *J* = 6.7 *Hz*, 3H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 100 MHz) δ 129.7 (CH), 129.6 (CH), 81.9 (CH), 78.0 (CH), 46.4 (CH_2), 38.5 (CH_2), 37.9 (CH_2), 30.2 (CH_2), 24.4 (CH), 23.5 (CH_3), 21.7 (CH_3), 10.9 (CH_3). HRMS (EI^+): *m/z* $[M]^+$ Calcd for $C_{12}H_{22}O$: 182.1671; Found: 182.1682. IR ($CHCl_3$): 2959, 2928, 2855, 1717, 1467, 1368, 1219 cm^{-1}.

***trans*-Δ⁴-2-ethyl-7-isobutyloxepene** (**10a**). 14.0 mg (14% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.66 (m, 2H), 4.06 (m, 1H), 3.88 (m, 1H), 2.34 (m, 2H), 2.17 (m, 2H), 1.76 (m, 1H), 1.53 (m, 2H), 1.48-1.37 (m, 1H), 1.10 (ddd, *J* = 4.5, 8.6 & 13.5 *Hz*, 1H), 0.91 (t, *J* = 7.4 *Hz*, 3H), 0.90 (d, *J* = 2.8 *Hz*, 3H), 0.89 (d, *J* = 2.9 *Hz*, 3H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 100 MHz) δ 128.6 (CH), 128.5 (CH), 74.8 (CH), 71.5 (CH), 45.2 (CH_2), 35.7 (CH_2), 35.0 (CH_2), 29.1 (CH_2), 24.5 (CH_3), 23.4 (CH_3), 22.1 (CH_3), 10.4 (CH). HRMS (EI^+): *m/z* $[M]^+$ Calcd for $C_{12}H_{22}O$: 182.1671; Found: 182.1682. IR ($CHCl_3$): 2959, 2928, 2855, 1717, 1467, 1368, 1219 cm^{-1}.

(2*R*,3*R*,4*R*,6*S*)-4-chloro-6-ethyl-2-isobutyl-3-methyltetrahydro-2*H*-pyran (11a). Following the previous general procedure, 16 mg of the product was obtained (14% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 3.69 (ddd, *J* = 4.7, 10.6 & 11.8 *Hz*, 1H), 3.15 (m, 1H), 2.99 (td, *J* = 2.8 & 9.8 *Hz*, 1H), 2.17 (dd, *J* = 4.7 & 12.8 *Hz*, 1H), 1.90 (m, 1H), 1.65 (dd, *J* = 11.6 & 24.1 *Hz*, 1H), 1.54-1.31 (m, 5H), 1.02 (d, *J* = 6.4 *Hz*, 3H), 0.96-0.91 (m, 6H), 0.86 (d, *J* = 6.5 *Hz*, 3H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 100 MHz) δ 80.0 (CH), 78.0 (CH), 64.6 (CH), 45.4 (CH), 43.0 (CH_2), 42.5 (CH_2), 28.8 (CH_2), 24.3 (CH),

23.9 (CH_3), 21.2 (CH_3), 14.6 (CH_3), 10.1 (CH_3). HRMS (EI^+): *m/z* $[M+H]^+$ Calcd for $C_{12}H_{24}ClO$: 219.1486; Found: 219.1465.

***cis*-Δ⁴-2-(but-3-en-1-yl)-7-ethyloxepene (1b).** Following the general procedure above, 4-pentenal (1.48 mmol, 1.1 eq.), TMSCl (1.48 mmol, 1.1 eq.) and $Fe(acac)_3$ (0.13 mmol, 0.10 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **7a** (1.34 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 99.0 mg of the product (41% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.83 (m, 1H), 5.74 (m, 2H), 5.02 (ddd, *J* = 1.6, 3.3 & 17.2 *Hz*, 1H), 4.95 (da, *J* = 10.2 *Hz*, 1H), 3.33 (ddt, *J* = 1.7, 3.7 & 9.5 *Hz*, 1H), 3.20 (m, 1H), 2.21 (m, 6H), 1.66 (m, 1H), 1.56 (m, 1H), 1.46 (m, 2H), 0.98 (t, *J* = 7.4 *Hz*, 3H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 100 MHz) δ 138.8 (CH), 129.6 (CH), 129.4 (CH), 114.4 (CH_2), 81.8 (CH), 79.3 (CH), 38.1 (CH_2), 37.7 (CH_2), 36.4 (CH_2), 30.5 (CH_2), 30.1 (CH_2), 11.0 (CH_3). HRMS (EI^+): *m/z* $[M]^+$ Calcd for $C_{12}H_{20}O$: 180.1514; Found: 180.1520. IR ($CHCl_3$): 2960, 2926, 2856, 1717, 1468, 1219 cm^{-1}.

***trans*-Δ⁴-2-(but-3-en-1-yl)-7-ethyloxepene (10b).** 29.0 mg (12% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.83 (m, 1H), 5.68 (m, 2H), 5.04 (m, 1H), 4.97 (da, *J* = 10.1 *Hz*, 1H), 4.00 (m, 1H), 3.91 (m, 1H), 2.23 (m, 1H), 2.21 (m, 5H), 1.66 (m, 1H), 1.56 (m, 1H), 1.46 (m, 2H), 0.95 (t, *J* = 7.4 *Hz*, 3H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 100 MHz) δ 138.7 (CH), 128.5 (CH), 128.4 (CH), 114.4 (CH_2), 75.0 (CH), 72.8 (CH), 35.4 (CH_2), 35.2 (CH_2), 34.9 (CH_2), 30.2 (CH_2), 29.0 (CH_2), 10.4 (CH_3). HRMS (EI^+): *m/z* $[M]^+$ Calcd for $C_{12}H_{20}O$: 180.1514; Found: 180.1520. IR ($CHCl_3$): 2960, 2926, 2856, 1717, 1468, 1219 cm^{-1}.

(2*R*,3*R*,4*R*,6*S*)-2-(but-3-en-1-yl)-4-chloro-6-ethyl-3-methyltetrahydro-2*H*-pyran (11b). 44.0 mg (15% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.82 (ddt, *J* = 6.7, 10.5 & 16.9 *Hz*, 1H), 4.99 (m, 2H), 3.68 (ddd, *J* = 5.6, 10.7 & 11.6 *Hz*, 1H), 3.17 (m, 1H), 2.96 (td, *J* = 2.5 & 9.5 *Hz*, 1H), 2.28 (m, 1H), 2.19-2.07 (m, 2H), 1.79-1.71 (m, 1H), 1.69-1.60 (dd, *J* = 11.7 & 24.1 *Hz*, 1H), 1.60-1.42 (m, 4H), 1.04 (d, *J* = 6.7 *Hz*, 3H), 0.95 (t, *J* = 7.4 *Hz*, 3H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 100 MHz) δ 138.6 (CH), 114.7 (CH_2), 80.9 (CH), 77.8 (CH), 64.5 (CH), 44.9 (CH), 42.9 (CH_2), 32.6 (CH_2), 29.6 (CH_2), 28.8 (CH_2), 14.5 (CH_3), 10.1 (CH_3). HRMS (ESI^+): *m/z* $[M-H]^-$ Calcd for $C_{12}H_{20}ClO$: 215.1203; Found: 215.1206.

***cis*-Δ⁴-2-decyl-7-isobutyloxepene (1c).** Following the general procedure above, isovaleraldehyde (0.99 mmol, 2.0 eq.) and $FeBr_3$ (0.025 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12a** (0.495 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 114.0 mg of the product (78% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz)

δ 5.74 (m, 2H), 3.38 (ddt, *J* = 1.6, 3.6 & 9.8 *Hz*, 1H), 3.28 (m, 1H), 2.18 (m, 4H), 1.86 (m, 1H), 1.53 (m, 3H), 1.26 (bs, 16H), 1.09 (m, 1H), 0.90 (d, *J* = 6.7 *Hz*, 3H), 0.88 (t, *J* = 6.7 *Hz*, 3H), 0.87 (d, *J* = 6.6 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 129.7 (CH), 129.6 (CH), 80.2 (CH), 78.0 (CH), 46.4 (CH_2), 38.5 (CH_2), 38.2 (CH_2), 37.2 (CH_2), 31.9 (CH_2), 29.63 (3 x CH_2), 29.6 (CH_2), 29.3 (CH_2), 26.2 (CH_2), 24.4 (CH), 23.6 (CH_3), 22.7 (CH_2), 21.7 (CH_3), 14.1 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{20}H_{38}ONa$: 317.2820; Found: 317.2818. IR ($CHCl_3$): 2957, 2928, 2856, 1717, 1467, 1368, 1219 cm^{-1}.

