Tandem Ene-Reaction/Intramolecular Sakurai Cyclisation (IMSC): A Novel Access to Polysubstituted Tetrahydropyrans and γ-Butyrolactones Using a Unique Allylation Strategy

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Abstract: The ene-reaction between a variety of aldehydes and allylsilane **22** generates highly functionalised homoallylic alcohols **23**. These adducts undergo a subsequent Intramolecular Sakurai Cyclisation (IMSC), affording in good yields polysubstituted tetrahydropyran derivatives. Furthermore, oxidative desilylation of **23** provides an efficient, connective access to a range of γ-butyrolactones and α-methylene-γ-butyrolactones.

Key words: ene-reactions, tetrahydropyrans, allylations, γ-butyrolactones, α-methylene-γ-butyrolactones

Numerous biologically active natural products contain, embeded in their complex architectural framework, one or more polysubstituted tetrahydrofuran or tetrahydropyran subunit. The ubiquitous presence of these heterocycles, associated with the challenge offered by the total synthesis of some of these natural products, has provided considerable impetus for the development of efficient methodologies for the preparation of tetrahydrofuran and tetrahydropyran derivatives.[1]

During the course of the total synthesis of polycavernoside A (**1**),[2] a potent marine toxin isolated by Yasumoto et al.[2a] in 1992 from the red alga *Polycavernosa tsudai* (*Gracilaria edulis*), we had the opportunity to examine novel and concise approaches towards the northern γ-butyrolactone-derived subunit and the southern tetrasubstituted terahydropyran fragment of **1** (Figure 1).[3]

In this article, we wish to report our results on the successful implementation of a connective methodology that allows the efficient access to both families of heterocycles.

Sometime ago, we discovered that the addition of a catalytic amount of trimethylsilyl triflate to a mixture of allylsilane **2**, a carbonyl derivative **3** and a silyl ether **4** led to the smooth formation of homoallylic ethers **5** (Scheme 1).[4] This three component coupling, coined as the Silyl-Modified Sakurai (SMS) reaction, possesses wide synthetic scope and has been employed, as a key-step, in several synthetic ventures.[5] Its intramolecular variant, the Intramolecular Silyl-Modified Sakurai (ISMS) cyclisation, which combines an homoallylic silyl ether such as **6** with an aldehyde or a ketone, provides a ready access to a wide range of stereodefined, polysubstituted, *exo*-methylene tetrahydropyrans **7**[6] (Scheme 1).

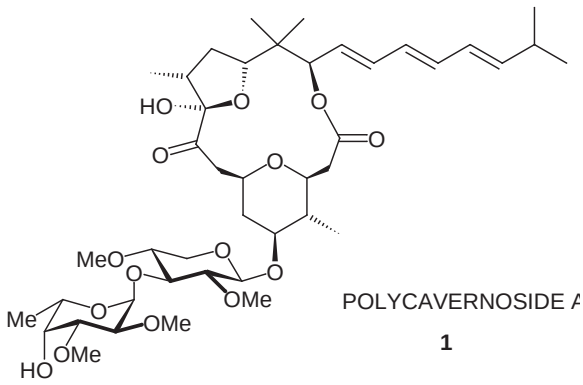

Figure 1 The structure of polycavernoside A (**1**).

During the course of these studies, we envisioned that the ISMS condensation of allyl silyl ether **8** and aldehydes **9** might afford an easy route to the homologous *exo*-methylene tetrahydrofuran skeleton **10**. However, and in stark contrast to our expectation, none of the desired furan derivatives **10** was obtained when a mixture of **8** and **9** was treated with a range of Lewis acids. Rather, diastereomerically pure, trisubstituted *exo*-methylene tetrahydropyrans **11** were produced, albeit in modest yields (Scheme 2).[7] Interestingly, product **11** was not formed when the corresponding acetals were used instead of the aldehydes in this coupling reaction.

Closer examination of heterocycles **11** clearly reveals that two molecules of aldehyde **9** have been appended onto allylsilane **8** via a novel three component coupling process. It is interesting to note that all three substituents occupy the thermodynamically more stable equatorial position. The nature of the products formed in this cascade process depends strongly upon the Lewis acid catalyst (Scheme 3).

Thus, whilst $TiCl_4$ promotes the Sakurai addition[8] of allylsilane **8** to aldehyde **9**, generating after workup the diol **12**, Et_2AlCl catalyses the formation of the unique hydroxysilyl enol ether **13**. Allylsilane **13** was isolated as a single geometric isomer, possessing the (*E*)-double bond config-

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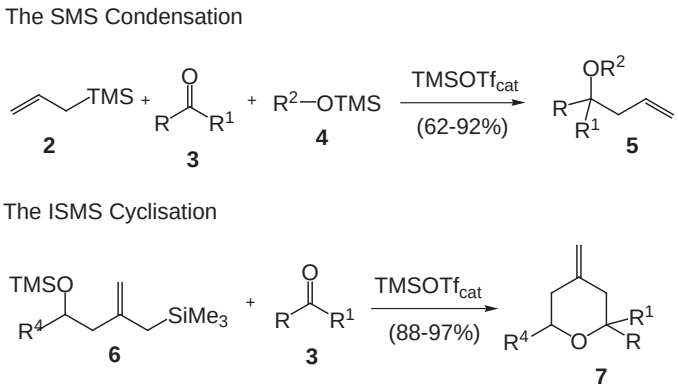
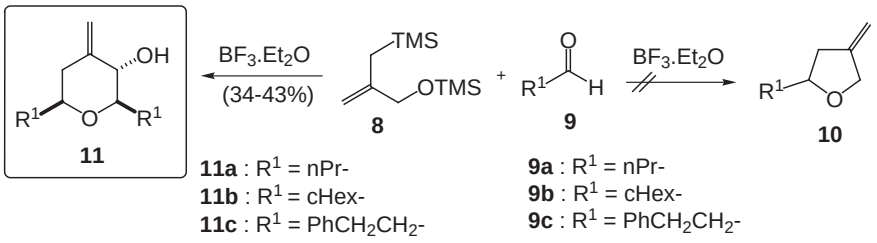
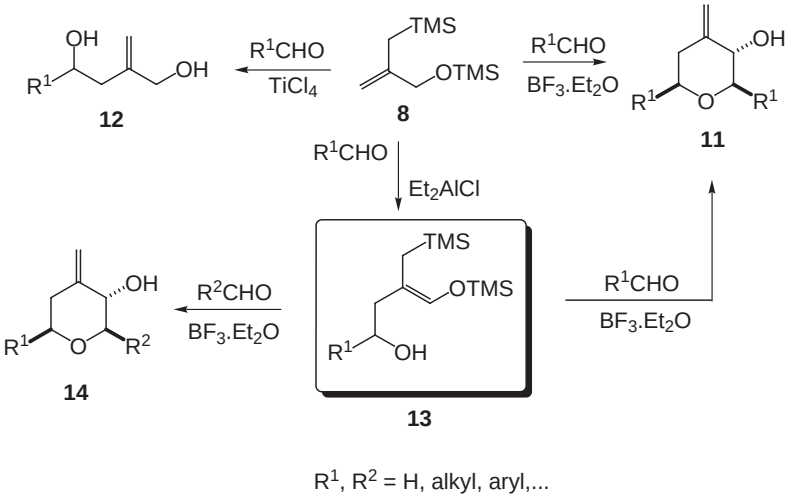


Scheme 1



Scheme 2



Scheme 3

uration. Subsequent addition of aldehyde **9** to **13**, in the presence of $BF_3{\cdot}OEt_2$, afforded the tetrahydropyran **11**, identical in all respect to the product obtained by the direct, three-component condensation protocol. This last result strongly suggests that the silyl enol ether **13** is an intermediate in the cascade transformation of **8** into **11**. The availability of functionalised homoallylic alcohol **13** offered a novel entry to the preparation of unsymmetrically substituted tetrahydropyrans **14**, by condensation of a second aldehyde with **13**.

Heterocycles **11** and **14** are useful synthetic intermediates that could be further elaborated into stereocontrolled polyoxygenated fragments (Scheme 4).

For example, ketone **15**, obtained by ozonolysis of **11**, was smoothly reduced to the corresponding *syn*-diol which afforded, after acetylation, the diastereomerically pure diacetate **16** in 82% yield. On the other hand, Luche reduction[9] of acetate **17** generated the stereocomplementary *anti*-diacetate **18** in 63% yield (Scheme 4). These readily available heterocycles can be viewed as structural analogues of the core subunits of interesting biologically active natural products such as pseudomonic acid and ambruticin.

Based upon these results, a simple retrosynthetic analysis of polysubstituted tetrahydropyrans **19** can be devised (Scheme 5).

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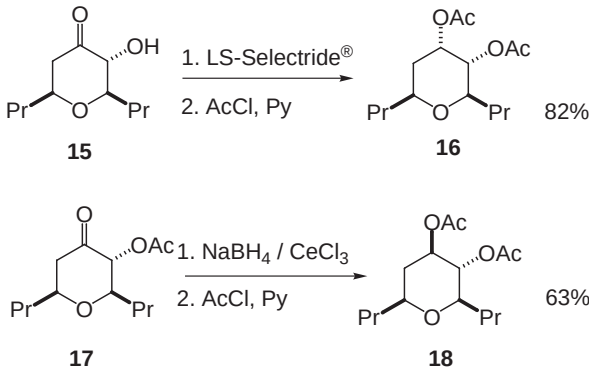


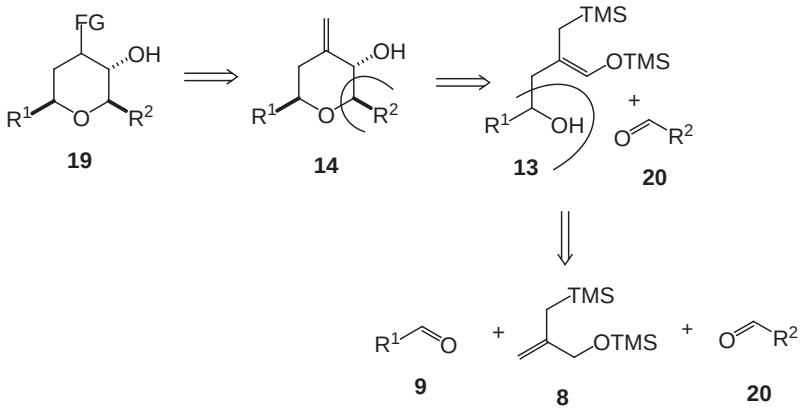
Scheme 4

Excision of carbon-C_2, bearing the R^2 substituent, opens the ring system of **14** and generates, besides the key-homoallylic alcohol **13**, the aldehyde **20**. Subsequent retroallyl cleavage of **13** produces aldehyde **9** and allylsilane **8**. In two straightforward operations, *exo*-methylene tetrahydropyrans **14** has been disconnected into three basic, commercially or readily available,[10] building blocks (Scheme 5). From the experiments described above, a mechanistic proposal, rationalising the formation of **11** and **14** can be advanced (Scheme 6).

