Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron
Tetrahedron 60 (2004) 2673–2692

Further observations on the rhodium (I)-catalysed tandem hydrosilylation-intramolecular aldol reaction

Marta Freiría,[a] Andrew J. Whitehead,[b] Derek A. Tocher[a] and William B. Motherwell[a,*]

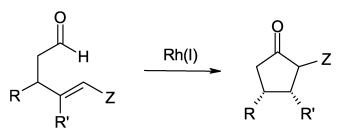
[a]*Department of Chemistry, University College London, Christopher Ingold Laboratories, 20 Gordon Street, London WC1H 0AJ, UK*
[b]*Chemical Development Division, GlaxoSmithKline Research and Development, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY, UK*

Received 3 October 2003; revised 3 December 2003; accepted 18 December 2003

Abstract—The rhodium (I) catalysed tandem hydrosilylation-intramolecular aldol reaction provides a simple strategy for construction of a range of usefully functionalised five-membered rings from readily prepared 6-oxo-2-hexenoates in good yield and with good to excellent stereoselectivity. A series of silanes and rhodium catalysts have been investigated. Stereoselectivity proved to be highly dependant on the catalyst as well as on the substitution pattern of the parent substrate. The extension of this methodology for the synthesis of larger ring sizes has also been evaluated.

1. Introduction

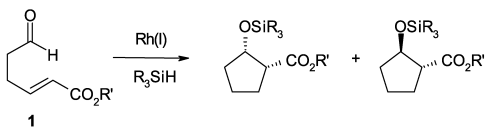
Highly stereoselective cyclisation methods provide a powerful tool for the construction of the carbocyclic skeletons found in both natural and non-natural molecules of biological importance. Moreover, the dictates of modern day organic synthesis also require that the overall process should be highly efficient in terms of atom economy. Within this context, the rhodium catalysed intramolecular hydroacylation reaction of 4-alkenals, first introduced by Sakai,[1] (Scheme 1, R=R′=alkyl, Z=H) provides a very good example of an extremely powerful method for the preparation of functionalised cyclopentanone derivatives,[2–9] especially in view of the *cis* stereoselectivities observed and the elegant studies by Bosnich[10] and Sakai[11] on the development of chiral catalysts for the asymmetric variant.



Scheme 1. General representation of the rhodium (**I**)-catalysed intramolecular hydroacylation of 4-alkenals.

On closer inspection, however, this protocol does suffer from some limitations, which include poorer yields for substrates either with heteroatom substituents or with additional groups located at the alkene terminus (Z), as well as in attempted cyclisations to give larger rings. Furthermore, competitive decarbonylation of the rhodium acyl complex generated after initial oxidative addition to the aldehyde can lead to undesired side reactions, and since the catalyst is then rendered inactive, relatively large amounts (20–50 mol%) have often been required for many examples.

In light of the above constraints, we therefore, sought to develop an alternative general methodology through the incorporation of ester functionality at the alkene terminus of the 4-pentenal unit (Scheme 1, Z=ester). The selection of a 6-oxo-2-hexenoate unit such as **1** then provides the opportunity for a tandem sequence involving transition metal mediated hydrosilylation followed by intramolecular aldol reaction as a route to substituted cycloalkanols (Scheme 2). Such an approach does of course find intermolecular precedent in terms of the sequential reductive aldol reaction which has witnessed spectacular development in recent years.[12] From the outset of our own study, even although it is often falsely assumed that an intramolecular variant of any given reaction will automatically follow on from its intermolecular congener, we were aware that chemoselectivity issues such as competing reduction of the aldehydic carbonyl group remained to be assessed, especially given that stepwise



Scheme 2. General representation of the rhodium (**I**)-catalysed tandem hydrosilylation-intramolecular aldol reaction of 6-oxo-2-hexenoates.

Keywords: Tandem hydrosilylation; Aldol; Rhodium; intramolecular; catalytic.
* Corresponding author. Tel.: +44-207-6797533; fax: +44-207-6797524; e-mail address: w.b.motherwell@ucl.ac.uk

0040–4020/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2003.12.057

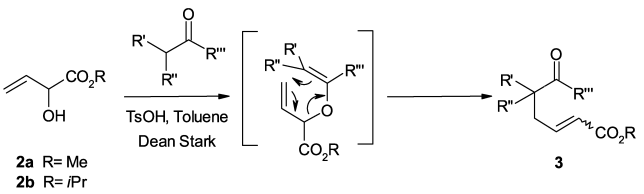
introduction of substrates is not possible in the intramolecular mode.

Within the large manifold of cascade reactions,[13] stereoselective tandem conjugate addition–cyclisation reactions have been extensively studied.[14] In particular, Michael addition followed by intramolecular aldolisation has proven to be a very useful strategy. Such ring closing reactions are believed to proceed via 1,4-addition of the organometallic or heteronucleophilic reagent to the enoate, with subsequent addition of the resultant enolate to the aldehyde.[15] Murphy[16] has recently reported a tandem Michael-intramolecular aldol mediated by secondary amines, thiols and phosphines. Lithium thiolates[14n] and $TiCl_4$–R_4NX combinations[17] have also been used to initiate such cyclisations; however, these heteronucleophiles remain covalently attached in the cyclisations products. There are also several examples in the literature of non-catalysed tandem Michael-intramolecular aldol reactions using stoichiometric amounts of organometallic hydrides such as Stryker's reagent $[(Ph_3P)CuH]_6$[18] and di-*n*-butyliodotin hydride (n-Bu_2SnIH).[19] We now report, in full detail[15] the results of our own study in which inexpensive and more environmentally benign organosilanes were selected for the initial conjugate addition step. An essentially contemporaneous parallel investigation by an American group[20] has also adopted a similar tandem-hydrosilylation intramolecular aldol sequence but chosen to investigate oxo-enone substrates and to use cobalt catalysts.

2. Results and discussion

2.1. Preparation of cyclisation substrates

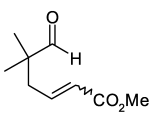
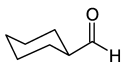
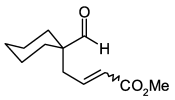
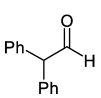
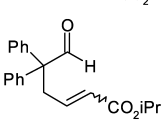
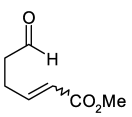
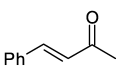
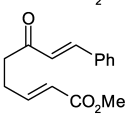
Substituted 6-oxo-2-hexenoate units such as **3** are proving to be especially valuable for a variety of tandem Michael addition-aldol processes and similar variants.[16,20] They are traditionally prepared either by Wittig olefination[21] or by relatively long multistep sequences.[22] For our present study, we elected to develop the simple atom efficient route[23] shown in Scheme 3 which requires acid catalysed condensation of a 2-hydroxy-3-butenoate ester with an aldehyde followed by in situ Claisen rearrangement of the allyl alkenyl ether intermediate (Scheme 3).



Scheme 3. General synthesis of substituted 6-oxo-2-hexenoates.

The required 2-hydroxy-3-butenoates **2a**–**b** were easily accessed from commercially available 2-acetoxy-3-butenenitrile using a literature method[24] involving dissolution in a saturated hydrochloric acid solution of the appropriate alcohol. A mixture of **2** with slightly more than one molar equivalent of the carbonyl compound was then refluxed in toluene for 48 h in the presence of a catalytic amount of *p*-toluenesulfonic acid and using a Dean and Stark trap for azeotropic removal of water. The corresponding 6-oxo-2-hexenoate products, produced as a mixture of geometric isomers, were then isolated by flash chromatography. Thus, as indicated in Table 1, aliphatic and aromatic 5,5-disubstituted 6-oxo-2-hexenoates **4**, **5a**, **5b** and **6** were obtained from the corresponding aldehydes in 49–64% yield in a 2:1 ratio (entries 1, 2 and 3). Synthesis of the parent unsubstituted derivative **7** was first attempted using acetaldehyde. However, this attempt was unsuccessful presumably due to the high volatility of acetaldehyde. However, when acetaldehyde was replaced by its less

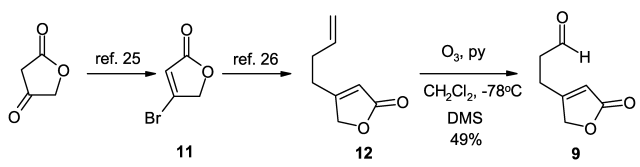
Table 1. Substituted 6-oxo-hexenoate derivatives produced via Scheme 3

Entry	Electrophile	Product		Yield (%)[a]	Ratio *E*/*Z*
1			**4**	53	2:1
2			**5a** (**5b**)	49 (61)[b]	1.5:1
3			**6**	64	2:1
4			**7**	46[c]	2.2:1
5			**8**	58	Only *E*

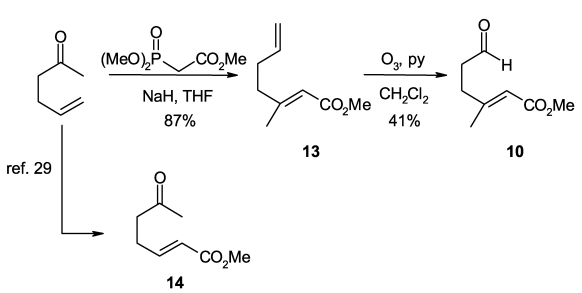
[a] Isolated yields.
[b] Yield of the correspondent isopropyl ester derivative starting from butenoate **2b**.
[c] The reaction was carried out using a Soxhlet extractor in the presence of 4 Å MS for the removal of ethanol.

volatile diethyl acetal congener, reaction proceeds to give **7** in 46% yield in a 2.2:1 ratio (entry 4). 6-Oxo-2,7-octadienoate **8** was also synthesised in 58% yield from benzylideneacetone as a single *E* diastereomer (entry 5). Additional examples and further preparative and stereochemical aspects on this [3,3] sigmatropic route have been discussed in our preliminary study.[23]

Substitution at *C*-3 was also sought and two different cyclisation substrates **9** and **10** were accordingly selected. Thus, 4-bromo-2(5*H*)-furanone **11** was prepared from tetronic acid following the procedure of Jas using oxalyl bromide and a catalylic amount of dimethylformamide in dichloromethane (Scheme 4).[25] Subsequent palladium-catalysed substitution reaction of **11** with a homoallylzinc reagent afforded **12** as described by Negishi.[26] Finally, 3-(5-oxo-2,5-dihydrofuran-3-yl)-propionaldehyde **9** was obtained in 49% yield by selective ozonolysis of the terminal double bond of alkene **12** in the presence of one volume percent of pyridine.[27] Methyl 3-methyl-6-oxo-2-hexenoate **10** was prepared from commercially available 5-hexen-2-one. We note parenthetically that the Horner–Wadsworth–Emmons olefination using trimethylphosphonoacetate and sodium hydride proceeded much more efficiently (87% vs. 43%) when the reaction was conducted in refluxing tetrahydrofuran rather than in 1,2-dimethoxyethane as previously reported for the corresponding ethyl ester.[28] Intermediate **13** was obtained as a 2:1 mixture of *E* and *Z* isomers, which were separated by chromatography (Scheme 5). Selective ozonolysis of **13** followed by reductive work up afforded **10** in 41% yield.



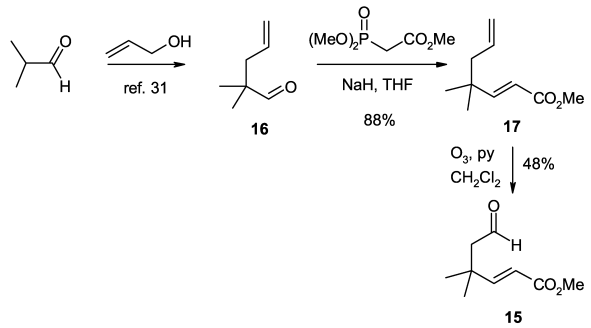
Scheme 4. Synthesis of 3-(5-oxo-2,5-dihydrofuran-3-yl)propionaldehyde.



Scheme 5. Syntheses of methyl (*E*)-3-methyl-6-oxo-2-hexenoate and methyl (*E*)-6-oxo-2-heptenoate from 5-hexen-2-one.

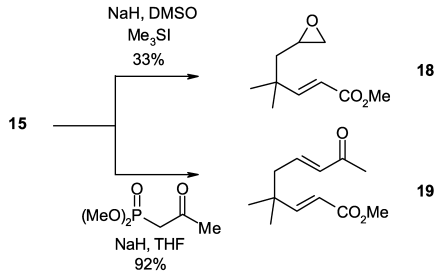
Methyl (*E*)-6-oxo-2-heptenoate **14** was also prepared from 5-hexen-2-one following a literature procedure.[29]

The synthesis of methyl 4,4-dimethyl-6-oxo-2-hexenoate **15** has already been reported by a multistep process which includes several protection and deprotection steps.[30] We have prepared it by an alternative procedure in three steps starting from isobutyraldehyde and allyl alcohol. Thus, 2,2-dimethyl-4-pentanal **16**, which is also commercially available, was synthesised by the method reported by Brannock from allyl alcohol and isobutyraldehyde via Claisen rearrangement of the allyl alkenyl ether intermediate.[31] Subsequent Horner–Wadsworth–Emmons olefination of the aldehyde with trimethylphosphonoacetate in the presence of sodium hydride afforded **17** in 88% yield as a single *E* diastereoisomer. Selective ozonolysis of the terminal alkene in **17** afforded compound **15** in 48% yield (Scheme 6). This method offers the advantage of permitting substituent variation at *C*-4 of the resulting 6-oxo-2-hexenoates of type **15** by a simple choice of the appropriate starting aldehyde.



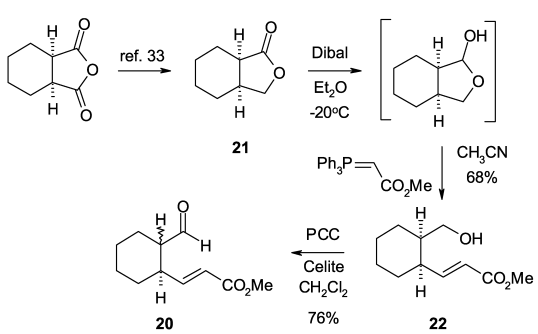
Scheme 6. Synthesis of methyl (*E*)-4,4-dimethyl-6-oxo-2-hexenoate.

Substrates **18** and **19** were also prepared from aldehyde **15** by Corey sulfur ylide epoxidation[32] and Horner–Wadsworth–Emmons olefination, respectively, (Scheme 7).



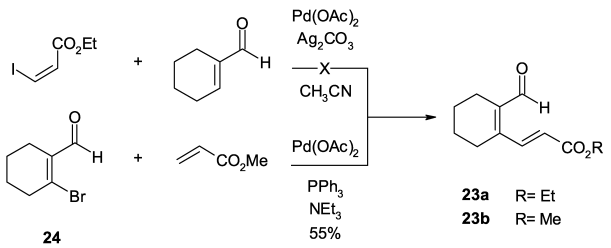
Scheme 7. Syntheses of methyl (*E*)-4,4-dimethyl- 5-oxiranyl-2-pentenoate and methyl (*E*)-4,4-dimethyl-8-oxo-2,6-nonadienoate.

In order to assess the feasibility of generating even more strained bicyclic systems in the tandem cyclisation sequence, substrate **20** was synthesised from commercially available *cis*-cyclohexane-1,2-dioic acid anhydride (Scheme 8). Lactone **21** was obtained in 70% yield by reduction of the corresponding anhydride with sodium borohydride, using the general procedure of Bailey and



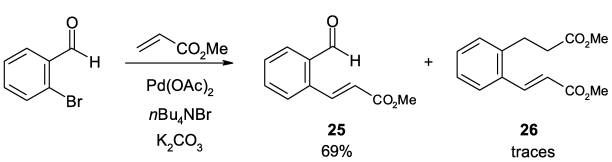
Scheme 8. Synthesis of methyl (*E*)-3-(2-formyl-cyclohexyl)-acrylate.

Johnson.[33] Treatment of lactone **21** with DIBAL in ether at −20 °C resulted in rapid and quantitative reduction to the lactol, which was subsequently reacted with methyl(triphenylphosphoranylidene)acetate in acetonitrile to afford alcohol **22** in an overall 68% yield as the single *E* isomer. Oxidation of alcohol **22** with pyridinium chlorochromate (PCC) gave the desired aldehyde **20** in 76% yield with some epimerization at the α centre of the newly formed aldehyde (*cis*/*trans*, 6:1). The viability of using a completely conjugated system in our cyclisation reaction was tested by selection of substrate **23** which was envisaged via a Heck strategy. In the first instance, 1-cyclohexene-1-carboxaldehyde and ethyl (*Z*)-3-iodo-propenoate, both commercially available, were stirred in acetonitrile at room temperature in the presence of 0.05 equiv. of palladium acetate and 1.5 equiv. of silver carbonate (Scheme 9). Coupling failed to occur and only starting material was recovered after 3 days. The yields and rates of reaction in Heck couplings are known to decrease with increasing size and number of substituents around the double bond in the olefin.[34] Coupling was, therefore, attempted between 2-bromo-1-cyclohexenecarboxaldehyde **24** and a monosubstituted olefin, methyl acrylate, in the presence of triethylamine and a catalytic amount of $Pd[(PPh_3)_3]_2(OAc)_2$ at reflux. In this way, the desired substrate **23b** was obtained in 55% yield as a single *E* diastereoisomer. The required aldehyde **24** was available from cyclohexanone by the bromo analogue of the Vilsmeier reaction according to the procedure of Arnold and Holy.[35]



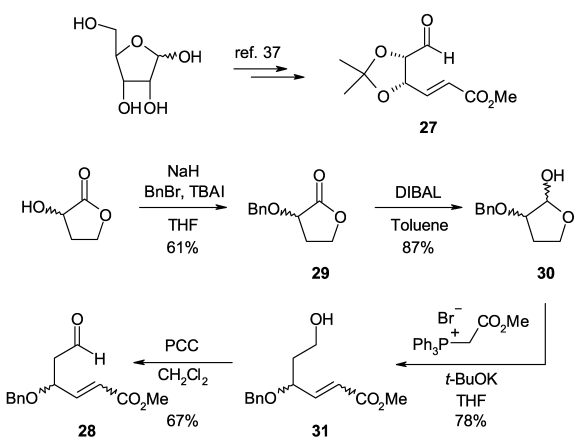
Scheme 9. Synthesis of methyl (*E*)-3-(2-formyl-cyclohex-1-enyl)-acrylate

Benzoannulated substrate **25** was then prepared from *o*-bromobenzaldehyde in order to investigate the compatibility of a 4,5-fused aromatic ring in the cyclisation reaction. Although Rodrigo[36] has observed that formation of the doubly substituted product **26** is favoured over the conventional Heck product **25** when the reaction is run in a concentrated solution in the presence of excess methyl acrylate (Scheme 10), the use of moderate amounts of methyl acrylate and more dilute solutions led to the optimum yield of our desired Heck product **25** which was obtained in 69% yield in pure form after chromatography.



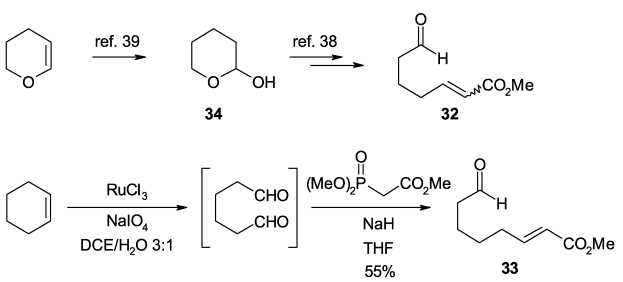
Scheme 10. Synthesis of methyl (*E*)-3-(2′-formylphenyl)-propenoate

Isopropylidene and benzyl ether functionalities were chosen to investigate whether tandem hydrosilylation cyclisation was compatible with heteroatomic substituents. Homochiral pentenal **27** was accessible from D-ribose by a literature procedure (Scheme 11).[37] Substrate **28** was prepared from commercially available racemic α-hydroxy-γ-butyrolactone, which was firstly protected using benzyl bromide in the presence of a catalytic quantity of tetrabutylammonium iodide. The resulting α-benzyloxy-γ-butyrolactone **29** was then reduced to the corresponding lactol **30** with DIBAL, which gave a mixture of *cis* and *trans* diastereoisomers in a 2:1 ratio. The observed *cis* selectivity presumably arises via subsequent equilibration which favours the *cis* lactol. Wittig olefination of lactol **30** with carbomethoxymethyltriphenylphosphonium bromide and potassium *tert*-butoxide gave **31** in 78% yield as a mixture of diastereoisomers. Subsequent oxidation of **31** with PCC afforded substrate **28** in 67% yield as two separable diastereoisomers.



Scheme 11. Methyl (4*S*, 5*S*)-6-oxo-4,5-isopropylidenedioxy-2-hexenoate and methyl 4-benzyloxy-6-oxo-2-hexenoate.