***trans*-Δ⁴-2-decyl-7-isobutyloxepene (10c).** 25.0 mg (17% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.65 (m, 2H), 4.05 (m, 1H), 3.95 (m, 1H), 2.33 (m, 2H), 2.17 (m, 2H), 1.75 (m, 1H), 1.52 (ddd, *J* = 5.3, 8.7 & 13.7 *Hz*, 2H), 1.44-1.34 (m, 2H), 1.34-1.19 (m, 18H), 1.10 (ddd, *J* = 4.5, 8.6 & 13.7 *Hz*, 1H), 0.91 (d, *J* = 1.5 *Hz*, 3H), 0.89 (d, *J* = 1.7 *Hz*, 3H), 0.88 (t, *J* = 7.0 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 128.6 (CH), 128.5 (CH), 73.4 (CH), 71.5 (CH), 45.3 (CH_2), 36.2 (CH_2), 35.8 (CH_2), 35.5 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (3 x CH_2), 29.3 (CH_2), 25.9 (CH_2), 24.5 (CH), 23.4 (CH_3), 22.7 (CH_2), 22.2 (CH_3), 14.1 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{20}H_{38}ONa$: 317.2820; Found: 317.2818. IR ($CHCl_3$): 2957, 2928, 2856, 1717, 1467, 1368, 1219 cm^{-1}.

(2*R*,3*R*,4*R*,6*S*)-4-chloro-6-decyl-2-isobutyl-3-methyltetrahydro-2*H*-pyran (11c). 16.4 mg (15% yield). (Table 1, entry 10). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 3.68 (ddd, *J* = 4.7, 10.6 & 15.3 *Hz*, 1H), 3.23 (m, 1H), 2.98 (td, *J* = 2.8 & 9.8 *Hz*, 1H), 2.15 (ddd, *J* = 1.7, 4.7 & 12.8 *Hz*, 1H), 1.89 (m, 1H), 1.66 (dd, *J* = 11.6 & 24.2 *Hz*, 1H), 1.55-1.24 (m, 21H), 1.02 (d, *J* = 6.5 *Hz*, 3H), 0.91 (d, *J* = 6.6 *Hz*, 3H), 0.86 (t, *J* = 6.6 *Hz*, 6H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 80.0 (CH), 76.5 (CH), 64.6 (CH), 45.4 (CH), 43.4 (CH_2), 42.5 (CH_2), 35.8 (CH_2), 31.9 (CH_2), 29.6 (3xCH_2), 29.4 (CH_2), 29.3 (CH_2), 25.6 (CH_2), 24.3 (CH), 23.9 (CH_3), 22.7 (CH_2), 21.2 (CH_3), 14.6 (CH_3), 14.1 (CH_3). HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{20}H_{39}ClO$: 330.2689; Found: 330.2686.

***cis*-Δ⁴-2-decyl-7-(3-butenyl)-oxepene (1d).** Following the general procedure above, 4-pentenal (0.99 mmol, 2.0 eq.) and $FeBr_3$ (0.025 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12a** (0.495 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 94.5 mg of the product (65% yield). Pale yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.82 (m, 1H), 5.73 (m, 2H), 5.02 (ddd, *J* = 1.6, 3.3 & 17.2 *Hz*, 1H), 4.95 (d, *J* = 10.2 *Hz*, 1H), 3.30 (m, 2H), 2.19 (m, 6H), 1.66 (m, 1H), 1.46 (m, 5H), 1.26 (bs, 14H), 0.88 (t, *J* = 6.7 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 138.8 (CH), 129.6 (CH), 129.4 (CH), 114.4

(CH_2), 80.1 (CH), 79.3 (CH), 38.2 (CH_2), 38.1 (CH_2), 37.2 (CH_2), 36.4 (CH_2), 31.9 (CH_2), 30.5 (CH_2), 29.63 (3 x CH_2), 29.6 (CH_2), 29.3 (CH_2), 26.4 (CH_2), 22.7 (CH_2), 14.1 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{20}H_{36}ONa$: 315.2664; Found: 315.2666. IR ($CHCl_3$): 3020, 2928, 2856, 1717, 1640, 1458, 1220 cm^{-1}.

***trans*-Δ⁴-2-decyl-7-(3-butenyl)-oxepene (10d).** 18.2 mg (13% yield). Pale yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.83 (m, 1H), 5.65 (m, 2H), 5.02 (ddd, *J* = 1.7, 3.5 & 17.1 *Hz*, 1H), 4.95 (bd, *J* = 10.1 *Hz*, 1H), 3.97 (m, 2H), 2.42-2.26 (m, 2H), 2.25-2.02 (m, 4H), 1.42-1.35 (m, 2H), 1.35-1.20 (bs, 18H), 0.88 (t, *J* = 6.8 *Hz*, 3H). $^{13}C\{^1H\}$-NMR ($CDCl_3$, 100 MHz) δ 138.7 (CH), 128.6 (CH), 128.4 (CH), 114.4 (CH_2), 73.6 (CH), 72.8 (CH), 36.1 (CH_2), 35.4 (CH_2), 35.3 (CH_2), 35.2 (CH_2), 31.9 (CH_2), 30.2 (CH_2), 29.7 (CH_2), 29.6 (3 x CH_2), 29.3 (CH_2), 26.0 (CH_2), 22.7 (CH_2), 14.1 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{20}H_{36}ONa$: 315.2664; Found: 315.2666. IR ($CHCl_3$): 3020, 2928, 2856, 1717, 1640, 1458, 1220 cm^{-1}.

(2*R*,3*R*,4*R*,6*S*)-2-(but-3-en-1-yl)-4-chloro-6-decyl-3-methyltetrahydro-2*H*-pyran (11d). 9.3 mg (8% yield). (Table 1, entry 11). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.87-5.75 (m, 1H), 5.06-4.98 (dd, *J* = 1.5 & 17.1 *Hz*, 1H), 4.98-4.93 (dd, *J* = 0.8 & 10.2 *Hz*, 1H), (td, *J* = 4.7 & 11.6 *Hz*, 1H), 3.24 (m, 1H), 2.95 (td, *J* = 2.4 & 9.6 *Hz*, 1H), 2.33-2.22 m, 1H), 2.18-2.03 (m, 2H), 1.79-1.71 (m, 1H), 1.71-1.59 (dd, *J* = 12.0 & 24.3 *Hz*, 1H), 1.54-1.46 (m, 2H), 1.46-1.21 (m, 18H), 1.03 (d, *J* = 6.5 *Hz*, 3H), 0.88 (t, *J* = 6.4 *Hz*, 3H). $^{13}C\{^1H\}$-NMR ($CDCl_3$, 125MHz) δ 138.6 (CH), 114.7 (CH_2), 80.9 (CH), 76.4 (CH), 64.5 (CH), 44.9 (CH), 43.2 (CH_2), 35.8 (CH_2), 32.6 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (3xCH_2), 29.5 (CH_2), 29.3 (CH_2), 25.6 (CH_2), 22.7 (CH_2), 14.5 (CH_3), 14.1 (CH_3). HRMS (EI): *m/z* $[M]^+$ Calcd for $C_{20}H_{37}ClO$:328.2533; Found: 328.2545.

***cis*-Δ⁴-2-decyl-7-vinyloxepene (1e).** Following the general procedure above, acrolein (0.99 mmol, 2.0 eq.) and $FeBr_3$ (0.025 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12a** (0.495 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 74.4 mg of the product (57% yield). Pale yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.88 (ddd, *J* = 4.8, 10.6 & 17.3 *Hz*, 1H), 5.76 (d, *J* = 3.5 *Hz*, 1H), 5.26 (td, *J* = 1.7 & 17.2 *Hz*, 1H), 5.06 (td, *J* = 1.8 & 10.6 *Hz*, 1H), 3.87 (m, 1H), 3.37 (m, 1H), 2.38-2.14 (m, 4H), 1.51-1.17 (m, 18H), 0.88 (t, *J* = 6.6 *Hz*, 3H). $^{13}C\{^1H\}$-NMR ($CDCl_3$, 100 MHz) δ 139.9 (CH), 129.9 (CH), 128.9 (CH), 113.8 (CH_2), 80.2 (CH), 80.1 (CH), 38.0 (CH_2), 37.5 (CH_2), 37.0 (CH_2), 31.9 (CH_2), 29.6 (3 x CH_2), 29.5 (CH_2), 29.3 (CH_2), 26.2 (CH_2), 22.7 (CH_2), 14.1 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{18}H_{32}ONa$: 287.2351; Found: 287.2359. IR ($CHCl_3$): 3020, 2928, 2856, 1718, 1466, 1458, 1218 cm^{-1}.

***trans*-Δ^4-2-decyl-7-vinyloxepene (10e).** 18.6 mg (14% yield). Pale yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.89 (ddd, *J* = 5.7, 10.5 & 17.2 *Hz*, 1H), 5.68 (m, 2H), 5.23 (td, *J* = 1.7 & 17.2 *Hz*, 1H), 5.08 (td, *J* = 1.7 & 10.5 *Hz*, 1H), 4.50 (m, 1H), 4.03 (m, 1H), 2.50 (m, 1H), 2.36 (m, 1H), 2.23 (m, 2H), 1.35-1.19 (m, 18H), 0.88 (t, *J* = 6.6 *Hz*, 3H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 100 MHz) δ 139.9 (CH), 129.2 (CH), 127.9 (CH), 114.5 (CH_2), 75.1 (CH), 73.9 (CH), 36.2 (CH_2), 35.7 (CH_2), 34.7 (CH_2), 31.9 (CH_2), 29.6 (4 x CH_2), 29.3 (CH_2), 26.0 (CH_2), 22.7 (CH_2), 14.1 (CH_3). HRMS (ESI$^+$): *m/z* [M+Na]$^+$ Calcd for $C_{18}H_{32}ONa$: 287.2351; Found: 287.2359. IR ($CHCl_3$): 3020, 2928, 2856, 1718, 1466, 1458, 1218 cm^{-1}.