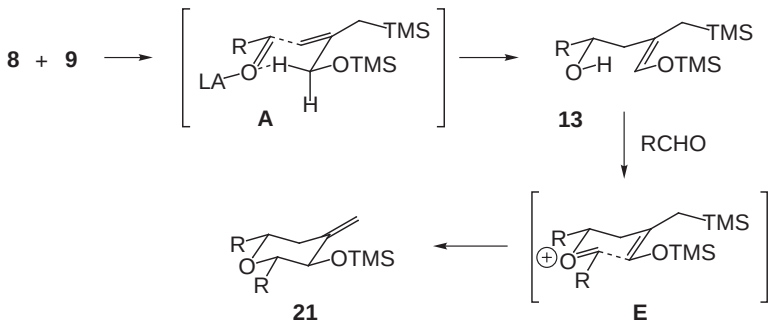
Upon activation of the aldehyde by a suitable Lewis acid, an initial ene reaction takes place via the six-membered transition state **A**, in which both the R substituent and the silyloxy group occupy pseudo equatorial positions.[11] The passage through a chair-like transition state, coupled with the equatorial disposition of the substituents, is responsible for the observed, highly stereocontrolled, configuration of the silyl enol ether double bond of **13**. Subsequent Lewis acid catalysed condensation of adduct **13** with a second equivalent of aldehyde, generates the oxocarbonium cation **E**, which undergoes intramolecular capture by the suitably positioned allylsilane residue, affording diastereomerically pure *exo*-methylene tetrahydropyran **21**[12] (Scheme 6).

The high regio- and stereo-selectivity observed in these ene-reactions can be nicely explained by considering, for all four possible transition states **A**–**D**, the stabilising β-silicon effect[13] and the repulsive 1,3-diaxial interactions, as shown in Figure 2.

Transition state **A**, leading to the observed ene-adduct **23**, contains no 1,3-diaxial interactions and benefits fully from the stabilising β-silicon effect. In contrast, transition state **B**, that would lead to the formation of the (*Z*)-double bond isomer **24**, suffers from severe 1,3-diaxial interactions between the silyloxy substituent and the C_2-hydrogen. The formation of the regioisomeric vinylsilanes **25** and **26** is also impeded by either the absence of a β-silicon effect (transition state **C**) or by a combination of destabilising 1,3-diaxial repulsions coupled with a weakening of the β-silicon effect due to a distorsion from the optimum angle of overlap between the interacting orbitals (transition state **D**).



Scheme 5



Scheme 6

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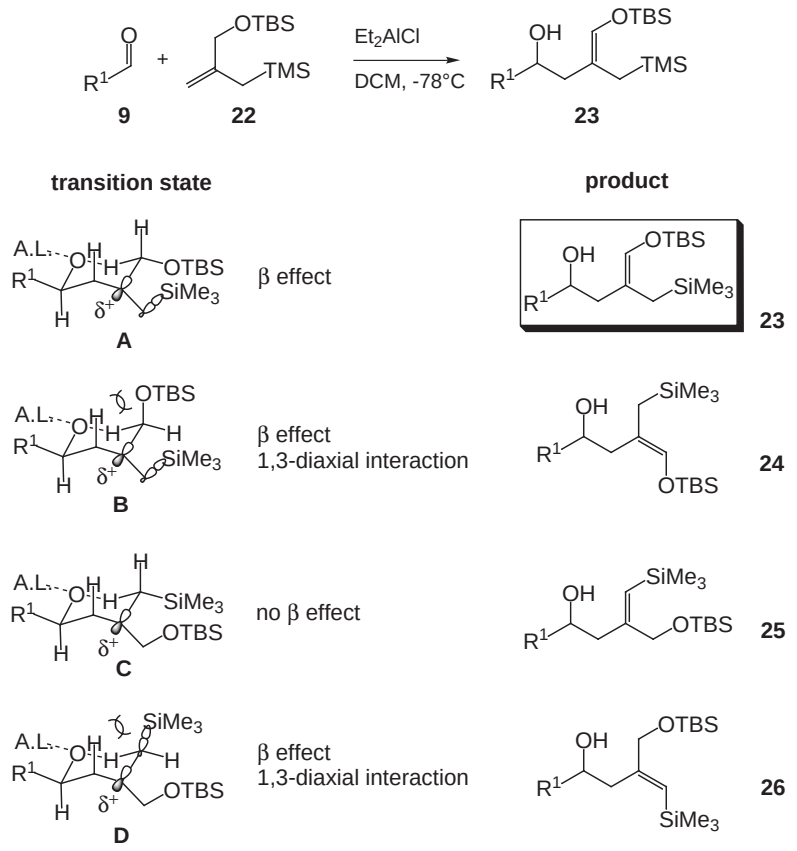

Figure 2 Transition states in the reaction of **9** with **22**.

As mentioned previously (vide supra), the yields of ene-adducts using the trimethylsilyloxy reagent **8** were rather moderate, probably owing to a competitive desilylation of enophile **8**. In order to improve the yield of homoallylic alcohols **13**, a more robust TBS protecting group was employed. Using reagent **22**, smooth allylation of aldehydes occurred, affording the desired silyl enol ethers **23** in good to excellent yields. Some selected examples are collected in Table 1.

As can be seen from Table 1, linear and branched aldehydes are good substrates for the ene-reaction (entries 2 and 3). The allylation process is also effective in the case of formaldehyde, though Yamamoto's bulky Lewis acid MAD[14] was required to promote the condensation. Interestingly, the ene-reaction tolerates a large number of functionalities, such as halides, (*Z*)-alkenes, alkynes and alkoxy groups (entries 4–7). In some cases, excellent diastereocontrol is exercised (entry 4) whilst in others the de can be rather modest (entry 7). Finally, it is worth mentioning that, using the Nakai–Mikami chiral titanium catalyst,[15] high levels of asymmetric induction can be achieved in this ene-reaction (entry 8). In all cases, only the (*E*)-silyl enol ether is formed.

With a variety of substituted homoallylic alcohols in hand, attention was then turned towards the Intramolecular Sakurai Cyclisation. Addition of an aldehyde or an acetal to allylsilanes **23**, in the presence of $BF_3{\cdot}OEt_2$, resulted in their smooth transformation into the desired *exo*-methylene tetrahydropyran derivatives **27**. Some representative examples are displayed in Table 2.

In general, good to excellent yields of heterocycles **27**, in which the robust TBS protecting group has been retained, were obtained. In all cases, the substituents around the ring system occupy equatorial positions, in accord with the previously suggested chair-like transition state **A** (vide supra). The reaction tolerates a wide range of functionalities, both in the aldehyde and the silyl enol ether fragments. For example, α,β-unsaturated esters (entry 1), TBS protected alcohols (entry 3) and cyclic acetals (entry 4) undergo efficient IMSC condensation with saturated or unsaturated aldehydes. It is noteworthy that allylic alcohol **23e**, a substrate which is prone to dehydration, readily adds to crotonaldehyde, affording the bis-unsaturated tetrahydropyran adduct **24e** in 85% yield (entry 5). In all these IMSC processes, ene-adduct **23** behaves as an allylsilane, undergoing addition of the activated allylic residue to the in situ generated oxocarbonium ion.

However, silyl enol ether **23** is also a masked aldehyde, originating from the addition of an aldehyde homoenolate (allylsilane **22**) to a carbonyl derivative. It was therefore envisioned that substituted γ-butyrolactones **28** could be readily accessed by chemoselective deprotection of the TBS function followed by subsequent oxidation of the resulting, cyclic lactol (Table 3).

In the event, treatment of **23** with TBAF in THF, at –78 °C, followed by the addition of TPAP and NMO[16] re-

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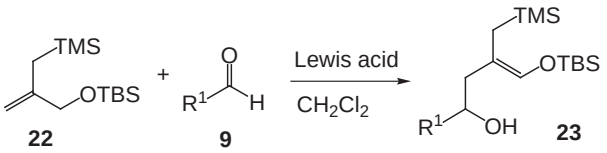
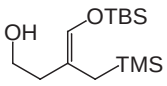
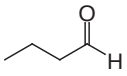
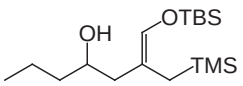
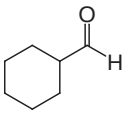
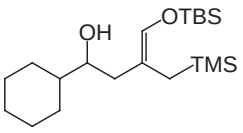
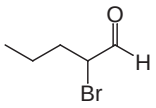
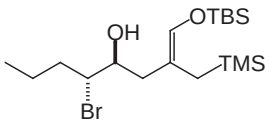
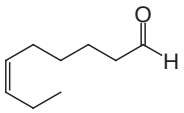
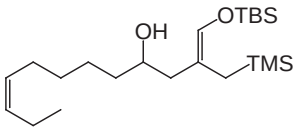
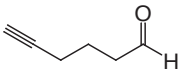
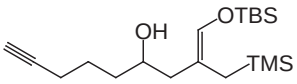
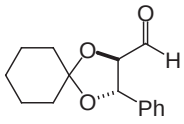
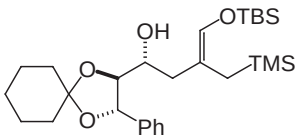
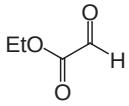
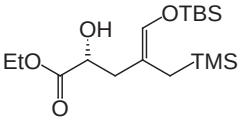
Table 1 Silyl Enol Ethers **23a–h**



Entry	Aldehyde	Product		Yield (%)[a]
1			**23a**	65
2			**23b**	73
3			**23c**	52
4			**23d**	79[b]
5			**23e**	55
6			**23f**	61
7			**23g**	59[c]
8			**23h**	51[d]

[a] Isolated yields after purification by column chromatography.
[b] de = 85%.
[c] de = 51%.
[d] ee = 95%.

sulted in the transformation of ene-adducts **23** into the desired γ-butyrolactones **28** in good to excellent overall yields. The procedure tolerates a range of substituents and protecting groups. The final lactones are usually obtained as a mixture of *cis*- and *trans*-isomers; the diastereoselectivity increasing as a function of the steric size of the R^1 substituent. These β-trimethylsilylmethyl-γ-butyrolactones **28** have been little studied previously[17] though they appear to be interesting precursors to a variety of 5-membered ring heterocycles.

To illustrate their synthetic utility, a simple conversion of **28** to *exo*-methylene-γ-butyrolactones **29** was devised (Table 4).

Thus, addition of lactone **28** to a THF solution of LDA, followed by capture of the resulting enolate with TMSCl, afforded the corresponding silylenol ether, which was immediately reacted with an equivalent of NBS. The in situ generated α-bromolactone was then treated with a slight excess of TBAF, inducing a rapid bromodesilylation, ulti-

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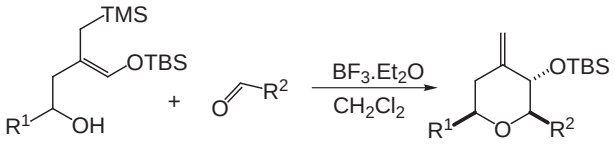
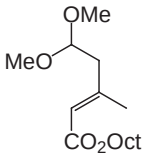
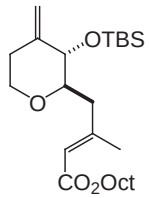
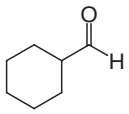
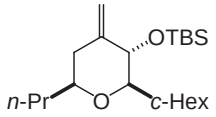
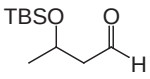
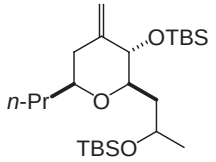
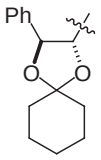
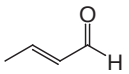
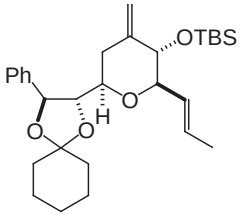
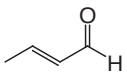
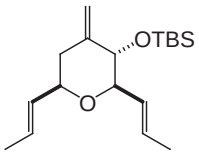
Table 2 *exo*-Methylene Tetrahydropyran Derivatives **27a**–**e** Prepared



23 **20** **27**

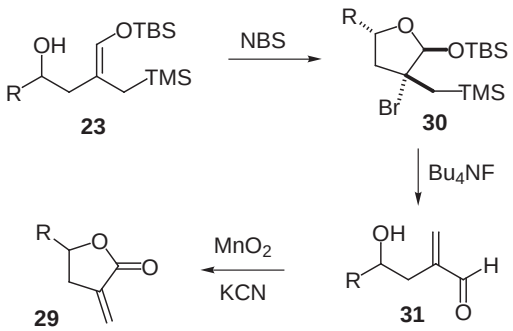
Entry	R^1	Aldehyde	Product		Yield (%)[a]
1	H			**27a**	80
2	Pr			**27b**	63
3	Pr			**27c**	79
4				**27d**	57
5	$CH_3CH=CH$			**27e**	85

[a] Isolated yields after purification by column chromatography.

mately providing the desired *exo*-methylene-γ-butyrolactones **29** in excellent overall yields[18] (Table 4).