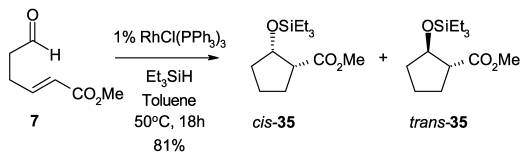
Finally, methyl 7-oxo-2-heptenoate **32** and its higher homologue **33** were prepared in order to explore the feasibility of constructing larger ring sizes. Thus, substrate **32** was prepared by a general route from 1-hydroxypyran **34**,[38] which was obtained by acid hydrolysis of commercially available 3,4-dihydropyran (Scheme 12).[39] Ruthenium trichloride catalysed oxidative cleavage of cyclohexene[40] followed by subsequent Horner–Wadsworth–Emmons olefination of resultant adipaldehyde, provided (*E*)-methyl 8-oxo-2-octenoate **33** in one step in 55% yield, accompanied by the doubly substituted diester (ca. 20%), which was easily separated by chromatography on silica gel.



Scheme 12. Methyl 7-oxo-2-heptenoate and methyl (*E*)-8-oxo-2-octenoate.

2.2. Cyclisation studies

In our preliminary study of the rhodium (I)-catalysed tandem hydrosilylation intramolecular aldol reaction, optimal conditions for the reaction of the model substrate methyl (*E*)-6-oxo-2-hexenoate (*E*)-**7** with Wilkinson's catalyst using triethylsilane as the hydride donor were first developed and these are summarized in Scheme 13 and Table 2 (entry 1). The significant observation was also made that the stereochemical outcome of the reaction was not altered when the (*Z*) geometrical isomer of **7** was employed as substrate in an otherwise identical reaction, thereby indicating that the initial alkene geometry does not play a crucial role in influencing the possible transition states adopted for the subsequent intramolecular aldol reaction. Since *E*/*Z* mixtures of α,β-unsaturated esters can, therefore, be used, this aspect is also clearly of preparative value.



Scheme 13. Rhodium (I)-catalysed tandem hydrosilylation-intramolecular aldol reaction of methyl (*E*)-6-oxo-2-hexenoate.

Table 2. Silane and catalyst screen

Entry	Silane[a]	Catalyst[b]	Ligand[c]	Yield[d] (%)	*c*-**35**/*t*-**35**
1	Et_3SiH	$RhCl(PPh_3)_3$	—	81	2.0:1.0
2	Me_2PhSiH	$RhCl(PPh_3)_3$	—	62	2.4:1.0
3	$MePh_2SiH$	$RhCl(PPh_3)_3$	—	49	2.8:1.0
4	Ph_3SiH	$RhCl(PPh_3)_3$	—	42	1.5:1.0
5	Et_3SiH	$[RhCl(C_8H_{14})_2]_2$[e]	PCy_3	79	2.5:1.0
6	Et_3SiH	$[RhCl(C_8H_{14})_2]_2$[e]	DIPHOS[f]	78	3.3:1.0
7	Et_3SiH	$[RhCl(C_8H_{14})_2]_2$[e]	$pTol_3P$	27	1.0:2.0
8	Et_3SiH	$[RhCl(C_8H_{14})_2]_2$[e]	$pTol_3P$	53	2.0:1.0
9	Et_3SiH	$[RhCl(C_8H_{14})_2]_2$[e]	pAn_3P[g]	61	1.0:1.6
10	Et_3SiH	$[RhCl(C_8H_{14})_2]_2$[e]	pAn_3P[g]	51	2.0:1.0
11	Et_3SiH	$RhH(PPh_3)_4$[h]	—	81	1.0:11.0

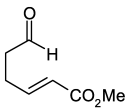
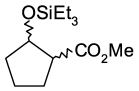
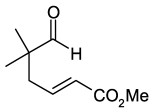
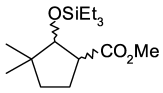
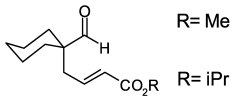
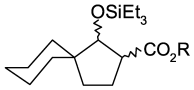
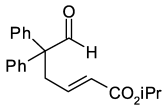
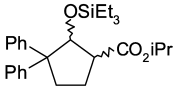
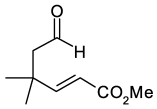
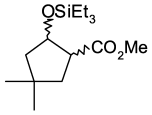
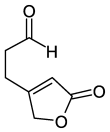
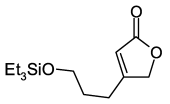
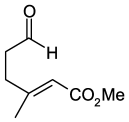
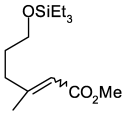
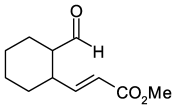
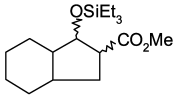
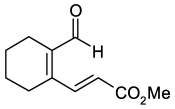
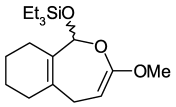
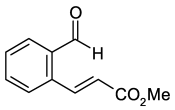
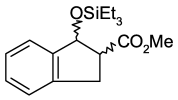
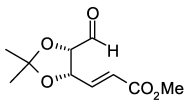
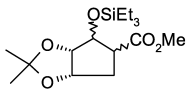
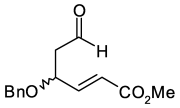
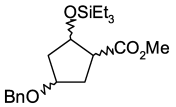
[a] 2.1 equiv. of silane used.
[b] 1 mol% catalyst unless otherwise stated.
[c] 4 equiv. ligand w.r.t. catalyst unless otherwise stated.
[d] Yield of isolated products.
[e] 2.5 mol% catalyst.
[f] 2 equiv. ligand w.r.t. catalyst, DIPHOS (1,2-bis(diphenylphosphino)ethane).
[g] An, anisole.
[h] Reaction complete after 6 h.

At this stage, examination of the results from a catalyst and silane screen (Table 2) revealed some useful trends. Thus, in reactions employing Wilkinson's catalyst, the use of silanes of increasing steric bulk (entries 1–4) led to reduced yields of the cyclopentanol **35**, even although the *cis* selectivity was maintained. Variation of the ancillary phosphine was also studied using triethylsilane and chlorobis(cyclooctene) rhodium (I) dimer (entries 5–10), and found to play a significant role, with the best combination of yield and *cis* stereoselectivity achieved through selection of the bidentate DIPHOS ligand (entry 6). The most intriguing observation of all, however, was that a complete reversal of stereoselectivity in favour of *trans*-**35** was noted when hydridotetrakis(triphenylphosphine) rhodium (I) was employed as the catalyst (entry 11). Although the observed preference in our preliminary study[15a] was relatively modest (*cis*/*trans*, 1:2) further work using carefully prepared rhodium catalyst now reproducibly favours the *trans* product in high yield and with excellent selectivity (*cis*/*trans*, 1.0:11.0).

We then elected to examine the synthetic utility of the reaction using both Wilkinson's catalyst[41] and hydridotetrakis(triphenylphosphine) rhodium (I).[42] The variety of variously functionalised substituted 6-oxo-2-hexenoate derivatives previously described were accordingly submitted to our optimised cyclisation conditions (2.1 M equiv. of triethylsilane and 1 mol% of rhodium catalyst in toluene at 50 °C) in order to probe such issues as chemoselectivity and the influence of the substitution pattern on the tandem sequence. The results are shown in Table 3.

Thus, comparison of entries 2–5 reveals that whilst geminal substitution at *C*-5 (entries 2–4) leads to a reduction in yield relative to the unsubstituted parent (entry 1) this is not necessarily the case for the *C*-4 *gem* dimethyl group (entry 5). Although all four cases might be anticipated to benefit from the Thorpe–Ingold effect,[43] it would, therefore, appear that the intramolecular aldol step is more sensitive to the presence of a neighbouring quaternary carbon atom than is the initial hydrosilylation step. Entry 3 also demonstrates that no significant difference in yield was observed when the methyl ester **5a** was replaced by its *iso*-propyl analogue in **5b**. Contrastingly, our examination of substrates possessing a trisubstituted α,β-unsaturated lactone or ester (entries 6 and 7) reveals that the incorporation of additional alkyl substitution at this site completely blocks the conjugate addition step and simple hydrosilylation of aldehydic functionality then becomes the dominant process. Comparison of entries 8, 9 and 10 reveals that the success of the intramolecular aldol addition step can be subject to very subtle conformational and stereoelectronic restrictions. Thus, whilst entries 8 and 10 provide a very encouraging basis for construction of the linearly fused bicyclo [4,3,0] system in both the hydrindane **42** (entry 8) and indane skeletons **44** (entry 10), the isolation of the hexahydrobenzo[*c*]oxepin **43** from the fully conjugated precursor **23b** was unexpected. In this latter instance, cyclisation of the ester enolate via oxygen to give the seven membered ring is clearly favoured, and formation of the silyl ether functionality in the product must be fast and hence preclude the reverse reaction. Finally, in view of the ever increasing importance of constructing carbocycles from the chiral pool of carbohydrates,[44–48] it was also of interest to examine substrates containing ancillary isopropylidene (entry 11) and benzyl ether (entry 12) functionality. The functional group tolerance exhibited in these latter two cyclisations provides an indication that this approach may be of promise for cyclopentanoid construction from carbohydrates. In terms of stereoselectivity, comparison of the two catalysts A and B reinforces the observation made in the parent system (entry 1) that the outcome can be significantly influenced by this choice. Thus, whilst Wilkinson's catalyst consistently exhibits a modest *cis* preference for formation of the β-triethylsiloxy ester unit, selection of hydridotetrakis(triphenylphosphine) rhodium (I) generally favours the *trans* congener. However, the diastereoisomeric ratios with the latter catalyst are evidently much more strongly

Table 3. Rhodium (I)-catalysed tandem cyclisation of substituted 6-oxo-2-hexenoate derivatives

Entry	Substrate		Product		Catalyst[a]	Yield (%)[b]	*cis*/*trans*[c]
1		**7**		**35**	A	81	3.0:1.0
					B	81	1.0:11.0
2		**4**		**36**	A	56	1.0:1.0
					B	62	6.4:1.0
3	 R= Me R= iPr	**5a**		**37a**	A	54	2.0:1.0
		5b		**37b**	B	59	1.0:2.0
4		**6**		**38**	B	68	1.0:2.5
5		**15**		**39**	A	93	2.2:1.0
					B	61	1.0:11.0
6		**9**		**40**	A	43	—
7		**10**		**41**	A	35	—
					B	39	—
8		**20**		**42**	B	81[d]	—
9		**23b**		**43**	B	88	—
10		**25**		**44**	A	61[e]	1.5:1.0
					B	69[e]	1.0:20.0
11		**27**		**45**	A	65	2.0:5.4:2.0:1.0[f]
					B	81	5.4:4.0:2.0:1.0[f]
12		**28**		**46**	A	81	1.7:1.5:1.0:1.0[g]
					B	72	1.2:1.0:1.2:1.7[g]

[a] A, $RhCl(PPh_3)_3$; B, $RhH(PPh_3)_4$.
[b] Isolated yields after chromatography on silica gel.
[c] Diastereomeric ratio in the crude material determined by ^1H NMR.
[d] Isolated as a complex mixture of diastereoisomers.
[e] Using 3 mol% of catalyst.
[f] See Figure 2 for assignment of the structures, *a*/*b*/*c*/*d*.
[g] Relative stereochemistry: OBn/$OSiEt_3$–$OSiEt_3$/CO_2Me; *trans*–*trans*/*cis*–*cis*/*cis*–*trans*; *trans*–*cis*.

influenced by the exact nature of the substrate substitution pattern and can, at times, be excellent (entries 1, 5 and 10).

In all cases, the structure of the major diastereoisomer was assigned on the basis of the values of coupling constants measured in ^{1}H NMR. In general, coupling constant $J(H^1-H^2)$=3.5–6.5 Hz indicates *cis* relative stereochemistry, whereas $J(H^1-H^2)$=5.5–9.5 Hz accounts for the *trans* isomer. This assignment could be confirmed by X-ray crystallographic analysis of compound **38**, since the minor *cis* diastereoisomer crystallised out of the mixture of isomers giving suitable crystals (Fig. 1).

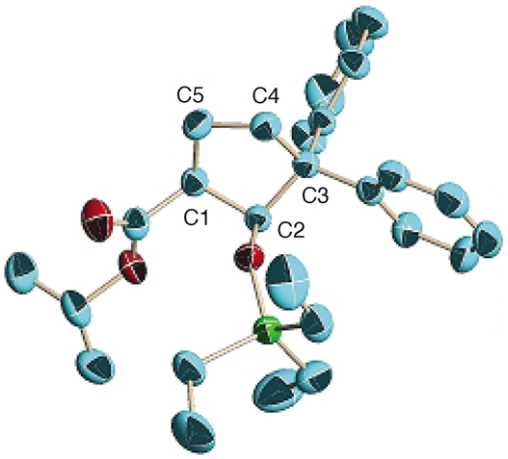


Figure 1. Crystal structure of compound **38**.

When more than two stereogenic centres are present, proton assignment and subsequent determination of all possible diastereoisomers by experimental means was extremely difficult. To our delight, however, careful column chromatography allowed the separation of three of the four possible isomers of substrate **45** and their structure and relative predominance (Table 3, entry 11) was determined by ^{1}H NMR (Fig. 2).

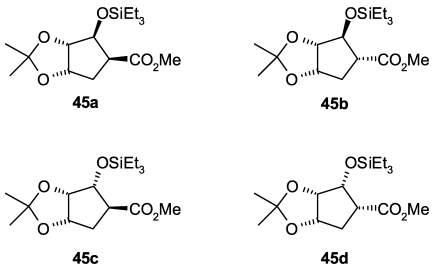


Figure 2. Structure of the four diastereoisomers of **45**.

A coupling constant $J(H_2-H_3)$=0.0–0.7 Hz was observed for both isomers **45a** and **45b**, indicating a dihedral angle close to 90 °C, which implies the equatorial configuration of H_2. The configuration of H_1 was assigned on the basis of NOE experiments (Fig. 3). A strong NOE effect between H_1 and H_{5eq} in **45a** indicates that H_1 occupies an axial position, whereas in **45b** the NOE effect was observed between H_1 and H_{5ax}, indicating that, in this case, it occupies an equatorial position.

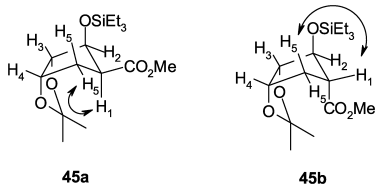


Figure 3. NOE mesurements of **45**.

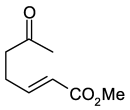
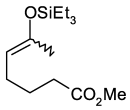
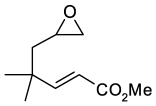
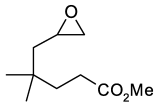
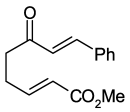
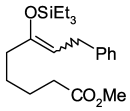
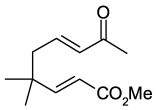
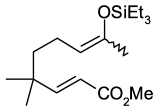
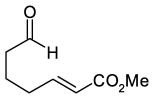
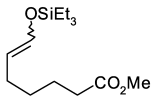
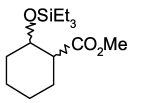
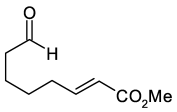
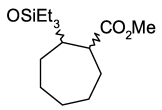
The structure of isomer **45c** was unequivocally assigned on the basis of a typical coupling constant $J(H_1-H_2)$=12.4 Hz for diaxial configuration. The minor isomer **45d** was not isolated but its structure was tentatively deduced as the all-*cis* isomer.

At this stage, in order to extend the scope of the reaction, cyclisation was also carried out on several substrates where the aldehyde functionality was replaced by alternative electrophilic acceptor groups. The construction of six- and seven-membered rings was also attempted. The results are shown in Table 4.

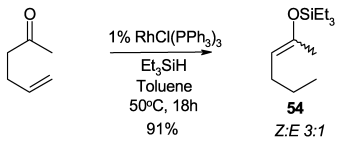
In the event, aldehyde functionality proved to be crucial in order to achieve cyclisation. Thus, as shown in entries 1 and 2, replacement of the aldehyde either by a methyl ketone or by an epoxide did not lead to the formation of cyclic products, even although the reduction of the acrylate unit by the silane in both cases implies formation of a hydrometallated ester enolate intermediate. In the case of the methyl ketone **14** (entry 1), the regiospecific and highly stereoselective formation of the silyl enol ether product was not anticipated but certainly of interest, especially since the control of regioselectivity in the case of unsymmetrical ketones[49] is always useful in organic synthesis. In order to understand this transformation commercially available 5-hexen-2-one was also subjected to the standard cyclisation conditions in the presence of Wilkinson's catalyst. As shown in Scheme 14, regiospecific silyl enol ether formation with concomitant double bond reduction occurred once again in excellent yield and with moderate stereoselectivity, thereby establishing that the ester group is not essential for this reaction to occur. A speculative intermediate is shown in Figure 4 and implies that substrate coordination around a silyl hydridorhodium intermediate may well direct the regiospecificity of the sequence and also produce molecular hydrogen for subsequent reduction of the double bond. At this stage, however, the reasons for the totally divergent behaviour of the aldehydic substrate **7** and its ketonic congener **14** still require further investigation.

The two enone substrates **8** and **19** shown in entries 3 and 4 were initially selected with the intention of probing a (non-rhodium catalysed) tandem hydrometallation–Michael addition sequence in which, as demonstrated by Evans[12a] for hydroboration, the α,β-unsaturated ketone unit should be the first point of attack. In the event, however, only acyclic products derived from 1,4-addition of the organosilane to the enones were isolated in the rhodium catalysed reactions and no evidence for a subsequent tandem Michael reaction was adduced. Interestingly, the use of Wilkinson's catalyst (entry 3) led to reduction of both the enone and the enoate whereas in the presence of hydridotetrakis(triphenylphosphine) rhodium (I) (entry 4) reduction occurred

Table 4. Rhodium (I)-catalysed tandem cyclisation of alternative acceptors and construction of larger ring sizes

Entry	Substrate		Product		Catalyst[a]	Yield (%)[b]	*cis*/*trans*[c]
1		**14**		**47**	A	83	5.0:1.0[d]
					B	61	5.0:1.0[d]
2		**18**		**48**	A	68	—
					B	60	
3		**8**		**49**	A	74	—
4		**19**		**50**	B	91	—
5		**32**		**51**	A	66	1.0:4.6
				**52**	B	65	1.0:3.0
6		**33**		**53**	B	68	2.5:1.0

[a] A, $RhCl(PPh_3)_3$; B, $RhH(PPh_3)_4$.
[b] Isolated yields after chromatography on silica gel.
[c] Diastereomeric ratio in the crude material determined by ^1H NMR.
[d] *Z*/*E* ratio.



Scheme 14. Formation of silyl enol ether **54** from 5-hexen-2-one.

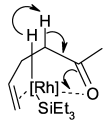


Figure 4. Speculative intermediate for the formation of **54** from 5-hexen-2-one.

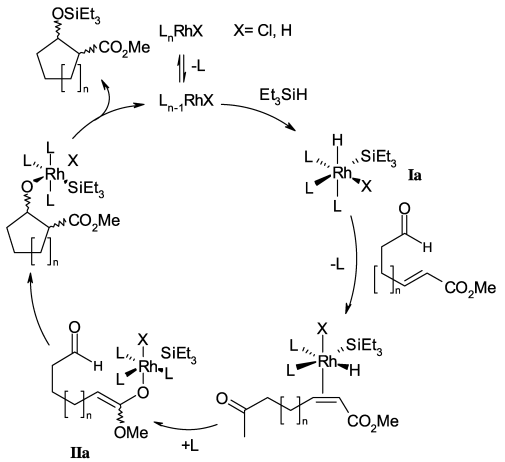
exclusively at the enone moiety. The contrasting behaviour of the two rhodium catalysts and the necessity for rigorous purification prior to their use was further highlighted in the case of 7-oxo-2-heptenoate **32** (entry 5). In our preliminary study,[15a] only a low yield of cyclised product was described using Wilkinson's catalyst. The results obtained under more stringent conditions reveal that, as in entry 1, the major product using Wilkinson's catalyst is the analogous reduced silyl enol ether **51**. To our delight, however, selection of hydridotetrakis-(triphenylphosphine) rhodium (I) affords the desired 2-carbomethoxycyclohexanol derivative **52** in 65% with *trans* selectivity. In similar fashion, octenoate **33** furnished the seven-membered ring analogue **53** in comparable yield (68%) but with a reversal in terms of stereoselectivity relative to the six-membered ring congener (entry 6). Significantly, and in contrast to the hydroacylation protocol, the applicability of this approach for the preparation of substituted five-, six- and seven-membered rings is, therefore, possible.

2.3. Mechanistic considerations and stereochemistry

From a mechanistic standpoint, it was of interest to determine whether the transformation described was indeed a consequence of intermolecular hydrosilylation followed by an intramolecular aldol reaction, and not in fact intramolecular hydroacylation followed by hydrosilylation. To this end, reduction of the ester, methyl-2-oxocyclopentane carboxylate, was attempted using an excess of triethylsilane in the presence of 1 mol% of Wilkinson's catalyst. Under identical conditions to those that yielded 81% of the products *c*-**35** and *t*-**35** from methyl (*E*)-6-oxo-2-hexenoate **7**, only traces of the β-triethylsiloxy ester were formed. We have also demonstrated that the *cis*-substituted cyclopentanol *c*-**35** was not interconverted to the *trans*-isomer *t*-**35** when resubmitted to the reaction conditions, neither in the presence of Wilkinson's catalyst nor in the presence of $RhH(PPh_3)_4$.