***cis*-Δ^4-2-decyl-7-cyclohexyloxepene (1f).** Following the general procedure above, cyclohexylcarboxaldehyde (0.99 mmol, 2.0 eq.) and $FeBr_3$ (0.025 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12a** (0.495 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 110.0 mg of the product (69% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.73 (m, 2H), 3.26 (m, 1H), 3.04 (brdd, *J* = 6.4 & 11.8 *Hz*, 1H), 2.28-2.10 (m, 4H), 1.97 (bd, *J* = 12.8 *Hz*, 1H), 1.77-1.69 (m, 2H), 1.69-1.60 (m, 2H), 1.60-1.41 (m, 2H), 1.39-1.02 (m, 22H), 0.88 (t, *J* = 6.8 *Hz*, 3H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 100 MHz) δ 129.7 (CH), 129.2 (CH), 84.6 (CH), 80.3 (CH), 44.0 (CH), 38.0 (CH_2), 37.2 (CH_2), 35.0 (CH_2), 31.9 (CH_2), 30.1 (CH_2), 29.63 (2 x CH_2), 29.60 (CH_2), 29.56 (CH_2), 29.3 (CH_2), 28.9 (CH_2), 26.6 (CH_2), 26.4 (CH_2), 26.3 (2 x CH_2), 22.7 (CH_2), 14.1 (CH_3). HRMS (ESI$^+$): *m/z* [M+Na]$^+$ Calcd for $C_{22}H_{40}ONa$: 343.2977; Found: 343.2981. IR ($CHCl_3$): 3019, 2929, 2856, 1716, 1451, 1218 cm^{-1}.

***trans*-Δ^4-2-decyl-7-cyclohexyloxepene (10f).** 19 mg (12% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.66 (m, 2H), 3.95 (m, 1H), 3.70 (m, 1H), 2.35 (m, 2H), 2.16 (m, 2H), 1.87 (d, *J* = 12.6 *Hz*, 1H), 1.74 (m, 2H), 1.65 (m, 2H), 1.43-1.16 (m, 22H), 1.06-0.95 (m, 2H), 0.88 (t, *J* = 6.7 *Hz*, 3H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 150 MHz) δ 128.8 (CH), 128.5 (CH), 77.9 (CH), 73.8 (CH), 42.8 (CH), 36.3 (CH_2), 35.2 (CH_2), 32.2 (CH_2), 31.9 (CH_2), 29.7 (CH_2), 29.6 (3xCH_2), 29.3 (CH_2), 29.1 (CH_2), 29.0 (CH_2), 26.7 (CH_2), 26.4 (CH_2), 26.3 (CH_2), 26.0 (CH_2), 22.7 (CH_2), 14.1 (CH_3). HRMS (ESI$^+$): *m/z* [M+Na]$^+$ Calcd for $C_{22}H_{40}ONa$: 343.2977; Found: 343.2981. IR ($CHCl_3$): 3019, 2929, 2856, 1716, 1451, 1218 cm^{-1}.

***cis*-Δ^4-2-decyl-7-phenyloxepene (1g).** Following the general procedure above, benzaldehyde (0.99 mmol, 2.0 eq.) and $FeBr_3$ (0.025 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12a** (0.495 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 64.5 mg of the product (41% yield). Pale yellow oil. ^{1}H-NMR ($CDCl_3$, 400

MHz) δ 7.38 (d, *J* = 7.2 *Hz*, 2H), 7.33 (t, *J* = 7.5 *Hz*, 2H), 7.24 (t, *J* = 7.3 *Hz*, 1H), 5.83 (t, *J* = 3.6 *Hz*, 2H), 4.45 (dd, *J* = 1.8 & 10.0 *Hz*, 1H), 3.51 (m, 1H), 2.62-2.42 (m, 2H), 2.42-2.20 (m, 2H), 1.61 (m, 1H), 1.50-1.39 (m, 2H), 1.35-1.21 (m, 15H), 0.88 (t, *J* = 6.7 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 144.1 (C), 130.1 (CH), 129.2 (CH), 128.1 (2 x CH), 126.8 (CH), 125.7 (2 x CH), 81.7 (CH), 80.6 (CH), 39.8 (CH_2), 37.9 (CH_2), 37.1 (CH_2), 31.9 (CH_2), 29.6 (4 x CH_2), 29.3 (CH_2), 26.2 (CH_2), 22.7 (CH_2), 14.1 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{22}H_{34}ONa$: 337.2507; Found: 337.2509. IR ($CHCl_3$): 3019, 2928, 2856, 1716, 1452, 1428, 1277, 1218, 1116 cm^{-1}.

***trans*-Δ^4-2-decyl-7-phenyloxepene (10g).** 20.2 mg (13% yield). Pale yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.38 (d, *J* = 7.9 *Hz*, 2H), 7.33 (t, *J* = 7.4 *Hz*, 2H), 7.24 (t, *J* = 7.0 *Hz*, 1H), 5.77 (m, 2H), 5.13 (dd, *J* = 1.6 & 10.2 *Hz*, 1H), 4.20 (m, 1H), 2.79 (m, 1H), 2.50 (m, 1H) 2.42-2.21 (m, 2H), 1.66 (ddd, *J* = 8.9, 8.9 & 16.9 *Hz*, 1H), 1.50-1.38 (m, 2H), 1.37-1.20 (m, 15H), 0.89 (t, *J* = 6.7 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 144.2 (C), 129.3 (CH), 128.8 (CH), 128.2 (2 x CH), 127.0 (CH), 126.2 (2 x CH), 76.5 (CH), 75.0 (CH), 37.2 (CH_2), 36.1 (CH_2), 35.2 (CH_2), 31.9 (CH_2), 29.6 (4 x CH_2), 29.3 (CH_2), 26.1 (CH_2), 22.7 (CH_2), 14.1 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{22}H_{34}ONa$: 337.2507; Found: 337.2509. IR ($CHCl_3$): 3019, 2928, 2856, 1716, 1452, 1428, 1277, 1218, 1116 cm^{-1}.

***cis*-Δ^4-2-decyl-7-*p*-methoxyphenyloxepene (1h).** Following the general procedure above, *p*-methoxybenzaldehyde (0.99 mmol, 2.0 eq.) and $FeBr_3$ (0.025 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12a** (0.495 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 64.7 mg of the product (38% yield). Pale yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.30 (d, *J* = 8.6 *Hz*, 2H), 6.86 (d, *J* = 8.6 *Hz*, 2H), 5.83 (m, 2H), 4.40 (dd, *J* = 1.8 & 10.2 *Hz*, 1H), 3.80 (s, 3H), 3.49 (m, 1H), 2.62-2.20 (m, 4H), 1.60 (dd, *J* = 8.6 & 17.7 *Hz*, 1H), 1.49-1.38 (m, 2H), 1.38-1.18 (m, 15H), 0.88 (t, *J* = 6.8 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 159.0 (C), 135.2 (C), 130.1 (CH), 129.2 (CH), 126.9 (2 x CH), 113.5 (2 x CH), 81.4 (CH), 80.5 (CH), 55.2 (CH_3), 39.6 (CH_2), 37.9 (CH_2), 37.1 (CH_2), 31.9 (CH_2), 29.62 (CH_2), 29.61 (CH_2), 29.58 (2 x CH_2), 29.3 (CH_2), 26.2 (CH_2), 22.7 (CH_2), 14.4 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{23}H_{36}O_2Na$: 367.2613; Found: 367.2616. IR ($CHCl_3$): 3019, 2928, 2856, 1613, 1514, 1466, 1427, 1248, 1217 cm^{-1}.

***trans*-Δ^4-2-decyl-7-*p*-methoxyphenyloxepene (10h).** 6.5 mg (4% yield). Pale yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.29 (d, *J* = 8.5 *Hz*, 2H), 6.86 (d, *J* = 8.8 *Hz*, 2H), 5.76 (m, 2H), 5.07 (dd, *J* = 1.9 & 10.2 *Hz*, 1H), 4.14 (m, 1H), 3.80 (s, 3H), 2.77 (m, 1H), 2.54-

2.40 (m, 1H), 2.40-2.18 (m, 2H) 1.68-1.60 (m, 1H), 1.45-1.40 (m, 2H), 1.33-1.19 (m, 15H), 0.88 (t, *J* = 6.8 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 158.7 (C), 136.4 (C), 129.3 (CH), 128.8 (CH), 127.4 (2 x CH), 113.6 (2 x CH), 76.1 (CH), 74.7 (CH), 55.2 (CH_3), 37.0 (CH_2), 36.2 (CH_2), 35.3 (CH_2), 31.9 (CH_2), 29.6 (2 x CH_2), 29.34 (CH_2), 29.31 (CH_2), 26.2 (CH_2), 26.1 (CH_2), 22.7(CH_2), 14.1 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{23}H_{36}O_2Na$: 367.2613; Found: 367.2616. IR ($CHCl_3$): 3019, 2928, 2856, 1613, 1514, 1466, 1427, 1248, 1217 cm^{-1}.