Although this protocol proved efficient on small scale, affording the desired products in a two-pot operation from the ene-adducts **23**, the stringent control of the reaction conditions precluded its easy transposition to larger quantitites. Therefore, a shorter procedure, more amenable to upscaling was developed, leading to *exo*-methylene-γ-butyrolactones **29** directly from homoallylic alcohols **23** (Scheme 7).[19]

Addition of NBS to ene-adduct **23** resulted in a quantitative bromocycloetherification, affording the corresponding TBS protected lactol **30** as a single diastereoisomer. Upon treatment with TBAF, double desilylation took



Scheme 7

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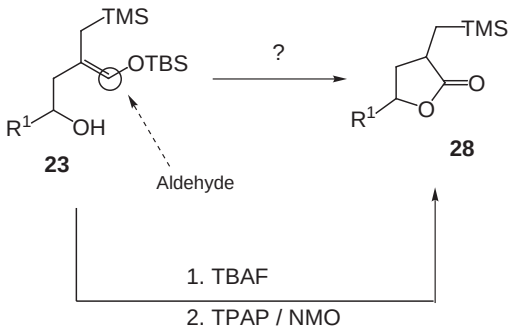
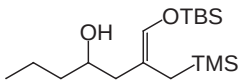
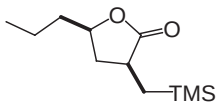
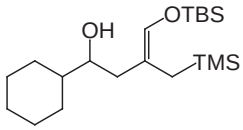
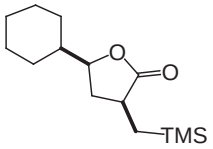
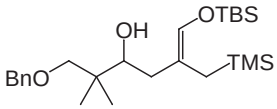
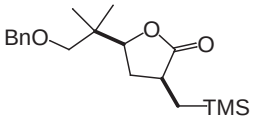
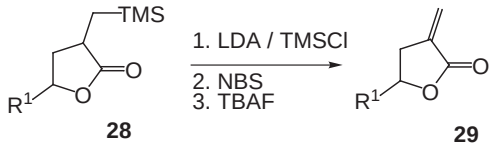
Table 3 γ-Butyrolactones **28a–c** Prepared

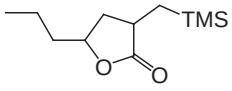
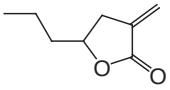
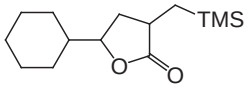
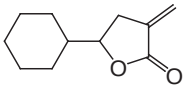
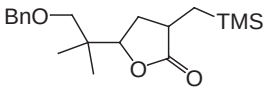
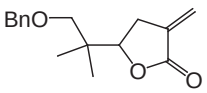


Entry	Ene adduct **23**	Lactone **28**		Yield (%)[a]
1			**28a**	80 (de = 45%)
2			**28b**	60 (de = 50%)
3			**28c**	99 (de = 75%)

[a] Isolated yields after purification by column chromatography.

Table 4 Conversion of **28** to *exo*-Methylene-γ-butyrolactones



Entry	Lactone **28**	Lactone **29**		Yield (%)[a]
1			**29a**	80
2			**29b**	70
3			**29c**	74

[a] Isolated yields after purification by column chromatography.

place, generating the α,β-unsaturated aldehyde **31**, in equilibrium with a small amount of the closed lactol. Under Corey's conditions,[20] this mixture of equilibrating species underwent smooth oxidative cyclisation, leading to the desired *exo*-methylene-γ-butyrolactones **29** in good to excellent overall yields (Scheme 7). Some selected examples are displayed in Table 5.

As can be seen from Table 5, a variety of primary, secondary and tertiary homoallylic alcohols can be efficiently converted into the final *exo*-methylene-γ-butyrolactones

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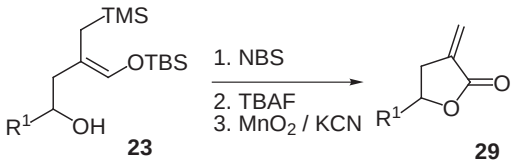
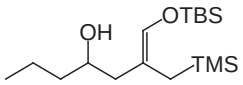
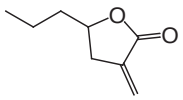
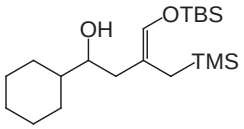
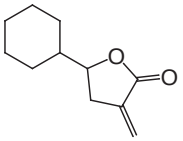
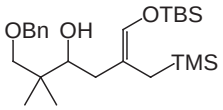
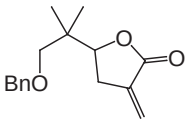
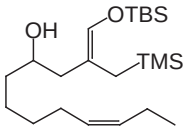
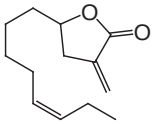
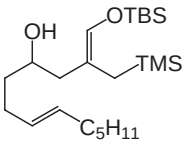
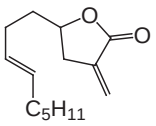
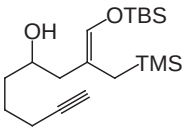
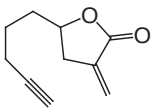
Table 5 Cyclization of **23** to exo-Methylene-g-butyrolactones **29**



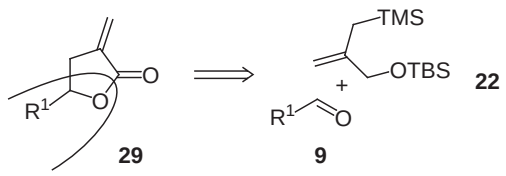
23 **29**

Entry	Ene-Adduct **23**	Lactone **29**		Yield (%)[a]
1			**29a**	61
2			**29b**	76
3			**29c**	66
4			**29d**	57
5			**29e**	60
6			**29f**	74

[a] Isolated yields after purification by column chromatography.

products by this simple protocol (entries 1–3). Interestingly, the reaction tolerates a range of functionalities and protecting groups, including (*E*)- and (*Z*)-disubstituted alkenes (entries 4 and 5) and terminal alkynes (entry 6). In this last case, no competitive cyclisation on the triple bond was observed.

From all these results, a simple and general disconnection for γ-butyrolactones and *exo*-methylene-γ-butyrolactones **29** can be proposed, as depicted in Scheme 8.



29 **9**

Scheme 8

In summary, we have shown that the ene-reaction between a variety of aldehydes and allylsilane **22** afforded, in good yields, the corresponding adducts **23**. These homoallylic alcohols, which embody an allylsilane and a silyl enol ether functions, are useful precursors to a range of polysubstituted heterocycles. By carefully selecting the reaction conditions, either the allylsilane or the enol ether function can be activated. Thus, addition of an aldehyde to ene-adduct **23**, in the presence of a Lewis acid, results in the preparation of trisubstituted, diastereomerically pure, *exo*-methylene tetrahydropyrans **27**. These functionalised, six-membered ring systems, are the core of a range of biologically active natural products. Furthermore, by recognising that adducts **23** were equivalent to aldehyde homoenolate addition products, two simple routes towards substituted γ-butyrolactones **28** and *exo*-methylene-γ-butyrolactones **29** have been established.

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Current efforts are now being directed towards delineating the full scope of these connective methodologies, defining enantioselective versions and applying them to the total synthesis of various natural products, including polycavernoside A (**1**).

All air or moisture sensitive reactions were carried out in flame dried glassware under Ar, unless otherwise noted. Reactive liquids were transferred by syringe and were added into the reaction flask through rubber septa. CH_2Cl_2 and THF were freshly distilled, the former from CaH_2 and the latter from sodium-benzophenone ketyl. Purchased reagents were used as received unless otherwise indicated. TLC was performed on aluminum sheets coated with 0.20 mm silica gel 60 G/UV_{254} (Macherey-Nagel). ^{1}H NMR spectra and ^{13}C NMR spectra were recorded on a Varian Gemini 200 (^{1}H 200 MHz, ^{13}C 50 MHz), Gemini 300 (^{1}H 300 MHz, ^{13}C 75 MHz) or Bruker Advanced TM 500 (^{1}H 500 MHz, ^{13}C 125 MHz) spectrometer using TMS as an internal standard. IR spectra were measured with a BIO-RAD FTS 135 infrared spectrometer. Mass spectra were determined on a Finnigan-Matt TSQ-70 or Varian Matt 44S spectrometer. High resolution mass spectra were performed in Prof R. Flamant's laboratory (Université de Mons-Hainaut, Belgium) and elemental analyses in Prof V. Jäger's laboratory (Institut für Organishe Chemie, Universität Stuttgart, Germany).

(2,3-*anti*,3,6-*anti*)-2,6-Dipropyl-4-methyleneoxacyclohexan-3-ol (11a); Typical Procedure

Neat $BF_3{\cdot}OEt_2$ (1.0 equiv, 0.390 g, 0.35 mL, 2.78 mmol) was added dropwise to a cold (–78 °C) mixture of butyraldehyde (2.0 equiv, 0.400 g, 5.56 mmol) and allylsilane **22** (1.0 equiv, 0.600 g, 2.78 mmol) in CH_2Cl_2 (15 mL). The resulting solution was allowed to warm slowly (over 2 h) to r.t., and then poured onto sat. aq $NaHCO_3$ (20 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extracts were dried (K_2CO_3) and the volatiles removed in vacuo. Purification by flash chromatography (silica gel, CH_2Cl_2) gave the title product (0.236 g, 43%) as a white solid (mp 36–38 °C).

IR (KBr): 3425, 2980, 2870, 1660, 1465, 1090, 895 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.99 (1 H, q, *J* = 2.1 Hz), 4.84 (1 H, q, *J* = 1.9 Hz), 3.74 (1 H, br d, *J* = 9.0 Hz), 3.21–3.31 (1 H, m), 2.98 (1 H, td, *J* = 9.0, 2.2 Hz), 2.38 (1 H, dd, *J* = 10.9, 2.3 Hz), 1.99–2.11 (1 H, m), 1.30–1.66 (1 H, m), 0.89–0.97 (6 H, m).

^{13}C NMR ($CDCl_3$): δ = 147.9 (C), 105.1 (CH_2), 82.4 (CH), 78.1 (CH), 73.8 (CH), 41.3 (CH_2), 37.9 (CH_2), 34.7 (CH_2), 18.9 (CH_2), 18.7 (CH_2), 14.0 (CH_3), 14.0 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 198 ($M^{+\cdot}$, 26), 181 (78), 137 (41), 126 (69), 109 (33), 97 (96), 71 (100), 55 (84), 43 (89).