As in the intermolecular variant of this reaction using enones and aldehydes,[50] the intermediacy of an oxygen bound rhodium ester enolate of the type suggested by Heathcock[51] seems most likely. The influence of the ancillary phosphine ligands, and the replacement of the chlorine atom by a hydride ligand on the stereochemical outcome of our reactions both provide strong support for this possibility. A possible pathway for the catalytic aldol cycloreduction is depicted in Scheme 15. Thus, oxidative addition of the silane to the rhodium (I) catalyst provides the hydridosilyl rhodium (III) intermediate **Ia**. 1,4 hydride transfer of the hydridosilyl rhodium (III) species to the α,β-unsaturated ester then generates a rhodium ester enolate **IIa**. Intramolecular aldol reaction followed by reductive elimination liberates the carbocyclic silyl ether product with concomitant regeneration of the active catalyst. It is interesting that the rhodium complex may catalyse both, the 1,4-addition and the aldol reaction, in one catalytic cycle. The chemoselectivity for both steps is very high, the intermediates **Ia** and **IIa** reacting with the α,β-unsaturated ester and the aldehyde, respectively, with perfect selectivity.

The stereochemical outcome of this reaction can be formally rationalised in terms of the preferential formation of one stereoisomer of the rhodium ester enolate **55** (Scheme 16). Thus, (*Z*)-enolate **56** undergoes the intramolecular aldol reaction via a chelated transition state and provides the *cis*-carbocyclic product **58a** in which one of the substituents occupies an axial position. On the other hand, (*E*)-enolate **57** cyclises with an all-equatorial orientation leading to the *trans*-substituted product **58b**.



Scheme 15. Mechanism of rhodium (I)-catalysed tandem hydrosilylation-intramolecular aldol reaction.

Although in the first instance it could be argued that the two rhodium complexes used in this study might well have converged to a common catalytic intermediate through oxidative addition of the silane to Wilkinson's catalyst and subsequent reductive elimination of chlorotriethylsilane, the experimental observations clearly do not substantiate this hypothesis. Consequently, the presence or absence of the rhodium chlorine bond will clearly influence the outcome of the reaction both in terms of the polarity of the rhodium hydride bond and the stereochemical outcome in the initial hydrometallation step as well as altering the Lewis acidic nature of the chelated rhodium intermediate postulated for the intramolecular aldol step.

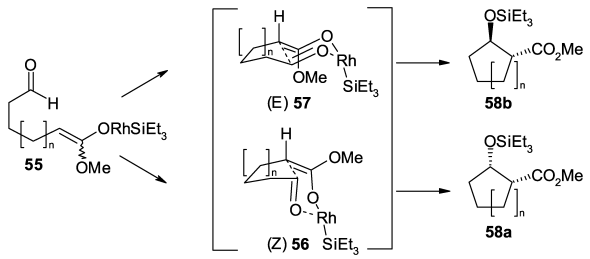
3. Conclusion

In summary, we have developed a highly stereoselective cyclisation sequence via a rhodium (I)-catalysed tandem hydrosilylation-intramolecular aldol reaction that can be used to prepare a range of usefully functionalised five-, six- and seven-membered rings in good yields under very mild conditions. Moreover, in many instances the required precursors can be easily prepared in a highly atom efficient way using the [3,3] sigmatropic rearrangement sequence. The scope and limitations of this novel reaction have been established. A range of substituents in the substrates is tolerated, however, aldehyde functionality proved to be crucial. The stereochemical outcome is highly dependant on the catalyst precursor, $RhH(PPh_3)_4$ is an efficient precatalyst for tandem hydrosilylation-aldol reaction and gave the best results in terms of selectivity. Further studies into the mechanism and stereochemistry of the tandem cyclisation and its applications in synthesis are ongoing.

4. Experimental

4.1. General

All cyclisations and air and/or moisture sensitive reactions were carried out in oven-dried glassware under a nitrogen atmosphere using standard Schlenk techniques. Unless otherwise noted, chemicals were commercially available and used without further purification. Solvents were distilled before use and degassed immediately prior to use. Toluene was distilled from sodium. Tetrahydrofuran and diethyl ether were distilled from sodium-benzophenone ketyl, methylene chloride and acetonitrile from calcium hydride and ethanol and methanol were used as supplied from Aldrich. $RhCl(PPh_3)_3$ was prepared according to



Scheme 16. Stereochemistry of rhodium (I)-catalysed tandem hydrosilylation-intramolecular aldol reaction.

Wilkinson's procedure[41] and $RhH(PPh_3)_4$ to Levison's procedure.[42]

Nuclear magnetic resonance spectra were recorded using a Bruker AMX-300 or a Bruker AMX-400 or a Bruker Avance 500. Chemical shifts (δ) are quoted in parts per million (ppm) relative to tetramethylsilane. The ^{1}H NMR spectra are reported relative to residual chloroform at 7.26 ppm. Coupling constants are reported in Hertz. ^{13}C NMR spectra were fully decoupled and are referenced to the middle peak of chloroform at 77.0 ppm. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and a combination of these. Melting points were determined using a Reichert hot stage or Electrothermal 9100 apparatus and are uncorrected. Optical rotations were recorded on a Perkin–Elmer 241 polarimeter (using the sodium D line; 589 nm) and $[\alpha]_D^T$ are given in units of 10^{-1} deg dm^2 g^{-1}. IR spectra were recorded on a Perkin–Elmer 1605 FT-IR spectrometer as thin films on NaCl or as KBr discs and are reported in cm^{-1}. Mass spectra were recorded on a Micromass 70-SE spectrometer using a cesium ion gun for FAB. X-ray crystallography was performed using a Bruker Smart Apex, CDD diffractometer. Elemental analyses and accurate mass measurements were performed at Christopher Ingold Laboratories, University College London.

Column chromatography was performed using BDH silica gel (40–60 μm). Analytical thin layer chromatography was performed on pre-coated aluminium-backed plates (Merck Keisekgel 60 F_{254}) and visualised by 254 nm UV or by staining with basic potassium permanganate solution followed by heat.

4.2. General procedure A for the synthesis of cyclisation substrates via Claisen rearrangement

A mixture of methyl 2-hydroxy-3-butenoate **2a** (2.0 g, 17.2 mmol), isobutyraldehyde (1.86 g, 25.8 mmol) and a small amount of *p*-toluenesulfonic acid (10 mg) in 10 mL of toluene, was heated under reflux for 48 h with provision of a Dean and Stark apparatus for the removal of water. After evaporation of the solvent under reduced pressure, the crude oil was purified by flash column chromatography employing P.E. 30–40 °C/EtOAc (80:20) as eluant to afford the desired product **4** (1.54 g, 53%) as two single diastereomers in a *E*/*Z* 2:1 ratio as a colorless oil.

4.2.1. Methyl (*E*)-5,5-dimethyl-6-oxo-2-hexenoate ((*E*)-4). R_f 0.20 (P.E. 30–40 °C/EtOAc, 80:20); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14 (s, 6H, C(CH_3)$_2$), 2.41 (dd, J=7.8, 1.4 Hz, 2H, CH_2), 3.79 (s, 3H, OCH_3), 5.93 (dt, J=15.6, 1.4 Hz, 1H, =CHCO$_2$CH$_3$), 6.93 (dt, J=15.6, 7.8 Hz, 1H, CH=CHCO$_2$CH$_3$), 9.60 (s, 1H, CHO); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.8 (C(*C*H$_3$)$_2$), 39.7 (*C*H$_2$), 46.2 (*C*(CH$_3$)$_2$), 51.9 (O*C*H$_3$), 124.6 (=*C*HCO$_2$CH$_3$), 144.2 (*C*H=CHCO$_2$CH$_3$), 166.8 (*C*O$_2$CH$_3$), 205.0 (*C*HO); FTIR (film) ν 1803, 1730, 1645 cm^{-1}; LRMS (EI$^+$) *m*/*z* 171 (M$^+$+1, 50), 139 (100), 109 (79), 81 (73), 41 (33); HRMS (EI$^+$) calcd for $C_9H_{14}O_3$ (M$^+$) 170.09429, found 170.09400.

4.2.2. Methyl (*Z*)-5,5-dimethyl-6-oxo-2-hexenoate ((*Z*)-4). R_f 0.25 (P.E. 30–40 °C/EtOAc, 80:20); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.05 (s, 6H, C(CH_3)$_2$), 2.83 (dd, J=7.8, 1.6 Hz, 2H, CH_2), 3.65 (s, 3H, OCH_3), 5.84 (dt, J=11.6, 1.6 Hz, 1H, =CHCO$_2$CH$_3$), 6.11 (dt, J=11.6, 7.8 Hz, 1H, CH=CHCO$_2$CH$_3$), 9.50 (s, 1H, CHO); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.7 (C(*C*H$_3$)$_2$), 35.9 (*C*H$_2$), 46.6 (*C*(CH$_3$)$_2$), 51.5 (O*C*H$_3$), 122.2 (=*C*HCO$_2$CH$_3$), 145.0 (*C*H=CHCO$_2$CH$_3$), 166.9 (*C*O$_2$CH$_3$), 205.5 (*C*HO); FTIR (film) ν 1797, 1724, 1656 cm^{-1}; LRMS (EI$^+$) *m*/*z* 170 (M, 8), 141 (58), 109 (87), 81 (70), 41 (100); HRMS (EI$^+$) calcd for $C_9H_{14}O_3$ (M$^+$) 170.09429, found 170.09417.

4.2.3. Methyl (*E*)-4-(1-formyl-cyclohexyl)-2-butenoate ((*E*)-5a). According to the general procedure A, reaction of methyl 2-hydroxy-3-butenoate **2a** (3.0 g, 25.8 mmol) and cyclohexanecarboxaldehyde (2.90 g, 25.8 mmol) gave, after purification by column chromatography eluting with P.E. 30–40 °C/EtOAc (80:20), the aldehyde **5a** (2.66 g, 49%) as two single diastereomers in a *E*/*Z* 1.5:1 ratio as a colorless oil. R_f 0.28 (P.E. 30–40 °C/EtOAc, 80:20); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.24–1.50 (m, 4H, CH_2), 1.62–1.70 (m, 4H, CH_2), 1.96–2.00 (m, 2H, CH_2), 2.44 (dd, J=8.0, 1.3 Hz, 2H, CH_2CH=), 3.84 (s, 3H, OCH_3), 5.96 (dt, J=15.6, 1.3 Hz, 1H, =CHCO$_2$CH$_3$), 6.93 (dt, J=15.6, 8.0 Hz, 1H, CH=CHCO$_2$CH$_3$), 9.66 (s, 1H, CHO); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 22.6 (*C*H$_2$), 25.8 (*C*H$_2$), 31.4 (*C*H$_2$), 38.8 (*C*H$_2$), 50.1 (*C*Cy), 51.9 (O*C*H$_3$), 124.6 (=*C*HCO$_2$CH$_3$), 143.7 (*C*H=CHCO$_2$CH$_3$), 166.7 (*C*O$_2$CH$_3$), 206.1 (*C*HO); FTIR (film) ν 1799, 1732, 1656 cm^{-1}; LRMS (APCI$^+$) *m*/*z* 211 (M$^+$+H, 44), 179 (100), 149 (39); HRMS (CI$^+$) calcd for $C_{12}H_{19}O_3$ (M$^+$+H) 211.13341, found 211.13323.

4.2.4. *i*-Propyl (*E*)-4-(1-formyl-cyclohexyl)-2-butenoate ((*E*)-5b). As for general procedure A. Reaction of *i*-propyl 2-hydroxy-3-butenoate **2b** (3.0 g, 20.8 mmol) and cyclohexanecarboxaldehyde (2.33 g, 20.8 mmol) gave, after purification by column chromatography eluting with P.E. 30–40 °C/EtOAc (80:20), the aldehyde **5b** (3.02 g, 61%) as two single diastereomers in a *E*/*Z* 1.5:1 ratio as a colorless oil. R_f 0.58 (P.E. 30–40 °C/EtOAc, 80:20); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.18 (d, J=6.3 Hz, 6H, OCH(CH_3)$_2$), 1.19–1.32 (m, 4H, CH_2), 1.39–1.57 (m, 4H, CH_2), 1.78–1.90 (m, 2H, CH_2), 2.24 (dd, J=7.8, 1.2 Hz, 2H, CH_2), 4.97 (m, 1H, OCH(CH$_3$)$_2$); 5.73 (dt, J=15.5, 1.2 Hz, 1H, =CHCO$_2$*i*Pr), 6.70 (dt, J=15.5, 7.8 Hz, 1H, CH=CHCO$_2$*i*Pr), 9.41 (s, 1H, CHO); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 22.2 (OCH(*C*H$_3$)$_2$), 22.6 (*C*H$_2$), 25.8 (*C*H$_2$), 31.2 (*C*H$_2$), 38.9 (*C*H$_2$CH=), 50.1 (*C*Cy), 68.1 (O*C*H(CH$_3$)$_2$), 125.6 (=*C*HCO$_2$*i*Pr), 143.0 (*C*H=CHCO$_2$-*i*Pr), 165.8 (*C*O$_2$*i*Pr), 206.2 (*C*HO); FTIR (film) ν 2934, 2856, 1798, 1719, 1655, 1452, 1273, 1200 cm^{-1}; LRMS (CI$^+$) *m*/*z* 239 (M$^+$+H, 58), 209 (83), 167 (100); HRMS (CI$^+$) calcd for $C_{14}H_{23}O_3$ (M$^+$+H) 239.16471, found 239.16435.

4.2.5. *i*-Propyl (*E*)-5,5-diphenyl-6-oxo-2-hexenoate ((*E*)-6). According to the general procedure A, reaction of *i*-propyl 2-hydroxy-3-butenoate **2b** (1.5 g, 10.4 mmol) and 2,2-diphenylacetaldehyde (2.04 g, 10.4 mmol) gave, after purification by column chromatography eluting with P.E. 30–40 °C/EtOAc (90:10), aldehyde **6** (2.15 g, 64%) as two isomers in a *E*/*Z* 2:1 ratio as a yellow oil. R_f 0.53 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (300 MHz, $CDCl_3$) δ

1.11 (d, J=6.3 Hz, 6H, CH(CH_3)$_2$), 3.11 (dd, J=7.4, 1.1 Hz, 2H, CH_2), 4.88 (m, 1H, CH(CH_3)$_2$), 5.62 (dt, J=15.6, 1.1 Hz, 1H, =$CH$$CO_2i$Pr), 6.62 (dt, J=15.6, 7.4 Hz, 1H, CH=CHCO$_2i$Pr), 7.08–7.33 (m, 10H, Ph), 9.74 (s, 1H, CHO); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 22.2 (CH(CH_3)$_2$), 37.4 (CH_2), 63.9 (CPh_2), 67.8 (CH(CH_3)$_2$), 125.4 (=CHCO$_2i$Pr), 128.1 (Ph), 129.3 (Ph), 139.3 (Ph), 144.1 (CH=CHCO$_2i$Pr), 165.9 (CO_2iPr), 197.9 (CHO); FTIR (film) ν 2982, 2936, 1796, 1720, 1656, 1277, 908, 735 cm^{-1}; LRMS (FAB$^+$) m/z 323 (M$^+$+H, 23), 307 (12), 263 (16), 245 (5), 167 (17), 154 (100); HRMS (FAB$^+$) calcd for $C_{21}H_{23}O_3$ (M$^+$+H) 323.16471, found 323.16428.

4.2.6. Methyl (*E*)-6-oxo-2-hexenoate ((*E*)-7). According to the general procedure A, methyl 2-hydroxy-3-butenoate **2a** (2.0 g, 17.2 mmol) and acetaldehyde diethyl acetal (3.05 g, 25.8 mmol) were heated under reflux using a Soxhlet extractor containing freshly conditioned 4 Å molecular sieves for 4 days. The sieves were replaced five times with a freshly conditioned batch. Purification by column chromatography eluting with P.E. 30–40 °C/EtOAc (60:40) gave the aldehyde **7**[52] (1.13 g, 46%) as two single diastereomers in a *E*/*Z* 2.2:1 ratio as a colorless oil. R_f 0.50 (P.E. 30–40 °C/EtOAc, 60:40); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.73–2.78 (m, 2H, CH_2CH=), 2.85 (t, J=7.3 Hz, 2H, CH_2CHO), 3.94 (s, 3H, OCH_3), 6.08 (dt, J=15.7, 1.5 Hz, 1H, =CHCO$_2$CH$_3$), 7.16 (dt, J=15.7, 6.7 Hz, 1H, CH=CHCO$_2$CH$_3$), 9.97 (s, 1H, CHO); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 24.8 (CH_2CH=), 42.2 (CH_2CHO), 51.9 (OCH_3), 122.4 (=CHCO$_2$CH$_3$), 147.0 (CH=CHCO$_2$CH$_3$), 167.0 (CO_2CH$_3$), 200.5 (CHO); FTIR (film) ν 2953, 2849, 2731, 1724, 1659, 1437, 1165 cm^{-1}.

4.2.7. Methyl (2*E*,7*E*)-6-oxo-8-phenyl-2,7-octadienoate (8). According to the general procedure A, reaction of methyl 2-hydroxy-3-butenoate **2a** (2.0 g, 17.2 mmol) and benzylideneacetone (2.48 g, 17.2 mmol) gave, after purification by column chromatography eluting with P.E. 30–40 °C/EtOAc (80:20), the ketone **8** (2.44 g, 58%) as a single *E*-diastereomer as a yellow oil. R_f 0.37 (P.E. 30–40 °C/EtOAc, 80:20); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.56 (qd, J=6.9, 1.4 Hz, 2H, CH_2CH=), 2.82 (t, J=6.9 Hz, 2H, CH_2CO), 3.70 (s, 3H, OCH_3), 5.86 (dt, J=15.6, 1.4 Hz, 1H, =CHCO$_2$CH$_3$), 6.72 (d, J=16.2 Hz, 1H, CH=CHPh), 6.99 (dt, J=15.6, 6.9 Hz, 1H, CH=CHCO$_2$CH$_3$), 7.37–7.54 (m, 5H, Ph), 7.60 (d, J=16.2 Hz, 1H, CH=CHPh); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 26.7 (CH_2CH=), 39.1 (CH_2CHO), 51.8 (OCH_3), 122.1 (=CHCO$_2$CH$_3$), 126.2 (CH=CHPh), 128.7 (Ph), 129.3 (Ph), 131.0 (Ph), 134.8 (Ph), 143.3 (CH=CHPh), 148.0 (CH=CHCO$_2$CH$_3$), 167.2 (CO_2CH$_3$), 198.4 (CO); FTIR (film) ν 3055, 1719, 1659, 1612, 1578, 1265, 739, 704 cm^{-1}; LRMS (FAB$^+$) m/z 245 (M$^+$+H, 100), 213 (78), 167 (39); HRMS (FAB$^+$) calcd for $C_{15}H_{17}O_3$ (M$^+$+H) 245.11776, found 245.11782.

4.3. General olefination procedure B for the synthesis of cyclisation substrates

A suspension of 80% sodium hydride dispersion in mineral oil (3.64 g, 121.2 mmol) in 100 mL of dry tetrahydrofuran under a positive nitrogen pressure was stirred in an ice bath while trimethylphosphonoacetate (22.07 g, 121.2 mmol) in 100 mL of dry tetrahydrofuran was added dropwise. The mixture becomes viscous near the end of the addition, but redissolved on continued stirring. After the addition was finished, the reaction mixture was stirred for further 1 h at 0 °C. Then, a solution of 5-hexen-2-one (10.0 g, 101.9 mmol) in 150 mL of dry tetrahydrofuran was added dropwise. The cold mixture was stirred for further 15 min after the addition. Then, it was slowly brought to reflux and stirred overnight. The clear ether layer was decanted from the oil. The remaining oil was dissolved in warm water and the upper organic layer was separated. The aqueous layer was extracted with ether. The combined organic layers were washed with saturated $NaHCO_3$, dried over Na_2SO_4, filtered and the solvents were removed in vacuo. Purification by flash column chromatography employing P.E. 30–40 °C/EtOAc (80:20) as eluant afforded the enoate **13** (13.67 g, 87%) as two single diastereomers in a *E*/*Z* 2:1 ratio as a colorless oil.