***cis*-Δ⁴-2-decyl-7-*p*-nitrophenyloxepene (1i).** Following the general procedure above, *p*-nitrobenzaldehyde (0.99 mmol, 2.0 eq.) and $FeBr_3$ (0.025 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12a** (0.495 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 68.8 mg of the product (39% yield). Pale yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.18 (d, *J* = 9.0 *Hz*, 2H), 7.54 (d, *J* = 8.6 *Hz*, 2H), 5.84 (m, 2H), 4.53 (dd, *J* = 3.5 & 8.9 *Hz*, 1H), 3.52 (m, 1H), 2.55-2.24 (m, 4H), 1.62 (m, 1H), 1.52-1.39 (m, 2H), 1.39-1.17 (m, 15H), 0.87 (t, *J* = 6.7 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 151.3 (C), 130.6 (CH), 128.5 (CH), 126.5 (2 x CH), 125.7 (C), 123.4 (2 x CH), 80.8 (CH), 80.7 (CH), 39.8 (CH_2), 37.8 (CH_2), 36.9 (CH_2), 31.9 (CH_2), 29.6 (2 x CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 26.1 (CH_2), 22.7 (CH_2), 14.1 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{22}H_{33}NO_3Na$: 382.2358; Found: 382.2349. IR ($CHCl_3$): 3020, 2928, 2856, 1606, 1522, 1466, 1458, 1349, 1219, 1107 cm^{-1}.

***cis*-Δ⁴-2-decyl-7-*p*-fluorophenyloxepene (1j).** Following the general procedure above, *p*-fluorobenzaldehyde (0.99 mmol, 2.0 eq.) and $FeBr_3$ (0.025 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12a** (0.495 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 104.0 mg of the product (63% yield). Pale yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.33 (dd, *J* = 5.5 & 8.6 *Hz*, 2H), 7.00 (t, *J* = 8.7 *Hz*, 2H), 5.82 (m, 2H), 4.42 (dd, *J* = 2.0 & 10.0 *Hz*, 1H), 3.50 (m, 1H), 2.58-2.21 (m, 4H), 1.60 (m, 1H), 1.50-1.37 (m, 2H), 1.36-1.18 (m, 15H), 0.88 (dd, *J* = 6.8 & 7.0 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 161.8 (d, *J* = 244.4 *Hz*, C), 139.9 (d, *J* = 3.0 *Hz*, C), 130.2 (CH), 129.0 (CH), 127.4 (CH), 127.3 (CH), 114.9 (CH), 114.7 (CH), 81.1 (CH), 80.6 (CH), 39.8 (CH_2), 37.9 (CH_2), 37.0 (CH_2), 31.9 (CH_2), 29.6 (2 x CH_2), 29.5 (2 x CH_2), 29.3 (CH_2), 26.2 (CH_2), 22.7 (CH_2), 14.1 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{22}H_{33}OFNa$: 355.2413; Found: 355.2418. IR ($CHCl_3$): 3019, 2928, 2856, 1716, 1605, 1509, 1278, 1217, 1155 cm^{-1}.

***trans*-Δ⁴-2-decyl-7-*p*-fluorophenyloxepene (10j).** 21.8 mg (13% yield). Pale yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.33 (dd, *J* = 5.5 & 8.5 *Hz*, 2H), 7.00 (t, *J* = 8.7 *Hz*, 2H),

5.75 (m, 2H), 5.09 (dd, *J* = 1.6 & 10.0 *Hz*, 1H), 4.17 (m, 1H), 2.75 (m, 1H), 2.48 (m, 1H), 2.36-2.21 (m, 2H), 1.67-1.58 (m, 1H), 1.46-1.37 (m, 2H), 1.36-1.22 (m, 15H), 0.88 (t, *J* = 6.8 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 150 MHz) δ 161.8 (d, *J* = 243.0 *Hz*, C), 139.9 (d, *J* = 3.1 *Hz*, C), 129.4 (CH), 128.6 (CH), 127.8 (CH), 127.7 (CH), 115.0 (CH), 114.9 (CH), 76.0 (CH), 75.1 (CH), 37.2 (CH_2), 36.1 (CH_2), 35.1 (CH_2), 31.9 (CH_2), 29.6 (4 x CH_2), 29.3 (CH_2), 26.1 (CH_2), 22.7 (CH_2), 14.1 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{22}H_{33}OFNa$: 355.2413; Found: 355.2418. IR ($CHCl_3$): 3019, 2928, 2856, 1716, 1605, 1509, 1278, 1217, 1155 cm^{-1}.

***cis*-Δ⁴-2-decyl-7-toluyloxepene (1k).** Following the general procedure above, *p*-methylbenzaldehyde (0.99 mmol, 2.0 eq.) and $FeBr_3$ (0.025 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12a** (0.495 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 98.3 mg of the product (60% yield). Pale yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.27 (d, *J* = 7.9 *Hz*, 2H), 7.13 (d, *J* = 7.9 *Hz*, 2H), 5.82 (bt, *J* = 3.8 *Hz*, 2H), 4.41 (dd, *J* = 1.8 & 10.3 *Hz*, 1H), 3.49 (m, 1H), 2.62-2.21 (m, 4H), 2.33 (s, 3H), 1.60 (m, 1H), 1.50-1.38 (m, 2H), 1.38-1.20 (m, 15H), 0.88 (t, *J* = 7.0 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 141.2 (C), 136.4 (C), 130.0 (CH), 129.3 (CH), 128.8 (2 x CH), 125.7 (2 x CH), 81.7 (CH), 80.6 (CH), 39.8 (CH_2), 38.0 (CH_2), 37.1 (CH_2), 31.9 (CH_2), 29.62 (2 x CH_2), 29.58 (CH_2), 29.57 (CH_2), 29.3 (CH_2), 26.2 (CH_2), 22.7 (CH_2), 21.1 (CH_3), 14.1 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{23}H_{36}ONa$: 351.2664; Found: 351.2665. IR ($CHCl_3$): 3019, 2928, 2856, 1715, 1612, 1278, 1214, 1106 cm^{-1}.

***trans*-Δ⁴-2-decyl-7-toluyloxepene (10k).** 19.2 mg (12% yield). Pale yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.26 (d, *J* = 7.8 *Hz*, 2H), 7.13 (d, *J* = 7.8 *Hz*, 2H), 5.75 (bt, *J* = 2.85 *Hz*, 2H), 5.09 (dd, *J* = 1.2 & 10.1 *Hz*, 1H), 4.16 (m, 1H), 2.78 (m, 1H), 2.48 (m, 1H), 2.38-2.22 (m, 2H), 2.33 (s, 3H), 1.64 (dd, *J* = 8.5 & 17.9 *Hz*, 1H), 1.45-1.38 (m, 2H), 1.34-1.23 (m, 15H), 0.88 (t, *J* = 7.1 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 141.2 (C), 136.6 (C), 129.8 (CH), 129.2 (CH), 128.8 (2 x CH), 127.7 (2 x CH), 76.3 (CH), 74.8 (CH), 37.1 (CH_2), 36.1 (CH_2), 35.2 (CH_2), 31.9 (CH_2), 29.6 (4 x CH_2), 29.3 (CH_2), 26.0 (CH_2), 22.7 (CH_2), 21.1 (CH_3), 14.1 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{23}H_{36}ONa$: 351.2664; Found: 351.2665. IR ($CHCl_3$): 3019, 2928, 2856, 1715, 1612, 1278, 1214, 1106 cm^{-1}.

***cis*-Δ⁴-2-decyl-7-methylphenyloxepene (1l).** Following the general procedure above, phenylacetaldehyde (0.99 mmol, 2.0 eq.) and $FeBr_3$ (0.025 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12a** (0.495 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 127.7 mg of the product (79% yield). ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 7.3-

7.29 (m, 2H), 7.27-7.21 (m, 3H), 5.76 (m, 2H), 3.62 (m, 1H), 3.26 (m, 1H), 2.90 (dd, *J* = 7.9 & 13.7 *Hz*, 1H), 2.76 (dd, *J* = 5.4 & 13.7 *Hz*, 1H), 2.37-2.31 (m, 1H), 2.31-2.25 (m, 2H), 2.17 (m, 1H), 1.48 (m, 1H), 1.38-1.21 (m, 11H), 1.21-1.16 (m, 5H), 1.09-1.02 (m, 1H), 0.93 (t, *J* = 7.1 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 150 MHz) δ 139.5 (C), 129.8 (CH), 129.4 (2 x CH), 129.1 (CH), 128.1 (2 x CH), 126.0 (CH), 81.3 (CH), 80.4 (CH), 43.6 (CH_2), 38.1 (CH_2), 37.5 (CH_2), 37.0 (CH_2), 31.9 (CH_2), 29.6 (2 x CH_2), 29.5 (2 x CH_2), 29.4 (CH_2), 25.8 (CH_2), 22.7 (CH_2), 14.1 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{23}H_{36}ONa$: 351.2664; Found: 351.2674. IR ($CHCl_3$): 3019, 2928, 2856, 1718, 1497, 1465, 1456, 1214, 1107 cm^{-1}.