Anal. Calcd for $C_{12}H_{22}O_2$ (198.3): C, 72.68; H, 11.18. Found: C, 72.56; H, 11.14.

(2,3-*anti*,3,6-*anti*)-2,6-Dicyclohexyl-4-methyleneoxacyclohexan-3-ol (11b)

Compound **11b** was prepared according to the protocol described for the synthesis of **11a**.

IR (KBr): 3390, 2925, 2855, 1660, 1455, 1075, 900 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 4.96 (1 H, s), 4.83 (1 H, s), 3.96 (1 H, br d, *J* = 6.8 Hz), 2.94 (1 H, ddd, *J* = 12.5, 8.3, 1.8 Hz), 2.79 (1 H, dd, *J* = 6.8, 1.9 Hz), 2.37 (1 H, dd, *J* = 12.5, 1.8 Hz), 0.90–2.10 (24 H, m).

^{13}C NMR ($CDCl_3$): δ = 149.1 (C), 104.8 (CH_2), 86.2 (CH), 82.6 (CH), 70.3 (CH), 42.8 (CH), 38.4 (CH), 38.3 (CH_2), 30.6 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 26.9 (CH_2), 26.6 (CH_2), 26.5 (CH_2), 26.2 (CH_2), 26.0 (CH_2), 25.5 (CH_2), 24.3 (CH_2).

MS (EI, 70 eV): *m*/*z* (%) = 278 ($M^{+\cdot}$, 3), 166 (47), 135 (24), 96 (80), 81 (60), 71 (58), 55 (100), 41 (87).

Anal. Calcd for $C_{18}H_{30}O_2$ (278.4): C, 77.65; H, 10.86. Found: C, 77.54; H, 10.73.

(2,3-*anti*,3,6-*anti*)-2,6-di-(2-phenylethyl)-4-methyleneoxacyclohexan-3-ol (11c)

Compound **11c** was prepared according to the protocol described for the synthesis of **11a**.

IR (KBr): 3416, 3040, 2925, 2860, 1649, 1594, 1497, 1460, 1105 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 7.15–7.40 (10 H, m), 4.96 (1 H, q, *J* = 2.0 Hz), 4.83 (1 H, q, *J* = 1.9 Hz), 3.77 (1 H, br d, *J* = 9.1 Hz), 3.22–3.36 (1 H, m), 2.67–3.03 (5 H, m), 2.38 (1 H, dd, *J* = 11.3, 2.1 Hz), 2.19–2.31 (1 H, m), 2.13 (1 H, br t, *J* = 11.3 Hz), 1.70–1.98 (3 H, m), 1.53 (1 H, br s).

^{13}C NMR ($CDCl_3$): δ = 149.4 (C), 144.3 (C), 144.1 (C), 130.7 (CH), 130.6 (CH), 130.5 (CH), 130.4 (CH), 127.9 (CH), 127.8 (CH), 107.6 (CH_2), 83.5 (CH), 79.2 (CH), 75.8 (CH), 43.3 (CH), 39.6 (CH), 36.5 (CH_2), 34.1 (CH_2), 33.8 (CH_2).

MS (EI, 70 eV): *m*/*z* = 322 ($M^{+\cdot}$, 37), 188 (20), 170 (17), 130 (33), 117 (25), 91 (100).

Anal. Calcd for $C_{22}H_{26}O_2$ (278.4): C, 81.95; H, 8.13. Found: C, 82.03; H, 8.10.

(2,3-*anti*,3,4-*syn*,4,6-*anti*)-2,6-dipropyl-3,4-diacetoxyoxacylohexane (16)

To a cold (–78 °C) solution of compound **15** (0.58 g, 2.9 mmol, 1.0 equiv) in THF (6 mL) was added a 1.0 M solution of LS-Selectride (3.77 mL, 3.77 mmol, 1.3 equiv). The resulting mixture was stirred at –78 °C for 2 h and then allowed to warm to r.t. over a further 2 h. The reaction was quenched by addition of H_2O (3 mL) and EtOH (9 mL) followed by further treatment with 2.5 M aq NaOH (6 mL) and 30% aq H_2O_2 (6 mL). This slurry was stirred vigorously at r.t. for 2 h and then diluted with H_2O (20 mL). The mixture was extracted with Et_2O (3 × 15 mL) and the combined organic extracts were dried ($MgSO_4$). The volatiles were removed in vacuo to leave a pale yellow oil, which was immediately dissolved in CH_2Cl_2 (10 mL) and the solution was cooled to 0 °C. To this solution was added, sequentially, acetyl chloride (2.5 equiv, 0.57 g, 0.52 mL, 7.25 mmol) and pyridine (2.6 equiv, 0.6 g, 0.61 mL, 7.54 mmol) and the reaction mixture was stirred at 0 °C for 7 h. The solution was poured onto aq sat. $NaHCO_3$ (20 ml), the layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic extracts were dried (K_2CO_3) and the solvent was removed under reduced pressure. Purification by flash column chromatography (silica gel, hexane–EtOAc 10:1) furnished the title product (0.68 g, 82%) as a colourless oil.

IR (film): 2955, 2865, 1750, 1375, 1255, 1060 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 5.38 (1 H, q, *J* = 3.0 Hz), 4.56 (1 H, dd, *J* = 10.0, 3.0 Hz), 3.56–3.70 (2 H, m), 2.10 (3 H, s), 2.00 (3 H, s), 1.81 (1 H, ddd, *J* = 14.5, 3.5, 2.4 Hz), 1.22–1.86 (9 H, m), 0.90 (6 H, t, *J* = 6.8 Hz).

^{13}C NMR ($CDCl_3$): δ = 170.2 (C), 170.0 (C), 73.1 (CH), 72.1 (CH), 71.6 (CH), 67.7 (CH), 37.5 (CH_2), 36.2 (CH_2), 33.9 (CH_2), 21.0 (CH_3), 20.7 (CH_3), 18.8 (CH_2), 18.3 (CH_2), 13.90 (CH_3).

MS (EI, 70 eV) : 287 (M^+, 18), 243 (11), 226 (17), 183 (30), 166 (54), 144 (25), 123 (48), 102 (46), 71 (27), 43 (100).

Anal. Calcd for $C_{15}H_{26}O_5$ (286.4): C, 62.91; H, 9.15. Found: C, 63.15; H, 9.26.

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(2,3-*anti*,3,4-*anti*,4,6-*syn*)-2,6-Dipropyl-3,4-diacetoxyoxacylohexane (18)

To a cold (–20 °C) mixture of the ketone **17** (1.0 equiv, 0.48 g, 1.98 mmol) and $CeCl_3 \cdot 7H_2O$ (1.2 equiv, 0.89 g, 2.38 mmol) in THF–MeOH (8 mL:4 mL) was added solid $NaBH_4$ (1.2 equiv, 0.09 g, 2.38 mmol). Effervescence occurred immediately. The reaction mixture was stirred at –20 °C for 1 h and then at r.t. for 1 h. The mixture was poured onto sat. aq $NaHCO_3$ (20 mL), the layers were separated and the aqueous phase was extracted with Et_2O (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$) and the solvents were removed in vacuo. The crude alcohol was dissolved in CH_2Cl_2 (10 mL) and treated, sequentially, with acetyl chloride (1.4 equiv, 0.22 g, 0.20 mL, 2.78 mmol) and pyridine (1.5 equiv, 0.24 g, 0.24 mL, 2.98 mmol) at 0 °C. The mixture was stirred at r.t. for 17 h and then poured onto sat. aq $NaHCO_3$ (15 mL). The combined organic extracts were dried (K_2CO_3) and the volatiles were removed under reduced pressure. Purification by flash column chromatography (silica gel, hexane-EtOAc, 10:1) provided the title compound (0.43 g, 76%) as a colourless oil.

IR (film): 2955, 2840, 1745, 1350, 1240, 1015 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.93 (1 H, ddd, *J* = 11.4, 9.3, 5.2 Hz), 4.72 (1 H, t, *J* = 9.3 Hz), 3.19–3.43 (2 H, m), 2.00–2.13 (2 H, m), 2.01 (3 H, s), 1.99 (3 H, s), 1.25–1.60 (8 H, m), 0.82–0.93 (6 H, m).

^{13}C NMR ($CDCl_3$): δ = 170.4 (C), 170.0 (C), 76.9 (CH), 74.6 (CH), 73.4 (CH), 72.6 (CH), 37.3 (CH_2), 36.6 (CH_2), 33.6 (CH_2), 20.7 (CH_3), 20.7 (CH_3), 18.6 (CH_2), 18.3 (CH_2), 13.7 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 287 ($M^{+\cdot}$, 3), 226 (53), 183 (50), 166 (100), 144 (50), 123 (97), 112 (82), 102 (64), 43 (39).

(*Z*)-4-{[(*tert*-Butyl(dimethyl)silyl]oxy}-3-[(trimethylsilyl)methyl]but-3-en-1-ol (23a)

Method A: To a solution of $AlMe_3$ in toluene (2 M, 10.8 mL, 21.5 mmol, 3.0 equiv) was added slowly and at r.t., a solution of 2,6-diphenylphenol (10.6 g, 43.0 mmol, 6 equiv) in freshly distilled CH_2Cl_2 (50 mL). The resulting yellow mixture was stirred for 30 min after which time the temperature was lowered to 0 °C. A solution of trioxane (645 mg, 21.5 mmol, 3.0 equiv) in anhyd CH_2Cl_2 (6 mL) was then added. After stirring for 1 h at 0 °C, a siolution of allylsilane **22** (1.86 g, 7.17 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was injected into the mixture. After 75 min, the solution was diluted with CH_2Cl_2 (400 mL) and poured onto a aq sat. solution of $NaHCO_3$. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 250 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated in vacuo. The residue, 12.3 g of a yellow solid, was purified by MPLC (silica gel: 1000 g, eluent: CH_2Cl_2, flow: 150 mL/min, 235 nm UV detection) to afford the homoallylic alcohol **23a** as a viscous colourless oil (1.35 g, 65%).

IR (film): 3354, 2955, 2931, 2888, 2859, 1664, 1249, 1160, 838 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 6.03 (1 H, br s), 3.55 (2 H, t, *J* = 10.0 Hz), 2.03 (2 H, td, *J* = 10.0, 1.0 Hz), 1.54 (1 H, br s), 1.45 (2 H, d, *J* = 1.0 Hz), 0.88 (9 H, s), 0.10 (6 H, s), 0.00 (9 H, s).

^{13}C NMR ($CDCl_3$): δ = 134.0 (CH), 114.4 (C), 60.1 (CH_2), 36.7 (CH_2), 25.8 (CH_3), 18.2 (C), 17.1 (CH_2), –0.62 (CH_3), –5.16 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 288 (M^+, 48), 257 (15), 233 (33), 231 (35), 185 (65), 157 (7), 147 (100), 75 (28), 73 (75).

Anal. Calcd for $C_{14}H_{32}O_2Si_2$ (288.6): C, 58.27; H, 11.18. Found: C, 58.17; H,11.06.

(*Z*)-1-{[(*tert*-Butyl(dimethyl)silyl]oxy}-2-[(trimethylsilyl)methyl]hept-1-en-4-ol (23b)

Method B: To a cold (–78 °C) mixture of butyraldehyde (0.89 g, 12.31 mmol, 1 equiv) and allylsilane **22** (3.182 g, 12.31 mmol, 1 equiv) in anhyd CH_2Cl_2 (100 mL) was added dropwise a 1 M hexane solution of Et_2AlCl (12.31 mL, 12.31 mmol, 1 equiv). The mixture was stirred at this temperature for 1 h after which time the cooling bath was removed and the solution was diluted by CH_2Cl_2 (50 mL). Aq sat. solution of $NaHCO_3$ was then added. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL). After washing the combined organic layers with H_2O (50 mL), the organic phase was dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified on silica gel using 30:1 hexane–EtOAc as eluent to afford the homoallylic alcohol **23b** as a viscous colourless oil (2.97 g, 73%).