4.3.1. Methyl (*E*)-3-methyl-2,6-heptadienoate ((*E*)-13). R_f 0.73 (P.E. 30–40 °C/EtOAc, 80:20); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.09 (d, J=1.3 Hz, 3H, CH_3), 2.16–2.18 (m, 4H, CH_2), 3.61 (s, 3H, OCH_3), 4.89 (dq, J=10.1, 1.8 Hz, 1H, CH=CH_{cis}H), 4.96 (dq, J=17.1, 1.8 Hz, 1H, CH=CHH_{trans}), 5.60 (m, 1H, =CHCO$_2$CH$_3$), 5.66–5.78 (m, 1H, CH=CH$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.7 (CH_3), 31.4 (CH_2), 40.1 (CH_2), 50.7 (OCH_3), 115.3 (=CH$_2$), 115.4 (=CHCO$_2$CH$_3$), 137.2 (CH=CH$_2$), 159.4 (C=CHCO$_2$CH$_3$), 167.1 (CO_2CH$_3$); FTIR (film) ν 3078, 2926, 2853, 1720, 1651, 1435, 1225, 1151 cm^{-1}; LRMS (DCI$^+$) m/z 155 (M$^+$+H, 100), 139 (8), 123 (26), 95 (63); HRMS (DCI$^+$) calcd for $C_9H_{15}O_2$ (M$^+$+H) 155.10719, found 155.10696.

4.3.2. Methyl (*E*)-4,4-dimethyl-2,6-heptadienoate (17). According to the general procedure B, reaction of 4,4-dimethyl pentenal **16** (23.0 g, 205.0 mmol) with a mixture of 80% sodium hydride dispersion in oil (6.77 g, 225.6 mmol) and trimethylphosphonoacetate (41.0 g, 225.6 mmol) gave, after purification by column chromatography eluting with P.E. 30–40 °C/EtOAc (80:20), the enoate **17** (30.3 g, 88%) as a single *E*-isomer as a colorless oil. R_f 0.67 (P.E. 30–40 °C/EtOAc, 80:20); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (s, 6H, C(CH_3)$_2$), 2.04 (d, J=7.4 Hz, 2H, CH_2CH=), 3.66 (s, 3H, OCH_3), 4.92–5.02 (m, 2H, CH=CH_2), 5.56–5.72 (m, 1H, CH=CH$_2$), 5.66 (d, J=15.7 Hz, 1H, =CHCO$_2$CH$_3$), 6.88 (d, J=15.7 Hz, 1H, CH=CHCO$_2$CH$_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 26.4 (C(CH_3)$_2$), 37.1 (C(CH$_3$)$_2$), 46.8 (CH_2), 51.8 (OCH_3), 117.9 (=CHCO$_2$CH$_3$), 118.2 (=CH_2), 134.6 (CH=CH$_2$), 158.3 (CH=CHCO$_2$CH$_3$), 167.9 (CO_2CH$_3$); FTIR (film) ν 2964, 2872, 1719, 1653, 1265 cm^{-1}; LRMS (APCI$^+$) m/z 169 (M$^+$+H, 10), 137 (10), 127 (63), 109 (100); HRMS (ES$^+$) calcd for $C_{10}H_{17}O_2$ (M$^+$+H) 169.1239, found 169.1232.

4.4. General ozonolysis procedure C for the synthesis of cyclisation substrates

A solution of 4-but-3-enyl-5*H*-furan-2-one **12** (0.6 g, 4.3 mmol) and pyridine (0.2 mL, 1% vol) in anhydrous dichloromethane (20 mL) was cooled to −78 °C. A stream of ozone was bubbled through the solution, and the reaction was carefully monitored by TLC. After consumption of the starting material the flask was flushed with nitrogen.

Dimethylsulfide was added (0.27 g, 43.4 mmol) and the mixture was allowed to warm to room temperature overnight. The solution was then extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered and the filtrate concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography eluting with EtOAc to afford the aldehyde **9** (0.33 g, 49%) as a yellow oil.

4.4.1. 3-(5-Oxo-2,5-dihydrofuran-3-yl)propionaldehyde (9). R_f 0.35 (EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.50–2.57 (m, 2H, CH_2CH$_2$CHO), 2.70 (t, J=7.4 Hz, 2H, CH_2CHO), 4.93 (d, J=1.5 Hz, 2H, OCH_2), 6.04–6.06 (m, 1H, =CHCO$_2$R), 9.79 (s, 1H, CHO); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.1 (*C*H$_2$CH$_2$CHO), 41.4 (*C*H$_2$CHO), 73.4 (O*C*H$_2$), 116.4 (=*C*HCO$_2$R), 168.7 (*C*=CHCO$_2$R), 173.8 (*C*O$_2$R), 199.4 (*C*HO); FTIR (film) ν 2853, 1744, 1636, 1391, 1182 cm^{-1}; HRMS (FAB$^+$) calcd for $C_7H_9O_3$ (M$^+$+H) 141.05516, found 141.05505.

4.4.2. Methyl (*E*)-3-methyl 6-oxo-2-hexenoate (10). According to the general procedure C, ozonolysis of methyl (*E*)-3-methyl-2,6-heptadienoate **13** (15.0 g, 97.3 mmol) gave, after purification by column chromatography eluting with P.E. 30–40 °C/EtOAc (90:10), the aldehyde **10**[53] (6.23 g, 41%) as a colorless oil. R_f 0.37 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.15 (d, J=1.3 Hz, 3H, CH_3), 2.45 (td, J=7.6, 1.1 Hz, 2H, CH_2CHO), 2.61 (td, J=7.6, 1.3 Hz, 2H, CH_2CH$_2$CHO), 3.65 (s, 3H, OCH_3), 5.61 (m, 1H, =CHCO$_2$CH$_3$), 9.77 (t, J=1.1 Hz, 1H, CHO); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.1 (*C*H$_3$), 33.0 (*C*H$_2$), 41.8 (*C*H$_2$), 51.3 (O*C*H$_3$), 116.4 (=*C*HCO$_2$CH$_3$), 157.7 (*C*=CHCO$_2$CH$_3$), 167.2 (*C*O$_2$CH$_3$), 200.8 (*C*HO); FTIR (film) ν 2951, 2845, 2729, 1719, 1649, 1437, 1362, 1229, 1153 cm^{-1}.

4.4.3. Methyl (*E*)-4,4-dimethyl-6-oxo-2-hexenoate (15). According to the general procedure C, ozonolysis of methyl (*E*)-4,4-dimethyl-2,6-heptadienoate **17** (30.0 g, 178.3 mmol) gave, after purification by column chromatography eluting with P.E. 30–40 °C/EtOAc (90:10), the aldehyde **15**[54] (14.57 g, 48%) as a colorless oil. R_f 0.28 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30 (s, 6H, C(CH_3)$_2$), 2.52 (d, J=2.7 Hz, 2H, CH_2CHO), 3.83 (s, 3H, OCH_3), 5.89 (d, J=16.0 Hz, 1H, =CHCO$_2$CH$_3$), 7.13 (d, J=16.0 Hz, 1H, CH=CHCO$_2$CH$_3$), 9.84 (t, J=2.7 Hz, 1H, CHO); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.2 (C(*C*H$_3$)$_2$), 36.2 (*C*(CH$_3$)$_2$), 52.0 (O*C*H$_3$), 54.6 (*C*H$_2$), 118.9 (=*C*HCO$_2$CH$_3$), 155.9 (*C*H=CHCO$_2$CH$_3$), 167.3 (*C*O$_2$CH$_3$), 201.6 (*C*HO); FTIR (film) ν 2930, 2853, 2729, 1730, 1654, 1462 cm^{-1}; LRMS (APCI$^+$) *m*/*z* 171 (M$^+$+H, 8), 155 (46), 139 (100); HRMS (ES$^+$) calcd for $C_9H_{15}O_3$ (M$^+$+H) 171.1007, found 171.1011.

4.5. Synthesis of other cyclisation substrates

4.5.1. Methyl (*E*)-4,4-dimethyl-5-oxiranyl-2-pentenoate (18). A mixture of 60% sodium hydride dispersion in mineral oil (0.13 g, 3.2 mmol) and excess anhydrous dimethylsulfoxide (5 mL) was stirred under nitrogen at 75 °C until the evolution of hydrogen ceases (1 h). The solution was then cooled down to room temperature, diluted with an equal volume of dry tetrahydrofuran to avoid freezing and then cooled in an ice–salt bath. A solution of trimethyl sulfonium iodide (0.66 g, 3.2 mmol) in 3 mL of dry dimethylsulfoxide was added and the mixture stirred for 5 min. The aldehyde **15** was then added (0.5 g, 2.9 mmol) and stirring was continued at salt–ice temperature for further 15 min, then for 1 h at room temperature. The mixture was diluted with 3 volumes of water and extracted with ether. The combined organic layers were dried over Na_2SO_4, filtered and the filtrate concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography eluting with P.E. 30–40 °C/EtOAc (90:10) to afford the epoxide **18** (0.18 g, 33%) as a colorless oil. R_f 0.28 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.11 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.47–1.54 (m, 2H, CH_2), 2.34 (dd, J=5.0, 2.7 Hz, 1H, CH_aHO), 2.66 (dd, J=5.0, 4.1 Hz, 1H, CHH_bO), 2.80–2.82 (m, 1H, CHO), 3.67 (s, 3H, OCH_3), 5.67 (d, J=16.0 Hz, 1H, =CHCO$_2$CH$_3$), 6.93 (d, J=16.0 Hz, 1H, CH=CHCO$_2$CH$_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 26.7 (*C*H$_3$), 27.3 (*C*H$_3$), 37.0 (*C*(CH$_3$)$_2$), 45.2 (*C*H$_2$), 47.0 (*C*H$_2$O), 49.4 (*C*HO), 51.9 (O*C*H$_3$), 118.3 (=*C*HCO$_2$CH$_3$), 157.6 (*C*H=CHCO$_2$CH$_3$), 167.7 (*C*O$_2$CH$_3$); FTIR (film) ν 3054, 2969, 2931, 2874, 1717, 1652, 1436, 1265 cm^{-1}; LRMS (FAB$^+$) *m*/*z* 185 (M$^+$+H, 66), 169 (8), 154 (100); HRMS (FAB$^+$) calcd for $C_{10}H_{17}O_3$ (M$^+$+H) 185.11775, found 185.11746.

4.5.2. Methyl (*E*)-4,4-dimethyl-8-oxo-2,6-nonadienoate (19). According to the general procedure B, reaction of methyl (*E*)-4,4-dimethyl-6-oxo-2-hexenoate **15** (1.5 g, 8.9 mmol) with a mixture of 80% sodium hydride dispersion in oil (0.26 g, 9.7 mmol) and dimethyl-(2-oxopropyl)-phosphonate (1.6 g, 9.7 mmol) gave, after purification by column chromatography eluting with P.E. 30–40 °C/EtOAc (90:10), the enoate **19**[55] (1.7 g, 92%) as a colorless oil. R_f 0.66 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.10 (s, 6H, C(CH_3)$_2$), 2.22 (s, 3H, CH_3CO), 2.28 (dd, J=7.6, 1.2 Hz, 2H, CH_2CH=), 3.74 (s, 3H, OCH_3), 5.76 (d, J=16.0 Hz, 1H, =CHCO$_2$CH$_3$), 6.07 (dt, J=15.8, 1.2 Hz, 1H, =CHCOCH$_3$), 6.65 (dt, J=15.8, 7.6 Hz, 1H, CH=CHCOCH$_3$), 6.93 (d, J=16.0 Hz, 1H, CH=CHCO$_2$CH$_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 26.8 (C(*C*H$_3$)$_2$), 27.5 (CO*C*H$_3$), 37.5 (*C*(CH$_3$)$_2$), 45.2 (*C*H$_2$), 51.9 (O*C*H$_3$), 118.7 (=*C*HCO$_2$CH$_3$), 134.3 (=*C*HCOCH$_3$), 143.6 (*C*H=CHCOCH$_3$), 156.9 (*C*H=CHCO$_2$CH$_3$), 167.5 (*C*O$_2$CH$_3$), 198.4 (*C*OCH$_3$); FTIR (film) ν 2964, 2845, 1724, 1655, 1628, 1437, 1367, 1256, 1171 cm^{-1}; LRMS (ES$^+$) *m*/*z*: 233 (M$^+$+Na, 96), 211 (M$^+$+H, 65), 179 (100); HRMS (ES$^+$) *m*/*z*: requires 211.1335 for $C_{12}H_{19}O_3$ (M$^+$+H), found 211.1334.

4.5.3. Methyl (*E*)-*cis*-3-(2-hydroxymethyl-cyclohexyl)-acrylate (22). To a stirred solution of hexahydro-isobenzofuran-1-one (5.5 g, 38.7 mmol) in 100 mL of anhydrous ether at −20 °C under positive nitrogen pressure, DIBAL (1.22 M solution in toluene) (33.3 mL, 40.6 mmol) was added dropwise over 1 h. The resulting solution was stirred at −20 °C for an additional 0.5 h, and was then quenched by the addition of methanol (30 mL). The solution was allowed to warm to room temperature and stirred overnight. The resulting suspension was diluted with 50 mL of 30% aqueous solution of Rochelle's salt and was stirred for 30 min. The organic layer was separated and washed with

30% aqueous solution of Rochelle's salt. The combined aqueous layers were extracted with ether. The organic layers were dried over Na_2SO_4, filtered and the filtrate concentrated under reduced pressure to afford the crude lactol that was added to a stirred solution of methyl(triphenylphosphoranylidene)acetate (18.55 g, 55 mmol) in 150 mL of dry acetonitrile and heated at reflux under a nitrogen atmosphere for 2 days. The heat was removed and most of the solvent was evaporated in vacuo. Ether (25 mL) was added and the mixture was stirred for an additional 2 h. The resulting mixture was filtered and the filtrate washed with 15 mL of ether. The solvent was removed in vacuo and 20 mL of 70% ether in pentane was added. After stirring for further 30 min, the suspension was filtered again and the filtrate concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography eluting with P.E. 30–40 °C/EtOAc (80:20) to afford the alcohol **22** (5.22 g, 68%) as a single *E* diastereoisomer as a colorless oil. R_f 0.33 (P.E. 30–40 °C/EtOAc, 80:20); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30–1.74 (m, 8H, CH_2), 1.86–1.97 (m, 1H, CHCH$_2$OH), 2.72–2.78 (m, 1H, CHCH=), 3.52 (d, J=7.2 Hz, 2H, CH_2OH), 3.80 (s, 3H, OCH_3), 5.95 (dd, J=15.6, 0.8 Hz, 1H, =CHCO$_2$CH$_3$), 7.23 (dd, J=15.6, 9.0 Hz, 1H, CH=CHCO$_2$CH$_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 22.7 (*C*H$_2$), 25.1 (*C*H$_2$), 25.5 (*C*H$_2$), 30.7 (*C*H$_2$), 29.7 (*C*HCH$_2$OH), 43.0 (*C*HCH=), 51.8 (O*C*H$_3$), 65.3 (*C*H$_2$OH), 121.9 (=*C*HCO$_2$CH$_3$), 150.4 (*C*H=CHCO$_2$CH$_3$), 167.4 (*C*O$_2$CH$_3$); FTIR (film) ν 3423, 2928, 2858, 1707, 1649, 1437, 1375, 1271, 1238, 1172 cm^{-1}; LRMS (EI$^+$) *m*/*z* 198 (M$^+$, 3), 167 (53), 81 (95), 67 (100); HRMS (EI$^+$) calcd for $C_{11}H_{18}O_3$ (M$^+$) 198.12558, found 198.12538.

4.5.4. Methyl (*E*)-3-(2-formyl-cyclohexyl)-acrylate (20). To a stirred suspension of pyridinium chlorochromate (1.95 g, 9.1 mmol) and celite (2.1 g) in 15 mL of anhydrous dichloromethane, was added at room temperature and under a positive pressure of nitrogen, a solution of methyl (*E*)-*cis*-3-(2-hydroxymethyl-cyclohexyl)-acrylate **22** (1.2 g, 6.1 mmol) in 3 mL of dichloromethane. The reaction mixture was stirred for 2 h at room temperature and was then diluted with 50 mL of ether. The resulting suspension was filtered through a short pad of Florisil®, rinsed with several portions of ether and the solvent concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography eluting with P.E. 30–40 °C/EtOAc (80:20) to afford the aldehyde **20** (0.90 g, 76%) as a colorless oil. R_f 0.67 (P.E. 30–40 °C/EtOAc, 80:20); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.52–1.98 (m, 8H, CH_2, *cis*+*trans*), 2.28–2.37 (m, 1H, CHCHO, *trans*), 2.49–2.61 (m, 1H, CHCH=, *trans*), 2.64–2.67 (m, 1H, CHCHO, *cis*), 2.86–2.89 (m, 1H, CHCH=, *cis*), 3.79 (s, 3H, OCH_3, *trans*), 3.80 (s, 3H, OCH_3, *cis*), 5.91 (dd, J=15.8, 1.2 Hz, 1H, =CHCO$_2$CH$_3$, *trans*), 5.94 (dd, J=15.8, 1.3 Hz, 1H, =CHCO$_2$CH$_3$, *cis*), 6.94 (dd, J=15.8, 8.0 Hz, 1H, CH=CHCO$_2$CH$_3$, *trans*), 7.20 (dd, J=15.8, 7.3 Hz, 1H, CH=CHCO$_2$CH$_3$, *cis*), 9.64 (d, J=2.3 Hz, 1H, CHO, *trans*), 9.73 (s, 1H, CHO, *cis*); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 23.7 (*C*H$_2$, *cis*), 23.9 (*C*H$_2$, *cis*), 24.3 (*C*H$_2$, *cis*), 24.9 (*C*H$_2$, *trans*), 25.1 (*C*H$_2$, *trans*), 25.9 (*C*H$_2$, *trans*), 29.6 (*C*H$_2$, *cis*), 31.3 (*C*H$_2$, *trans*), 39.5 (*C*HCHO, *cis*), 40.5 (*C*HCHO, *trans*), 51.9 (O*C*H$_3$, *cis*+*trans*), 52.2 (*C*HCH=, *cis*), 54.2 (*C*HCH=, *trans*), 121.5 (=*C*HCO$_2$CH$_3$, *trans*), 122.0 (=*C*HCO$_2$CH$_3$, *cis*), 149.7 (*C*H=CHCO$_2$CH$_3$, *cis*), 151.0 (*C*H=CHCO$_2$CH$_3$, *trans*), 167.1 (*C*O$_2$CH$_3$, *cis*+*trans*), 203.6 (*C*HO, *trans*), 204.1 (*C*HO, *cis*); FTIR (film) ν 2937, 2858, 1719, 1655, 1437, 1277, 1175 cm^{-1}; LRMS (FAB$^+$) *m*/*z* 197 (M$^+$+H, 15), 181 (24), 165 (30); HRMS (FAB$^+$) calcd for $C_{11}H_{17}O_3$ (M$^+$+H) 197.11776, found 197.11916.

4.5.5. Methyl (*E*)-3-(2-formyl-cyclohex-1-enyl)-acrylate (23b). A mixture of 2-bromo-cyclohexene-1-carboxaldehyde **24** (1.5 g, 7.9 mmol), methyl acrylate (0.81 g, 9.5 mmol), triethylamine (0.96 g, 9.5 mmol), palladium acetate (18 mg, 0.079 mmol) and triphenylphosphine (42 mg, 0.158 mmol), was heated at reflux under a positive pressure of nitrogen for 3 days. The heat was removed and the reaction mixture was diluted with ether and filtered. The solids were washed several times with small portions of ether, and the filtrate was concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography eluting with P.E. 30–40 °C/EtOAc (90:10) to afford the aldehyde **23b** (0.85 g, 55%) as a colorless oil. R_f 0.39 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.54–1.67 (m, 4H, CH_2), 2.29–2.36 (m, 4H, CH_2), 3.73 (s, 3H, OCH_3), 6.07 (d, J=15.6 Hz, 1H, =CHCO$_2$CH$_3$), 8.22 (d, J=15.6 Hz, 1H, CH=CHCO$_2$CH$_3$), 10.35 (s, 1H, CHO); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.5 (*C*H$_2$), 22.0 (*C*H$_2$), 23.8 (*C*H$_2$), 27.3 (*C*H$_2$), 52.3 (O*C*H$_3$), 122.2 (=*C*HCO$_2$CH$_3$), 138.9 (*C*H=CHCO$_2$CH$_3$), 141.0 (=*C*CHO), 148.2 (*C*=CCHO), 167.2 (*C*O$_2$CH$_3$), 190.3 (*C*HO); FTIR (film) ν 2937, 2864, 1720, 1668, 1622, 1587, 1435, 1375, 1300, 1277, 1175 cm^{-1}; LRMS (EI$^+$) *m*/*z* 195 (M$^+$+H, 8), 165 (38), 135 (100); HRMS (EI$^+$) calcd for $C_{11}H_{15}O_3$ (M$^+$+H) 195.10210, found 195.10196.

