A synthesis of (±)-lavandulol using a silyl-to-hydroxy conversion in the presence of 1,1-disubstituted and trisubstituted double bonds

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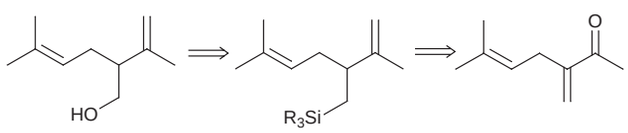
Silylcuprates and silylzincates react with α,β-unsaturated aldehydes, esters, ketones and amides 19 unsubstituted at the β-position in higher yield if trimethylsilyl chloride is present. Applying this method, conjugate addition of the silylcuprate 26 derived from (*Z*)-chloro(2-methylbut-2-enyl)diphenylsilane 24, itself prepared by an improved route, to 3-methylene-6-methylhept-5-en-2-one 25 gave 3-[(*Z*)-2-methylbut-2-enyl(diphenyl)silyl]methyl–6-methylhept-5-en-2-one 27. A Wittig reaction gave 3-[(*Z*)-2-methylbut-2-enyl(diphenyl)silyl]methyl–2,6-dimethylhepta-1,5-diene 28 and silyl-to-hydroxy conversion gave lavandulol 1, even in the presence of the 1,1-disubstituted and trisubstituted double bonds. The hydroxy group of the 3-hydroxysilane, 2,6-dimethyl-3-{[(*Z*)-2-methylbut-2-enyl]diphenylsilyl}methylhept-5-en-2-ol 30, activated the allylsilane group towards protodesilylation. Chloro(diphenyl)methallylsilane 35 is easier to make than the chloride 24, and should be an alternative allylsilane that can make a lithium and hence a cuprate reagent like 26.

Introduction

We described in the immediately preceding paper in this series,[1] that the 2-methylbut-2-enylsilyl group may be introduced into an organic molecule as a cuprate reagent, and is also converted into a hydroxy in the presence of a 1,2-disubstituted double bond within an allylsilane substructure. We were still faced with some uncertainties about how effective this group might be in the presence of a 1,1-disubstituted double bond, where protonation is easier because it gives a tertiary cation. One allylsilane in the preceding paper (**21** in that paper) did have a 1,1-disubstituted double bond, which, although reassuringly untouched during the silyl-to-hydroxy conversion, was so disposed relative to the silyl group that it was not quite a fully satisfying test. We also had Mayr's work on the relative nucleophilicities of alkenes and allylsilanes to go on, since that indicated that an allylsilyl group like ours ought to be more nucleophilic than a 1,1-dialkylalkene and even than a trialkylalkene.[2] This ought still to be the case even though the two phenyl groups, necessary for forming the lithium reagent that the cuprate is made from, are mildly deactivating relative to having alkyl groups attached to the silicon atom. We can estimate that the double bond on our allylsilane group can be expected to be something like two orders of magnitude more nucleophilic than, say, 2-methylbut-2-ene. Although Mayr's work measures the nucleophilicity towards a carbocation, we were hopeful that the relative nucleophilicity towards a proton would be similar, and that the 2-methylbut-2-enylsilyl group would undergo protodesilylation selectively in the presence of 1,1-disubstituted and trisubstituted alkenes. If it was, it could be converted into a hydroxy group, since the second step, the Tamao oxidation, is entirely compatible with simple double bonds of any degree of substitution. We wanted to engineer a fitting test, and found one in a synthesis of lavandulol **1**, as we reported in a preliminary communication,[3] and report in full as part of this series, even though it has no stereochemical complications.

This very simple target molecule, in addition to giving us a chance to see whether the conversion **2** ⟶ **1** would work in a testing situation, also exposed us to a limitation in our methods that we had met earlier. Further disconnection of the target molecule (Scheme 1) led to the enone **3** and the need to carry out a conjugate addition reaction with the silylcuprate reagent. In this type of reaction, we have sometimes found the intermediate enolate of the first addition reacting again in a Michael reaction with another molecule (or two) of the enone. Thus



1 **2** **3**

Scheme 1

methyl cinnamate gave more or less of the (1+ 3) ketodiester **6** in addition to the normal product **5** (Scheme 2).[4]

We more or less solved this problem using silylzincates[5] in place of the cuprates, but, even with the silylzincate, ethyl crotonate **7** has, from time to time, given, in addition to the usual β-silyl ester **8**,[6] the (1+2) diester **9** in yields up to 15%.[7] The remarkable diastereoselectivity in this reaction, although well understood with respect to the relationship between C-2 and C-3,[8] was unpredictable for the sense between C-3 and C-4. Accordingly, we proved it by the silyl-to-hydroxy conversion **9** ⟶ **10** followed by the formation of a lactone **11** with diagnostic ^{1}H NMR coupling constants.[7] Unfortunately, this type of byproduct is not useful, because we have been unable to make it a major pathway. On the other hand we have often found it difficult to suppress, and *the problem is especially acute when the enone system is unsubstituted at the β position*, as it will be in a synthesis of lavandulol along the lines illustrated in Scheme 1. Silylzincates do not solve this limitation at all, and we needed to overcome it. The synthesis, even of a trivial molecule like lavandulol, was therefore worth tackling.

Results and discussion

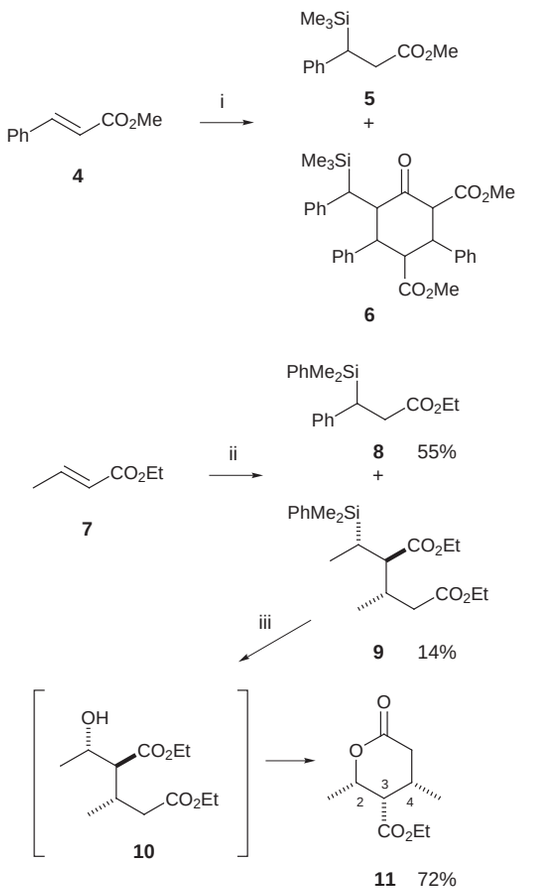
Illustrating the nature of the problem, we observed in an earlier approach to lavandulol that the addition of the zincate **13** to methyl acrylate **12** and to the unsaturated ester **16** gave low yields of mixtures of compounds, from which we were able to separate what appear to be the normal products **14** and **17** and the (1+2) products **15** and **18** in comparable amounts, although not always pure enough for full characterisation (Scheme 3).