IR (film): 3452 (O–H), 2956–2860 (C–H), 1645 (C=C), 1255, 1050, 835 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 6.09 (1 H, s), 3.65–3.57 (1 H, m), 2.04 (1 H, ddd, *J* = 13.7, 3.1, 1.3 Hz), 1.81 (1 H, br s), 1.76 (1 H, dd, *J* = 13.7, 9.6 Hz), 1.76 (1 H, d, *J* = 13.4 Hz), 1.55–1.32 (4 H, m), 1.19 (1 H, d, *J* = 13.4 Hz), 0.93 (3 H, t, *J* = 7.2 Hz), 0.91 (9 H, s), 0.10 (6 H, s), 0.01 (9 H, s).

^{13}C NMR ($CDCl_3$): δ = 134.2 (CH), 115.1 (C), 67.7 (CH), 41.8 (CH_2), 39.0 (C-3), 25.7 (CH_3), 18.9 (CH_2), 18.1 (C), 17.2 (CH_2), 14.0 (CH_3), –0.74 (CH_3), –5.26 (CH_3), –5.39 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 330 ($M^{+\cdot}$, 7), 257 (7), 199 (26), 115 (11), 75 (100), 73 (47).

(*Z*)-4-{[(*tert*-Butyldimethyl)silyl]oxy}-1-cyclohexyl-3-[(trimethylsilyl)methyl]but-3-en-1-ol (23c)

The ene adduct **23c** was prepared from cyclohexanecarboxaldehyde and **22** according to method B; colourless oil; yield: 52%.

IR (film): 3567 (O–H), 2954–2855 (C–H), 1658 (C=C), 1472, 1450, 1250, 1161, 1001, 838 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 6.09 (1 H, s), 3.35 (1 H, ddd, *J* = 10.3, 5.9, 2.7 Hz), 2.10 (1 H, ddd, *J* = 13.7, 2.5, 1.4 Hz), 1.92–1.81 and 1.38–0.95 (12 H, m), 1.82 (1 H, d, *J* = 13.4 Hz), 1.74 (1 H, dd, *J* = 13.7, 10.4 Hz), 1.15 (1 H, d, *J* = 13.4 Hz), 0.92 (9 H, s), 0.10 (6 H, s), 0.01 (9 H, s).

^{13}C NMR ($CDCl_3$): δ = 134.3 (CH), 115.2 (C), 71.5 (CH), 43.2 (CH), 38.4 (CH_2), 29.1 (CH_2), 28.5 (CH_2), 26.6 (CH_2), 26.3 (CH_2), 26.2 (CH_2), 25.7 (CH_3), 18.1 (C), 16.8 (CH_2), –0.73 (CH_3), –5.23 (CH_3), –5.39 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 370 ($M^{+\cdot}$, 19), 355 (2), 257 (30), 239 (2), 185 (100), 147 (16), 127 (16), 73 (29).

Anal. Calcd for $C_{20}H_{42}O_2Si_2$: C, 64.80; H, 11.42. Found: C, 64.83; H, 11.40.

(*Z*)-5-Bromo-1-{[*tert*-butyl(dimethyl)silyl]oxy}-2-[(trimethylsilyl)methyl]oct-1-en-4-ol (23d)

The ene adduct **23d** was prepared from 2-bromopentanal and **22** according to method B. This compound is rather sensitive and should be used as soon as possible in the subsequent step; colourless oil; yield: 79%; de = 85%.

IR (film): 447, 2958, 2933, 2888, 2860, 1660, 1468, 1251, 1201, 1158, 1105, 840, 781 cm^{-1}.

^1H NMR ($CDCl_3$): δ (major isomer) = 6.09 (1 H, s), 4.05 (1 H, dt, *J* = 8.4, 5.1 Hz), 3.68–3.79 (1 H, m), 2.29 (1 H, dd, *J* = 14.3, 3.7 Hz), 2.13 (1 H, m), 1.19–2.01 (7 H, m), 0.89 (9 H, s), 0.89–0.92 (3 H, m), 0.09 (6 H, s), 0.01 (9 H, s).

^{13}C NMR ($CDCl_3$): δ (major isomer) = 135.4 (CH), 114.9 (C), 71.9 (CH), 62.8 (CH), 38.8 (CH_2), 36.4 (CH_2), 26.3 (CH_3), 21.7 (CH_2), 18.7 (C), 17.8 (CH_2), 14.1 (CH_3), –0.05 (CH_3), –4.54 (CH_3), –4.64 (CH_3).

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^{1}H NMR ($CDCl_3$): δ (minor isomer) = 6.13 (1 H, s), 4.04 (1 H, ddd, *J* = 9.0, 4.8, 2.4 Hz), 3.54 (1 H, br t, *J* = 4.9 Hz), 1.21–2.19 (8 H, m), 0.91 (9 H, s), 0.87–0.94 (3 H, m), 0.09 (6 H, s), 0.00 (9 H, s).

^{13}C NMR ($CDCl_3$): δ (minor isomer) = 135.4 (CH), 114.7 (C), 71.5 (CH), 63.4 (CH), 40.4 (CH_2), 38.4 (CH_2), 26.3 (CH_3), 21.7 (CH_2), 18.7 (C), 17.9 (CH_2), 14.0 (CH_3), –0.06 (CH_3), –4.61 (CH_3).

(*Z*)-1-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-[(trimethylsilyl)methyl]dodeca-1,9-dien-4-ol (23e)

The ene adduct **23e** was prepared from aldehyde **9e** and allylsilane **22** according to method B; colourless oil; yield: 55%.

IR (film): 3447 (O–H), 3005–2858 (C–H), 1659 (C=C), 1472, 1463, 1405, 1362, 1248, 1167, 1100, 838 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 6.09 (1 H, s), 5.41–5.23 (2 H, m), 3.62–3.48 (1 H, m), 2.10–1.93 and 1.47–1.13 (5 H and 7 H, m), 1.77 (1 H, d, *J* = 13.2 Hz), 1.75 (1 H, dd, *J* = 13.4, 8.2 Hz), 1.19 (1 H, d, *J* = 13.4 Hz), 0.95 (3 H, t, *J* = 7.7 Hz), 0.91 (9 H, s), 0.10 (6 H, s), 0.01 (9 H, s).

^{13}C NMR ($CDCl_3$): δ = 134.4 (CH), 131.7 (CH), 129.1 (CH), 115.2 (C), 68.0 (CH), 41.9 (CH_2); 36.8 (CH_2), 29.9 (CH_2), 27.1 (CH_2), 25.8 (CH_3), 25.5 (CH_2), 20.2 (CH_2), 18.2 (C), 17.3 (CH_2), 14.4 (CH_3), –0.63 (CH_3), –5.13 (CH_3), –5.26 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 398 ($M^{+\cdot}$, 92), 383 (9), 257 (81), 213 (100), 147 (31), 123 (37), 73 (56).

Anal. Calcd for $C_{22}H_{46}O_2Si_2$: C, 66.26; H, 11.63. Found: C, 66.28; H, 11.60.

(*Z*)- 1-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-[(trimethylsilyl)methyl]non-1-en-8-yn-4-ol (23f)

The ene adduct **23f** was prepared from aldehyde **9f** and allylsilane **22** according to method B; colorless oil; yield: 61%.

IR (film): 3449 (O–H), 3313, 2954–2858 (C–H), 1660 (C=C), 1463, 1408, 1362, 1248, 1144, 1101, 838 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 6.10 (1 H, s), 3.79–3.63 (1 H, m), 2.24 (2 H, td, *J* = 6.6, 2.7 Hz), 2.04 (1 H, ddd, *J* = 13.5, 2.7, 1.5 Hz), 1.95 (1 H, t, *J* = 2.7 Hz), 1.79 (1 H, dd, *J* = 13.2, 11.1 Hz), 1.77 (1 H, d, *J* = 13.2 Hz), 1.76–1.48 (4 H, m), 1.19 (1 H, d, *J* = 13.8 Hz), 0.91 (9 H, s), 0.10 (6 H, s), 0.01 (9 H, s).

^{13}C NMR ($CDCl_3$): δ = 134.4 (CH), 114.9 (C), 84.2 (C), 68.4 (CH), 67.5 (CH_2), 41.9 (CH_2), 35.8 (CH_2), 25.7 (CH_3), 24.9 (CH_2), 18.5 (CH_2), 18.2 (C), 17.2 (CH_2), –0.66 (CH_3), –5.15 (CH_3), –5.29 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 354 ($M^{+\cdot}$, 72), 339 (4), 257 (68), 169 (100), 147 (43), 129 (33), 95 (41), 79 (44), 73 (56).

Anal. Calcd for $C_{19}H_{38}O_2Si_2$: C, 64.34; H, 10.80. Found: C, 63.88; H, 10.60.

4-{[*tert*-butyl(dimethyl)silyl]oxy}-1-(3-phenyl-1,4-dioxaspiro[4.5]dec-2-yl)-3-[(trimethylsilyl)methyl]but-3-en-1-ol (23g)

The ene adduct **23g** was prepared from the corresponding aldehyde and allylsilane **22** according to method B; colourless oil; yield: 59%; de 51%.

IR (film): 3500, 2934, 2886, 2858, 1685, 1249, 1164, 1103, 838, 780 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ (major isomer) = 7.30–7.53 (5 H, m), 5.96 (1 H, s), 5.06 (1 H, d, *J* = 7.4 Hz), 3.93 (1 H, dd, *J* = 7.4, 5.4 Hz), 3.88–3.96 (1 H, m), 2.23 (1 H, dd, *J* = 14.6, 3.0 Hz), 2.02 (1 H, br s), 1.91 (1 H, dd, *J* = 14.3, 9.1 Hz), 1.48–1.87 (11 H, m), 1.29 (1 H, d, *J* = 13.5 Hz), 0.96 (9 H, s), 0.12 (6 H, s), 0.07 (9 H, s).

^{1}H NMR ($CDCl_3$): δ (minor isomer) = 7.35–7.57 (5 H, m), 6.14 (1 H, s), 5.09 (1 H, d, *J* = 8.5 Hz), 3.86 (1 H, dd, *J* = 8.5, 1.9 Hz), 3.70 (1 H, br q, *J* = 6.9 Hz), 2.65–2.17 (2 H, m), 1.30–1.95 (13 H, m), 0.98 (9 H, s), 0.15 (6 H, s), 0.06 (9 H, s).

^{13}C NMR ($CDCl_3$): δ (major isomer) = 139.3 (C), 134.3 (CH), 128.4 (CH), 128.0 (CH), 127.4 (CH), 114.0 (C), 109.6 (C), 84.8 (CH), 80.2 (CH), 69.1 (CH), 37.3 (CH_2), 36.8 (CH_2), 36.7 (CH_2), 25.6 (CH_3), 25.1 (CH_2), 23.9 (CH_2), 18.0 (C), 16.9 (CH_2), –0.72 (CH_3), –5.21 (CH_3), –5.33 (CH_3).