***trans*-Δ^4-2-decyl-7-methylphenyloxepene (10l).** 12.4 mg (8% yield). ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.30-7.26 (m, 2H), 7.26-7.15 (m, 3H), 5.63 (m, 2H), 4.24 (m, 1H), 3.98 (m, 1H), 2.90 (dd, *J* = 6.2 & 13.4 *Hz*, 1H), 2.75 (dd, *J* = 6.8 & 13.4 *Hz*, 1H), 2.4-2.27 (m, 2H), 2.25-2.11 (m, 2H), 1.42 (m, 1H), 1.35-1.11 (m, 17H), 0.88 (t, *J* = 6.8 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 139.2 (C), 129.5 (2 x CH), 128.7 (CH), 128.4 (CH), 128.1 (2 x CH), 126.0 (CH), 74.7 (CH), 74.2 (CH), 42.8 (CH2), 36.0 (CH2), 35.2 (CH2), 34.6 (CH2), 31.9 (CH2), 29.6 (4 x CH2), 29.3 (CH2), 25.9 (CH2), 22.7 (CH2), 14.1 (CH3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{23}H_{36}ONa$: 351.2664; Found: 351.2674. IR ($CHCl_3$): 3019, 2928, 2856, 1718, 1497, 1465, 1456, 1214, 1107 cm^{-1}.

***cis*-Δ^4-2-isobutyl-7-(oct-7-en-1-yl)-oxepene (1m).** Following the general procedure above, isovaleraldehyde (0.93 mmol, 2.0 eq.) and $FeBr_3$ (0.023 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12b** (0.465 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 87.2 mg of the product (71% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.81 (m, 1H), 5.74 (m, 2H), 4.99 (m, 1H), 4.93 (m, 1H), 3.38 (ddt, *J* = 1.7, 3.7 & 9.8 *Hz*, 1H), 3.28 (m, 1H), 2.24 (m, 2H), 2.19-2.08 (m, 2H), 2.04 (m, 2H), 1.86 (m, 1H), 1.62-1.52 (m, 3H), 1.42-1.23 (m, 8H), 1.10 (ddd, *J* = 3.7, 9.6 & 13.7 *Hz*, 1H), 0.90 (d, *J* = 6.7 *Hz*, 3H), 0.88 (d, *J* = 6.7 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 139.2 (CH), 129.7 (CH), 129.6 (CH), 114.1 (CH_2), 80.1 (CH), 77.9 (CH), 46.4 (CH_2), 38.5 (CH_2), 38.2 (CH_2), 37.2 (CH_2), 33.8 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 26.1 (CH_2), 24.5 (CH), 23.5 (CH_3), 21.7 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{18}H_{32}ONa$: 287.2351; Found: 287.2349. IR ($CHCl_3$): 3077, 2930, 2857, 2361, 1718, 1639, 1467, 1367, 1261, 1091, 1014 cm^{-1}.

***trans*- Δ^4-2-isobutyl-7-(oct-7-en-1-yl)-oxepene (10m).** 20.5 mg (17% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 5.81 (m, 1H), 5.65 (m, 2H), 4.99 (m, 1H), 4.93 (m, 1H), 4.04 (m, 1H), 3.95 (m, 1H), 2.33 (m, 2H), 2.17 (m, 2H), 2.04 (m, 2H), 1.75 (m, 1H),

1.52 (m, 2H), 1.38 (m, 4H), 1.30 (m, 5H), 1.10 (ddd, *J* = 4.6, 8.6 & 13.6 *Hz*, 1H), 0.91 (d, *J* = 2.0 *Hz*, 3H), 0.89 (d, *J* = 2.2 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 125 MHz) δ 139.2 (CH), 128.6 (CH), 128.5 (CH), 114.1 (CH_2), 73.3 (CH), 71.5 (CH), 45.3 (CH_2), 36.2 (CH_2), 35.8 (CH_2), 35.4 (CH_2), 33.8 (CH_2), 29.5 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 25.9 (CH_2), 24.5 (CH), 23.4 (CH_3), 22.2 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{18}H_{32}ONa$: 287.2351; Found: 287.2349. IR ($CHCl_3$): 3077, 2930, 2857, 2361, 1718, 1639, 1467, 1367, 1261, 1091, 1014 cm^{-1}.

***cis*-Δ⁴-2-(but-3-en-1-yl)-7-(oct-7-en-1-yl)-oxepene (1n).** Following the general procedure above, 4-pentenal (0.93 mmol, 2.0 eq.) and $FeBr_3$ (0.023 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12b** (0.465 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 85.6 mg of the product (71% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 5.82 (m, 2H), 5.73 (m, 2H), 5.05-4.99 (m, 1H), 4.97 (m, 1H), 4.97-4.90 (m, 1H), 3.30 (m, 2H), 2.30-2.20 (m, 3H), 2.19-2.10 (m, 3H), 2.04 (m, 2H), 1.66 (m, 1H), 1.60-1.42 (m, 4H), 1.42-1.24 (m, 8H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 125 MHz) δ 139.2 (CH), 138.7 (CH), 129.6 (CH), 129.4 (CH), 114.4 (CH_2), 114.1 (CH_2), 80.1 (CH), 79.3 (CH), 38.1 (CH_2), 38.0 (CH_2), 37.2 (CH_2), 36.4 (CH_2), 33.8 (CH_2), 30.5 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 26.3 (CH_2). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{18}H_{30}ONa$: 285.2194; Found: 285.2194. IR ($CHCl_3$): 3000, 2931, 2858, 1718, 1639, 1456, 1436, 1228, 1105, 996, 915 cm^{-1}.

***trans*-Δ⁴-2-(but-3-en-1-yl)-7-(oct-7-en-1-yl)-oxepene (10n).** 18.8 mg (15% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 5.82 (m, 2H), 5.65 (m, 2H), 5.06-4.90 (m, 4H), 3.97 (m, 2H), 2.35 (m, 2H), 2.22-2.14 (m, 3H), 2.11 (m, 1H), 2.04 (m, 2H), 1.64 (m, 1H), 1.53 (m, 1H), 1.48-1.35 (m, 5H), 1.34-1.27 (m, 5H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 125 MHz) δ 139.2 (CH), 138.7 (CH), 128.6 (CH), 128.4 (CH), 114.4 (CH_2), 114.1 (CH_2), 73.6 (CH), 72.9 (CH), 36.2 (CH_2), 35.4 (CH_2), 35.3 (CH_2), 35.3 (CH_2), 33.8 (CH_2), 30.2 (CH_2), 29.5 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 25.9 (CH_2). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{18}H_{30}ONa$: 285.2194; Found: 285.2194. IR ($CHCl_3$): 3000, 2931, 2858, 1718, 1639, 1456, 1436, 1228, 1105, 996, 915 cm^{-1}.

***cis*-Δ⁴-2-(furan-3-yl)-7-(oct-7-en-1-yl)-oxepene (1o).** Following the general procedure above, 3-furancarboxaldehyde (1.16 mmol, 2.0 eq.) and $FeBr_3$ (0.029 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12b** (0.58 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 73.1 mg of the product (46% yield). Yellow oil.^{1}H-NMR ($CDCl_3$, 500 MHz) δ 7.37 (s, 2H), 6.38 (s, 1H), 5.86-5.75 (m, 3H), 4.99 (dd, *J* = 1.5 & 17.1 *Hz*, 1H), 4.93 (d, J = 10.1 Hz, 1H), 4.38 (dd, *J* = 1.7 & 10.2 *Hz*, 1H), 3.47 (m, 1H), 2.57 (m,

1H), 2.51 (m, 1H), 2.32 (m, 1H), 2.23 (dd, *J* = 6.2 & 16.5 *Hz*, 1H), 2.04 (ddd, *J* = 7.0, 7.0 & 14.1 *Hz*, 2H), 1.64-1.55 (m, 2H), 1.42-1.26 (m, 8H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 142.8 (CH), 139.2 (CH), 138.5 (CH), 130.3 (CH), 128.9 (CH), 128.5 (C), 114.1 (CH_2), 109.2 (CH), 80.6 (CH), 75.4 (CH), 38.1 (CH_2), 38.0 (CH_2), 37.0 (CH_2), 33.8 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 26.2 (CH_2). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{18}H_{26}O_2Na$: 297.1831; Found: 297.1838. IR ($CHCl_3$): 2929, 2857, 1772, 1734, 1717, 1649, 1540, 1507, 1457, 1227, 1108 cm^{-1}.

***trans*-Δ^4-2-(furan-3-yl)-7-(oct-7-en-1-yl)-oxepene (10o).** 15.6 mg (9% yield). Yellow oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.36 (m, 2H), 6.37 (brs, 1H), 5.80 (m, 1H), 5.74 (brs, 2H), 5.04 (brdd, *J* = 2.4 & 9.2 Hz, 1H), 4.99 (brdd, *J* = 1.8 & 17.3 *Hz*, 1H), 4.93 (brdd, *J* = 1.9 & 1.1 Hz, 1H), 3.98 (m, 1H), 2.71 (m, 1H), 2.49 (m, 1H), 2.40 (m, 1H), 2.23 (m, 1H), 2.03 (brddd, *J* = 6.8, 6.8 & 14.1 *Hz*, 2H), 1.58 (m, 1H), 1.37 (m, 4H), 1.27 (brs, 5H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 125 MHz) δ 142.8 (CH), 139.4 (CH), 139.2 (CH), 129.6 (CH), 128.0 (CH), 127.7 (C), 114.1 (CH_2), 109.6 (CH), 73.5 (CH), 69.4 (CH), 36.2 (CH_2), 35.8 (CH_2), 35.4 (CH_2), 33.7 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 25.9 (CH_2). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{18}H_{26}O_2Na$: 297.1831; Found: 297.1838. IR ($CHCl_3$): 2929, 2857, 1772, 1734, 1717, 1649, 1540, 1507, 1457, 1227, 1108 cm^{-1}.