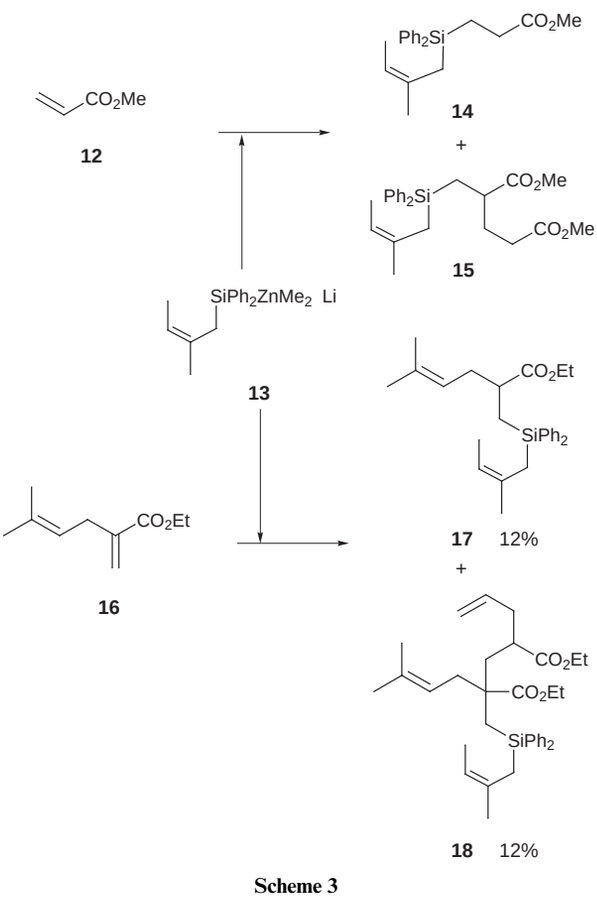
Trimethylsilyl chloride has been found to be useful in the conjugate additions of carbon-based cuprates—it affects the yield, the rate, and the regio- and stereoselectivity of these reactions,[9] but it has not been used in silylcuprate chemistry before. By adding trimethylsilyl chloride to the esters **12** and **16**, before adding them to the silylcuprate, we suppressed the Michael

Table 1 Yields (%) of conjugate addition products **20a-f** and **22** (Scheme 4) in the presence and absence of trimethylsilyl chloride

	Cuprate		Zincate	
Substrate	with TMSCl	without TMSCl	with TMSCl	without TMSCl
19a	71[a]	24[b]	78[a]	36[a]
19b	57[b]	42[b]	64[a]	37[a]
19c	80,[a] 80,[b] 47[a,c]	29,[a] 36[b]	73,[a] 72,[b] 50[a,d]	25[a]
19d	74[a]	22[b]	74[a]	25[a]
19e	57[b]	6[b]	64[a]	5[a]
16 = **19f**	83[a]	23[b]	75[a]	35[a]
21	50[a]	29[b]	93[a]	21[a]
methyl crotonate	72,[a] 71[b]	95[b]	72[a]	80,[a] 32[a,d]

[a] Without added TMEDA. [b] With added TMEDA. [c] $PhMe_2SiCu$ in place of $(PhMe_2Si)_2CuLi$. [d] $PhMe_2SiZnBr$ in place of $PhMe_2SiZnMe_2Li$





Scheme 3

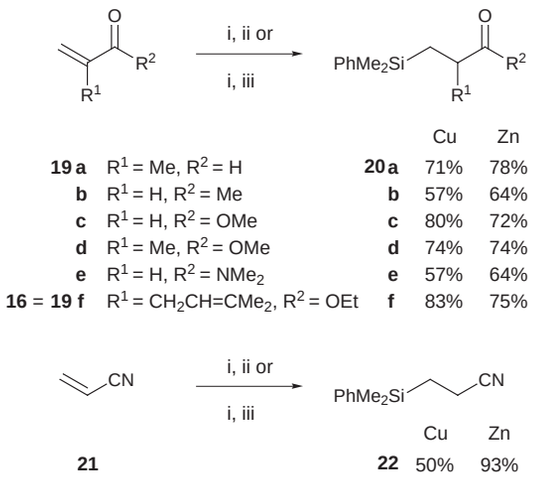
Scheme 2 *Reagents*: i, $(Me_3Si)_2CuLi$; ii, $PhMe_2SiZnMe_2Li$; iii, $Hg(OAc)_2$, AcOOH, AcOH

reaction that had caused so much trouble—the conjugate additions took place cleanly and in high yield, even though the unsaturated esters had no β-substituents. We obtained the ester **14** in 76% yield and the ester **17** in 89% yield from the silylcuprate in the presence of trimethylsilyl chloride.

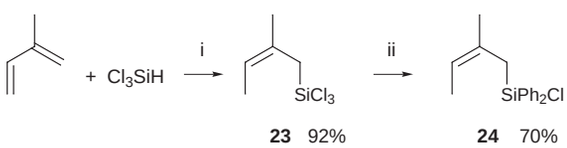
To test the generality of this solution to the problem, we carried out conjugate additions of our usual phenyldimethylsilylcuprate and zincate reagents to methacrolein, methyl vinyl ketone, methyl acrylate, methyl methacrylate, *N*,*N*-dimethylacrylamide **19a**–**f** and acrylonitrile **21** in the presence of trimethylsilyl chloride. In each case, we obtained better yields of the conjugate addition products **20a**–**f** and **22** (Scheme 4) than in its absence (Table 1). However, the yields with methyl crotonate, which does have a β-substituent, did not improve in the presence of trimethylsilyl chloride—if anything they were worse. Simply using the cuprate or zincate is still the best method here.

The scene was now set for the synthesis, and we needed to prepare again the silyl chloride **24** used in the preparation of the silylcuprate. The preparation described in the preceding paper, although entirely successful, had not made it easy to purify the chloride. A better prospect was to make the bonds to the silicon atom in the opposite order. Hydrosilylation of isoprene using trichlorosilane and Ojima's catalyst gave the known[10] allylsilane **23** (Scheme 5), which was amenable to simple vacuum distillation. On treatment with two equivalents of phenyllithium, this gave the silyl chloride **24**, which could be distilled without complication, presumably because it is free of transition metal impurities. This appears to be the better way to prepare the reagent—not only can the silyl chloride be distilled, but trichlorosilane is much cheaper than diphenylsilane, and the total time involved is significantly less.

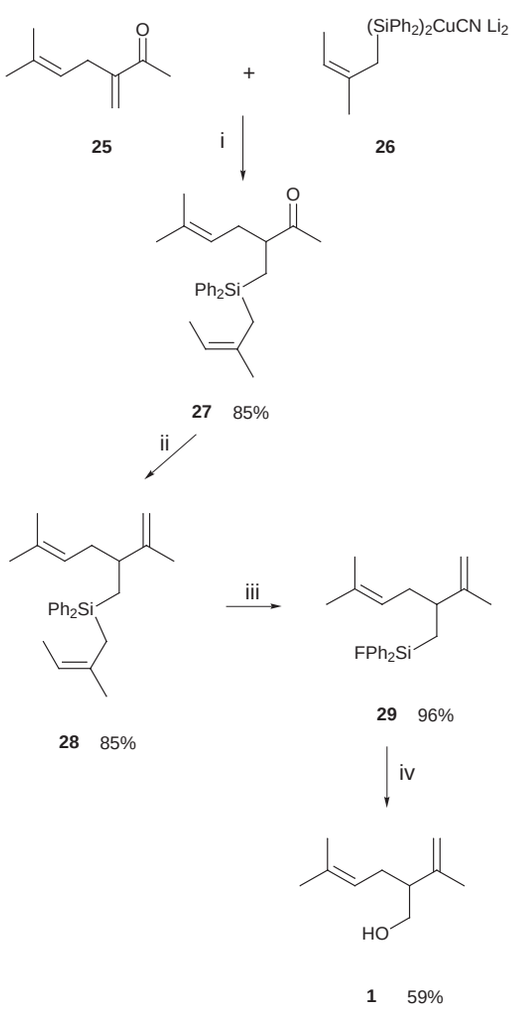
We prepared the enone **25**, by alkylating pentane-2,4-dione with prenyl bromide and treating the product with base and formaldehyde, following a method developed by Ayed and Amri.[11] Conjugate addition of the silyl cuprate **26** in the presence of trimethylsilyl chloride gave the β-silyl ketone **27**, and a Wittig reaction gave the diene **28** (Scheme 6). The protodesilylation proved to be a fairly delicate matter, and we had to search to find mild enough conditions not to damage the rest of the structure. Eventually we found that methanolic hydrogen



Scheme 4 *Reagents*: i, Me_3SiCl; ii, $(PhMe_2Si)_2CuCN\ Li_2$; iii, $Me_2(PhMe_2Si)ZnLi$