4.5.6. Methyl (*E*)-3-(2′-formylphenyl)-propenoate (25). Tetrabutylammonium bromide (0.56 g, 1.7 mmol), potassium carbonate (0.80 g, 5.8 mmol), palladium acetate (156 mg, 0.69 mmol) and methyl acrylate (2.97 g, 34.8 mmol) were stirred for 5 min under nitrogen, forming a dark orange solution. A solution of *o*-bromobenzaldehyde (1.28 g, 6.9 mmol) in 4 mL of degassed dimethylformamide was then added and the reaction was stirred at 70 °C for 16 h. The resulting mixture was diluted with ethyl acetate and filtered through a short pad of celite. The filtrate was diluted with water and extracted with ethyl acetate. The combined organic extracts were dried over $MgSO_4$, filtered and the filtrate concentrated under reduced pressure. Purification by flash column chromatography eluting with P.E. 30–40 °C/EtOAc (90:10) enabled *o*-bromobenzaldehyde to be removed from the crude mixture, with the desired aldehyde being isolated in 69% yield (when adjusted for recovered starting material). All spectroscopic and analytical data were in agreement with the literature values.[36] R_f 0.32 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (s, 3H, OCH_3), 6.40 (d, J=15.9 Hz, 1H, =CHCO$_2$CH$_3$), 7.56–7.91 (m, 4H, Ph), 8.55 (d, J=15.9 Hz, 1H, CH=CHCO$_2$CH$_3$), 10.31 (s, 1H, CHO); FTIR (film) ν 1728, 1699, 1621 cm^{-1}.

4.5.7. α-Benzyloxy-γ-butyrolactone (29). A suspension of 60% sodium hydride dispersion in mineral oil (2.15 g, 54 mmol) and α-hydroxy-γ-butyrolactone (5.0 g, 49 mmol) in dry tetrahydrofuran (50 mL) was stirred at 0–5 °C for

0.5 h. Benzyl bromide (7.3 mL, 61.3 mmol) and tetrabutylammonium iodide (1.18 g, 4.9 mmol) were then added. The resulting suspension was stirred at ambient temperature for 3 h, and then a saturated $NaHCO_3$ solution (50 mL) was cautiously added. The aqueous layer was extracted with dichloromethane and the combined organic extracts were dried over $MgSO_4$, filtered and the filtrate concentrated under reduced pressure. The resulting brown oil was purified by flash column chromatography eluting with P.E. 30–40 °C/EtOAc (60:40) to afford the product **29** (5.70 g, 61%) as a colorless oil. R_f 0.34 (P.E. 30–40 °C/EtOAc, 60:40); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.24–2.56 (m, 2H, CH_2CH$_2$O), 4.15–4.26 (m, 2H, OCH_2CH$_2$), 4.43 (t, J=8.0 Hz, 1H, OCHCH$_2$), 4.74 (d, J=12.0 Hz, 1H, PhCH_a-H$_b$O), 4.95 (d, J=12.0 Hz, 1H, PhCH$_a$$H_b$O), 7.30–7.42 (m, 5H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.9 (*C*H$_2$), 65.5 (*C*H$_2$OCO), 72.2 (O*C*H$_2$Ph), 72.5 (O*C*H), 128.1 (Ph), 128.2 (Ph), 128.6 (Ph), 137.0 (Ph), 175.0 (*C*O$_2$R); FTIR (film) ν 1781, 1175, 1142, 699 cm^{-1}; LRMS (ES$^+$) *m/z* 210 (M$^+$+NH$_4$, 100), 193 (M$^+$+H, 31), HRMS (ES$^+$) calcd for $C_{11}H_{13}O_3$ (M$^+$+H) 193.0852, found 193.0860.

4.5.8. α-Benzyloxy-γ-butyrolactol (30). DIBAL (1.22 M solution in toluene) (13.9 mL, 21 mmol) was added dropwise to a stirred solution of α-benzyloxy-γ-butyrolactone **29** (3.66 g, 19 mmol) in toluene (55 mL) at −75 °C under positive nitrogen pressure. The resulting solution was stirred at −70 °C for 3 h, and was then quenched by the addition of methanol (1.5 mL). The mixture was allowed to warm −10 to 0 °C, treated with 20% (w/v) aqueous solution of Rochelle's salt (50 mL) and the resulting mixture stirred at ambient temperature for 30 min. The biphasic mixture was separated, the aqueous layer extracted with toluene and the combined organic layers washed with water. The combined water washes were back extracted with toluene and the combined organics dried over Na_2SO_4, filtered and the filtrate concentrated under reduced pressure to afford a pale green oil of sufficient purity for further use (3.19 g, 87%). R_f 0.27 (P.E. 30–40 °C/EtOAc, 60:40); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.96–2.28 (m, 2H, CH_2CH$_2$O), 2.49 (d, J=2.5 Hz, 1H, O*H*), 3.80–3.86 (m, 1H, BnOC*H*CH$_2$, *trans*), 4.00–4.12 (m, 3H, BnOC*H*CH$_2$, *cis* and CH_2O), 4.57 (s, 2H, PhCH_2O, *cis*), 4.63 (d, J=6.0 Hz, 2H, PhCH_2O, *trans*), 5.35 (dd, J=17.0, 6.0 Hz, 1H, C*H*OH, *trans*), 5.45 (d, J=2.5 Hz, 1H, C*H*OH, *cis*), 7.25–7.40 (m, 5H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.9 (*C*H$_2$, *cis*+*trans*), 64.8 (*C*H$_2$O, *trans*), 67.0 (*C*H$_2$O, *cis*), 71.4 (O*C*H$_2$Ph, *cis*), 72.5 (O*C*H$_2$Ph, *trans*), 78.1 (O*C*H, *trans*), 83.4 (O*C*H, *cis*), 96.3 (HO*C*H, *trans*), 100.7 (HO*C*H, *cis*), 127.9 (Ph, *cis*), 128.1 (Ph, *trans*), 128.2 (Ph, *cis*+*trans*), 128.5 (Ph, *cis*), 128.6 (Ph, *trans*), 137.2 (Ph, *trans*), 137.9 (Ph, *cis*); FTIR (film) ν 3397, 1071, 739, 699 cm^{-1}; LRMS (ES$^+$) *m/z* 218 (M$^+$+NH$_4$), 195 (M$^+$+H), 177 (M$^+$−H$_2$O).

4.5.9. Methyl 6-hydroxy-4-benzyloxy-2-hexenoate (31). A solution of α-benzyloxy-γ-butyrolactol **30** (1.8 g, 9.3 mmol) in toluene (10 mL) was added to a stirred suspension of carbomethoxymethyl triphenylphosphonium bromide (4.25 g, 10 mmol) and potassium *t*-butoxide (1.12 g, 10 mmol) in dry tetrahydrofuran (40 mL) which were premixed at 0 °C for 30 min. The resulting suspension was heated at 80 °C for 3 h, then cooled to ambient temperature, diluted with water (30 mL), and extracted with dichloromethane. The combined organic extracts were dried over $MgSO_4$, filtered and the filtrate concentrated under reduced pressure. Purification of the pale green oil by flash column chromatography eluting with P.E. 30–40 °C/EtOAc (60:40) afforded the title compound as a mixture of *Z* and *E* isomers in a 1:4.3 ratio (1.89 g, 78%). R_f 0.29 (P.E. 30–40 °C/EtOAc, 60:40); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.82–1.88 (m, 2H, CH_2CH$_2$OH), 3.73–3.79 (m, 5H, CH_2OH and OCH_3), 4.23 (q, J=7.0 Hz, 1H, BnOC*H*, *E*), 4.41–4.57 (dd, J=11.0, 6.0 Hz, 2H, PhCH_2O, *Z*), 4.31–4.65 (dd, J=11.0, 6.0 Hz, 2H, PhCH_2O, *E*), 5.19–5.25 (q, J=7.0 Hz, 1H, BnOC*H*, *Z*); 5.95 (d, J=12.0 Hz, 1H, =C*H*CO$_2$CH$_3$, *Z*), 6.05–6.10 (d, J=17.0 Hz, 1H, =C*H*CO$_2$CH$_3$, *E*), 6.25 (dd, J=12.0, 6.0 Hz, 1H, C*H*=CHCO$_2$CH$_3$, *Z*), 6.90 (dd, J=17.0, 6.0 Hz, 1H, C*H*=CHCO$_2$CH$_3$, *E*), 7.28–7.38 (m, 5H, Ph); ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.2 (*C*H$_2$CH$_2$OH, *E*), 37.3 (*C*H$_2$-CH$_2$OH, *Z*), 51.7 (O*C*H$_3$, *Z*), 51.8 (O*C*H$_3$, *E*), 59.8 (*C*H$_2$OH, *E*), 60.0 (*C*H$_2$OH, *Z*), 71.4 (*C*HOBn, *E*), 71.7 (*C*HOBn, *Z*), 74.5 (Ph*C*H$_2$O, *Z*), 76.7 (Ph*C*H$_2$O, *E*), 121.3 (=*C*HCO$_2$-CH$_3$, *Z*), 122.0 (=*C*HCO$_2$CH$_3$, *E*), 127.9 (Ph, *E*), 128.0 (Ph, *Z*), 128.5 (Ph, *Z*), 128.6 (Ph, *E*), 137.6 (Ph, *E*), 137.7 (Ph, *Z*), 147.7 (*C*H=CHCO$_2$CH$_3$, *E*), 150.9 (*C*H=CHCO$_2$CH$_3$, *Z*), 166.5 (*C*O$_2$CH$_3$, *E*), 166.6 (*C*O$_2$CH$_3$, *Z*); FTIR (film) ν 3431, 1730, 738, 699 cm^{-1}; LRMS (ES$^+$) *m/z* 268 (M$^+$+NH$_4$, 38), 251 (M$^+$+H, 100), 233 (17), 210 (13); HRMS (ES$^+$) calcd for $C_{14}H_{22}NO_4$ (M$^+$+NH$_4$) 268.1549, found 268.1549.

4.5.10. Methyl 6-oxo-4-benzyloxy-2-hexenoate (28). To a stirred suspension of pyridinium chlorochromate (2.1 g, 9.6 mmol) in 10 mL of anhydrous dichloromethane, was added at room temperature and under a positive pressure of nitrogen, a solution of methyl 6-hydroxy-4-benzyloxy-2-hexenoate **31** (1.6 g, 6.4 mmol) in 10 mL of dichloromethane. The reaction mixture was stirred for 12 h at room temperature and the solvent removed under reduced pressure. The resulting crude oil was purified by flash column chromatography eluting with P.E. 30–40 °C/EtOAc (80:20) which allowed separation of *Z* and *E* isomers as clear oils (1.08 g, 67%).

Z isomer. R_f 0.48 (P.E. 30–40 °C/EtOAc, 80:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.60–2.84 (m, 2H, CH_2CHO), 3.75 (s, 3H, OCH_3), 4.45–4.63 (dd, J=12.0, 6.0 Hz, 2H, PhCH_2O), 5.50–5.63 (m, 1H, BnOC*H*CH$_2$); 6.00 (d, J=12.0 Hz, 1H, =C*H*CO$_2$CH$_3$), 6.80–6.95 (m, 1H, C*H*=CHCO$_2$CH$_3$), 7.25–7.38 (m, 5H, Ph), 9.75 (s, 1H, C*H*O); ^{13}C NMR (100 MHz, $CDCl_3$) δ 48.4 (*C*H$_2$CHO), 51.6 (O*C*H$_3$), 71.0 (*C*HOBn), 71.7 (Ph*C*H$_2$O), 121.5 (=*C*HCO$_2$CH$_3$), 127.9 (Ph), 128.4 (Ph), 137.7 (Ph), 149.7 (*C*H=CHCO$_2$CH$_3$), 166.1 (*C*O$_2$CH$_3$), 200.8 (*C*HO); FTIR (film) ν 2952, 1725, 698 cm^{-1}; LRMS (ES$^+$) *m/z* 514 (2M$^+$+NH$_4$, 43), 266 (M$^+$+NH$_4$, 100), 249 (M$^+$+H, 27), 210 (14); HRMS (ES$^+$) calcd for $C_{14}H_{17}O_4$ (M$^+$+H) 249.1116, found 249.1127.

E isomer. R_f 0.45 (P.E. 30–40 °C/EtOAc, 80:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.68–2.90 (m, 2H, CH_2CHO), 3.77 (s, 3H, OCH_3), 4.42–4.65 (dd, J=12.0, 6.0 Hz, 2H, PhCH_2O), 5.50–5.63 (m, 1H, BnOC*H*CH$_2$); 6.15 (d, J=17.0 Hz, 1H, =C*H*CO$_2$CH$_3$), 6.85–6.98 (m, 1H, C*H*=CHCO$_2$CH$_3$), 7.21–7.45 (m, 5H, Ph), 9.78 (s, 1H, C*H*O); ^{13}C NMR (100 MHz, $CDCl_3$) δ 48.4 (*C*H$_2$CHO),

51.8 (OCH_3), 71.5 (*C*HOBn), 73.0 ($PhCH_2O$), 122.7 (=*C*HCO_2CH_3), 127.9 (Ph), 128.5 (Ph), 137.3 (Ph), 146.2 (*C*H=CHCO_2CH_3), 166.3 (CO_2CH_3), 199.0 (*C*HO); HRMS (ES^+) calcd for $C_{14}H_{17}O_4$ (M^++H) 249.1116, found 249.1125.

4.5.11. Methyl (*E*)-8-oxo-2-octenoate (33). To a stirred mixture of cyclohexene (2.5 g, 30.4 mmol) and aqueous ruthenium trichloride stock solution (130 mg, 0.627 mmol, 0.035 M) in 1,2-dichloroethane (120 mL) and distilled water (90 mL), was added, in portions, sodium periodate (9.75 g, 45.7 mmol) over a period of 5 min at room temperature. The colour turned from black to yellow immediately. The reaction was monitored by TLC. After completion in 3 h, the reaction was quenched with a saturated aqueous solution of $Na_2S_2O_3$ and the two layers were separated. The aqueous layer was extracted with 1,2-dichloroethane (3×30 mL). The organic layers were dried over anhydrous Na_2SO_4, filtered and the filtrate containing the crude adipaldehyde was directly used without further purification. A suspension of 60% sodium hydride dispersion in mineral oil (0.49 g, 12.2 mmol) in 25 mL of dry 1,2-dichloroethane under a positive nitrogen pressure, was stirred in an ice bath while trimethylphosphonoacetate (2.22 g, 12.2 mmol) in 25 mL of dry 1,2-dichloroethane was added dropwise. After the addition was finished, the reaction mixture was stirred for further 1 h at 0 °C. Then, the solution of crude adipaldehyde in 1,2-dichloroethane was added dropwise. The cold mixture was stirred for further 15 min after the addition. Then, it was slowly brought to reflux and stirred overnight. The clear organic layer was decanted from the oil. The remaining oil was dissolved in warm water and the upper organic layer was separated. The aqueous layer was extracted with dichloromethane. The combined organic layers were washed with saturated $NaHCO_3$, dried over anhydrous Na_2SO_4, filtered and the solvents were removed in vacuo. The resulting crude oil was purified by flash column chromatography eluting with P.E. 30–40 °C/EtOAc (80:20) to afford the aldehyde **33**[54] (2.85 g, 55%) as a colorless oil. R_f 0.66 (P.E. 30–40 °C/EtOAc, 80:20); ^1H NMR (300 MHz, $CDCl_3$) δ 1.38–1.46 (m, 2H, CH_2CH_2CH=), 1.55–1.62 (m, 2H, CH_2CH_2CHO), 2.17 (qd, J=7.1, 1.4 Hz, 2H, CH_2CH=), 2.39 (td, J=7.3, 1.5 Hz, 2H, CH_2CHO), 3.66 (s, 3H, OCH_3), 5.76 (dt, J=15.7, 1.4 Hz, 1H, =C*H*CO_2CH_3), 6.87 (dt, J=15.7, 7.1 Hz, 1H, C*H*=CHCO_2CH_3), 9.69 (t, J=1.5 Hz, 1H, C*H*O); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 21.9 (CH_2), 27.8 (CH_2), 32.2 (CH_2), 43.9 (CH_2), 51.8 (OCH_3), 121.8 (=*C*HCO_2CH_3), 149.0 (*C*H=CHCO_2CH_3), 167.4 (CO_2CH_3), 202.5 (*C*HO); FTIR (film) ν 2949, 2862, 2725, 1724, 1655, 1437, 1275 cm^{-1}; LRMS (ES^+) *m/z* 188 (M^++NH_4, 38), 171 (M^++H, 100), 139 (19).

4.6. Typical procedure for the rhodium catalysed tandem hydrosilylation-aldol reaction

Triethylsilane (0.86 g, 7.4 mmol, 2.1 equiv.) was added slowly to a stirred solution of methyl (*E*)-6-oxo-hexenoate (*E*)-**7** and tris(triphenylphosphine) rhodium (I) chloride (48 mg, 0.05 mmol, 1 mol%) in anhydrous, degassed toluene (20 mL) at ambient temperature. The resulting solution was heated for 16 h at 50 °C and then cooled to room temperature. The reaction mixture was diluted with 2 M aqueous sodium hydroxide (10 mL) and extracted with dichloromethane (60 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the filtrate concentrated under reduced pressure. The resulting crude oil was purified by flash column chromatography eluting with P.E. 30–40 °C/EtOAc (90:10) to afford the product **32** (0.73 g, 81%) as a 3:1 mixture of *cis* and *trans* diastereomers as a colorless oil. An identical procedure was followed when using hydridotetrakis(triphenylphosphine) rhodium (I).

4.6.1. 2-Triethylsilyloxy-cyclopentane carboxylic acid methyl ester (35). R_f 0.69 (P.E. 30–40 °C/EtOAc, 90:10); ^1H NMR (400 MHz, $CDCl_3$) δ 0.48–0.72 (q, J=6.0 Hz, 6H, OSiCH_2CH$_3$, *cis*+*trans*), 0.98–1.02 (t, J=6.0 Hz, 9H, OSiCH$_2$CH_3, *cis*+*trans*), 1.49–2.05 (m, 6H, CH_2, *cis*+*trans*), 2.70–2.81 (m, 1H, C*H*CO_2CH_3, *cis*+*trans*), 3.67 (s, 3H, OCH_3, *cis*), 3.68 (s, 3H, OCH_3, *trans*), 4.40 (q, J=6.0 Hz, 1H, C*H*OSi, *trans*), 4.50 (q, J=4.0 Hz, 1H, C*H*OSi, *cis*); ^{13}C NMR (100 MHz, $CDCl_3$) δ 3.6 (OSi*C*H$_2$-CH$_3$, *trans*), 3.8 (OSi*C*H$_2$CH$_3$, *cis*), 5.6 (OSiCH$_2$*C*H$_3$, *trans*), 5.7 (OSiCH$_2$*C*H$_3$, *cis*), 21.7 (CH$_2$*C*H$_2$CH$_2$, *cis*), 22.7 (CH$_2$*C*H$_2$CH$_2$, *trans*), 23.4 (CH$_2$*C*H$_2$CH, *cis*), 28.1 (CH$_2$*C*H$_2$CH, *trans*), 34.5 (OCH*C*H$_2$, *cis*), 35.5 (OCH*C*H$_2$, *trans*), 50.5 (*C*HCO_2CH_3, *cis*), 50.6 (O*C*H$_3$, *cis*), 51.1 (O*C*H$_3$, *trans*), 53.1 (*C*HCO_2CH_3, *trans*), 74.3 (*C*HOSi, *cis*), 78.3 (*C*HOSi, *trans*), 172.3 (CO_2CH_3, *cis*), 174.6 (CO_2CH_3, *trans*); FTIR (film) ν 2955, 2878, 1738, 1200, 1007 cm^{-1}; LRMS (FAB^+) *m/z* 259 (M^++H, 5), 229 (10), 115 (40), 87 (100); HRMS (FAB^+) calcd for $C_{13}H_{27}O_3Si$ (M^++H) 259.1729, found 259.1710.