***cis*-Δ^4-2-(3-propyl benzoate)-7-(oct-7-en-1-yl)-oxepene (1p).** Following the general procedure above, 4-benzoyloxybutanal (**9l**) (1.08 mmol, 2.0 eq.) and $FeBr_3$ (0.027 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12b** (0.54 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 142.2 mg of the product (70% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 8.04 (brdd, *J* = 1.2 & 8.2 *Hz*, 2H), 7.55 (t, *J* = 7.4 *Hz*, 1H), 7.43 (t, *J* = 7.7 *Hz*, 2H), 5.84-5.76 (m, 1H), 5.76-5.70 (m, 2H), 4.97 (brddd, *J* = 1.8, 3.6 & 17.0 *Hz*, 1H), 4.91 (m, 1H), 4.36 (m, 2H), 3.37 (m, 1H), 3.31 (m, 1H), 2.33-2.21 (m, 2H), 2.21-2.13 (m, 2H), 2.02 (m, 3H), 1.84 (m, 1H), 1.68 (m, 1H), 1.58 (m, 2H), 1.47 (m, 1H), 1.43-1.21 (m, 8H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 166.6 (C), 139.1 (CH), 132.8 (CH), 130.5 (C), 129.7 (CH), 129.5 (2xCH), 129.3 (CH), 128.3 (2xCH), 114.1 (CH_2), 80.2 (CH), 79.5 (CH), 65.0 (CH_2), 38.1 (CH_2), 38.0 (CH_2), 37.2 (CH_2), 33.7 (CH_2), 33.6 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 26.2 (CH_2), 25.6 (CH_2). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{24}H_{34}O_3Na$: 393.2406; Found: 393.2404. IR ($CHCl_3$): 3028, 2998, 2931, 2858, 1714, 1638, 1602, 1452, 1316, 1279, 1216, 1114, 1071 cm^{-1}.

***trans*-Δ^4-2-(3-propyl benzoate)-7-(oct-7-en-1-yl)-oxepene (10p).** 27.1 mg (13% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 8.04 (brdd, *J* = 1.3 & 8.2 *Hz*, 2H), 7.55 (m,

1H), 7.43 (t, *J* = 7.7 *Hz*, 2H), 5.79 (m, 1H), 5.67 (m, 2H), 4.98 (ddd, *J* = 1.7, 3.6 & 17.1 *Hz*, 1H), 4.92 (m, 1H), 4.34 (m, 2H), 4.04 (m, 1H), 3.98 (m, 1H), 2.38 (m, 2H), 2.21 (m, 1H), 2.17 (m, 1H), 2.02 (m, 2H), 1.98-1.88 (m, 1H), 1.81 (m, 1H), 1.67 (m, 1H), 1.61-1.48 (m, 2H), 1.45-1.33 (m, 4H), 1.32-1.24 (m, 5H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 150 MHz) δ 166.6 (C), 139.2 (CH), 132.8 (CH), 130.5 (C), 129.5 (2xCH), 128.7 (CH), 128.4 (CH), 128.3 (2xCH), 114.1 (CH_2), 73.9 (CH), 73.1 (CH), 65.1 (CH_2), 36.1 (CH_2), 35.4 (CH_2), 35.2 (CH_2), 33.8 (CH_2), 32.7 (CH_2), 29.5 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 25.9 (CH_2), 25.4 (CH_2). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{24}H_{34}O_3Na$: 393.2406; Found: 393.2404. IR ($CHCl_3$): 3028, 2998, 2931, 2858, 1714, 1638, 1602, 1452, 1316, 1279, 1216, 1114, 1071 cm^{-1}.

***cis*-Δ^4-2-benzyl-7-isobutyl-oxepene (1q).** Following the general procedure above, isovaleraldehyde (1.44 mmol, 2.0 eq.) and $FeBr_3$ (0.036 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12c** (0.72 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 133.8 mg of the product (77% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.30-7.24 (m, 2H), 7.23-7.17 (m, 3H), 5.73 (m, 2H), 3.59 (m, 1H), 3.30 (m, 1H), 2.86 (dd, *J* = 8.0 & 13.6 *Hz*, 1H), 2.73 (dd, *J* = 5.5 & 13.6 *Hz*, 1H), 2.37-2.20 (m, 3H), 2.09 (m, 1H), 1.44 (m, 2H), 1.00 (m, 1H), 0.77 (d, *J* = 6.6 *Hz*, 3H), 0.58 (d, *J* = 6.5 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 125 MHz) δ 139.5 (C), 129.8 (CH), 129.4 (2xCH), 129.2 (CH), 128.1 (2xCH), 125.9 (CH), 81.5 (CH), 78.3 (CH), 46.2 (CH_2), 43.6 (CH_2), 38.4 (CH_2), 37.6 (CH_2), 24.2 (CH), 23.4 (CH_3), 21.4 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{17}H_{24}ONa$: 267.1725; Found: 267.1723. IR ($CHCl_3$): 3029, 2997, 2958, 2927, 2870, 1718, 1654, 1604, 1497, 1655, 1367, 1131, 1099 cm^{-1}.

***trans*-Δ^4-2-benzyl-7-isobutyl-oxepene (10q).** 20 mg (11% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.26 (m, 2H), 7.18 (m, 3H), 5.68-5.62 (m, 1H), 5.62-5.56 (m, 1H), 4.22 (m, 1H), 4.07 (m, 1H), 2.85 (dd, *J* = 6.2 & 13.3 *Hz*, 1H), 2.71 (dd, *J* = 6.9 & 13.5 *Hz*, 1H), 2.32 (m, 2H), 2.24-2.16 (m, 1H), 2.15-2.09 (m, 1H), 1.64-1.57 (m, 1H), 1.42 (ddd, *J* = 5.2, 8.9 & 13.9 *Hz*, 1H), 1.00 (ddd, *J* = 4.3, 8.8 & 13.4 *Hz*, 1H), 0.83 (d, *J* = 6.5 *Hz*, 3H), 0.79 (d, *J* = 6.6 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 125 MHz) δ 139.1 (C), 129.5 (2xCH), 128.6 (CH), 128.5 (CH), 128.1 (2xCH), 126.0 (CH), 74.6 (CH), 72.2 (CH), 45.1 (CH_2), 42.9 (CH_2), 35.5 (CH_2), 34.5 (CH_2), 24.4 (CH), 23.4 (CH_3), 22.0 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{17}H_{24}ONa$: 267.1725; Found: 267.1723. IR ($CHCl_3$): 3029, 2997, 2958, 2927, 2870, 1718, 1654, 1604, 1497, 1655, 1367, 1131, 1099 cm^{-1}.

***cis*-Δ^4-2-benzyl-7-(but-3-en-1-yl)-oxepene (1r).** Following the general procedure above, 4-pentenal (1.4 mmol, 2.0 eq.) and $FeBr_3$ (0.035 mmol, 0.05 eq.) were added to a solution

of the *bis*-homoallylsilyl alcohol **12c** (0.7 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 129.6 mg of the product (77% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.31-7.25 (m, 2H), 7.24-7.17 (m, 3H), 5.77-5.69 (m, 2H), 5.69-5.60 (m, 1H), 4.86 (m, 1H), 4.80 (brddd, *J* = 1.6, 3.5 & 17.1 *Hz*, 1H), 3.57 (m, 1H), 3.24 (m, 1H), 2.87 (dd, *J* = 7.7 & 13.3 *Hz*, 1H), 2.73 (dd, *J* = 5.2 & 13.7 *Hz*, 1H), 2.36-2.20 (m, 3H), 2.12 (m, 1H), 1.95-1.85 (m, 1H), 1.85-1.74 (m, 1H), 1.61-1.50 (m, 1H), 1.37 (m, 1H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 100 MHz) δ 139.5 (C), 138.8 (CH), 129.6 (CH), 129.5 (2xCH), 129.1 (CH), 128.1 (2xCH), 126.0 (CH), 114.2 (CH_2), 81.2 (CH), 79.4 (CH), 43.6 (CH_2), 38.0 (CH_2), 37.5 (CH_2), 36.1 (CH_2), 29.9 (CH_2). HRMS (ESI$^+$): *m/z* $[M+Na]^+$ Calcd for $C_{17}H_{22}ONa$: 265.1568; Found: 265.1563. IR ($CHCl_3$): 3066, 3030, 2999, 2925, 2883, 1639, 1604, 1497, 1454, 1338, 1235, 1106, 1029, 996, 915 cm^{-1}.