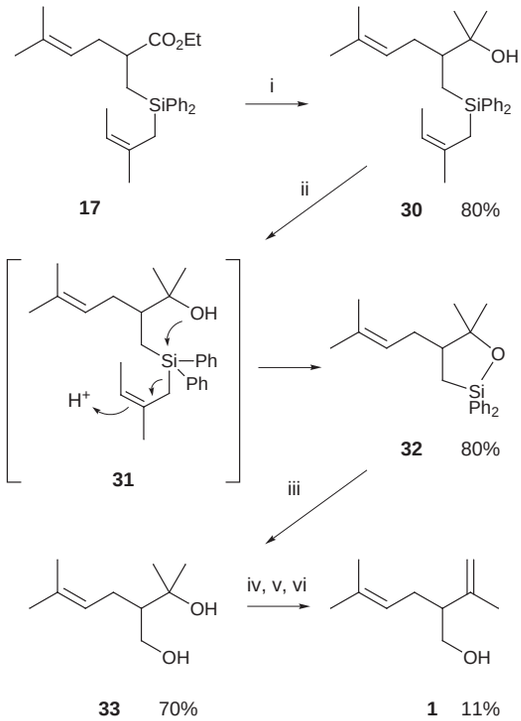


Scheme 5 *Reagents*: i, $PdCl_2(PhCN)_2$ cat., Ph_3P; ii, 2PhLi

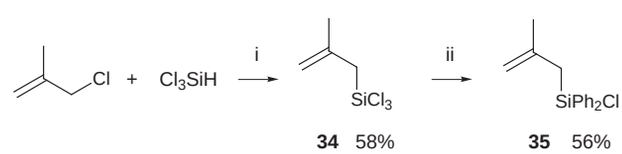


Scheme 6 *Reagents*: i, Me_3SiCl; ii, $CH_2{=}PPh_3$; iii, HCl, KF, MeOH, CH_2Cl_2; iv, H_2O_2, $NaHCO_3$, KF

chloride in dichloromethane in the presence of potassium fluoride cleanly gave the fluoride **29** in high yield. The final oxidation under Tamao's conditions then gave a mixture of phenol and



Scheme 7 *Reagents*: i, MeMgBr; ii, HCl, MeOH, or $SOCl_2$, or $POCl_3$; iii, H_2O_2, KF, $KHCO_3$, THF, MeOH; iv, TBDMSCl, Et_3N, DMAP; v, PCl_3, DMF; vi, TBAF



Scheme 8 *Reagents*: i, Et_3N; ii, 2PhLi

lavandulol **1**, which were separated by extracting the former with alkali and chromatographing the residue. The product was identical (TLC, ^1H NMR) with an authentic sample obtained from commercial lavandulyl acetate, and the 3,5-dinitrobenzoate had the correct melting point.

This was not the only synthesis of lavandulol that we developed, but it is the best. In an earlier approach, we used the ester **16** to make the ketone **25**, by converting it into the Weinreb amide and treating that with methylmagnesium bromide, but the overall yield 17% was much inferior to the route based on the work of Ayed and Amri. Even earlier, we had taken the ester **17** and treated it with two equivalents of methylmagnesium bromide to make the tertiary alcohol **30** (Scheme 7). All attempts to dehydrate this alcohol, using such reagents as phosphorus pentachloride, phosphorus oxychloride, toluene-*p*-sulfonyl chloride or protic acid, all under the mildest conditions, gave instead the cyclic silyl ether **32**. We believe that the well placed hydroxy group coordinates to the silicon atom, enhancing its capacity to donate electrons into the allylsilane system **31**, and making this allylsilane even more susceptible to such reactions as protodesilylation than it is inherently. Intramolecular nucleophilic participation by an alkoxide is known to activate an allylsilane,[12] and so is participation by the carbonyl oxygen atom of an amide group.[13] This is the first time it has been seen with the hydroxy group itself. Oxidation of the silyl ether gave the diol **33** in good yield. The primary alcohol group was easily protected, although it may not have been necessary to protect it, and the tertiary alcohol was now easily dehydrated, although only in low yield in our one attempt. Removal of the silyl ether gave lavandulol **1**. This was not as good a synthesis overall, nor had it allowed us to test the very feature for which we had set up the synthesis.

One final development is that we offer an alternative silyl chloride **35**, that is even easier to make than the silyl chloride **24**, and which will probably function just as well in all the work we have done so far with the latter. Trichloro(methallyl)silane **34** is readily available from the known reaction of trichlorosilane with methallyl chloride catalysed by triethylamine (Scheme 8).[14] Treatment of this compound with two equivalents of phenyllithium gave methallyl(diphenyl)chlorosilane **35**, which could be distilled, as usual, with an even easier fractionation from the volatile byproducts and unchanged starting materials, making a Vigreux column unnecessary.

Experimental

Light petroleum refers to the fraction bp 40–60 °C. ^{13}C NMR spectra using the attached proton test, are identified as +, if the peak is on the same side as the solvent peak, and as − if it is on the opposite side. The NMR machine is identified by its frequency for ^{1}H NMR spectroscopy. Ether refers to diethyl ether.

Ethyl (3*RS*,4*SR*,5*RS*)-5-[dimethyl(phenyl)silyl]-4-ethoxycarbonyl-3-methylhexanoate 9

(Carried out by R. N. Wesley) Dimethyl(phenyl)silyllithium (1.2 mol dm^{-3} in THF, 8.8 cm^3, 10.6 mmol) was added to a stirred solution of dimethylzinc (2.0 mol dm^{-3} in toluene, 5.4 cm^3, 10.8 mmol) in THF (40 cm^3) at 0 °C under argon. The mixture was stirred at this temperature for 5 min and then cooled to −78 °C. Ethyl crotonate (1.0 cm^3, 8 mmol) in THF (5 cm^3) was added dropwise over 5 min. After a further 30 min stirring, the reaction was quenched with saturated aqueous ammonium chloride (20 cm^3) and allowed to warm to room temperature. Hydrochloric acid (3 mol dm^{-3}, 20 cm^3) was added to dissolve the precipitated zinc salts, and the THF was evaporated under reduced pressure. The residue was extracted with dichloromethane (3 × 50 cm^3) and the combined organic fractions were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed (SiO_2, Et_2O–light petroleum, 10:90) to give ethyl 3-[dimethyl(phenyl)silyl]butanoate **8** (1.1 g, 55%)[6] and the *Michael addition product* **9** (0.4 g, 14%); R_f(Et_2O–light petroleum, 10:90) 0.27; ν_{max}(film)/cm^{-1} 1732 (C=O) and 1589 (Ph); δ_H(400 MHz; $CDCl_3$) 7.52–7.27 (5 H, m, Ph), 4.10 (2 H, q, *J* 7.1, OCH_2Me) 3.87 (1 H, dq, *J* 10.9, 7.1, OCH_AH$_B$Me), 3.77 (1 H, dq, *J* 10.9, 7.1, OCH$_A$-H_BMe), 2.53 (1 H, dd, *J* 15.4, 2.1, CH_ACH$_B$CO$_2$Et), 2.38 (1 H, m, CH$_2$C*H*Me), 2.31 (1 H, dd, *J* 10.6, 4.9, C*H*CO$_2$Et), 2.01 (1 H, dd, *J* 15.4 and 10.9, CH$_A$CH_BCO$_2$Et), 1.39 (1 H, dq, *J* 10.6 and 7.6, MeC*H*Si), 1.22 (3 H, t, *J* 7.1, OCH$_2$*Me*), 1.18 (3 H, t, *J* 7.1, OCH$_2$*Me*), 0.93 (6 H, d, *J* 7.6, 2 × *Me*CH), 0.27 (3 H, s, Si*Me*$_A$Me$_B$) and 0.25 (3 H, s, SiMe$_A$*Me*$_B$); δ_C(400 MHz; $CDCl_3$) 174.4, 173.5, 138.0, 134.1 (2 C), 128.9, 127.6 (2 C), 60.2, 59.9, 51.9, 36.1, 29.5, 18.8, 18.7, 14.2, 14.1, 12.5, −3.9 and −4.4 (Found: C, 66.1; H, 8.55. $C_{20}H_{32}O_4Si$ requires C, 65.9; H, 8.85%).