^{13}C NMR ($CDCl_3$): δ (minor isomer) = 138.2 (C), 134.3 (CH), 128.5 (CH), 128.1 (CH), 126.8 (CH), 114.1 (C), 109.5 (C), 84.0 (CH), 78.8 (CH), 66.1 (CH), 39.0 (CH_2), 36.8 (CH_2), 36.5 (CH_2), 25.7 (CH_3), 25.1 (CH_2), 23.9 (CH_2), 18.1 (C), 17.2 (CH_2), –0.78 (CH_3), –5.33 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 504.3 ($M^{+\cdot}$, 100), 309.2 (98), 257.2 (46), 205.2 (62), 195.1 (49), 147.0 (45), 73.1 (69), 44.1 (62).

Anal. Calcd for $C_{28}H_{48}O_4Si_2$ (504.9): C, 66.61; H, 9.58. Found: C, 66.12; H, 9.37.

(2*S*,4*Z*)-Ethyl 5-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-hydroxy-4-[(trimethylsilyl)methyl]pent-4-enoate (23h)

Method C: A solution of $Cl_2Ti(i\text{PrO})_2$ (0.488 M, 225 μL, 100 μmol, 0.1 equiv) in toluene was added to (*S*)-Binol (29 mg, 100 μmol, 0.1 equiv) in anhyd CH_2Cl_2 (1 mL). The mixture turned at once to red-brown. In another flask, a suspension of hydrated molecular sieves (4Å) was prepared by the addition of H_2O (30 μL) to activated MS (500 mg) in CH_2Cl_2 (3 mL). The titanate solution was then transferred, via canula, on the molecular sieve suspension. The mixture was stirred for 1 h at 17 °C, after which time it was cooled to 0 °C. Allylsilane **22** (320 μL, 258 mg, 1.0 mmol, 1.0 equiv) was added directly, followed by a solution of ethyl glyoxylate in toluene (refluxed 1 h before, 50% weight, 300 μL, 306 mg, 1.5 mmol, 1.5 equiv). After stirring for 20 h at this temperature, the reaction was worked up by the addition of aq sat. solution of $NaHCO_3$ and Et_2O. The layers were separated and the aqueous phase was extracted twice with Et_2O. The organic phase was dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified on silica gel using CH_2Cl_2 as eluent, affording homoallylic alcohol **23h** as a viscous colourless oil (185 mg, 51%). Enantiomerical excess was determined by CGC on a chiral phase (160 °C isotherm, 95% ee).

IR (film): 3482, 2956, 2931, 2869, 1735, 1664, 1251, 1201, 1162, 1101, 838 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 6.07 (1 H, br s), 4.14–4.24 (3 H, m), 2.49 (0.8 H, d, *J* = 5.9 Hz), 2.32 (1 H, ddd, *J* = 14.1, 4.4, 1.0 Hz), 2.13 (1 H, dd, *J* = 14.1, 7.8 Hz), 1.56 (1 H, d, *J* = 13.6 Hz), 1.41 (1 H, d, *J* = 13.6 Hz), 1.27 (1 H, t, *J* = 7.1 Hz), 0.89 (9 H, s), 0.07 (6 H, s), 0.00 (9 H, s).

^{13}C NMR ($CDCl_3$): δ = 174.6 (C), 134.9 (CH), 113.1 (C), 69.0 (CH), 61.3 (CH_2), 38.7 (CH_2), 25.7 (CH_3), 18.1 (C), 17.2 (CH_2), 14,2 (CH_3), –0.73 (CH_3), –5.24 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 360.3 ($M^{+\cdot}$, 25), 257.2 (75), 185.2 (100), 157.1 (15), 147.1 (18), 73.1 (30).

Anal. Calcd for $C_{17}H_{36}O_4Si_2$ (360.2): C, 56.69; H, 10.07. Found: C, 57.24; H,10.17

***tert*-butyl[2-cyclohexyl-4-methylene-6-propyltetrahydro-2*H*-pyran-3yl)oxy]dimethylsilane (27b); Typical Procedure**

To a cold (–78 °C) solution of silyl enol ether **23c** (1.0 equiv, 0.227 g, 0.692 mmol) and cyclohexanecarboxaldehyde (1.0 equiv, 0.085 g, 0.761 mmol) in CH_2Cl_2 (5 mL) was added $BF_3{\cdot}OEt_2$ (1.1 equiv, 0.108 g, 0.096 mL, 0.761 mmol). The reaction mixture was allowed to warm slowly (over 2 h) to r.t. before being poured onto sat. aq $NaHCO_3$ (20 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 20 mL). The combined organic extracts were dried (K_2CO_3) and the solvent was removed under reduced pressure. Purification by flash column chromatography

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(silica gel, hexane–EtOAc, 50:1) afforded **27b** (0.153 g, 63%) as a colourless oil.

IR (film): 2925, 2860, 1640, 1460, 1250, 1120, 835 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.93 (1 H, s), 4.73 (1 H, s), 3.85 (1 H, d, *J* = 8.9 Hz), 3.10–3.23 (1 H, m), 2.81 (1 H, d, *J* = 8.9 Hz), 2.26 (1 H, dd, *J* = 12.8, 1.9 Hz), 1.91 (1 H, t, *J* = 12.8 Hz), 1.10–1.78 (15 H, m), 0.92 (9 H, s), 0.88 (3 H, t, *J* = 6.9 Hz), 0.05 (3 H, s), 0.00 (3 H, s).

^{13}C NMR ($CDCl_3$): δ = 148.9 (C), 105.7 (CH_2), 87.3 (CH), 78.5 (CH), 71.2 (CH), 41.8 (CH_2), 38.0 (CH_2), 37.5 (CH), 31.4 (CH_2), 27.1 (CH_2), 26.6 (CH_2), 26.3 (CH_2), 26.0 (CH_3), 25.3 (CH_2), 18.9 (CH_2), 18.3 (C), 14.0 (CH_3), –4.07 (CH_3), –4.90 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 352 ($M^{+\cdot}$, 100), 295 (9), 280 (19), 269 (22), 240 (44), 223 (58), 198 (29), 183 (95), 127 (25), 75 (24).

Octyl (*E*)-4-((2*S*-3*S*)-3-{[*tert*-butyl(dimethyl)silyl]oxy}-4-methylenetetrahydro-2*H*-pyran-2-yl)-3-methylbut-2-enoate (27a)

Compound **27a** was prepared according to the protocol described for the synthesis of **27b**; colourless oil; yield: 80%.

IR (film): 2956, 2854, 1717, 1654, 1147, 838 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 5.71 (1 H, s), 5.00 (1 H, br s), 4.82 (1 H, br s), 4.84 (1 H, t, *J* = 6.7 Hz), 3.90–4.00 (1 H, ddd, *J* = 10.8, 4.7, 2.0 Hz), 3.70 (1 H, br d, *J* = 8.8 Hz), 3.28 (1 H, dt, *J* = 10.5, 4.7 Hz), 3.21 (1 H, ddd, *J* = 10.6, 8.8, 2.2 Hz), 1.91 (1 H, dd, *J* = 14.3, 9.1 Hz), 1.48–1.87 (11 H, m), 1.29 (1 H, d, *J* = 13.5 Hz), 0.96 (9 H, s), 0.12 (6 H, s), 0.07 (9 H, s).

^{13}C NMR ($CDCl_3$): δ = 139.3 (C), 134.3 (CH), 128.4 (CH), 128.0 (CH), 127.4 (CH), 114.0 (C), 109.6 (C), 84.8 (CH), 80.2 (CH), 69.1 (CH), 37.3 (CH_2), 36.8 (CH_2), 36.7 (CH_2), 25.6 (CH_3), 25.1 (CH_2), 23.9 (CH_2), 18.0 (C), 16.9 (CH_2), –0.72 (CH_3), –5.21 (CH_3), –5.33 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 438.3 ($M^{+\cdot}$, 5), 257.1 (100), 157.1 (92), 114.1 (88), 97.1 (60), 73.1 (88), 57.1 (60), 43.1 (80).

Anal. Calcd for $C_{28}H_{48}O_4Si_2$ (504.9): C, 68.44; H, 10.57. Found: C, 68.40; H, 10.65.

3-{[*tert*-Butyl(dimethyl)silyl]oxy}-2-[1-{[*tert*-butyl(dimethyl)silyl]oxy}propyl-4-methylene-6-propyltetrahydro-2*H*-pyran (27c)

Compound **27c** was prepared according to the protocol described for the synthesis of **27b**; colourless oil; yield: 79%.

IR (film): 2958, 2930, 2858, 1468, 1254, 1110, 836, 775 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 4.98 (1 H, d, *J* = 1.3 Hz), 4.77 (1 H, d, 1.8 Hz), 3.96–4.21 (1 H, m), 3.67 (1 H, d, *J* = 9.0 Hz), 3.16–3.23 (1 H, m), 3.00 (1 H, ddd, *J* = 10.4, 8.9, 2.7 Hz), 2.33 (1 H, dd, *J* = 13.1, 2.2 Hz), 2.02 (1 H, br t, *J* = 12.1 Hz), 1.86 (1 H, ddd, *J* = 13.3, 9.1, 2.6 Hz), 1.63 (1 H, ddd, *J* = 13.5, 10.4, 4.1 Hz), 1.24–1.54 (4 H, m), 1.12 (3 H, d, *J* = 6.1 Hz), 0.94 (12 H, br s), 0.88 (9 H, s), 0.08 (3 H, s), 0.05 (6 H, br s), 0.03 (3 H, s).

^{13}C NMR ($CDCl_3$): δ = 148.5 (C), 106.6 (CH_2), 81.5 (CH), 79.1 (CH), 75.8 (CH), 66.8 (CH), 43.8 (CH_2), 42.4 (CH_2), 38.6 (CH_2), 22.7 (CH_3), 23.5 (CH_3), 19.6 (CH_2), 18.9 (C), 14.7 (CH_3), –3.69 (CH_3), –3.79 (CH_3), –3.93 (CH_3).

MS (EI, 70 eV): *m*/*z* = 442.3 ($M^{+\cdot}$, 80), 385.2 (38), 253.2 (28), 159.1 (100), 73.0 (47).

HRMS: *m*/*z* calcd for $C_{24}H_{50}O_3Si_2$, 442.3298; found, 442.3305.

***tert*-Butyl(dimethyl){[4-methylene-6-(3-phenyl-1,4-dioxaspiro[4.5]dec-2-yl)prop-2-enyltetrahydro-2*H*-pyran-3-yl]oxy}silane (27d)**

Compound **27d** was prepared according to the protocol described for the synthesis of **27b**; colourless oil; yield: 57%.

IR (film): 2931, 2861, 1449, 1254, 1118, 1065, 831, 777 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 7.30–7.41 (5 H, m), 5.58 (1 H, dq, *J* = 15.4, 6.3 Hz), 5.45 (1 H, dd, *J* = 15.4, 6.6 Hz), 5.08 (1 H, s), 4,91 (1 H, s), 4.83 (1 H, d, *J* = 8.0 Hz), 3.90 (1 H, dd, *J* = 8.0, 5.2 Hz), 3.74 (1 H, d, *J* = 9.1 Hz), 3.42–3.49 (2 H, m), 2.56 (1 H, br d, *J* = 11.3 Hz), 2.33 (1 H, br t, *J* = 12.3 Hz), 0.82–1.96 (10 H, m), 1.67 (3 H, d, *J* = 6.3 Hz), 0.90 (9 H, s), 0.01 (6 H, s).