4.6.2. 3,3-Dimethyl-2-triethylsilyloxy-cyclopentane carboxylic acid methyl ester (36). R_f 0.63 (P.E. 30–40 °C/EtOAc, 90:10); ^1H NMR (500 MHz, $CDCl_3$) δ 0.55 (q, J=7.9 Hz, 6H, OSiCH_2CH$_3$, *cis*), 0.56 (q, J=7.9 Hz, 6H, OSiCH_2CH$_3$, *trans*), 0.87 (s, 3H, CH$_3$, *cis*), 0.92 (s, 3H, CH$_3$, *trans*), 0.93 (t, J=7.9 Hz, 9H, OSiCH$_2$CH_3, *cis*), 0.94 (t, J=7.9 Hz, 9H, OSiCH$_2$CH_3, *trans*), 0.97 (s, 3H, CH$_3$, *trans*), 0.98 (s, 3H, CH$_3$, *cis*), 1.50 (dd, J=7.4, 8.4 Hz, 2H, CH_2CH$_2$CH, *cis*+*trans*), 1.67–1.71 (dq, J=13.6, 7.4 Hz, 1H, CH_{eq}H$_{ax}$CHCO_2CH_3, *cis*), 1.69–1.72 (m, 1H, CH_{eq}-H$_{ax}$CHCO_2CH_3, *trans*), 1.97 (ddt, J=13.6, 10.8, 8.4 Hz, 1H, CH$_{eq}$H$_{ax}$CHCO_2CH_3, *cis*), 2.12–2.21 (m, 1H, CH$_{eq}$-H$_{ax}$CHCO_2CH_3, *trans*), 2.73 (dt, J=10.8, 7.4 Hz, 1H, C*H*CO_2CH_3, *cis*), 2.96 (td, J=10.4, 7.0 Hz, 1H, C*H*CO_2-CH$_3$, *trans*), 3.66 (s, 3H, OCH_3, *cis*), 3.67 (s, 3H, OCH_3, *trans*), 3.94 (d, J=10.4 Hz, 1H, C*H*OSi, *trans*), 3.94 (d, J=7.4 Hz, 1H, C*H*OSi, *cis*); ^{13}C NMR (125 MHz, $CDCl_3$) δ 4.9 (OSi*C*H$_2$CH$_3$, *cis*), 5.0 (OSi*C*H$_2$CH$_3$, *trans*), 6.8 (OSiCH$_2$*C*H$_3$, *cis*), 6.9 (OSiCH$_2$*C*H$_3$, *trans*), 19.7 (*C*H$_2$CH, *trans*), 21.1 (*C*H$_3$, *cis*), 22.9 (*C*H$_3$, *trans*), 24.7 (*C*H$_2$CH, *cis*), 26.7 (*C*H$_3$, *cis*), 27.7 (*C*H$_3$, *trans*), 36.9 (*C*H$_2$CH$_2$CH, *cis*), 37.0 (*C*H$_2$CH$_2$CH, *trans*), 42.3 (*C*(CH$_3$)$_2$, *cis*), 43.7 (*C*(CH$_3$)$_2$, *trans*), 49.8 (*C*HCO_2CH_3, *trans*), 50.8 (*C*HCO_2CH_3, *cis*), 51.4 (O*C*H$_3$, *trans*), 51.5 (O*C*H$_3$, *cis*), 83.1 (*C*HOSi, *trans*), 83.5 (*C*HOSi, *cis*), 174.3 (CO_2CH_3, *trans*), 176.9 (CO_2CH_3, *cis*); FTIR (film) ν 1738 cm^{-1}; LRMS (FAB^+) *m/z* 287 (M^++H, 3), 257 (10), 255 (5), 155 (18), 125 (60), 95 (100); HRMS (CI^+) calcd for $C_{15}H_{31}O_3Si$ (M^++H) 287.20423, found 287.20397.

4.6.3. 2-Triethylsilyloxyspiro[4.5]decane carboxylic acid

methyl ester (37a). R_f 0.60 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.55–0.60 (q, J=7.8 Hz, 6H, OSiCH_2CH$_3$, *cis*+*trans*), 0.94 (t, J=7.8 Hz, 9H, OSiCH$_2$-CH_3, *trans*), 0.95 (t, J=7.8 Hz, 9H, OSiCH$_2$CH_3, *cis*), 1.23–1.31 (m, 6H, CH_2, *cis*+*trans*), 1.44–1.49 (m, 1H, CH_{eq}-H$_{ax}$CH$_2$CH, *cis*+*trans*), 1.53–1.58 (m, 4H, CH_2, *cis*+*trans*), 1.62–1.65 (m, 1H, CH$_{eq}H_{ax}$CH$_2$CH, *cis*+*trans*), 1.69–1.74 (m, 1H, CH_{eq}H$_{ax}$CHCO$_2$CH$_3$, *cis*), 1.75–1.81 (m, 1H, CH_{eq}H$_{ax}$CHCO$_2$CH$_3$, *trans*), 1.89–1.97 (m, 1H, CH$_{eq}H_{ax}$CHCO$_2$CH$_3$, *trans*), 2.12–2.20 (m, 1H, CH$_{eq}$-H_{ax}CHCO$_2$CH$_3$, *cis*), 2.74 (td, J=10.4, 7.9 Hz, 1H, CHCO$_2$-CH$_3$, *trans*), 2.99 (td, J=9.0, 5.3 Hz, 1H, CHCO$_2$CH$_3$, *cis*), 3.64 (s, 3H, OCH_3, *cis*), 3.65 (s, 3H, OCH_3, *trans*), 3.90 (d, J=7.9 Hz, 1H, CHOSi, *trans*), 3.98 (d, J=5.3 Hz, 1H, CHOSi, *cis*); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.4 (OSiCH$_2$-CH$_3$, *trans*), 5.5 (OSiCH$_2$CH$_3$, *cis*), 7.0 (OSiCH$_2$$CH_3$, *trans*), 7.1 (OSiCH$_2$$CH_3$, *cis*), 22.8 ($CH_2$, Cy, *trans*), 23.3 ($CH_2$, Cy, *cis*), 23.7 ($CH_2$, Cy, *cis*), 23.9 ($CH_2$CH, *cis*), 24.2 ($CH_2$, Cy, *trans*), 25.0 ($CH_2$CH, *trans*), 26.8 ($CH_2$, Cy, *cis*), 26.9 ($CH_2$, Cy, *trans*), 30.0 ($CH_2$, Cy, *trans*), 31.9 ($CH_2$-CH$_2$CH, *trans*), 32.2 ($CH_2CH_2$CH, *cis*), 32.3 ($CH_2$, Cy, *cis*), 36.4 ($CH_2$, Cy, *cis*), 36.6 ($CH_2$, Cy, *trans*), 46.2 ($C$Cy, *trans*), 47.9 ($C$Cy, *cis*), 49.7 ($CHCO_2CH_3$, *cis*), 50.7 ($CHCO_2CH_3$, *trans*), 51.4 (OC$H_3$, *cis*), 51.7 (OC$H_3$, *trans*), 83.9 ($C$HOSi, *cis*), 84.4 ($C$HOSi, *trans*), 175.7 ($CO_2CH_3$, *cis*), 178.8 ($CO_2CH_3$, *trans*); FTIR (film) ν 1738 cm^{-1}; LRMS (CI$^+$) *m/z* 326 (M$^+$, 10), 298 (100), 195 (49), 135 (54); HRMS (CI$^+$) calcd for $C_{18}H_{34}O_3Si$ (M$^+$) 326.22771, found 326.22536.

4.6.4. 2-Triethylsilyloxyspiro[4.5]decane carboxylic acid *i*-propyl ester (37b). R_f 0.75 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.50–0.54 (q, J=7.8 Hz, 6H, OSiCH_2CH$_3$, *cis*+*trans*), 0.86–0.90 (t, J=7.8 Hz, 9H, OSiCH$_2$CH_3, *trans*), 0.95 (t, J=7.8 Hz, 9H, OSiCH$_2$CH_3, *cis*), 1.15–1.21 (m, 12H, CH_2, (CH_3)$_2$, *cis*+*trans*), 1.24–1.41 (m, 1H, CH_{eq}CH$_{ax}$CH$_2$CH, *cis*+*trans*), 1.42–1.56 (m, 4H, CH_2, *cis*+*trans*), 1.57–1.61 (m, 1H, CH$_{eq}$CH_{ax}CH$_2$CH, *cis*+*trans*), 1.64–1.71 (m, 1H, CH_{eq}H$_{ax}$CHCO$_2$*i*Pr, *cis*+*trans*), 1.85–1.93 (m, 1H, CH$_{eq}$-H_{ax}CHCO$_2$*i*Pr, *trans*), 2.07–2.12 (m, 1H, CH$_{eq}H_{ax}$CHCO$_2$-*i*Pr, *cis*), 2.60 (dt, J=10.4, 7.3 Hz, 1H, CHCO$_2$*i*Pr, *trans*), 2.84 (td, J=9.2, 5.2 Hz, 1H, CHCO$_2$*i*Pr, *cis*), 3.88 (d, J=7.3 Hz, 1H, CHOSi, *trans*), 3.89 (d, J=5.2 Hz, 1H, CHOSi, *cis*), 4.89 (m, 1H, OCH(CH$_3$)$_2$, *cis*), 4.91 (m, 1H, OCH(CH$_3$)$_2$, *trans*); ^{13}C NMR (125 MHz, $CDCl_3$) δ 4.1 (OSiCH$_2$CH$_3$, *trans*), 4.2 (OSiCH$_2$CH$_3$, *cis*), 5.9 (OSiCH$_2$-CH$_3$, *trans*), 6.0 (OSiCH$_2$$CH_3$, *cis*), 20.0 ($CH_3$, *trans*), 20.8 ($CH_3$, *cis*), 21.6 ($CH_2$, Cy, *trans*), 22.0 ($CH_2$, Cy, *cis*), 22.3 ($CH_2$, Cy, *cis*), 22.6 ($CH_2$CH, *cis*), 22.7 ($CH_2$, Cy, *trans*), 24.1 ($CH_2$CH, *trans*), 25.3 ($CH_2$, Cy, *cis*), 25.5 ($CH_2$, Cy, *trans*), 27.9 ($CH_2$, Cy, *trans*), 30.9 ($CH_2CH_2$CH, *trans*), 31.1 ($CH_2CH_2$CH, *cis*), 33.1 ($CH_2$, Cy, *cis*), 34.8 ($CH_2$, Cy, *trans*), 35.4 ($CH_2$, Cy, *cis*), 45.0 ($C$Cy, *trans*), 46.2 ($C$Cy, *cis*), 48.9 ($CHCO_2$*i*Pr, *cis*), 50.0 ($CHCO_2$*i*Pr, *trans*), 66.4 (OCH(CH$_3$)$_2$, *cis*), 66.5 (OCH(CH$_3$)$_2$, *trans*), 82.3 (CHOSi, *trans*), 82.4 (CHOSi, *cis*), 171.8 (CO$_2$*i*Pr, *cis*), 174.7 (CO$_2$*i*Pr, *trans*); FTIR (film) ν 2934, 2858, 1717, 1452, 1375, 1107, 908 cm^{-1}; LRMS (CI$^+$) *m/z* 355 (M$^+$+H, 80), 313 (18), 283 (39), 223 (100); HRMS (CI$^+$) calcd for $C_{20}H_{39}O_3Si$ (M$^+$+H) 355.26683, found 355.26676.

4.6.5. 3,3-Diphenyl-2-triethylsilyloxy-cyclopentane carboxylic acid *i*-propyl ester (38). R_f 0.73 (P.E. 30–40 °C/EtOAc, 95:5); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.09–0.26 (q, J=7.8 Hz, 6H, OSiCH_2CH$_3$, *cis*+*trans*), 0.56 (t, J=7.8 Hz, 9H, OSiCH$_2$CH_3, *cis*), 0.59 (t, J=7.8 Hz, 9H, OSiCH$_2$CH_3, *trans*), 1.02 (d, J=6.3 Hz, 3H, CH_3, *trans*), 1.03 (d, J=6.3 Hz, 3H, CH_3, *cis*), 1.05 (d, J=6.3 Hz, 3H, CH_3, *trans*), 1.06 (d, J=6.3 Hz, 3H, CH_3, *cis*), 1.42–1.48 (m, 1H, CH_{eq}H$_{ax}$CHCO$_2$*i*Pr, *cis*), 1.49–1.54 (m, 1H, CH_{eq}H$_{ax}$-CHCO$_2$*i*Pr, *trans*), 1.79–1.86 (m, 1H, CH$_{eq}H_{ax}$CHCO$_2$*i*Pr, *trans*), 2.11–2.16 (m, 1H, CH$_{eq}H_{ax}$CHCO$_2$*i*Pr, *cis*), 2.17 (dt, J=12.9, 7.7 Hz, 1H, CH_{eq}H$_{ax}$CH$_2$CH, *trans*), 2.27 (ddd, J=12.9, 7.7, 5.9 Hz, 1H, CH$_{eq}H_{ax}$CH$_2$CH, *trans*), 2.29–2.32 (m, 1H, CH_{eq}H$_{ax}$CH$_2$CH, *cis*), 2.68 (ddd, J=12.0, 11.0, 9.2 Hz, 1H, CH$_{eq}H_{ax}$CH$_2$CH, *cis*), 2.70 (dt, J=11.0, 6.3 Hz, 1H, CHCO$_2$*i*Pr, *trans*), 2.89 (ddd, J=11.0, 7.4, 3.7 Hz, 1H, CHCO$_2$*i*Pr, *cis*), 4.74–4.82 (m, 1H, OCH(CH$_3$)$_2$, *cis*+*trans*), 4.85 (d, J=6.3 Hz, 1H, CHOSi, *trans*), 5.13 (d, J=3.7 Hz, 1H, CHOSi, *cis*), 6.93–7.19 (m, 10H, Ph, *cis*+*trans*); ^{13}C NMR (125 MHz, $CDCl_3$) δ 5.2 (OSiCH$_2$-CH$_3$, *trans*), 5.4 (OSiCH$_2$CH$_3$, *cis*), 7.2 (OSiCH$_2$$CH_3$, *trans*), 7.4 (OSiCH$_2$$CH_3$, *cis*), 22.2 ($CH_3$, *trans*), 22.3 ($CH_3$, *cis*), 22.5 ($CH_2CH_2$CH, *cis*), 25.7 ($CH_2CH_2$CH, *trans*), 32.8 ($CH_2$CHCO$_2$*i*Pr, *cis*), 35.5 ($CH_2$CHCO$_2$*i*Pr, *trans*), 50.2 ($CHCO_2$*i*Pr, *cis*), 51.7 ($CHCO_2$*i*Pr, *trans*), 59.5 ($CPh_2$, *trans*), 61.7 ($CPh_2$, *cis*), 68.2 (OC$H$(CH$_3$)$_2$, *cis*), 68.3 (OC$H$(CH$_3$)$_2$, *trans*), 81.2 ($C$HOSi, *cis*), 82.1 ($C$HOSi, *trans*), 126.1 (Ph, *cis*+*trans*), 126.4 (Ph, *cis*+*trans*), 126.9 (Ph, *cis*), 127.8 (Ph, *trans*), 127.9 (Ph, *trans*), 128.0 (Ph, *trans*), 128.4 (Ph, *cis*), 128.6 (Ph, *cis*), 128.9 (Ph, *cis*), 129.8 (Ph, *trans*), 145.1 (Ph, *trans*), 145.8 (Ph, *cis*), 146.6 (Ph, *cis*), 146.8 (Ph, *trans*), 172.6 (CO$_2$*i*Pr, *cis*), 175.2 (CO$_2$*i*Pr, *trans*); FTIR (film) ν 3059, 3028, 2955, 2912, 2876, 1728, 1661, 1651, 1599, 1495, 1447, 1373, 1265, 1109 cm^{-1}; LRMS (FAB$^+$) *m/z* 439 (M$^+$+H, 33), 409 (42), 367 (25), 349 (38), 219 (77); HRMS (FAB$^+$) calcd for $C_{27}H_{39}O_3Si$ (M$^+$+H) 439.26680, found 439.26640; Crystal data for $C_{27}H_{38}O_3Si$,[56] M=438.66, triclinic, a=8.6086(11) Å, b=8.9819(12) Å, c=17.411(2) Å, U=1285.6(3) Å^3, T=293 K, space group $P\,1$, Z=2, μ(Mo Kα) 0.115 mm^{-1}, 11181 reflections measured, 5848 unique F^2 values used in refinement (R_{int}=0.0210), R_1[4707 with $F^2>2\sigma$]=0.0543, wR_2(all data)=0.1570.

4.6.6. 4,4-Dimethyl-2-triethylsilyloxy-cyclopentane carboxylic acid methyl ester (39). R_f 0.59 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.50–0.56 (q, J=7.9 Hz, 6H, OSiCH_2CH$_3$, *cis*+*trans*), 0.88–0.93 (t, J=7.9 Hz, 9H, OSiCH$_2$CH_3, *cis*+*trans*), 0.95 (s, 3H, CH_3, *cis*), 1.05 (s, 3H, CH_3, *trans*), 1.06 (s, 3H, CH_3, *trans*), 1.13 (s, 3H, CH_3, *cis*), 1.45 (dd, J=12.9, 7.2 Hz, 1H, CH$_{eq}H_{ax}$CHOSi, *trans*), 1.54 (dd, J=12.9, 7.7 Hz, 1H, CH_{eq}H$_{ax}$CHCO$_2$CH$_3$, *cis*), 1.56 (dd, J=13.3, 3.7 Hz, 1H, CH_{eq}H$_{ax}$CHOSi, *cis*), 1.58 (dd, J=12.9, 10.0 Hz, 1H, CH$_{eq}H_{ax}$CHCO$_2$CH$_3$, *trans*), 1.71 (dd, J=13.3, 5.7 Hz, 1H, CH$_{eq}H_{ax}$CHOSi, *cis*), 1.77 (dd, J=12.9, 7.2 Hz, 1H, CH_{eq}H$_{ax}$CHOSi, *trans*), 1.79 (dd, J=12.9, 8.9 Hz, 1H, CH_{eq}H$_{ax}$CHCO$_2$CH$_3$, *trans*), 2.09 (dd, J=12.9, 11.0 Hz, 1H, CH$_{eq}H_{ax}$CHCO$_2$CH$_3$, *cis*), 2.83 (ddd, J=10.0, 8.9, 7.2 Hz, 1H, CHCO$_2$CH$_3$, *trans*), 2.93 (ddd, J=11.0, 7.7, 5.7 Hz, 1H, CHCO$_2$CH$_3$, *cis*), 3.63 (s, 3H, OCH_3, *cis*), 3.65 (s, 3H, OCH_3, *trans*), 4.45 (q, J=7.2 Hz, 1H, CHOSi, *trans*), 4.53 (td, J=5.7, 3.7 Hz, 1H, CHOSi, *cis*); ^{13}C NMR (125 MHz, $CDCl_3$) δ 4.4 (OSiCH$_2$CH$_3$, *cis*),

4.6 ($OSiCH_2CH_3$, *trans*), 6.4 ($OSiCH_2CH_3$, *cis*), 6.7 ($OSiCH_2CH_3$, *trans*), 27.3 (CH_3, *cis*), 30.3 (CH_3, *trans*), 36.6 ($C(CH_3)_2$, *cis*), 37.2 ($C(CH_3)_2$, *trans*), 40.6 (CH_2, *cis*), 43.0 (CH_2, *trans*), 50.1 (CH_2, *trans*), 50.5 (CH_2, *cis*), 50.8 ($CHCO_2CH_3$, *cis*), 51.2 (OCH_3, *cis*), 51.5 ($CHCO_2CH_3$, *trans*), 53.2 (OCH_3, *trans*), 75.4 (*C*HOSi, *cis*), 76.5 (*C*HOSi, *trans*), 173.1 (CO_2CH_3, *cis*), 175.9 (CO_2CH_3, *trans*); FTIR (film) ν 2955, 2876, 1740, 1460, 1435, 1171 cm^{-1}; LRMS (FAB^+) *m/z* 287 (M^++H, 3), 257 (10), 255 (5), 155 (18), 125 (60), 95 (100); HRMS (CI^+) calcd for $C_{15}H_{31}O_3Si$ (M^++H) 287.20423, found 287.20397.

4.6.7. 4-(3-Triethylsilanyloxy-propyl)-5*H*-furan-2-one (40). R_f 0.62 (EtOAc); ^1H NMR (300 MHz, CD_2Cl_2) δ 0.49 (q, *J*=7.8 Hz, 6H, $OSiCH_2CH_3$), 0.88 (t, *J*=7.8 Hz, 9H, $OSiCH_2CH_3$), 1.70–1.75 (m, 2H, CH_2CH_2OSi), 2.42 (td, *J*=7.9, 1.8 Hz, 2H, CH_2CH_2C=), 3.58 (t, *J*=7.8 Hz, 2H, CH_2OSi), 4.67 (d, *J*=1.8 Hz, 2H, =CCH_2O), 5.71–5.76 (m, 1H, =$CHCO_2R$); ^{13}C NMR (75.5 MHz, CD_2Cl_2) δ 3.2 ($OSiCH_2CH_3$), 5.7 ($OSiCH_2CH_3$), 24.4 (CH_2CH_2OSi), 29.6 (CH_2CH_2C=), 60.8 (CH_2OSi), 72.4 (OCH_2C=), 114.3 (=$CHCO_2R$), 170.0 (C=$CHCO_2R$), 173.1 (CO_2R); FTIR (film) ν 2957, 2876, 1747, 1655, 1456, 1414, 1379, 1238, 1074 cm^{-1}; LRMS (DCI^+) *m/z* 257 (M^++H, 81), 227 (47), 197 (12), 115 (15); HRMS (DCI^+) calcd for $C_{13}H_{25}O_3Si$ (M^++H) 257.15728, found 257.15669.