Ethyl (2*RS*,3*RS*,4*RS*)-tetrahydro-2,4-dimethyl-6-oxo-2*H*-pyran-3-carboxylate 11

(Carried out by R. N. Wesley) Mercuric acetate (0.49 g, 1.54 mmol) was added to a stirred solution of the silyl ester (0.38 g, 1.05 mmol) in peracetic acid (35–40% in AcOH, 5 cm^3, *ca.* 25 mmol) and the mixture was stirred for 3 h at room temperature. Toluene (25 cm^3) was added and the solvents removed under reduced pressure. The residue was taken up in ethyl acetate–methanol (99:1), which was filtered and then concentrated under reduced pressure. The residue was chromatographed (SiO_2, CH_2Cl_2–Et_2O, 67:33) to give the *lactone* (0.15 g, 72%); R_f(CH_2Cl_2–Et_2O, 67:33) 0.56; ν_{max}(film)/cm^{-1} 1727 (C=O); δ_H(400 MHz; $CDCl_3$) 4.53 (1 H, dq, *J* 3.2, 6.6, H_{ax} on C-2), 4.19 (1 H, dq, *J* 14.3, 7.1, OCH_AH$_B$Me), 4.16 (1 H, dq, *J* 14.3, 7.1, OCH$_A$$H_B$Me), 2.67 (1 H, t, *J* 3.8, H_{eq} on C-3), 2.62 (1 H, dd, *J* 18.5, 8.2, H_{eq} on C-5), 2.55 (1 H, dd, *J* 18.5, 11.3, H_{ax} on C-5), 2.29 (1 H, m, H_{eq} on C-4), 1.36 (3 H, d, *J* 6.6, Me on C-2), 1.25 (3 H, t, *J* 7.1, OCH$_2$*Me*) and 1.03 (3 H, d, *J* 6.7, Me on C-4); δ_C(400 MHz; $CDCl_3$) 170.6, 170.0, 76.4, 60.8, 48.6, 34.0, 29.6, 19.1, 18.7 and 14.3 (Found: M$^+$, 200.1047. $C_{10}H_{16}O_4$ requires *M*, 200.1049). Irradiation of the signal at δ_H = 4.53 resulted in enhancements of the signals at 2.67, 2.29 and 1.36; irradiation at δ_H = 2.67 gave enhancements at 4.53, 2.29 and 1.03; irradiation at δ_H = 2.29 gave enhancements at 4.53, 2.67 and 1.03; irradiation at δ_H = 1.36 gave enhancements at 4.53 and 2.67; irradiation at δ_H = 1.03 gave enhancements at 2.67, 2.62, 2.55 and 2.29.

Ethyl 5-methyl-2-methylenehex-4-enoate 16

Sodium hydride (60% suspension in mineral oil, 3.8 g, 9.9 mmol) was added in 20 portions over 20 min to a stirred solution of triethyl phosphonoacetate (18.1 g, 8.1 mmol) in THF (40 cm^3) at 0 °C under argon. After 10 min, prenyl bromide (9.4 g, 6.3 mmol) was added over 20 min and the mixture stirred at room temperature for 6 h. Potassium carbonate (18 g, 130 mmol), water (10 cm^3) and aqueous formaldehyde (37% in H_2O, 20 cm^3) were added to the solution. The mixture was warmed to 80 °C and stirred at this temperature for 2 h. After cooling the mixture, the organic phase was separated and diluted with ether (50 cm^3), washed with water (30 cm^3), and the aqueous layer was extracted with ether (2 × 30 cm^3). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. The residue was chromatographed (SiO_2, light petroleum–EtOAc, 10:1) to give the α,β-unsaturated ester[15] (7.54 g, 71%); R_f(light petroleum–EtOAc, 20:1) 0.34; ν_{max}(neat)/cm^{-1} 2979 and 2929 (aliphatic CH), 1719 (C=O), 1632 (C=C) and 1136 (C–O); δ_H(250 MHz; $CDCl_3$) 6.11 (1 H, s, CH_AH$_B$=), 5.50 (1 H, s, CH$_A$$H_B$=), 5.16 (1 H, t, *J* 7.3, =CH), 4.19 (2 H, q, *J* 7.1, OCH$_2$), 2.97 (2 H, d, *J* 7.3, CH$_2$), 1.72 (3 H, s, C*Me*$_A$Me$_B$), 1.61 (3 H, s, CMe$_A$*Me*$_B$) and 1.28 (3 H, t, *J* 7.1, *Me*CH$_2$O); δ_C(250 MHz; $CDCl_3$) 167.30+, 139.92+, 133.99+, 124.14+, 120.53−, 60.55+, 30.25+, 25.69−, 17.60− and 14.17−.

General procedures for conjugate addition of silylcuprates and zincates

Method A. Silyllithium[1,16] (0.54 mol dm^{-3} in THF, 13.3 cm^3, 7.2 mmol), freshly prepared from the corresponding silyl chloride and lithium shot, was stirred with dried copper(I) cyanide (322 mg, 3.6 mmol) [optionally treated with TMEDA (1.05 g, 9 mmol) at room temperature for 20 min] at −20 °C for 45 min, and then cooled to −78 °C. A mixture of chlorotrimethylsilane (978 mg, 9 mmol) and the substrate (3 mmol) in THF (4 cm^3) was added under argon over 10 min, and the mixture kept for a further 15 min. Saturated aqueous ammonium chloride (20 cm^3) was added to the mixture at −78 °C, and the mixture extracted with ether (100 cm^3). The organic phase was washed with saturated aqueous ammonium chloride (2 × 40 cm^3) and brine (40 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Tetrabutylammonium fluoride (1 mol dm^{-3} in THF, 4 cm^3) and THF (10 cm^3) were added to the residue and the mixture stirred at room temperature for 2 h. Water (20 cm^3) was added and the mixture was extracted with ether (2 × 30 cm^3). The combined organic extracts were dried ($MgSO_4$), concentrated under reduced pressure, and the residue chromatographed.

Method B. As in method A, but without the chlorotrimethylsilane, the reaction mixture was kept at −78 °C for 40 min before quenching, and the treatment with tetrabutylammonium fluoride was omitted.

Method C. The silyllithium (0.54 mol dm^{-3} in THF, 6.7 cm^3, 3.6 mmol) and dimethylzinc (2.0 mol dm^{-3} solution in toluene, 1.8 cm^3, 3.6 mmol) were stirred in THF (3 cm^3) under argon at 0 °C for 30 min and cooled to −78 °C. A mixture of substrate (3 mmol) and chlorotrimethylsilane (978 mg, 9 mmol) in THF (3 cm^3) was added dropwise by syringe over 30 min and the

mixture stirred for 25 min. The usual work-up, treatment with tetrabutylammonium fluoride, and chromatography gave the products.

Method D. As in method C, but without the chlorotrimethylsilane, the reaction mixture was kept at −78 °C for 30 min before quenching, and the treatment with tetrabutylammonium fluoride was omitted.

Method E. Dimethyl(phenyl)silyllithium (3.6 mmol) was added to dried zinc bromide (811 mg, 3.6 mmol) in THF (5 cm^3) under argon at −50 °C to −60 °C over 10 min. A mixture of substrate (3 mmol) and chlorotrimethylsilane (978 mg, 9 mmol) in THF (5 cm^3) was added over 30 min, and the mixture stirred for 30 min at −78 °C and for 15 h at room temperature. The usual work-up and chromatography (SiO_2, light petroleum–EtOAc, 20:1) gave the products.