^{13}C NMR ($CDCl_3$): δ = 146.5 (C), 139.0 (C), 129.6 (CH), 129.2 (CH), 128.3 (CH), 128.0 (CH), 127.1 (CH), 110.4 (C), 107.2 (CH_2), 84.5 (CH), 84.4 (CH), 80.8 (CH), 78.6 (CH), 74.0 (CH), 36.8 (CH_2), 36.5 (CH_2), 29.7 (CH_2), 25.7 (CH_3), 25.1 (CH_2), 23.8 (CH_2), 18.2 (C), 17.8 (CH_3), –4.54 (CH_3), –4.79 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 484.3 ($M^{+\cdot}$, 14), 266.2 (100), 149.1 (14).

Anal. Calcd for $C_{29}H_{44}O_4Si$ (484.8): C, 71.85; H, 9.15. Found: C, 72.05; H, 9.29.

***tert*-Butyl(dimethyl)({4-methylene-2,6-di[(*E*)-prop-1-enyl]tetrahydro-2*H*-pyran-3-yl}oxy)silane (27e)**

Compound **27e** was prepared according to the protocol described for the synthesis of **27b**; colourles oil; yield: 85%.

IR (film): 2934, 2857, 1656, 1462, 1253, 1121, 1063, 836, 776 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 5.66–5.80 (2 H, m), 5.42–5.56 (2 H, m), 5.05 (1 H, q, *J* = 1.3 Hz), 4.84 (1 H, q, *J* = 1.8 Hz), 3.77–3.84 (1 H, m), 3.76 (1 H, d, *J* = 8.7 Hz), 3.52 (1 H, t, *J* = 8.2 Hz), 2.39 (1 H, dd, *J* = 13.2, 2.5 Hz), 2.19 (1 H, bt, *J* = 12.3 Hz), 1.69 (3 H, d, *J* = 6.4 Hz), 1.68 (3 H, d, *J* = 6.4 Hz), 0.90 (9 H, s), 0.03 (3 H, s), 0.02 (3 H, s).

^{13}C NMR ($CDCl_3$): δ = 146.7 (C), 131.1 (CH), 130.1 (CH), 130.0 (CH), 128.0 (CH), 106.7 (CH_2), 84.3 (CH), 79.0 (CH), 74.0 (CH), 41.4 (CH_2), 25.8 (CH_3), 18.2 (C), 17.9 (CH_3), 17.8 (CH_3), –4.49 (CH_3), –4.72 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 308.1 (M^+, 2), 238.2 (100), 181.1 (82), 163.1 (19), 74.9 (28).

Anal. Calcd for $C_{18}H_{32}O_2Si$ (308.5): C, 70.07; H, 10.45. Found: C, 69.94; H, 10.48.

5-Propyl-3-[(trimethylsilyl)methyl]dihydrofuran-2(3*H*)-one (28a); Typical Procedure

A 1 M solution of TBAF (3.51 mL, 3.51 mmol, 2 equiv) in THF was added slowly to a solution of the ene adduct **23b** (0.58 g, 1.75 mmol, 1 equiv) in anhy THF (10 mL). The mixture was stirred overnight (14 h), diluted with Et_2O (10 mL) and then transferred to a separatory funnel containing brine (15 mL). The aqueous phase was washed with Et_2O (3 × 20 mL) and the combined organic extracts dried ($MgSO_4$), filtered and concentrated in vacuo. The crude material was judged to be of sufficient purity to be used as such in the following oxidation step. A solution of this material in CH_2Cl_2 (5 mL) was injected into a 2-necked flask containing 0.9 g of dry 4 Å molecular sieves. Solid NMO (0.31 g, 2.63 mmol, 1.5 equiv) was then added. After cooling to 0 °C, TPAP (20 mg, 0.06 mmol, 0.03 equiv) was added portionwise and the mixture allowed to warm to r.t. The reaction was monitored by TLC, and after 1 h of vigorous stirring, the mixture was filtered on silica gel. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography (silica gel, hexane–EtOAc, 15:1). After removal of the eluent, 304 mg of the title compound was isolated (80%) as a colorless oil.

IR (film): 2958–2857 (C–H), 1772 (C=O), 1466, 1250, 1185, 842 cm^{-1}.

^1H NMR ($CDCl_3$): δ (major isomer) = 4.30 (1 H, ddt, *J* = 10.4, 7.4, 5.3 Hz), 2.58 (1 H, tdd, *J* = 11.9, 8.5, 3.5 Hz), 2.48 (1 H, ddd, *J* = 12.2, 8.5, 5.4 Hz), 1.80–1.70 (1 H, m), 1.60–1.30 (4 H, m), 1.29

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(1 H, dd, *J* = 14.8, 3.3 Hz), 0.94 (3 H, t, *J* = 7.2 Hz), 0.58 (1 H, dd, *J* = 14.8, 11.4 Hz), 0.07 (9 H, s).

^{1}H NMR ($CDCl_3$): δ (minor isomer) = 4.49 (1 H, tt, *J* = 7.7, 4.8 Hz), 2.58 (1 H, m), 2.07 (1 H, ddd, *J* = 12.7, 8.8, 4.7 Hz), 1.95 (1 H, dt, *J* = 12.7, 7.7 Hz), 1.70 (1 H, m), 1.60–1.30 (3 H, m), 1.18 (1 H, dd, *J* = 14.8, 4 Hz), 0.94 (3 H, t, *J* = 7.2 Hz), 0.66 (1 H, dd, *J* = 14.8, 11.1 Hz), 0.07 (9 H, s).

^{13}C NMR ($CDCl_3$): δ = 180.2 (C), 78.2 (CH), 77.9 (CH), 37.8 (CH_2), 37.7 (CH_2), 35.9 (CH_2), 35.5 (CH), 18.7 (CH_2), 18.6 (CH_2), 18.0 (CH_2), 13.8 (CH_3), 13.7 (CH_3), –1.20 (CH_3).

MS (EI, 70 eV): 214 ($M^{+\cdot}$, 13), 199 (100), 171 (9), 143 (12), 129 (16), 73 (38), 55 (13), 43 (18).

Anal. Calcd for $C_{11}H_{22}O_2Si$: C, 61.63; H, 10.34. Found: C 61.65; H 10.47.

5-Cyclohexyl-3-[(trimethylsilyl)methyl]dihydrofuran-2(3*H*)-one (28b)

Compound **28b** was prepared according to the protocol described for the synthesis of **28a**; colourless oil; yield: 70%.

IR (film): 2926–2854 (C–H), 1751 (C=O), 1448, 1249, 1201, 1184, 848 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ (major isomer) = 4.00 (1 H, ddd, *J* = 10.7, 7.7, 5.3 Hz), 2.59–2.47 (1 H, m), 2.38 (1 H, ddd, *J* = 12.1, 8.4, 5.2 Hz), 2.00–1.90 (1 H, m), 1.53–1.40 (2 H, m), 1.24 (1 H, dd, *J* = 14.9, 3.6 Hz), 1.79–1.56 and 1.29–0.75 (9 H, 2 m), 0.57 (1 H, dd, *J* = 14.8, 11.0 Hz), 0.06 (9 H, s).

^{1}H NMR ($CDCl_3$): δ (minor isomer) = 4.21 (1 H, td, *J* = 7.5, 5.6 Hz), 2.59–2.47 (1 H, m), 2.15 (1 H, ddd, *J* = 12.9, 9.1, 5.5 Hz), 2.00–1.90 (1 H, m), 1.86 (1 H, dt, *J* = 12.9, 7.3 Hz), 1.53–1.40 (1 H, m), 1.12 (1 H, dd, *J* = 14.8, 4.1 Hz), 1.79–1.56 and 1.29–0.75 (9 H, 2 m), 0.67 (1 H, dd, *J* = 14.8, 11.3 Hz), 0.06 (9 H, s).

^{13}C NMR ($CDCl_3$): δ (major isomer) = 180.0 (C), 82.3 (CH), 42.6 (CH), 37.4 (CH), 35.5 (CH_2), 29.2 (CH_2), 27.6 (CH_2), 26.2 (CH_2), 25.6 (CH_2), 25.4 (CH_2), 17.86 (CH_2), –1.25 (CH_3).

^{13}C NMR ($CDCl_3$): δ (minor isomer) = 180.7 (C), 82.1 (CH), 42.4 (CH), 35.7 (CH), 33.4 (CH_2), 29.58 (CH_2), 28.6 (CH_2), 28.1 (CH_2), 26.2 (CH_2), 25.2 (CH_2), 19.0 (CH_2), –1.25 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 254 ($M^{+\cdot}$, 8), 239 (100), 221 (44), 171 (8), 159 (48), 147 (82), 143 (64), 130 (22), 73 (98).

Anal. Calcd for $C_{14}H_{26}O_2Si$: C, 66.06; H, 10.30. Found: C, 66.09; H, 10.32.

5-(2-Benzyloxy-1,1-dimethylethyl)-3-[(trimethylsilyl)methyl]dihydrofuran-2(3*H*)-one (28c)

Compound **28c** was prepared according to the protocol described for the synthesis of **28a**; colourless oil; yield: 74%.

IR (film): 3031–2879 (C–H), 1771 (C=O), 1453, 1249, 1181, 843 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ (major isomer) = 7.39–7.28 (5 H, m), 4.53 (1 H, d, *J* = 12.1 Hz), 4.45 (1 H, d, *J* = 12.1 Hz), 4.38 (1 H, dd, *J* = 11.1, 5.5 Hz), 3.35 (1 H, d, *J* = 9 Hz), 3.25 (1 H, d, *J* = 9 Hz), 2.62–2.50 (1 H, m), 2.21 (1 H, ddd, *J* = 12.4, 8.5, 5.5 Hz), 1.63 (1 H, q, *J* = 12.3 Hz), 1.28 (1 H, dd, *J* = 14.9, 3.6 Hz), 0.96 (3 H, s), 0.92 (3 H, s), 0.57 (1 H, dd, *J* = 14.9, 11.1 Hz), 0.04 (9 H, s).

^{1}H NMR ($CDCl_3$): δ (minor isomer) = 7.39–7.28 (5 H, m), 4.53 (1 H, d, *J* = 12.1 Hz), 4.45 (1 H, d, *J* = 12.1 Hz), 4.53–4.45 (1 H, m), 3.33 (1 H, d, *J* = 8.9 Hz), 3.24 (1 H, d, *J* = 8.9 Hz), 2.62–2.50 (1 H, m), 2.79 (1 H, ddd, *J* = 13, 9.5, 6.7 Hz), 1.77 (1 H, ddd, *J* = 13.5, 8, 5.8 Hz), 1.15 (1 H, dd, *J* = 14.8, 3.9 Hz), 0.96 (3 H, s), 0.92 (3 H, s), 0.72 (1 H, dd, *J* = 14.7, 11.4 Hz), 0.04 (9 H, s).

^{13}C NMR ($CDCl_3$): δ = 180.8 (C), 138.8 (C), 128.7 (CH), 127.84 (CH), 127.9 (CH), 82.2 (CH), 76.8 (CH_2), 73.7 (CH_2), 38.1 (CH), 37.8 (C), 36.7 (CH), 32.6 (CH_2), 31.0 (CH_2), 20.5 (CH_3), 20.2 (CH_3), 19.8 (CH_2), 18.1 (CH_2), 0.8 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 334 ($M^{+\cdot}$, 100), 319 (21), 243 (9), 228 (16), 211 (16), 171 (4), 153 (20), 143 (15), 129 (10), 91 (64), 73 (19).

Anal. Calcd for $C_{19}H_{30}O_3Si$: C, 68.22; H, 9.04. Found: C, 68.18; H, 9.10.