4.6.8. Methyl (*E*)-3-methyl-6-triethylsilanyloxy-hex-2-enoate (41). R_f 0.70 (P.E. 30–40 °C/EtOAc, 95:5); ^1H NMR (300 MHz, $CDCl_3$) δ 0.52 (q, *J*=7.8 Hz, 6H, $OSiCH_2CH_3$), 0.89 (t, *J*=7.8 Hz, 9H, $OSiCH_2CH_3$), 1.60–1.65 (m, 2H, CH_2CH_2OSi), 2.09 (d, *J*=1.2 Hz, 3H, CH_3), 2.14 (td, *J*=7.8, 1.1 Hz, 2H, CH_2CH_2C=), 3.52 (t, *J*=6.5 Hz, 2H, CH_2OSi), 3.61 (s, 3H, OCH_3), 5.61–5.64 (m, 1H, =$CHCO_2CH_3$); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 3.5 ($OSiCH_2CH_3$), 5.7 ($OSiCH_2CH_3$), 17.8 (CH_3), 29.7 (CH_2CH_2OSi), 36.3 (CH_2CH_2C=), 49.7 (OCH_3), 61.1 (CH_2OSi), 114.2 (=$CHCO_2CH_3$), 159.0 (C=$CHCO_2CH_3$), 166.2 (CO_2CH_3); FTIR (film) ν 2876, 1728, 1651, 1435, 1360, 1101 cm^{-1}; LRMS (DCI^+) *m/z* 273 (M^++H, 100), 258 (5), 243 (34), 132 (28); HRMS (DCI^+) calcd for $C_{14}H_{29}O_3Si$ (M^++H) 273.18858, found 273.18821.

4.6.9. Methyl 1-triethylsilanyloxy-octahydro-indene-2-carboxylate (42). R_f 0.80 (P.E. 30–40 °C/EtOAc, 90:10); ^1H NMR (500 MHz, $CDCl_3$) δ 0.55–0.58 (q, *J*=7.8 Hz, 6H, $OSiCH_2CH_3$), 0.90–0.97 (t, *J*=7.8 Hz, 9H, $OSiCH_2CH_3$), 1.05–2.34 (m, 12H, CH_2 and CH), 2.58–3.10 (m, 1H, $CHCO_2CH_3$), 3.64–3.68 (s, 3H, OCH_3), 3.73–4.39 (m, 1H, CHOSi); ^{13}C NMR (125 MHz, $CDCl_3$) δ 3.4–3.9 ($OSiCH_2CH_3$), 5.7–5.8 ($OSiCH_2CH_3$), 19.9–33.5 (CH_2), 33.9–52.3 (CH, OCH_3), 75.6 (CHOSi), 77.7 (CHOSi), 78.2 (CHOSi), 78.3 (CHOSi), 78.5 (CHOSi), 80.2 (CHOSi), 172.9 (CO_2CH_3), 173.2 (CO_2CH_3), 173.6 (CO_2CH_3), 175.7 (CO_2CH_3), 176.2 (CO_2CH_3), 176.4 (CO_2CH_3); FTIR (film) ν 3053, 2930, 2878, 2855, 1732, 1435, 1265 cm^{-1}; LRMS (FAB^+) *m/z* 313 (M^++H, 8), 283 (100), 267 (5), 251 (31), 221 (34), 207 (25); HRMS (FAB^+) calcd for $C_{17}H_{33}O_3Si$ (M^++H) 313.21988, found 313.21948.

4.6.10. Triethyl-(3-methoxy-1,5,6,7,8,9-hexahydro-benzo[c]oxepin-1-yloxy)-silane (43). R_f 0.57 (P.E. 30–40 °C/EtOAc, 90:10); ^1H NMR (300 MHz, $CDCl_3$) δ 0.56 (q, *J*=7.9 Hz, 6H, $OSiCH_2CH_3$), 0.88 (t, *J*=7.9 Hz, 9H, $OSiCH_2CH_3$), 1.51–1.54 (m, 4H, $CH_2CH_2CH_2CH_2$), 1.90–1.94 (m, 2H, CH_2CH_2C=), 2.08–2.11 (m, 2H, CH_2CH_2C=), 2.95 (d, *J*=6.6 Hz, 2H, =CCH_2CH=), 3.59 (s, 3H, OCH_3), 5.35 (t, *J*=6.6 Hz, 1H, CH_2CH=), 6.02 (s, 1H, OCHOSi); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 4.8 ($OSiCH_2CH_3$), 6.8 ($OSiCH_2CH_3$), 28.5 (CH_2), 28.8 (CH_2), 31.9 (CH_2), 35.3 (CH_2), 37.3 (=CCH_2CH=), 51.8 (OCH_3), 116.2 (CH=$C(O)OCH_3$), 119.4 (CH_2C=CCH_2), 132.4 (OCHOSi), 138.4 (CH_2C=CCH_2), 174.1 (=$C(O)OCH_3$); FTIR (film) ν 2934, 2878, 1736, 1439, 1265, 1173 cm^{-1}; LRMS (ES^+) *m/z* 328 (M^++NH_4, 18), 311 (M^++H, 100), 246 (11); HRMS (ES^+) calcd for $C_{17}H_{31}O_3Si$ (M^++H) 311.2042, found 311.2439.

4.6.11. 2-Triethylsilyloxy-3,4-phenyl-cyclopentane carboxylic acid methyl ester (44). R_f 0.79 (P.E. 30–40 °C/EtOAc, 90:10); ^1H NMR (500 MHz, $CDCl_3$) δ 0.62 (q, *J*=7.9 Hz, 6H, $OSiCH_2CH_3$, *cis*+*trans*), 0.91 (t, *J*=7.9 Hz, 9H, $OSiCH_2CH_3$, *cis*+*trans*), 2.88 (dd, *J*=11.2, 7.8 Hz, 1H, $CH_{eq}H_{ax}CHCO_2CH_3$, *cis*), 2.98 (dd, *J*=15.0, 8.5 Hz, 1H, $CH_{eq}H_{ax}CHCO_2CH_3$, *trans*), 3.11 (dt, *J*=8.5, 6.7 Hz, 1H, $CH_2CHCO_2CH_3$, *trans*), 3.19 (dd, *J*=15.0, 8.5 Hz, 1H, $CH_{eq}H_{ax}CHCO_2CH_3$, *trans*), 3.28 (dt, *J*=7.8, 6.2 Hz, 1H, $CH_2CHCO_2CH_3$, *cis*), 3.47 (dd, *J*=11.2, 7.8 Hz, 1H, $CH_{eq}H_{ax}CHCO_2CH_3$, *cis*), 3.68 (s, 3H, OCH_3, *trans*), 3.73 (s, 3H, OCH_3, *cis*), 5.34 (d, *J*=6.2 Hz, 1H, CHOSiEt$_3$, *cis*), 5.51 (d, *J*=6.7 Hz, 1H, CHOSiEt$_3$, *trans*), 7.13–7.64 (m, 4H, Ph, *cis*+*trans*); ^{13}C NMR (125 MHz, $CDCl_3$) δ 4.0 ($OSiCH_2CH_3$, *trans*), 5.7 ($OSiCH_2CH_3$, *trans*), 33.2 (CH_2, *trans*), 50.6 (OCH_3, *trans*), 53.6 ($CHCO_2CH_3$, *trans*), 78.2 (CHOSiEt$_3$, *trans*), 123.0 (Ph, *trans*), 123.4 (Ph, *trans*), 126.1 (Ph, *trans*), 127.5 (Ph, *trans*), 138.6 (Ph, *trans*), 142.9 (Ph, *trans*), 174.0 (CO_2CH_3); FTIR (film) ν 2955, 2877, 1731, 1637, 1437, 1351, 909 cm^{-1}; LRMS (ES^+) *m/z* 324 (M^++NH_4, 100), 307 (M^++H, 44), 246 (61), 175 (93); HRMS (ES^+) calcd for $C_{17}H_{27}O_3Si$ (M^++H) 307.1729, found 307.1735.

4.6.12. Methyl (1*S*,2*S*,3*S*,4*S*)-2-triethylsilyloxy-3,4-isopropylidene-dioxy-cyclopentane carboxylate (45a). R_f 0.53 (P.E. 30–40 °C/EtOAc, 95:5); ^1H NMR (500 MHz, $CDCl_3$) δ 0.51 (q, *J*=7.7 Hz, 6H, $OSiCH_2CH_3$), 0.86 (t, *J*=7.7 Hz, 9H, $OSiCH_2CH_3$), 1.21 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.89 (dd, *J*=13.8, 6.3 Hz, 1H, $CH_{eq}H_{ax}CHCO_2CH_3$), 2.24 (ddd, *J*=13.8, 10.7, 5.4 Hz, 1H, $CH_{eq}H_{ax}CHCO_2CH_3$), 3.02 (ddd, *J*=10.7, 6.3, 4.0 Hz, 1H, $CHCO_2CH_3$), 3.60 (s, 3H, OCH_3), 4.20 (d, *J*=5.4 Hz, 1H, CHCHOSiEt$_3$), 4.28 (d, *J*=4.0 Hz, 1H, CHOSiEt$_3$), 4.67 (t, *J*=5.4 Hz, 1H, CH_2CHO); ^{13}C NMR (125 MHz, $CDCl_3$) δ 3.7 ($OSiCH_2CH_3$), 5.7 ($OSiCH_2CH_3$), 22.8 (CH_3), 25.1 (CH_3), 30.8 (CH_2), 46.2 ($CHCO_2CH_3$), 50.4 (OCH_3), 76.8 (CHOSiEt$_3$), 78.2 (CH_2CHO), 84.9 (OCHCHOSiEt$_3$), 108.9 ($OC(CH_3)_2$), 171.1 (CO_2CH_3); FTIR (film) ν 2936, 2878, 1733, 1439, 1376, 1262, 902 cm^{-1}; LRMS (FAB^+) *m/z* 331 (M^++H, 20), 301 (100), 241 (15), 211 (10), 187 (10); HRMS (FAB^+) calcd for $C_{16}H_{31}O_5Si$ (M^++H) 331.19406, found 331.19408; $[\alpha]_D^{20}$: −20.7 (*c*=0.50, $CHCl_3$/MeOH 9:1).

4.6.13. 2-Triethylsilanyloxy-4-benzyloxy-cyclopentane carboxylic acid methyl ester (46a). R_f 0.68 (P.E. 30–40 °C/EtOAc, 90:10); ^1H NMR (500 MHz, $CDCl_3$) δ 0.54 (q, *J*=7.7 Hz, 6H, $OSiCH_2CH_3$), 0.90 (t, *J*=7.7 Hz, 9H,

OSiCH$_2$CH$_3$), 1.71 (ddd, J=13.6, 7.0, 6.6 Hz, 1H, CH$_{eq}$-H$_{ax}$CHOSiEt$_3$), 1.93 (ddd, J=13.3, 9.9, 6.5 Hz, 1H, CH$_{eq}$-H$_{ax}$CO$_2$CH$_3$), 2.09 (ddd, J=13.3, 8.1, 3.6 Hz, 1H, CH$_{eq}$H$_{ax}$CO$_2$CH$_3$); 2.31 (ddd, J=13.6, 7.2, 6.7 Hz, 1H, CH$_{eq}$H$_{ax}$CHOSiEt$_3$), 2.92 (ddd, J=9.9, 8.1, 7.8 Hz, 1H, CHCO$_2$CH$_3$), 3.64 (s, 3H, OCH$_3$), 3.95 (m, 1H, CHOBn), 4.29 (ddd, J=7.8, 7.2, 7.0 Hz, 1H, CHOSiEt$_3$), 4.42 (s, 2H, ArCH$_2$O); 7.29–7.42 (m, 5H, Ph); ^{13}C NMR (100 MHz, CDCl$_3$) δ 4.6 (OSiCH$_2$CH$_3$), 6.7 (OSiCH$_2$CH$_3$), 34.6 (CH$_2$), 42.0 (CH$_2$), 51.1 (OCH$_3$), 51.7 (CHCO$_2$CH$_3$), 70.7 (OCH$_2$Ph), 74.5 (CHOBn), 76.9 (CHOSiEt$_3$), 127.5 (Ph), 127.6 (Ph), 128.4 (Ph), 138.5 (Ph), 175.6 (CO$_2$CH$_3$); FTIR (film) ν 2953, 2912, 2876, 1739, 1496, 1455, 1436, 1354, 1116, 1058, 736, 697 cm^{-1}; LRMS (ES$^+$) m/z 382 (M$^+$+NH$_4$, 72), 365 (M$^+$+H, 100), 251 (10); HRMS (ES$^+$) calcd for C$_{20}$H$_{36}$NO$_4$Si (M$^+$+NH$_4$) 382.2414, found 382.2404.

4.6.14. 6-Triethylsilanyloxy-5-heptenoate (47). R_f 0.69 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.62–0.66 (q, J=8.0 Hz, 6H, OSiCH$_2$CH$_3$, *cis*+*trans*), 0.94–0.99 (t, J=8.0 Hz, 9H, OSiCH$_2$CH$_3$, *cis*+*trans*), 1.62–1.65 (m, 2H, CH$_2$CH$_2$CH$_2$, *cis*+*trans*), 1.71 (d, J=1.0 Hz, 3H, CH$_3$, *trans*), 1.77 (d, J=1.1 Hz, 3H, CH$_3$, *cis*), 1.95 (q, J=7.5 Hz, 2H, CH$_2$CH$_2$CH=, *trans*), 2.02 (q, J=7.2 Hz, 2H, CH$_2$CH$_2$CH=, *cis*), 2.29 (t, J=7.5 Hz, 2H, CH$_2$CO$_2$CH$_3$, *cis*+*trans*), 3.65 (s, 3H, OCH$_3$, *cis*), 3.66 (s, 3H, OCH$_3$, *trans*), 4.33 (tq, J=7.2, 1.1 Hz, 1H, CH=C(OSi)CH$_3$, *cis*), 4.60 (tq, J=7.5, 1.0 Hz, 1H, CH=C(OSi)CH$_3$, *trans*); ^{13}C NMR (125 MHz, CDCl$_3$) δ 4.9 (OSiCH$_2$CH$_3$, *cis*), 5.0 (OSiCH$_2$CH$_3$, *trans*), 6.4 (OSiCH$_2$CH$_3$, *cis*), 6.5 (OSiCH$_2$CH$_3$, *trans*), 17.6 (CH$_3$, *trans*), 22.6 (CH$_3$, *cis*), 24.6 (CH$_2$CH$_2$C=, *cis*), 25.6 (CH$_2$CH$_2$CH$_2$, *cis*+*trans*), 26.5 (CH$_2$CH$_2$C=, *trans*), 33.3 (CH$_2$CO$_2$CH$_3$, *trans*), 33.7 (CH$_2$CO$_2$CH$_3$, *cis*), 51.3 (OCH$_3$, *cis*), 51.4 (OCH$_3$, *trans*), 106.4 (CH=C(OSi)CH$_3$, *trans*), 107.0 (CH=C(OSi)CH$_3$, *cis*), 147.5 (CH=C(OSi)CH$_3$, *cis*), 148.7 (CH=C(OSi)CH$_3$, *trans*), 174.2 (CO$_2$CH$_3$, *trans*), 174.3 (CO$_2$CH$_3$, *cis*); FTIR (film) ν 3053, 2955, 2914, 2878, 1732, 1670, 1437, 1362, 1265 cm^{-1}; LRMS (CI$^+$) m/z 273 (M$^+$+H, 51), 243 (24), 103 (100); HRMS (CI$^+$) calcd for C$_{14}$H$_{29}$O$_3$Si (M$^+$+H) 273.18858, found 273.18830.

4.6.15. Methyl 4,4-dimethyl-5-oxiranyl-pentanoate (48). R_f 0.28 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.91 (s, 3H, CH$_3$), 0.93 (s, 3H, CH$_3$), 1.34–1.36 (m, 2H, CH$_2$CHOCH$_2$), 1.56–1.66 (m, 2H, CH$_2$CH$_2$CO$_2$CH$_3$); 2.20–2.27 (m, 2H, CH$_2$CH$_2$CO$_2$CH$_3$); 2.35 (dd, J=5.0, 2.7 Hz, 1H, CH$_a$HO), 2.69 (dd, J=5.0, 4.1 Hz, 1H, CHH_bO), 2.89–2.90 (m, 1H, CHO), 3.59 (s, 3H, OCH$_3$); ^{13}C NMR (125 MHz, CDCl$_3$) δ 26.8 (CH$_3$), 26.9 (CH$_3$), 29.3 (CH$_2$CH$_2$CO$_2$CH$_3$); 32.8 (CH$_2$CO$_2$CH$_3$); 36.6 (C(CH$_3$)$_2$), 44.4 (CH$_2$), 46.7 (CH$_2$O), 49.2 (CHO), 51.6 (OCH$_3$), 174.5 (CO$_2$CH$_3$); FTIR (film) ν 2958, 2924, 2850, 1730, 1463, 1436, 1264, 1172 cm^{-1}; LRMS (ES$^+$) m/z 187 (M$^+$+H, 100), 204 (M$^+$+NH$_4$, 25); HRMS (ES$^+$) calcd for C$_{10}$H$_{19}$O$_3$ (M$^+$+H) 187.1320, found 187.1328.

4.6.16. 7-Phenyl-6-triethylsilanyloxy-6-heptenoic acid methyl ester (49). R_f 0.76 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (300 MHz, CDCl$_3$) δ 0.60 (q, J=7.8 Hz, 6H, OSiCH$_2$CH$_3$), 0.90 (t, J=7.8 Hz, 9H, OSiCH$_2$CH$_3$), 1.40–1.62 (m, 4H, CH$_2$CH$_2$CH$_2$CH$_2$), 1.96–2.02 (m, 2H, CH$_2$-C(OSiEt$_3$)=), 2.24 (t, J=7.2 Hz, 2H, CH$_2$CO$_2$CH$_3$), 3.31 (d, J=7.1 Hz, 1H, =CHCH$_2$Ph), 3.59 (s, 3H, OCH$_3$), 4.55 (t, J=7.1 Hz, 1H, =CHCH$_2$Ph), 7.09–7.28 (m, 5H, Ph); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 5.7 (OSiCH$_2$CH$_3$), 7.2 (OSiCH$_2$CH$_3$), 27.0 (CH$_2$), 31.9 (CH$_2$), 34.6 (CH$_2$), 36.7 (CH$_2$), 51.9 (OCH$_3$), 54.8 (CH$_2$Ph), 107.0 (=CHCH$_2$Ph), 128.6 (Ph), 128.7 (Ph), 129.0 (Ph), 132.6 (Ph), 151.1 (C(OSiEt$_3$)=CH), 167.1 (CO$_2$CH$_3$); FTIR (film) ν 3051, 2930, 2876, 1736, 1435, 1264, 1016 cm^{-1}; LRMS (CI$^+$) m/z 363 (M$^+$+H, 30), 348 (28), 332 (19), 232 (14); HRMS (CI$^+$) calcd for C$_{21}$H$_{35}$O$_3$Si (M$^+$+H) 363.23553, found 363.23519.

4.6.17. (2*E*)-4,4-Dimethyl-triethylsilanyloxy-nona-2,7-dienoic acid methyl ester (50). R_f 0.79 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (300 MHz, CDCl$_3$) δ 0.56 (q, J=7.9 Hz, 6H, OSiCH$_2$CH$_3$), 0.89 (t, J=7.9 Hz, 9H, OSiCH$_2$CH$_3$), 0.99 (s, 6H, C(CH$_3$)$_2$), 1.25–1.32 (m, 2H, CH$_2$CH$_2$CH=), 1.70 (s, 3H, CH$_3$C(OSiEt$_3$)=CH), 1.79–1.80 (m, 2H, CH$_2$CH=), 3.68 (s, 3H, OCH$_3$), 4.24 (t, J=6.6 Hz, 1H, CH$_2$CH=), 6.65 (d, J=15.8 Hz, 1H, =CHCO$_2$CH$_3$), 6.84 (d, J=15.8 Hz, 1H, CH=CHCO$_2$CH$_3$); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 6.0 (OSiCH$_2$CH$_3$), 7.1 (OSiCH$_2$CH$_3$), 21.0 (CH$_2$CH$_2$CH=), 23.1 (CH=CCH$_3$), 26.6 (C(CH$_3$)$_2$), 37.2 (C(CH$_3$)$_2$), 42.6 (CH$_2$CH=), 51.8 (OCH$_3$), 108.5 (=CHCH$_2$), 117.7 (=CHCO$_2$CH$_3$), 147.2 (CH=CHCO$_2$CH$_3$), 159.0 (CH=C(CH$_3$)OSiEt$_3$), 167.5 (CO$_2$CH$_3$); FTIR (film) ν 2959, 2914, 2877, 1717, 1651, 1465, 1437, 1380, 902 cm^{-1}; LRMS (FAB$^+$) m/z 327 (M$^+$+H, 100), 297 (60), 253 (34), 225 (21), 185 (79); HRMS (CI$^+$) calcd for C$_{18}$H$_{35}$O$_3$Si (M$^+$+H) 327.23553, found 327.23496.