***trans*-Δ^4-2-benzyl-7-(but-3-en-1-yl)-oxepene (10r).** 11.3 mg (7% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.31-7.25 (m, 2H), 7.24-7.17 (m, 3H), 5.75 (m, 1H), 5.70-5.57 (m, 2H), 5.00-4.88 (m, 2H), 4.24 (m, 1H), 4.01 (m, 1H), 2.87 (dd, *J* = 6.5 & 13.5 *Hz*, 1H), 2.72 (dd, *J* = 6.7 & 13.5 *Hz*, 1H), 2.35 (m, 2H), 2.19 (m, 2H), 2.00 (m, 2H), 1.55 (m, 1H), 1.37 (m, 1H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 125 MHz) δ 139.1 (C), 138.7 (CH), 129.5 (2xCH), 128.5 (CH), 128.5 (CH), 128.2 (2xCH), 126.1 (CH), 114.3 (CH_2), 74.7 (CH), 73.6 (CH), 42.8 (CH_2), 35.1 (2xCH_2), 34.6 (CH_2), 30.1 (CH_2). HRMS (ESI$^+$): *m/z* $[M+Na]^+$ Calcd for $C_{17}H_{22}ONa$: 265.1568; found: 265.1563. IR ($CHCl_3$): 3066, 3030, 2999, 2925, 2883, 1639, 1604, 1497, 1454, 1338, 1235, 1106, 1029, 996, 915 cm^{-1}.

***cis*-Δ^4-2-benzyl-7-(furan-3-yl)-oxepene (1s).** Following the general procedure above, 3-furancarboxaldehyde (2.56 mmol, 2.0 eq.) and $FeBr_3$ (0.064 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12c** (1.28 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 123.9 mg of the product (38% yield, 74% conversion). Amorphous white solid. mp 68-69 ºC. ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 7.33-7.27 (m, 3H), 7.26-7.21 (m, 3H), 7.19 (brs, 1H), 6.07 (brs, 1H), 5.81 (m, 2H), 4.32 (d, *J* = 10.4 *Hz*, 1H), 3.78 (m, 1H), 2.92 (dd, *J* = 8.2 & 13.8 *Hz*, 1H), 2.79 (dd, *J* = 5.2 & 13.8 *Hz*, 1H), 2.59 (m, 1H), 2.50 (m, 1H), 2.40 (m, 1H), 2.32 (m, 1H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 150 MHz) δ 142.7 (CH), 139.4 (C), 138.6 (CH), 129.9 (CH), 129.4 (2xCH), 129.1 (CH), 128.2 (2xCH), 128.1 (C), 126.1 (CH), 109.2 (CH), 81.6 (CH), 75.4 (CH), 43.4 (CH_2), 37.6 (CH_2), 37.5 (CH_2). HRMS (ESI$^+$): *m/z* $[M+Na]^+$ Calcd for $C_{17}H_{18}O_2Na$: 277.1204; Found: 277.1210. IR ($CHCl_3$): 3029, 3007, 2929, 2887, 1602, 1505, 1497, 1456, 1326, 1162, 1106, 1062 cm^{-1}.

***trans*-Δ^4-2-benzyl-7-(furan-3-yl)-oxepene (10s).** 13.4 mg (4% yield, 74% conversion). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.31-7.25 (m, 3H), 7.23-7.14 (m, 4H), 6.11 (brs, 1H), 5.73 (m, 2H), 5.07 (dd, *J* = 2.6 & 8.7 *Hz*, 1H), 4.24 (m, 1H), 2.91 (dd, *J* = 7.0 & 13.5 *Hz*, 1H), 2.77-2.70 (dd, *J* = 6.3 & 13.5 *Hz*, 1H), 2.70-2.64 (m, 1H), 2.56-2.39 (m, 2H), 2.27 (dd, *J* = 6.4 & 17.3 *Hz*, 1H), ^{13}C{^{1}H}-NMR ($CDCl_3$, 150 MHz) δ 142.7 (CH), 139.4 (CH), 139.0 (C), 129.5 (2xCH), 129.4 (CH), 128.2 (CH), 128.1 (2xCH), 127.3 (C), 126.1 (CH), 109.4 (CH), 74.7 (CH), 70.0 (CH), 42.8 (CH_2), 35.3 (CH_2), 35.0 (CH_2). HRMS (ESI$^+$): *m/z* [M+Na]$^+$ Calcd for $C_{17}H_{18}O_2Na$: 277.1204; Found: 277.1210. IR ($CHCl_3$): 3029, 3007, 2929, 2887, 1602, 1505, 1497, 1456, 1326, 1162, 1106, 1062 cm^{-1}.

***cis*-Δ^4-2-(3-propylbenzoate)-7-benzyl-oxepene (1t).** Following the general procedure above, 4-benzoyloxybutanal (**9l**) (1.3 mmol, 2.0 eq.) and $FeBr_3$ (0.033 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12c** (0.7 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 176.3 mg of the product (75% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 8.02 (brdd, *J* = 1.0 & 8.1 *Hz*, 2H), 7.57 (t, *J* = 7.4 *Hz*, 1H), 7.44 (t, *J* = 7.7 *Hz*, 2H), 7.26-7.23 (m, 2H), 7.23-7.19 (m, 2H), 7.13 (t, *J* = 7.1 *Hz*, 1H), 5.73 (m, 2H), 4.07 (m, 2H), 3.61 (m, 1H), 3.26 (m, 1H), 2.83 (dd, *J* = 8.5 & 13.7 *Hz*, 1H), 2.75 (dd, *J* = 5.0 & 13.8 *Hz*, 1H), 2.30 (m, 3H), 2.14 (m, 1H), 1.57-1.48 (m, 2H), 1.48-1.36 (m, 2H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 150 MHz) δ 166.6 (C), 139.5 (CH), 132.8 (CH), 130.5 (C), 129.5 (2xCH), 129.4 (2xCH), 129.2 (CH), 128.3 (2xCH), 128.1 (2xCH), 126.0 (CH), 81.5 (CH), 79.6 (CH), 64.8 (CH_2), 43.5 (CH_2), 38.1 (CH_2), 37.6 (CH_2), 33.2 (CH_2), 24.9 (CH_2). HRMS (ESI$^+$): *m/z* [M+Na]$^+$ Calcd for $C_{23}H_{26}O_3Na$: 373.1780; Found: 373.1783. IR ($CHCl_3$): 3028, 3011, 2925, 2883, 1714, 1603, 1496, 1453, 1316, 1279, 1114, 1070, 1027 cm^{-1}.

***trans*-Δ^4-2-(3-propylbenzoate)-7-benzyl-oxepene (10t).** 11.3 mg (5% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 600 MHz) δ 8.03 (brdd, *J* = 1.4 & 8.4 *Hz*, 2H), 7.56 (m, 1H), 7.44 (m, 2H), 7.29-7.23 (m, 2H), 7.23-7.14 (m, 3H), 5.65 (m, 2H), 4.31-4.24 (m, 1H), 4.24-4.14 (m, 2H), 4.05 (m, 1H), 2.86 (dd, *J* = 6.9 & 13.5 *Hz*, 1H), 2.72 (dd, *J* = 6.3 & 13.5 *Hz*, 1H), 2.46-2.30 (m, 2H), 2.29-2.12 (m, 2H), 1.77-1.59 (m, 2H), 1.55-1.40 (m, 2H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 150 MHz) δ 166.6 (C), 139.1 (CH), 132.8 (CH), 130.5 (C), 129.5 (2xCH), 129.5 (2xCH), 128.7 (CH), 128.3 (2xCH), 128.2 (C), 128.1 (2xCH), 126.1 (CH), 74.6 (CH), 73.9 (CH), 65.0 (CH_2), 42.7 (CH_2), 34.9 (CH_2), 34.8 (CH_2), 32.4 (CH_2), 25.2 (CH_2). HRMS (ESI$^+$): *m/z* [M+Na]$^+$ Calcd for $C_{23}H_{26}O_3Na$: 373.1780; Found: 373.1783.

IR ($CHCl_3$): 3028, 3011, 2925, 2883, 1714, 1603, 1496, 1453, 1316, 1279, 1114, 1070, 1027 cm^{-1}.

8-(oct-7-en-1-yl)-7-oxaspiro[5.6]dodec-10-ene (14). Following the general procedure above, cyclohexanone (1.1 mmol, 2.0 eq.) and $FeBr_3$ (0.027 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12b** (0.55 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 79.9 mg of the product (53% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 5.81 (m, 1H), 5.66 (m, 1H), 5.57 (m, 1H), 4.99 (ddd, *J* = 1.7, 3.7 & 17.2 *Hz*, 1H), 4.93 (m, 1H), 3.79 (m, 1H), 2.30 (dd, *J* = 6.2 & 15.3 *Hz*, 1H), 2.24-2.14 (m, 3H), 2.04 (m, 2H), 1.84 (brd, *J* = 13.6 *Hz*, 1H), 1.67 (m, 2H), 1.52-1.24 (m, 17H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 125 MHz) δ 139.2 (CH), 129.9 (CH), 125.9 (CH), 114.1 (CH_2), 75.7 (C), 68.7 (CH), 38.7 (2xCH_2), 37.8 (CH_2), 33.8 (CH_2), 33.5 (CH_2), 29.6 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 26.3 (2xCH_2), 26.1 (CH_2), 22.3 (CH_2), 22.1 (CH_2). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{19}H_{32}ONa$: 299.2351; Found: 299.2353. IR ($CHCl_3$): 2986, 2933, 2857, 1637, 1457, 1105, 997, 914.cm^{-1}.