3-Methylene-5-propyldihydrofuran-2(3*H*)-one (29a); Typical Procedures

*Method A, Strating from **28a***: A 1.6 M solution of BuLi in hexane (405 μL, 0.65 mmol, 1.15 equiv) was added to freshly distilled diisopropylamine (95 μL, 0.68 mmol, 1.2 equiv) and anhyd THF (3 mL) cooled at –10 °C. The solution was stirred for 30 min, after which time the temperature was lowered to –78 °C and a solution of the lactone **28a** (121 mg, 0.56 mmol, 1 equiv) in THF (2 mL) was injected dropwise. The mixture was stirred for 1 h. After the addition of TMSCl (143 μL, 1.13 mmol, 2 equiv), the cooling bath was removed and the solution stirred for an additional hour. The mixture was then cooled again to –10 °C and NBS (110 mg, 0.62 mmol, 1.1 equiv) was added. After 15 min, TBAF (1 M in THF, 677 μL, 0.68 mmol, 1.2 equiv) was injected dropwise, and the mixture was stirred for 15 min before being diluted with Et_2O (10 ml) and poured onto aq sat. solution of NH_4Cl (15 mL). The aqueous layer was separated and extracted with Et_2O (2 × 10 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. Purification of the resulting pale yellow oil by silica gel chromatography (eluent: hexane–EtOAc, 13:1) afforded the title compound (63 mg, 80%) as a colourless liquid.

*Method B, Starting from **23b***: To a solution of the ene adduct **23b** (0.40 g, 1.22 mmol, 1 equiv) in anhyd THF (10 mL) was added a solution of NBS (0.22 g, 1.22 mmol, 1 equiv) in THF (2 mL). After stirring for 10 min, the THF was removed in vacuo. The resulting white precipitate was filtered off and washed with pentane (20 mL). The filtrate was concentrated under reduced pressure. This crude and extremely sensitive material was directly used in the subsequent double desilylation step. A 1 M solution of TBAF in THF (2.44 mL, 2.44 mmol, 2 equiv) was added to a solution of the crude product dissolved in CH_2Cl_2 (15 mL). The resulting yellow mixture was stirred for 5 min after which time TLC monitoring clearly indicated the end of the reaction. The solution was then diluted with Et_2O (20 mL) and transferred to a separatory funnel containing brine (20 mL). After separation, the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. To a cold (0 °C) solution the resulting oil in MeCN (23 mL) were successively introduced freshly prepared MnO_2 (4 g, 46 mmol, 20 equiv) and KCN (0.15 g, 2.3 mmol, 1 equiv). The resulting black slurry was stirred for 25 min after which time it was filtered through silica gel. The solvent was removed in vacuo and the residue purified by flash column chromatography (silica gel, eluent: 13:1 hexane–EtOAc). Evaporation of the eluent afforded 275 mg of the pure lactone as a colourless oil (61%).

IR (film): 2961–2874 (C–H), 1765 (C=O), 1666 (C=C), 1466, 1399, 1273, 1187, 1001, 940, 813 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 6.20 (1 H, t, *J* = 2.8 Hz), 5.61 (1 H, t, *J* = 2.7 Hz), 4.56–4.47 (1 H, m), 3.00 (1 H, ddt, *J* = 17, 7.6, 2.5 Hz), 2.56 (1 H, ddt, *J* = 17, 5.9, 2.8 Hz), 1.48–1.33 (4 H, m), 0.95 (3 H, t, *J* = 7.2 Hz).

^{13}C NMR ($CDCl_3$): δ = 170.2 (C), 134.9 (C), 121.7 (CH_2), 77.2 (CH), 38.4 (CH_2), 33.6 (CH_2), 18.2 (CH_2), 13.7 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 141 ($M^{+\cdot}$ + H^+, 80), 140 ($M^{+\cdot}$, 36), 111 (12), 97 (100), 69 (22), 43 (21).

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5-Cyclohexyl-3-methylenedihydrofuran-2(3*H*)-one (29b)
This lactone was prepared using the reaction conditions described for compound **29a**, starting from **28b** (70%) as well as from **23c** (76%); colourless oil.

IR (film): 2932–2851 (C–H), 1754 (C=O), 1666 (C=C), 1445, 1278, 985, 945, 893 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 6.20 (1 H, t, *J* = 2.7 Hz), 5.60 (1 H, t, *J* = 2.7 Hz), 4.24 (1 H, q, *J* = 7.1 Hz), 2.95 (1 H, ddt, *J* = 17, 7.7, 2.7 Hz), 2.67 (1 H, ddt, *J* = 17, 6.6, 2.7 Hz), 1.98–1.44 and 1.28–0.97 (6 H and 5 H, 2 m).

^{13}C NMR ($CDCl_3$): δ = 170.2 (C), 134.9 (C), 121.3 (CH_2), 81.2 (CH), 43.0 (CH), 31.2 (CH_2), 28.0 (CH_2), 27.6 (CH_2), 26.2 (CH_2), 25.6 (CH_2), 25.5 (CH_2).

MS (EI, 70 eV): *m*/*z* (%) = 180 ($M^{+\cdot}$, 60), 152 (42), 134 (40), 97 (100), 83 (12), 69 (20), 68 (16), 55 (19), 41 (8).

5-(2-Benzyloxy-1,1-dimethylethyl)-3-methylenedihydrofuran-2(3*H*)-one (29c)
This lactone was prepared using the reaction conditions described for compound **29a**, starting from **28c** (74%) as well as from the ene-adduct **23c** (66%); colourless oil.

IR (film): 3036, 3030, 2966–2851 (C–H), 1764 (C=O), 1664 (C=C), 1477, 1280, 1130, 1100, 985, 945, 813, 737, 698 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 7.41–7.20 (5 H, m), 6.20 (1 H, t, *J* = 3.0 Hz), 5.60 (1 H, t, *J* = 2.7 Hz), 4.57 (1 H, t, *J* = 7.4 Hz), 4.52 (1 H, d, *J* = 11.5 Hz), 4.44 (1 H, d, *J* = 11.5 Hz), 3.37 (1 H, d, *J* = 9 Hz), 3.25 (1 H, d, *J* = 9 Hz), 2.83 (2 H, dt, *J* = 7.5, 2.7 Hz), 0.95 (6 H, s).

^{13}C NMR ($CDCl_3$): δ = 170.3 (C), 138.4 (C), 135.2 (C), 128.5 (CH), 127.4 (CH), 121.3 (CH_2), 80.9 (CH), 76.1 (CH_2), 73.35 (CH_2), 38.3 (C), 28.6 (CH_2), 19.9 (CH_3), 19.4 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 261 ($M^{+\cdot}$ + H^+, 4), 242 (40), 213 (17), 186 (38), 139 (22), 91 (100), 69 (21).

HRMS: *m*/*z* calcd for $C_{16}H_{20}O_3$, 260.1412; found, 260.1413.

(*Z*)-3-Methylene-5-oct-5-enyldihydrofuran-2(3*H*)-one (29d)
This lactone was prepared using the reaction conditions described for compound **29a**, starting from ene adduct **23e**; colourless oil; yield: 57%.

IR (film): 3003–2859 (C–H), 1765 (C=O), 1665 (C=C), 1462, 1275, 1002 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 6.21 (1 H, t, *J* = 2.7 Hz), 5.61 (1 H, t, *J* = 2.7 Hz), 5.45–5.19 (2 H, m), 4.51 (1 H, m), 3.04 (1 H, ddt, *J* = 17, 7.7, 2.7 Hz), 2.56 (1 H, ddt, *J* = 17, 6.3, 2.7 Hz), 2.06–1.98 (4 H, m), 1.75–1.30 (6 H, m), 0.94 (3 H, t, *J* = 7.7 Hz).

^{13}C NMR ($CDCl_3$): δ = 170.2 (C), 134.8 (C), 132.0 (CH), 128.5 (CH), 121.7 (CH_2), 77.5 (CH), 36.2 (CH_2), 33.6 (CH_2), 29.4 (CH_2), 26.9 (CH_2), 24.5 (CH_2), 20.5 (CH_2), 14.3 (CH_3).

MS (EI, 70 eV): *m*/*z* (%) = 208 ($M^{+\cdot}$, 40), 180 (4), 179 (22), 123 (100), 97 (46), 81 (40), 67 (40), 55 (12), 41 (8).

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.33; H, 9.63.

3-Methylene-5-non-3-enyldihydrofuran-2(3*H*)-one (29e)
This lactone was prepared using the reaction conditions described for compound **29a**, starting from the corresponding ene adduct; colourless oil; yield: 60%.

IR (film): 2956, 2926, 2854, 1766, 1666, 1398, 1278, 1120, 970 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 6.21 (1 H, t, *J* = 2.8 Hz), 5.61 (1 H, t, *J* = 2.6 Hz), 5.54 (1 H, dt, *J* = 15.0, 6.3 Hz), 5.43 (1 H, dt, *J* = 15.3, 6.3 Hz), 4.51 (1 H, tt, *J* = 7.6, 6.0 Hz), 3.04 (1 H, ddt, *J* = 17.1, 7.5, 2.6 Hz), 2.57 (1 H, ddt, *J* = 17.1, 6.3, 2.8 Hz), 2.04–2.17 (2 H, m), 1.96 (1 H, q, *J* = 6.7 Hz), 1.58–1.86 (2 H, m), 1.16–1.36 (3 H, m), 0.87 (3 H, t, *J* = 6.9 Hz).

^{13}C NMR ($CDCl_3$): δ = 170.2 (C), 134.7 (C), 132.1 (CH), 128.0 (CH), 121.8 (CH_2), 76.8 (CH), 38.2 (CH_2), 33.5 (CH_2), 32.5 (CH_2), 31.3 (CH_2), 29.1 (CH_2), 27.9 (CH_2), 22.5 (CH_2), 14.0 (CH_3).

MS (EI, 70 eV) : 222.2 (M^+, 7), 205.2 (12), 177.2 (38), 123.1 (9), 110.1 (100), 97.0 (23), 81.1 (28), 68.1 (16).

Anal. Calcd for $C_{14}H_{22}O_2$ (222.7): C, 75.46; H, 10.02. Found: C, 75.50; H, 9.96.

3-Methylene-5-pent-4-enyldihydrofuran-2(3*H*)-one (29f)
This lactone was prepared using the reaction conditions described for compound **29a**, starting from ene adduct **23f**.

IR (film): 3288, 2950–2859, 2116, 1760 (C=O), 1665 (C=C), 1436, 1344, 1276, 1130, 997 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 6.23 (1 H, t, *J* = 2.7 Hz), 5.64 (1 H, t, *J* = 2.5 Hz), 4.55 (1 H, quint, *J* = 6.3 Hz), 3.08 (1 H, ddt, *J* = 17.3, 7.7, 2.7 Hz), 2.56 (1 H, ddt, *J* = 17, 6, 3 Hz), 2.29–2.21 (2 H, m), 1.97 (1 H, t, *J* = 2.8 Hz), 1.82–1.53 (4 H, m).

^{13}C NMR ($CDCl_3$): δ = 170.0 (C), 134.5 (C), 121.3 (CH_2), 83.4 (C), 76.8 (CH), 70.0 (CH), 35.1 (CH_2), 33.6 (CH_2), 23.8 (CH_2), 18.0 (CH_2).

MS (EI, 70 eV): *m*/*z* (%) = 163 ($M^{+\cdot}$, 8), 136 (20), 123 (44), 120 (9), 97 (100), 69 (21), 68 (24).

Anal. Calcd for $C_{13}H_{20}O_2$: C, 73.15; H, 7.37. Found: C, 72.88; H, 7.39.

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