4.6.18. Methyl 7-triethylsilanyloxy-6-heptenoate (51). R_f 0.70 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.53–0.67 (q, J=7.9 Hz, 6H, OSiCH$_2$CH$_3$, *cis*+*trans*), 0.88–0.98 (t, J=7.9 Hz, 9H, OSiCH$_2$CH$_3$, *cis*+*trans*), 1.27–1.40 (m, 2H, CH$_2$CH$_2$CH=, *cis*+*trans*), 1.56–1.68 (m, 2H, CH$_2$CH$_2$CO$_2$CH$_3$, *cis*+*trans*), 1.83–1.92 (qd, J=7.4, 1.0 Hz, 2H, CH$_2$CH=, *trans*), 2.05–2.11 (qd, J=7.2, 1.3 Hz, 2H, CH$_2$CH=, *cis*), 2.25–2.35 (m, 2H, CH$_2$CO$_2$CH$_3$, *cis*+*trans*), 3.65 (s, 3H, OCH$_3$, *cis*+*trans*), 4.41 (q, J=7.2 Hz, 1H, =CHCH$_2$, *cis*), 4.96 (dt, J=12.0, 7.4 Hz, 1H, =CHCH$_2$, *trans*), 6.21 (d, J=7.2 Hz, 1H, =CHOSi, *cis*), 6.24 (d, J=12.0 Hz, 1H, =CHOSi, *trans*); ^{13}C NMR (75.5 MHz, CDCl$_3$) δ 4.4 (OSiCH$_2$CH$_3$, *cis*), 5.4 (OSiCH$_2$CH$_3$, *trans*), 6.9 (OSiCH$_2$CH$_3$, *cis*), 7.1 (OSiCH$_2$CH$_3$, *trans*), 23.5 (CH$_2$), 24.7 (CH$_2$), 24.9 (CH$_2$), 27.3 (CH$_2$), 29.5 (CH$_2$), 30.3 (CH$_2$), 34.3 (CH$_2$), 34.4 (CH$_2$), 51.7 (OCH$_3$, *cis*+*trans*), 110.4 (=CHCH$_2$, *cis*), 111.3 (=CHCH$_2$, *trans*), 139.0 (=CHOSi, *cis*), 140.6 (=CHOSi, *trans*), 174.3 (CO$_2$CH$_3$, *cis*), 174.6 (CO$_2$CH$_3$, *trans*); FTIR (film) ν 2937, 2877, 1732, 1652, 1436, 907 cm^{-1}; LRMS (CI$^+$) m/z 273 (M$^+$+H, 25), 243 (19), 211 (12); 175 (60); HRMS (CI$^+$) calcd for C$_{14}$H$_{29}$O$_3$Si (M$^+$+H) 273.18858, found 273.18832.

4.6.19. Methyl 2-triethylsilyloxycyclohexanecarboxylate (52). R_f 0.55 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (500 MHz, CDCl$_3$) δ 0.50–0.57 (q, J=7.9 Hz, 6H, OSiCH$_2$-CH$_3$, *cis*+*trans*), 0.89–0.92 (t, J=7.9 Hz, 9H, OSiCH$_2$CH$_3$,

cis+*trans*), 1.15–1.90 (m, 8H, CH_2, *cis*+*trans*), 2.27–2.30 (m, 1H, CHCO_2CH_3, *cis*), 2.30–2.34 (ddd, *J*=9.7, 9.2, 3.5 Hz, 1H, CHCO_2CH_3, *trans*), 3.63 (s, 3H, OCH_3, *cis*), 3.64 (s, 3H, OCH_3, *trans*), 3.77 (dt, *J*=9.7, 4.3 Hz, 1H, CHOSi, *trans*), 3.96–4.00 (m, 1H, CHOSi, *cis*); ^{13}C NMR (125 MHz, $CDCl_3$) δ 4.4 (OSiCH_2CH$_3$, *cis*), 4.9 (OSiCH_2-CH$_3$, *trans*), 6.5 (OSiCH$_2$$CH_3$, *cis*), 6.8 (OSiCH$_2$$CH_3$, *trans*), 19.7 ($CH_2$, *cis*), 22.0 ($CH_2$, *cis*), 24.3 ($CH_2$, *trans*), 24.4 ($CH_2$, *trans*), 24.5 ($CH_2$, *cis*), 28.6 ($CH_2$, *trans*), 33.6 ($CH_2$, *cis*), 35.2 ($CH_2$, *trans*), 48.4 ($CHCO_2CH_3$, *cis*), 51.2 (OCH$_3$, *cis*), 51.3 (OCH$_3$, *trans*), 52.5 ($CHCO_2CH_3$, *trans*), 68.2 ($C$HOSi, *cis*), 72.2 ($C$HOSi, *trans*), 174.3 ($CO_2CH_3$, *cis*), 175.6 ($CO_2CH_3$, *trans*); FTIR (film) ν 2937, 2876, 1740, 1435, 1173 cm^{-1}; LRMS (CI$^+$) *m*/*z* 272 (M$^+$, 14), 243 (35), 175 (10), 57 (100); HRMS (CI$^+$) calcd for $C_{14}H_{28}O_3Si$ (M$^+$) 272.18076, found 272.17809.

4.6.20. 2-Triethylsilyloxy-cycloheptane carboxylic acid methyl ester (53). R_f 0.70 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.54 (q, *J*=7.9 Hz, 6H, OSiCH_2CH$_3$, *cis*+*trans*), 0.92 (t, *J*=7.9 Hz, 9H, OSiCH$_2$-CH_3, *trans*), 0.93 (t, *J*=7.9 Hz, 9H, OSiCH$_2$CH_3, *cis*), 1.34–1.88 (m, 10H, CH_2, *cis*+*trans*), 2.50–2.55 (m, 1H, CHCO$_2$CH$_3$, *cis*+*trans*), 3.65 (s, 3H, OCH_3, *cis*), 3.66 (s, 3H, OCH_3, *trans*), 4.00 (dt, *J*=8.3, 3.6 Hz, 1H, CHOSi, *trans*), 4.00 (dt, *J*=6.8, 3.4 Hz, 1H, CHOSi, *cis*); ^{13}C NMR (125 MHz, $CDCl_3$) δ 3.9 (OSiCH_2CH$_3$, *cis*), 4.0 (OSiCH_2-CH$_3$, *trans*), 5.7 (OSiCH$_2$$CH_3$, *trans*), 5.8 (OSiCH$_2$$CH_3$, *cis*), 21.0 ($CH_2$, *trans*), 21.3 ($CH_2$, *cis*), 22.3 ($CH_2$, *cis*), 25.1 ($CH_2$, *trans*), 25.6 ($CH_2$, *cis*), 26.3 ($CH_2$, *trans*), 26.8 ($CH_2$, *trans*), 27.4 ($CH_2$, *cis*), 35.1 ($CH_2$, *cis*), 35.6 ($CH_2$, *trans*), 50.3 (OCH$_3$, *cis*), 50.8 (OCH$_3$, *trans*), 50.9 ($CHCO_2CH_3$, *cis*), 53.6 ($CHCO_2CH_3$, *trans*), 70.7 ($C$HOSi, *cis*), 73.7 ($C$HOSi, *trans*), 174.1 ($CO_2CH_3$, *cis*), 175.4 ($CO_2CH_3$, *trans*); FTIR (film) ν 2937, 2878, 1734, 1458, 1437, 1007, 908 cm^{-1}; LRMS (FAB$^+$) *m*/*z* 287 (M$^+$+H, 18), 257 (100), 115 (45), 87 (69); HRMS (FAB$^+$) calcd for $C_{15}H_{31}O_3Si$ (M$^+$+H) 287.20420, found 287.20413.

4.6.21. Triethyl-(1-methyl-pent-1-enyloxy)-silane (54). R_f 0.86 (P.E. 30–40 °C/EtOAc, 90:10); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.61–0.68 (q, *J*=8.1 Hz, 6H, OSiCH_2CH$_3$, *cis*+*trans*), 0.86 (t, *J*=7.4 Hz, 3H, CH$_2$CH_3, *trans*), 0.87 (t, *J*=7.4 Hz, 3H, CH$_2$CH_3, *cis*), 0.93–0.97 (t, *J*=8.1 Hz, 9H, OSiCH$_2$CH_3, *cis*+*trans*), 1.27–1.34 (m, 2H, CH$_2$CH_2-CH$_3$, *cis*+*trans*), 1.71 (d, *J*=0.7 Hz, 3H, CH_3, *trans*), 1.77 (d, *J*=1.1 Hz, 3H, CH_3, *cis*), 1.87 (q, *J*=7.2 Hz, 2H, CH$_2$CH_2CH=, *trans*), 1.97 (q, *J*=7.3 Hz, 2H, CH$_2$CH_2-CH=, *cis*), 4.37 (tq, *J*=7.3, 1.1 Hz, 1H, CH=C(OSi)CH$_3$, *cis*), 4.63 (tq, *J*=7.2, 0.7 Hz, 1H, CH=C(OSi)CH$_3$, *trans*); ^{13}C NMR (125 MHz, $CDCl_3$) δ 4.9 (OSiCH_2CH$_3$, *cis*), 5.0 (OSiCH_2CH$_3$, *trans*), 6.4 (OSiCH$_2$$CH_3$, *cis*), 6.6 (OSiCH$_2$-$CH_3$, *trans*), 13.6 ($CH_3$, *trans*), 13.9 ($CH_3$, *cis*), 17.6 ($CH_3$C=, *trans*), 22.7 ($CH_3$C=, *cis*), 23.0 (CH$_2$$CH_2CH_2$, *cis*), 23.6 (CH$_2$$CH_2CH_2$, *trans*), 27.4 (CH$_2$$CH_2$C=, *cis*), 29.3 (CH$_2$$CH_2$C=, *trans*), 107.7 ($C$H=C(OSi)CH$_3$, *trans*), 108.4 ($C$H=C(OSi)CH$_3$, *cis*), 146.6 (CH=$C$(OSi)CH$_3$, *cis*), 147.8 (CH=$C$(OSi)CH$_3$, *trans*); FTIR (film) ν 2957, 2878, 1670, 1460, 1240 cm^{-1}; LRMS (CI$^+$) *m*/*z* 215 (M$^+$+H, 21), 185 (41), 157 (14), 115 (68); HRMS (CI$^+$) calcd for $C_{12}H_{27}OSi$ (M$^+$+H) 215.18310, found 215.18272.

Acknowledgements

We wish to thank GlaxoSmithKline for the provision of a studentship to M. F.

References and notes

1. Sakai, K.; Ido, J.; Oda, O.; Nakamura, N. *Tetrahedron Lett.* **1972**, *13*, 128.
2. Lachow, C.; Miller, R. *J. Am. Chem. Soc.* **1976**, *98*, 1281.
3. Suggs, J. *J. Am. Chem. Soc.* **1979**, *101*, 489.
4. Larock, R.; Oertle, K.; Potter, G. *J. Am. Chem. Soc.* **1980**, *102*, 90.
5. Miller, R.; Campbell, R.; Lachow, C.; Krishnakant, P. *J. Am. Chem. Soc.* **1980**, *102*, 5824.
6. Milstein, D. *J. Chem. Soc., Chem. Commun.* **1982**, 1357.
7. Sakai, K.; Ishiguro, Y.; Funakoshi, K.; Ueno, K.; Suemune, H. *Tetrahedron Lett.* **1991**, *25*, 961.
8. Bosnich, B.; Fairlie, D. *Organometallics* **1988**, *7*, 936.
9. Bosnich, B.; Fairlie, D. *Organometallics* **1988**, *7*, 946.
10. (a) Bosnich, B.; Barnhart, R.; McMorran, D. *Inorg. Chim. Acta* **1997**, *263*, 1. (b) Bosnich, B.; Barnhart, R.; Wang, X.; Noheda, P.; Bergan, S.; Whelan, J. *J. Am. Chem. Soc.* **1994**, *116*, 1821.
11. (a) Sakai, K.; Taura, Y.; Tanaka, M.; Funakoshi, K. *Tetrahedron Lett.* **1989**, *30*, 6349. (b) Sakai, K.; Wu, X.; Funakoshi, K. *Tetrahedron Lett.* **1992**, *33*, 6331. (c) Sakai, K.; Wu, X.; Funakoshi, K. *Tetrahedron Lett.* **1993**, *34*, 5927.
12. (a) Evans, D. A.; Fu, G. C. *J. Org. Chem.* **1990**, *55*, 5678. (b) Boldrini, G. P.; Bortolotti, M.; Mancini, F.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem.* **1991**, *56*, 5820. (c) Zhao, C.-X.; Duffey, M. O.; Taylor, S. J.; Morken, J. P. *J. Org. Lett.* **2001**, *3*, 1829. (d) Taylor, S. J.; Morken, J. P. *J. Am. Chem. Soc.* **1999**, *121*, 12202. (e) Taylor, S. J.; Duffey, M. O.; Morken, J. P. *J. Am. Chem. Soc.* **2000**, *122*, 4528.
13. (a) Little, R. D.; Masjedizadeh, M. R.; Wallquist, O.; McLoughlin, J. I. *Org. React.* **1995**, *47*, 315. (b) Ho, T. L. *Tandem organic reactions*; Wiley: New York, 1992. (c) Tietze, L. F.; Beifuss, U. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 131.
14. (a) Ihara, M.; Fukumoto, K. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1010. (b) Kamenecka, T. M.; Overman, L. E.; Ly Sakata, S. K. *Org. Lett.* **2002**, *4*, 79. (c) Yoshizaki, H.; Tanaka, T.; Yoshii, E.; Koizumi, T.; Takeda, K. *Tetrahedron Lett.* **1998**, *39*, 47. (d) Takeda, K.; Ohkawa, N.; Hori, K.; Koizumi, T.; Yoshii, E. *Heterocycles* **1998**, *4*, 277. (e) Yoshii, E.; Hori, K.; Nomura, K.; Yamaguchi, K. *Synlett* **1995**, 568. (f) Klimko, P. G.; Singleton, D. A. *J. Org. Chem.* **1992**, *57*, 1733. (g) Nagaoka, Y.; Tomioka, K. *Org. Lett.* **1999**, *1*, 1467. (h) Urones, J. G.; Garrido, N. M.; Diez, D.; Dominguez, S. H.; Davies, S. G. *Tetrahedron: Asymmetry* **1999**, *10*, 1637. (i) Uyehara, T.; Shida, N.; Yamamoto, Y. *J. Org. Chem.* **1992**, *57*, 3139. (j) Shida, N.; Uyehara, T.; Yamamoto, Y. *J. Org. Chem.* **1992**, *57*, 5049. (k) Frank, S. A.; Mergott, D. J.; Roush, W. R. *J. Am. Chem. Soc.* **2002**, *124*, 2404. (l) Wang, L.-C.; Luis, A. L.; Agapiou, K.; Jang, H.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2002**, *124*, 2402. (m) Sato, Y.; Takimoto, M.; Hayashi, K.; Katsuhara, T.; Takagi, K.; Mori, M. *J. Am. Chem. Soc.* **1994**, *116*, 9771. (n) Ono, M.; Nishimura, K.; Nagaoka, Y.; Tomioka, K. *Tetrahedron Lett.* **1999**, *40*, 6979.
15. (a) Emiabata-Smith, D.; McKillop, A.; Mills, C.; Motherwell, W. B.; Whitehead, A. J. *Synlett* **2001**, *8*, 1302. (b) Whitehead, A. J. MSc Dissertation, University of East Anglia, 1995.

16. (a) Richards, E. L.; Murphy, P. J.; Dinon, F.; Fratucello, S.; Brown, P. M.; Gelbrich, T.; Hursthouse, M. B. *Tetrahedron* **2001**, *57*, 7771. (b) Black, G. P.; Dinon, F.; Fratucello, S.; Murphy, P. J.; Nielsen, M.; Williams, H. L. *Tetrahedron Lett.* **1997**, *38*, 8561.
17. Yagi, K.; Turitani, T.; Shinokubo, H.; Oshima, K. *Org. Lett.* **2002**, *4*, 3111.
18. (a) Chiu, P.; Szeto, C.-P.; Geng, Z.; Cheng, K.-F. *Org. Lett.* **2001**, *3*, 1901. (b) Chiu, P.; Szeto, C.-P.; Geng, Z.; Cheng, K.-F. *Tetrahedron Lett.* **2001**, *42*, 4091.
19. Suwa, T.; Nishino, K.; Miyatake, M.; Shibata, I.; Baba, A. *Tetrahedron Lett.* **2000**, *41*, 3403.
20. Baik, T.-G.; Luis, A. L.; Wang, L.-C.; Krische, M. J. *J. Am. Chem. Soc.* **2001**, *123*, 5112.
21. Kigoshi, H.; Suzuki, K.; Aoki, K.; Uemura, D. *Tetrahedron Lett.* **2000**, *41*, 3927.
22. Procter, D. J.; Johnston, D.; McCusker, C. F.; Muir, K. *J. Chem. Soc., Perkin Trans. 1* **2000**, 681.
23. Freiría, M.; Whitehead, A. J.; Motherwell, W. B. *Synlett* **2003**, *6*, 805.
24. Stach, H.; Huggenberg, W.; Hesse, M. *Helv. Chim. Acta* **1987**, *70*, 369.
25. Jas, G. *Synthesis* **1991**, *11*, 965.
26. Kobayashi, M.; Negishi, E.-I. *J. Org. Chem.* **1980**, *45*, 5223.
27. Slomp, G.; Johnson, J. L. *J. Am. Chem. Soc.* **1958**, *80*, 915.
28. Wolff, S.; Barany, F.; Agosta, W. *J. Am. Chem. Soc.* **1980**, *102*, 2378.
29. Molander, G. A.; del Pozo Losada, C. *J. Org. Chem.* **1997**, *62*, 2935.
30. Mulzer, J.; Bock, H.; Eck, W.; Buschmann, J.; Luger, P. *Angew. Chem.* **1991**, *103*, 450.
31. Brannock, K. C. *J. Am. Chem. Soc.* **1959**, *81*, 3379.
32. Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.
33. (a) Bailey, D. M.; Johnson, R. E. *J. Org. Chem.* **1970**, *35*, 3574. (b) Haggis, G. H.; Owens, L. N. *J. Chem. Soc.* **1953**, 389.
34. Heck, R. F. *Org. React.* **1982**, *27*, 345.
35. (a) Arnold, Z.; Holy, A. *Collect. Czech. Chem. Commun.* **1961**, *26*, 3059. (b) Coates, R. M.; Senter, P. D.; Baker, W. R. *J. Org. Chem.* **1982**, *47*, 3597.
36. Meegalla, S. K.; Taylor, N. J.; Rodrigo, R. *J. Org. Chem.* **1992**, *57*, 2422.
37. Cooper, R. D.; Jigajinni, V. B.; Wightman, R. H. *Tetrahedron Lett.* **1984**, *25*, 5215.
38. Denmark, S. E.; Middleton, D. S. *J. Org. Chem.* **1998**, *63*, 1604.
39. Restrepo-Sanchez, N. E.; Gomez, F. J.; Jaramillo-Gomez, L. M.; Hudlicky, T. *Synth. Commun.* **1999**, *29*, 2795.
40. Yang, D.; Zhang, C. *J. Org. Chem.* **2001**, *66*, 4814.
41. Osborn, J. A.; Wilkinson, G. *Inorg. Synth.* **1967**, *10*, 67.
42. Levison, J. J.; Robinson, S. D. *J. Chem. Soc. (A)* **1970**, 2947.
43. (a) Beesley, R. M.; Ingold, C. K.; Thorpe, J. F. *J. Chem. Soc.* **1915**, *105*, 1080. (b) Galli, C.; Mandolini, L. *Eur. J. Org. Chem.* **2000**, 3117.
44. Ferrier, R. J.; Middleton, S. *Chem. Rev.* **1993**, *93*, 2779.
45. Ferrier, R. J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 1455.
46. RajanBabu, T. V. *Acc. Chem. Res.* **1991**, *24*, 139.
47. Taguchi, T.; Ito, H.; Motoki, Y.; Hanzawa, Y. *J. Am. Chem. Soc.* **1993**, *115*, 8835.
48. Sudha, A. V. R. L.; Nagarajan, M. *J. Chem. Soc., Chem. Commun.* **1998**, 925.
49. (a) Nakamura, E.; Hashimoto, K.; Kuwajima, I. *Tetrahedron Lett.* **1978**, *19*, 2079. (b) Reich, H. J.; Rusek, J. J.; Olson, R. E. *J. Am. Chem. Soc.* **1979**, *101*, 2225. (c) Cahiez, G.; Figadere, B.; Clery, P. *Tetrahedron Lett.* **1994**, *35*, 6295. (d) Aggarwal, V. K.; Sheldon, C. G.; Macdonald, G. J.; Martin, W. P. *J. Am. Chem. Soc.* **2002**, *124*, 10300.
50. Matsuda, I.; Takahashi, K.; Sato, S. *Tetrahedron Lett.* **1990**, *31*, 5331.
51. Slough, G. A.; Bergman, R. G.; Heathcock, C. H. *J. Am. Chem. Soc.* **1989**, *111*, 938.
52. Denmark, S. E.; Senanayake, C. B. W. *J. Org. Chem.* **1993**, *58*, 1853.
53. (a) Johnson, W. S.; Li, T.; Faulkner, D. J.; Campbell, S. F. *J. Am. Chem. Soc.* **1968**, *90*, 6225. (b) Henrick, C. A.; Schaub, F.; Siddall, J. B. *J. Am. Chem. Soc.* **1972**, *94*, 5374.
54. Mulzer, J.; Bock, H.; Eck, W.; Buschmann, J.; Luger, P. *Angew. Chem., Int. Ed. Engl.* **1991**, *103*, 450.
55. Nakayama, M. *Chem. Lett.* **1979**, 1245.
56. Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 220626. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].