Method F. Dimethyl(phenyl)silyllithium (3.6 mmol) was stirred with dried copper(I) cyanide (322 mg, 3.6 mmol) in THF (5 cm^3) under argon at 0 °C for 1.5 h, and then cooled to −78 °C. A mixture of methyl acrylate (3 mmol) and chlorotrimethylsilane (978 mg, 9 mmol) in THF (5 cm^3) was added over 20 min, and the solution stirred at −78 °C for 3 h and then at room temperature for 15 h. The usual work-up, treatment with tetrabutylammonium fluoride, and chromatography (SiO_2, light petroleum–EtOAc, 20:1) gave methyl 3-dimethyl(phenyl)-silylpropanoate.

The following compounds were made by one or more of these methods.

Methyl 3-{[(*Z*)-2-methylbut-2-enyl]diphenylsilyl}propanoate 14. As an oil (76% by Method A with TMEDA, low yield by Method D) from the methyl acrylate and eluting with light petroleum–EtOAc, 10:1; R_f(light petroleum–EtOAc, 5:1) 0.73; ν_{max}(neat)/cm^{-1} 3069 (=CH), 2951 (aliphatic C–H), 1739 (C=O), 1590 and 1429 (aromatic C=C) and 1118 (C–O); δ_H(250 MHz; $CDCl_3$) 7.57–7.53 (4 H, m, *m*-ArH), 7.42–7.37 (6 H, m, *o*- and *p*-ArH), 5.11 (1 H, q, *J* 6.7, MeC*H*=), 3.61 (3 H, s, OMe), 2.37–2.30 (2 H, m, CH_2CO_2Me), 2.11 (2 H, s $SiCH_2CMe$=), 1.60 (3 H, s, $SiCH_2CMe$=), 1.54–1.46 (2 H, m, $SiCH_2CH_2CO$) and 1.35 (3 H, d, *J* 6.7, CH*Me*=); δ_C(250 MHz; $CDCl_3$) 175.1+, 134.98−, 132.11+, 129.51−, 127.9−, 118.0−, 51.6−, 28.56+, 26.29−, 18.96+, 13.85– and 8.28+; *m*/*z* (EI) 307 (35%, M − OMe) and 269 (100%, M − C_5H_9).

Methyl 5-{[(*Z*)-2-methylbut-2-enyl]diphenylsilyl}-4-methoxycarbonylpentanoate 15. As an oil (low yield by Method D using Et_2Zn instead of Me_2Zn) from methyl acrylate and eluting with light petroleum–EtOAc, 20:1. The product was isolated by preparative thin layer chromatography (SiO_2, light petroleum–EtOAc; 10:1); R_f(light petroleum–EtOAc; 5:1) 0.55; ν_{max}(neat)/cm^{-1} 3071 and 3008 (=CH), 2954 and 2921 (aliphatic CH), 1733 (C=O), 1660 and 1438 (aromatic C=C) and 1206 and 1165 (C–O); δ_H(250 MHz; $CDCl_3$) 7.55–7.47 (4 H, m, *m*-ArH), 7.29–7.38 (6 H, m, *o*- and *p*-ArH), 5.05 (1 H, q, *J* 6.7, MeC*H*=), 3.60 (3 H, s, CO_2Me), 3.20 (3 H, s, CO_2Me), 2.53 (1 H, tt, *J* 9.8 and 4.9, CH_2CHCH_2), 2.24–2.16 (2 H, m, CH_2CO), 2.09 (2 H, s, $SiCH_2CMe$=), 1.92–1.76 (2 H, m, CH_2CH_2CO), 1.61 (1 H, dd, *J* 14.9 and 9.9, $SiCH_AH_BCH$), 1.48 (3 H, s, $SiCH_2CMe$=) and 1.30–1.13 (4 H, m, *Me*CH= and $SiCH_AH_BCH$); δ_C(250 MHz; $CDCl_3$) 175.98+, 173.25+, 135.20−, 135.14−, 135.01−, 134.91+, 132.17+, 129.47−, 129.40−, 127.77−, 127.70−, 118.07−, 51.57−, 51.22−, 40.25−, 31.61+, 31.04+, 26.30−, 19.26+, 16.44+ and 13.80−; *m*/*z* (EI) 393 (42%, M − OMe), 355 (65%, M − C_5H_9), 199 (100%, M − 225) (Found: M^+ − OMe, 393.1898. $C_{25}H_{32}O_4Si$ requires *M* − OMe, 393.1886).

Ethyl 5-methyl-2-{[(*Z*)-2-methylbut-2-enyl]diphenylsilyl}-methylhex-4-enoate 17. As an oil (89% by Method A with TMEDA, 17% by Method B, 12% by Method D) from the ester **16** and eluting with light petroleum–EtOAc, 20:1. R_f(light petroleum–EtOAc, 10:1) 0.51; ν_{max}(neat)/cm^{-1} 3048 (=CH), 2970 and 2924 (aliphatic CH) and 1731 (C=O); δ_H(400 MHz; $CDCl_3$) 7.46–7.49 (4 H, m, *m*-ArH), 7.25–7.40 (6 H, m, *o*- and *p*-ArH), 5.04 (1 H, q, *J* 6.7, =C*H*Me), 4.96 (1 H, t, *J* 7.2, $=CHCH_2$), 3.65 (1 H, dq, *J* 10.8 and 7.1, OCH_AH_BMe), 3.64 (1 H, dq, *J* 10.8 and 7.1, OCH_AH_BMe), 2.45 (1 H, m, CH_2CH CO_2Et), 2.22 (1 H, m, $=CHCH_AH_BCH$), 2.13–2.04 (3 H, m, $SiCH_2MeC$= and $=CHCH_AH_BCH$), 1.64 (3 H, s, $SiCH_2MeC$=), 1.57 (1 H, m, $CHCH_AH_BSi$), 1.48 (3 H, s, Me_AMe_BC=), 1.47 (3 H, s, Me_AMe_BC=), 1.30–1.25 (4 H, m, $CHCH_AH_BSi$ and *Me*HC=) and 1.01 (3 H, t, *J* 7.1, OCH_2Me); δ_C(400 MHz; $CDCl_3$) 176.2,+ 135.6+, 135.5+, 135.3−, 135.2−, 133.8+, 132.4+, 129.34−, 129.30−, 127.7−, 127.6−, 121.2−, 117.9−, 60.0+, 41.3−, 34.7+, 26.3−, 25.8−, 19.4+, 17.8−, 15.6+, 14.0− and 13.8− (Found: M^+ − 1, 419.2406. $C_{27}H_{36}SiO_2$ requires *M* − 1, 419.2406).

Ethyl 4-ethoxycarbonyl-4-{[(*Z*)-2-methylbut-2-enyl]diphenylsilyl}methyl-7-methyl-2-(3-methylbut-2-enyl)oct-6-enoate 18. As a mixture of diastereoisomers, an oil (18% by Method B, 12% by Method D) from the ester **16** and preparative thin layer chromatography eluting with light petroleum–EtOAc, 20:1. R_f(light petroleum–EtOAc, 10:1) 0.51; ν_{max}(neat)/cm^{-1} 3048, 2973 and 2914 (aliphatic C–H), 1730 (C=O), 1445 (CH_2) and 1377 (Me); δ_H(250 MHz, $CDCl_3$) 7.67–7.48 (4 H, m, *m*-ArH), 7.39–7.24 (6 H, m, *o*- and *p*- ArH), 5.01–4.91 (3 H, m, 3 × =CH), 3.71–3.56 (4 H, m, 2 × OCH_2), 2.37- 1.83 (7 H, m, 3 × $=CCH_2$ and C*H*CO), 1.63–1.40 (18 H, m, 6 × *Me*C=) and 1.24–0.99 [10 H, m, 2 × CO_2CH_2Me and $=CCH_2CH_2C(CO_2Et)CH_2Si$]; δ_C(400 MHz, $CDCl_3$) 176.3+, 176.2+, 136.2+, 136.1+, 136.0+, 135.6– (2 peaks), 134.0+, 133.8+, 133.7+, 133.6+, 132.8+, 132.7+, 129.1−, 127.4−, 121.0−, 119.5−, 119.9−, 117.9−, 60.3+, 60.2+ (2 peaks), 60.1+, 48.0+, 47.8+, 42.2−, 42.1−, 40.5+, 35.6+, 35.3+, 33.1+, 26.4−, 26.0−, 25.8−, 22.3+, 21.8+, 20.7+, 20.6+, 18.1−, 17.7−, 14.2−, 13.9– (2 peaks) and 13.7–.