8-benzyl-7-oxaspiro[5.6]dodec-10-ene (15). Following the general procedure above, cyclohexanone (1.38 mmol, 2.0 eq.) and $FeBr_3$ (0.034 mmol, 0.05 eq.) were added to a solution of the *bis*-homoallylsilyl alcohol **12c** (0.69 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 86.3 mg of the product (49% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.34-7.28 (m, 2H), 7.27-7.19 (m, 3H), 5.6 (m, 1H), 5.60 (m, 1H), 4.05 (quin, *J* = 6.4 *Hz*, 1H), 2.83 (dd, *J* = 7.1 & 13.4 *Hz*, 1H), 2.71 (dd, *J* = 5.9 & 13.4 *Hz*, 1H), 2.33-2.25 (m, 3H), 2.21 (dd, *J* = 6.8 & 15.6 *Hz*, 1H), 1.72 (m, 2H), 1.69-1.56 (m, 1H), 1.45-1.25 (m, 3H), 1.23-1.02 (m, 4H). ^{13}C{^{1}H}-NMR ($CDCl_3$, 100 MHz) δ 139.6 (C), 129.7 (2xCH), 129.6 (CH), 128.0 (2xCH), 126.2 (CH), 126.0 (CH), 75.9 (C), 70.4 (CH), 44.3 (CH_2), 39.2 (CH_2), 38.7 (CH_2), 37.9 (CH_2), 33.0 (CH_2), 26.0 (CH_2), 22.0 (CH_2), 21.4 (CH_2). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{18}H_{24}ONa$: 279.1725; Found: 279.1720. IR ($CHCl_3$): 2935, 2860, 1603, 1496, 1454, 1220, 1084, 980 cm^{-1}.

***tert*-butyl(((*S*)-1-((2*R*,7*R*)-7-isobutyl-2,3,6,7-tetrahydrooxepin-2-yl)but-3-en-1-yl)oxy)diphenylsilane (19).** Following the general procedure above, isovaleraldehyde (0.2 mmol, 2.0 eq.) and $FeBr_3$ (2 mg, 0.005 mmol, 0.05 eq.) were added to a solution of the alcohol **18** (0.1 mmol, 1.0 eq.) in dry DCM (0.08 M) to obtain 24.4 mg of the product (53% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.69 (ddd, *J* = 1.5, 7.9 & 14.4 *Hz*, 4H), 7.45-7.31 (m, 6H), 5.73 (m, 2H), 4.90 (m, 2H), 3.79 (dd, *J* = 4.8 & 11.0 *Hz*, 1H), 3.32 (m, 2H), 2.48-2.10 (m, 6H), 1.71 (hep, *J* = 6.7 *Hz*, 1H), 1.48 (ddd, *J* = 5.4, 8.6 & 13.8 *Hz*, 1H), 1.15-1.09 (m, 1H) 1.08 (s, 9H), 0.86 (d, *J* = 6.7 *Hz*, 3H), 0.84 (d, *J* = 6.6

Hz, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 136.3 (2 x CH), 136.1 (2 x CH), 134.7 (CH), 134.5 (C), 134.0 (C), 129.8 (CH), 129.5 (CH), 129.5 (CH), 129.4 (CH), 127.4 (2 x CH), 127.3 (2 x CH), 116.8 (CH_2), 81.4 (CH), 77.9 (CH), 76.0 (CH), 46.4 (CH_2), 38.1 (CH_2), 37.9 (CH_2), 32.4 (CH_2), 27.1 (3 x CH_3), 24.5 (CH), 23.3 (CH), 22.3 (CH), 19.6 (2xCH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{30}H_{42}O_2SiNa$: 485.2852; Found: 485.2849. $[\alpha]_D^{25}$ = +7.2 (*c* = 1.22, $CHCl_3$). IR ($CHCl_3$): 3019, 2959, 2932, 2860, 1472, 1428, 1218, 1112 cm^{-1}.

(((*S*)-1-((2*R*,7*R*)-7-(but-3-en-1-yl)-2,3,6,7-tetrahydrooxepin-2-yl)but-3-en-1-yl)oxy)(tert-butyl)diphenylsilane (20). Following the general procedure above, 4-pentenal (0.06 mL, 0.54 mmol, 2.0 eq.) and $FeBr_3$ (4 mg, 0.014 mmol, 0.05 eq.) were added to a solution of the alcohol **18** (0.27 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 87 mg of the product (70% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 7.73 (ddd, *J* = 1.5, 7.9 & 16.8 *Hz*, 4H), 7.48-7.31 (m, 6H), 5.86-5.63 (m, 4H), 4.98 (bdd, *J* = 17.1 & 27.0 *Hz*, 4H), 3.81 (dd, *J* = 4.7 & 11.1 *Hz*, 1H) 3.29 (m, 2H), 2.44-1.95 (m, 8H), 1.60 (m, 1H), 1.49 (m, 1H), 1.09 (s, 9H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 138.8 (CH), 136.3 (2 x CH), 136.1 (2 x CH), 134.8 (CH), 134.5 (C), 134.0 (C), 129.8 (CH), 129.5 (CH), 129.4 (CH), 129.2 (CH), 127.4 (2 x CH), 127.3 (2 x CH), 116.9 (CH_2), 114.3 (CH_2), 81.5 (CH), 79.2 (CH), 76.0 (CH), 38.2 (CH_2), 37.6 (CH_2), 36.3 (CH_2), 32.2 (CH_2), 30.4 (CH_2), 27.1 (3 x CH_3), 19.6 (C). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{30}H_{40}O_2SiNa$: 483.2695; Found: 483.2686. $[\alpha]_D^{25}$ = +4.9 (*c* = 1.38, $CHCl_3$). IR ($CHCl_3$): 3074, 3014, 2932, 2859, 1639, 1473, 1428, 1219, 1112 cm^{-1}.

(*R*)-1-((2*S*,7*R*)-7-((*S*)-1-((*tert*-butyldiphenylsilyl)oxy)but-3-en-1-yl)-2,3,6,7-tetrahydrooxepin-2-yl)propyl benzoate (25). Following the general procedure above, aldehyde **24** (0.18g, 0.94 mmol, 2.0 eq.) and $FeBr_3$ (7 mg, 0.025 mmol, 0.05 eq.) were added to a solution of the alcohol **18** (0.31g, 0.47 mmol, 1.0 eq.) in dry DCM (0.1 M) to obtain 107 mg of the product (40% yield). Colorless oil. ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 8.03 (d, *J* = 8.77 *Hz*, 2H), 7.76-7.68 (ddd, *J* = 1.5, 7.9 & 15.9 *Hz*, 4H), 7.55 (m, 2H), 7.46-7.34 (m, 9H), 5.82 (m, 2H), 5.68 (ddt, *J* = 7.0, 10.5 & 16.9 *Hz*, 1H), 5.02 (ddd, *J* = 4.0, 5.7 & 8.2 *Hz*, 1H), 4.85 (m, 2H), 3.83 (dt, *J* = 4.5 & 6.7 *Hz*, 1H), 3.51 (ddd, *J* = 2.9, 5.7 & 9.1 *Hz*, 1H), 3.36 (dt, *J* = 3.9 & 8.2 *Hz*, 1H), 2.40-2.26 (m, 4H), 2.23-2.14 (m, 1H), 1.76-1.66 (m, 1H), 1.07 (s, 9H), 0.90 (t, *J* = 7.4 *Hz*, 3H). $^{13}C\{^{1}H\}$-NMR ($CDCl_3$, 100 MHz) δ 166.1 (C), 136.2 (2 x CH), 136.1 (2 x CH), 134.6 (CH), 132.8 (CH), 129.8 (CH), 129.6 (2 x CH), 129.55 (CH), 129.5 (CH), 128.6 (CH), 128.3 (2 x CH), 127.4 (2 x CH), 127.38 (2 x CH), 116.9 (CH_2), 82.0 (CH), 80.4 (CH), 77.9 (CH), 76.1 (CH), 38.3 (CH_2),

33.1 (CH_2), 31.9 (CH_2), 27.1 (3 x CH_3), 23.4 (CH_2), 19.5 (C), 9.8 (CH_3). HRMS (ESI^+): *m/z* $[M+Na]^+$ Calcd for $C_{36}H_{44}O_4SiNa$: 591.2907; Found: 591.2906. $[\alpha]_D^{25}$ = +5.6 (*c* = 0.97, $CHCl_3$). IR ($CHCl_3$): 3018, 2962, 2933, 2893, 1714, 1452, 1428, 1277, 1212, 1112 cm^{-1}.

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Notes

The authors declare no competing financial interest

Supporting Information

^1H and ^{13}CNMR and Goesy spectra of all new compounds. Configuration analysis of diastereoisomers of **12a**. X-ray crystallographic analysis and data of **1s**.

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