(±)-2-Methyl-3-dimethyl(phenyl)silylpropanal 20a. As an oil (71% by Method A without TMEDA, 24% by Method B, 78% by Method C and 36% by Method D) from methacrolein and eluting with light petroleum–EtOAc, 20:1. R_f(light petroleum–EtOAc, 9:1) 0.73; ν_{max}(neat)/cm^{-1} 3069 and 3048 (aromatic CH), 2957 (aliphatic CH), 2705 (aldehyde CH), 1724 (CO), 1456 and 1427 (aromatic C=C) and 1113 (Si–Ph); δ_H(250 MHz; $CDCl_3$) 9.53 (1 H, d, *J* 1.8, CHO), 7.54–7.50 (2 H, m, *m*-ArH), 7.39–7.35 (3 H, m, *o*- and *p*-ArH), 2.47–2.31 (1 H, m, C*H*), 1.25 (1 H, dd, 14.9 and 5.1, $SiCH_AH_B$), 1.07 (3 H, d, *J* 7.0, CH*Me*), 0.77 (1 H, dd, *J* 14.9 and 2.9, $SiCH_AH_B$) and 0.29 (6 H, s, $SiMe_2$); δ_C(250 MHz; $CDCl_3$) 204.6−, 138.5+, 133.5−, 129.2−, 127.8−, 42.5−, 16.9+, 16.2– and −2.3– (Found: M^+, 206.1141. $C_{12}H_{18}SiO$ requires *M*, 206.1127).

4-Dimethyl(phenyl)silylbutan-2-one 20b.[6] As an oil (57% by Method A with TMEDA, 42% by Method B, 64% by Method C and 37% by Method D) from methyl vinyl ketone freshly distilled from DCC eluting with light petroleum–EtOAc, 20:1; R_f(light petroleum–EtOAc, 9:1) 0.42; ν_{max}(neat)/cm^{-1} 3415 (CO overtone), 3068 and 3049 (aromatic CH), 2954 and 2896 (aliphatic CH), 1717 (CO), 1589 and 1426 (aromatic C=C), 1357 (Me) and 1113 (Si–Ph); δ_H(250 MHz; $CDCl_3$) 7.52–7.46 (2 H, m, *m*-ArH), 7.38–7.33 (3 H, m, *o*- and *p*-ArH), 2.37 (2 H, m not 1st order, CH_2CO), 2.06 (3 H, s, COMe), 1.00 (2 H, m not 1st order, $SiCH_2$) and 0.28 (6 H, s, $SiMe_2$), matching data in the literature.[6]

Methyl 3-dimethyl(phenyl)silylpropanoate 20c.[17] As an oil (80% by Method A with and without TMEDA, 36% by Method B with TMEDA and 29% without, 73% by Method C without TMEDA and 72% with TMEDA, 25% by Method D, 50% by Method E and 47% by Method F) from methyl acrylate and dimethyl(phenyl)silyllithium eluting with light petroleum–EtOAc, 20:1. R_f(light petroleum–EtOAc, 9:1) 0.60; ν_{max}(neat)/cm^{-1} 3069 and 3049 (aryl CH), 2999 and 2899 (aliphatic CH), 1740 (C=O), 1590 and 1427 (aromatic C=C), 1115 (Si–Ph) and 836, 786 and 701 (Ar); δ_H(250 MHz; $CDCl_3$) 7.55–7.49 (2 H, m, *m*-ArH), 7.42–7.34 (3 H, m, *o*- and *p*-ArH), 3.64 (3 H, s, OMe), 2.30 (2 H, m not

first order, CH_2CH_2CO), 1.10 (2 H, m, $SiCH_2CH_2CO$) and 0.31 (6 H, s, $SiMe_2$).

(±)-Methyl 2-dimethyl(phenyl)silylmethylpropanoate 20d. As an oil (74% by Method A without TMEDA, 22% by Method B, 74% by Method C and 25% by Method D) from methyl methacrylate eluting with light petroleum–EtOAc, 20:1. R_f(light petroleum–EtOAc, 9:1) 0.65; ν_{max}(neat)/cm^{-1} 3069 (aromatic CH), 2952 (aliphatic CH), 1736 (C=O), 1458 and 1428 (aromatic C=C), 1250 and 1203 (C–O) and 1113 (Si–Ph); δ_H(250 MHz; $CDCl_3$) 7.53–7.48 (2 H, m, *m*-ArH), 7.38–7.32 (3 H, m, *o*- and *p*-ArH), 3.55 (3 H, s, OMe), 2.55 (1 H, m, CH), 1.29 (1 H, dd, *J* 14.8 and 7.0, $SiCH_AH_B$), 1.15 (3 H, d, *J* 1.5, $CHMe$), 0.92 (1 H, dd, *J* 14.8 and 7.7, $SiCH_AH_B$) and 0.31 (6 H, s, $SiMe_2$) (Found: M$^+$, 236.1217. $C_{13}H_{20}SiO_2$ requires *M*, 236.1232).

***N*,*N*-Dimethyl-3-dimethyl(phenyl)silylpropanamide 20e**. As an oil (57% by Method A with TMEDA, 6% by Method B, 64% by Method C, 5% by Method D) from *N*,*N*-dimethylacrylamide eluting with light petroleum–EtOAc, 10:1; R_f(light petroleum–EtOAc, 9:1) 0.24; ν_{max}(neat)/cm^{-1} 3047 and 3018 (aromatic CH), 2952 (aliphatic CH), 1650 (C=O), 1589, 1488 and 1426 (aromatic C=C) and 1113 (Si–Ph); δ_H(250 MHz; $CDCl_3$) 7.54–7.47 (2 H, m, *m*-ArH), 7.37–7.31 (3 H, m, *o*- and *p*-ArH), 2.89 (3 H, s, NMe_AMe_B), 2.81 (3 H, s, NMe_AMe_B), 2.25 (2 H, m not 1st order, $SiCH_2CH_2$), 1.10 (2 H, m, not 1st order, $SiCH_2CH_2$) and 0.29 (6 H, s, $SiMe_2$); δ_C(250 MHz; $CDCl_3$) 174.0+, 138.5+, 133.1−, 128.9−, 127.8−, 37.1−, 35.5−, 28.0+ and 10.7+ (Found: M$^+$ − 1, 234.1314. $C_{13}H_{21}NSiO$ requires *M* − 1, 234.1314).

(±)-Ethyl 2-dimethyl(phenyl)silylmethyl-5-methylhex-4-enoate 20f. As an oil (83% by Method A without TMEDA, 23% by Method B, 75% by Method C and 35% by Method D) from ester **16** eluting with light petroleum–EtOAc, 20:1. R_f(light petroleum–EtOAc, 9:1) 0.64; ν_{max}(neat)/cm^{-1} 3448 (carbonyl overtone), 3068 and 3049 (aliphatic CH), 1732 (C=O), 1590 and 1427 (aromatic C=C), 1375 (Me) and 1113 (Si–Ph); δ_H(250 MHz; $CDCl_3$) 7.53–7.46 (2 H, m, *m*-ArH), 7.37–7.31 (3 H, m, *o*- and *p*-ArH), 5.01 (1 H, m not 1st order, $=CHCH_2$), 4.05–3.84 (2 H, m, OCH_2Me), 2.42 (1 H, m, $CHCH_2Si$), 2.28 (1 H, m, $=CHCH_AH_B$), 2.12 (1 H, m, $=CHCH_AH_B$), 1.66 (3 H, s, CMe_AMe_B), 1.55 (3 H, s, CMe_AMe_B), 1.17 (3 H, t, *J* 7.1, OCH_2Me), 0.95 (1 H, dd, *J* 14.8 and 5.0, CH_AH_BSi), 0.87 (1 H, dd, *J* 14.8 and 6.5, CH_AH_BSi) and 0.32 (6 H, s, $SiMe_2$); δ_C(250 MHz; $CDCl_3$) 176.5+, 138.8+, 133.6−, 128.9−, 127.7−, 121.3−, 60.0+, 41.7−, 34.5+, 25.8−, 18.5+, 17.8−, 14.1−, −2.6– and −2.7–. One carbon ($=CMe_2$) is not seen (Found: M$^+$ − 1, 303.1778. $C_{18}H_{28}SiO_2$ requires *M* – 1, 303.1780).

3-Dimethyl(phenyl)silylpropanonitrile 22.[18] As an oil (50% by Method A without TMEDA, 29% by Method B, 93% by Method C and 21% by Method D) from acrylonitrile eluting with light petroleum–EtOAc, 20:1. R_f(light petroleum–EtOAc, 9:1) 0.34; ν_{max}(neat)/cm^{-1} 3070, 3050 and 3010 (aromatic CH), 2956 and 2898 (aliphatic CH), 2246 (CN), 1590, 1487 and 1427 (aromatic C=C) and 1115 (Si–Ph); δ_H(250 MHz; $CDCl_3$) 7.50–7.44 (2 H, m, *m*-ArH), 7.43–7.32 (3 H, m, *o*- and *p*-ArH), 2.27 (2 H, m not 1st order, CH_2CN), 1.16 (2 H, m not 1st order, $SiCH_2$) and 0.37 (6 H, s, $SiMe_2$); δ_C(250 MHz; $CDCl_3$) 136.7+, 133.5−, 129.6−, 128.2−, 121.2+, 12.2+, 12.0+ and −3.5–.

(±)-Methyl 3-dimethyl(phenyl)silylbutanoate.[19] As an oil (72% by Method A without TMEDA, 71% by Method A with TMEDA, 95% by Method B, 72% by Method C, 80% by Method D and 32% by Method E) from methyl crotonate eluting with light petroleum–EtOAc, 20:1. R_f(light petroleum–EtOAc, 9:1) 0.73; ν_{max}(neat)/cm^{-1} 3066 and 3016 (aromatic CH), 2953, 2906 and 2869 (aliphatic CH), 1738 (C=O), 1589 and 1423 (aromatic C=C), 1250 and 1210 (C–O) and 1112 (Si–Ph); δ_H(250 MHz; $CDCl_3$) 7.52–7.48 (2 H, m, *m*-ArH), 7.38–7.33 (3 H, m, *o*- and *p*-ArH), 3.62 (3 H, s, OMe), 2.23 (1 H, dd, *J* 15.2 and 4.2, CH_AH_B), 2.07 (1 H, dd, *J* 15.2 and 11.0, CH_AH_B), 1.45 (1 H, dqd, *J* 11.0, 7.3 and 4.2, SiCH), 0.98 (3 H, d, *J* 7.3, $CHMe$) and 0.30 (6 H, s, $SiMe_2$); δ_C(250 MHz; $CDCl_3$) 177.8+, 138.7+, 133.5−, 129.0−, 127.8−, 51.4−, 35.5−, 20.9+, 20.6– and −2.6– (two peaks).

(*Z*)-Trichloro(2-methylbut-2-enyl)silane 23

Trichlorosilane (8.13 g, 60 mmol), isoprene (4.36 g, 64 mmol), bis(benzonitrile)palladium(II) chloride (0.05 g, 0.13 mmol) and triphenylphosphine (0.08 g, 0.30 mmol) were heated in a sealed tube at 70 °C for 7 h. Simple distillation of the dark brown liquid under reduced pressure gave the trichlorosilane[10] (11.18 g, 92%) (bp 58–60 °C at 18 mmHg); ν_{max}(neat)/cm^{-1} 3028 (vinyl CH), 2974, 2919 and 2862 (aliphatic CH), 1669 (C=C), 1441 (CH_2), 1398 and 1380 (Me), 807, 761 and 721 (C=C); δ_H(250 MHz; $CDCl_3$) 5.42 (1 H, q, *J* 6.7, =CH), 2.40 (3 H, s, $=CMeCH_2$), 1.83 (3 H, q, *J* 1.4, *Me*C=CHMe) and 1.60 (3 H, d, *J* 6.7, $=CHMe$).

Chloro[(*Z*)-2-methylbut-2-enyl]diphenylsilane 24

Phenyllithium (1.8 mol dm^{-3} in cyclohexane–ether, 7:3, 67 cm^3, 120.6 mmol) was slowly added to (*Z*)-trichloro(2-methylbut-2-enyl)silane (12.20 g, 60 mmol) in ether (90 cm^3) at −78 °C under argon, and the mixture kept at −78 °C for 2 h and at room temperature overnight. The precipitated salt was filtered off through a sintered glass filter. The solvent was evaporated off under reduced pressure, and the residue distilled to give the silane[1] (12.03 g, 70%) (bp 149–155 °C/0.09 mmHg).

3-Acetyl-6-methylhept-5-en-2-one

Sodium hydride (60%, 1.95 g, 49 mmol) was added to pentane-2,4-dione (4.5 g, 45 mmol) in ethanol (30 cm^3) in 30 portions at 0 °C. Prenyl bromide (7.5 g, 50 mmol) was added dropwise at the same temperature, and the mixture stirred at room temperature for 12 h. The precipitated salt was filtered off, volatile materials were evaporated off under reduced pressure, and the residue was distilled to give a 1 : 1 mixture of the keto and enol forms of the dione (5.46 g, 72%) bp 68–72 °C/0.4 mmHg (lit.[20] 107–108 °C/33 mmHg); δ_H(250 MHz; $CDCl_3$) 4.94–4.85 (2 H, m, CH_2CH=CMe_2 keto and enol), 3.54 (1 H, t, *J* 7.4, $CHCH_2$ keto), 2.84 (2 H, d, *J* 6.5, CH_2CH=enol), 2.46 (2 H, t, *J* 7.4, $CHCH_2CH$=keto), 2.09 [6 H, s, COMe and *Me*C(OH)=], 2.04 (6 H, s, MeCO keto), 1.97 (1 H, s, OH) and 1.64–1.56 (6 H, m, $=CMe_2$).

3-Methylene-6-methyl-hept-5-en-2-one 25

Aqueous formaldehyde (37% w/w, 4 cm^3) was added to the gelatinous mixture of potassium carbonate (5.53 g, 40.0 mmol), water (4 cm^3) and 3-acetyl-6-methylhept-5-en-2-one (3.37 g, 20 mmol), and the mixture was stirred at room temperature for 3 days. Water (30 cm^3) was added and the mixture was extracted with ether (3 × 30 cm^3). The combined organic extracts were dried ($MgSO_4$) and the solvent evaporated off under reduced pressure. Chromatography of the residue gave the ketone (1.95 g, 71%); R_f(light petroleum–EtOAc, 9:1) 0.57; ν_{max}(neat)/cm^{-1} 2970 and 2916 (aliphatic CH), 1681 (conjugated C=O), 1626 (C=C), 1364 (Me) and 974, 944 and 843 (C=C); δ_H(250 MHz; $CDCl_3$) 6.00 (1 H, s, $=CH_AH_B$), 5.73 (1 H, s, $=CH_AH_B$), 5.12 (1 H, t, *J* 7.3, $=CHCH_2$), 2.93 (2 H, d, *J* 7.3, $=CHCH_2$), 2.34 (3 H, s, COMe), 1.72 (3 H, s, CMe_AMe_B) and 1.65 (3 H, s, CMe_AMe_B); δ_C(250 MHz; $CDCl_3$) 199.8+, 148.1+, 134.0+, 124.9+, 120.7−, 28.9+, 26.0−, 25.7– and 17.6– (Found: M$^+$, 138.1046. $C_9H_{14}O$ requires *M*, 138.1045).

(±)-3-[(*Z*)-2-Methylbut-2-enyl(diphenyl)silyl]methyl-6-methylhept-5-en-2-one 27

The ketone **27** was prepared by the silyl conjugate addition method A without TMEDA from the silylcuprate reagent **26** (4.4 mmol), the ketone **25** (396 mg, 2.87 mmol) and chlorotrimethylsilane (935 mg, 8.61 mmol) as an oil (972 mg, 87%); R_f(light petroleum–EtOAc, 10:1) 0.55; ν_{max}(neat)/cm^{-1} 3068 and 3048 (vinyl CH), 1712 (C=O), 1664 (C=C), 1589, 1487 and 1428

(aromatic C=C), 1110 (Si–Ph), 842, 736 and 700 (Ar); δ_H(250 MHz; $CDCl_3$) 7.64–7.30 (10 H, m, ArH), 5.05 (1 H, q, *J* 6.3, MeC*H*=), 4.93 (1 H, t, *J* 7.3, =C*H*CH_2), 2.57 (1 H, quint, *J* 6.3, CH_2CHCH_2), 2.23–1.90 (5 H, m, =CHCH_2CH and COMe), 1.67 (3 H, s, =C$Me_A$$Me_B$), 1.66 (3 H, s, =C*Me*$CH_2$), 1.54 (1 H, dd *J* 15.0 and 4.8, CHC$H_A$$H_B$Si), 1.49 (5 H, s, =C$Me_A$$Me_B$ and =CMeCH_2Si), 1.30 (3 H, d, *J* 6.4, *Me*CH=) and 1.18 (1 H, dd, *J* 15.0 and 4.8, CHC$H_A$$H_B$Si) (Found: $M^+ - C_5H_9$, 321.1677. $C_{26}H_{34}SiO$ requires $M - C_5H_9$, 321.1675).

(±)-3-[(*Z*)-2-Methylbut-2-enyl(diphenyl)silyl]methyl-2,6-dimethylhepta-1,5-diene 28

Sodium bis(trimethylsilyl)amide (1.0 mol dm^{-3} in THF, 2.74 cm^3, 2.74 mmol) was added to a mixture of the ketone **27** (357 mg, 0.91 mmol) and methyltriphenylphosphonium iodide (1.11 g, 2.74 mmol) in toluene (5 cm^3), and the mixture was refluxed for 30 min. Ether (30 cm^3) was added, and the mixture was washed with brine (20 cm^3) and water (20 cm^3). The organic layer was dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. Column chromatography (SiO_2, light petroleum–EtOAc, 20:1) of the residue gave the *diene* (302 mg, 85%); R_f(light petroleum) 0.15; ν_{max}(neat)/cm^{-1} 3069 and 3047 (vinyl CH), 2964 and 2913 (aliphatic CH), 1643 (C=C), 1589 and 1428 (aromatic C=C), 1375 (Me) and 1110 (Si–Ph); δ_H(500 MHz; $CDCl_3$) 7.57–7.54 (2 H, m, *m*-ArH), 7.39–7.35 (3 H, m, *o*- and *p*-ArH), 5.05 (1 H, br s, =C*H*CH_2), 4.92 (1 H, br s, =C*H*CH_2), 4.60 (2 H, s, H_2C=), 2.35–2.27 (1 H, m, CH_2CHCH_2), 2.18–2.06 (2 H, m, =CHCH_2CH), 1.99–1.87 (2 H, m, =CMeCH_2Si), 1.64 (3 H, s, $Me_A$$Me_B$C=), 1.54–1.52 (6 H, m, $Me_A$$Me_B$C= and =CCH*Me*), 1.44 (3 H, s, =C*Me*CH_2) and 1.31–1.29 (5 H, m, *Me*C=CH_2 and CHCH_2Si); δ_C(250 MHz; $CDCl_3$) 149.3+, 136.6+, 136.2+, 135.4−, 132.8+, 131.9+, 129.5−, 127.7−, 123.0−, 117.7−, 110.9+, 43.0−, 34.9+, 26.4−, 25.8−, 19.5+, 18.5+, 18.3−, 18.1– and 13.8–.

(±)-3-(Fluoro)diphenylsilylmethyl-2,6-dimethylhepta-1,5-diene 29

Anhydrous methanolic hydrogen chloride (25% w/w, 20 drops) was slowly added to a mixture of the allylsilane **28** (190 mg, 0.49 mmol) and potassium fluoride (58 mg, 1.0 mmol) in dichloromethane (10 cm^3) at room temperature over 10 min, and the mixture was stirred for 2 h. Dichloromethane (20 cm^3) was added and the solution was washed with water (20 cm^3). The organic layer was dried ($MgSO_4$) and the solvent was evaporated off under reduced pressure to give the *fluorosilane* (160 mg, 96%); R_f(light petroleum–EtOAc, 9:1) 0.39; ν_{max}(neat)/cm^{-1} 3070 and 3050 (vinyl CH), 2967 and 2914 (aliphatic CH), 1643 (C=C), 1591 and 1429 (aromatic C=C), 1375 (Me) and 1123 (Si–Ph); δ_H(250 MHz; $CDCl_3$) 7.65–7.58 (2 H, m, *m*-ArH), 7.54–7.25 (3 H, m, *o*- and *p*-ArH), 4.98 (1 H, tt, *J* 7.0 and 1.3, =C*H*CH_2), 4.65 (1 H, br s, =C$H_A$$H_B$), 4.58 (1 H, s, =C$H_A$$H_B$), 2.40 (1 H, quint, *J* 6.8, CH_2CHCH_2), 2.18–1.93 (2 H, m, =CHCH_2CH), 1.66 (3 H, s, C$Me_A$$Me_B$), 1.59 (3 H, s, C$Me_A$$Me_B$), 1.52 [3 H, s, =C(CH)*Me*] and 1.44–1.35 (2 H, m, CHCH_2SiF); δ_C(250 MHz; $CDCl_3$) 148.6+, 134.1 (two peaks)−, 132.3+, 130.4−, 128.0−, 122.6−, 111.0+, 34.6+, 25.8−, 19.3+, 19.1+, 18.4– and 17.8– (Found: M^+, 338.1865. $C_{22}H_{27}SiF$ requires *M*, 338.1866).

(±)-Lavandulol 1

Hydrogen peroxide (30% w/w in H_2O, 1.50 g, 13.2 mmol), sodium hydrogen carbonate (1.2 g, 14.3 mmol) and the fluorosilane (0.57 g, 1.68 mmol) were refluxed in methanol (5 cm^3) and THF (5 cm^3) for 12 h. The mixture was concentrated under reduced pressure and ether (30 cm^3) was added to the residue. The ether layer was washed with water (20 cm^3), with aqueous sodium hydroxide (10%, 2 × 20 cm^3) and dried ($MgSO_4$). The solvent was evaporated off under reduced pressure to give the crude alcohol (160 mg, 62%). Column chromatography (SiO_2, light petroleum–EtOAc, 10:1) gave lavandulol (154 mg, 59%); R_f(light petroleum–EtOAc, 10:1) 0.17; δ_H(250 MHz; $CDCl_3$) 5.07 (1 H, m, =C*H*CH_2), 4.93 (1 H, m, H_AH_BC=), 4.82(1 H, m, H_AH_BC=), 3.57 (1 H, dd, *J* 10.6 and 5.2, CH_AH_BO), 3.48 (1 H, dd, *J* 10.6 and 8.0, CH_AH_BO), 2.28 (1 H, ddd, *J* 14.9, 7.3 and 5.2, CH_2CHCH_2), 2.05 [2 H, q (approximately), *J* 7.0, CH_2CHCH_2], 1.68 [6 H, s, Me_2C=], 1.60 [3 H, s, =C(CH)*Me*] and 1.43 (1 H, br s, O*H*), identical (TLC, ^{1}H NMR) with data in the literature,[21] and with an authentic sample obtained (97%) by hydrolysis (KOH, EtOH, room temperature for 3 h) of (±)-lavandulyl acetate. In another reference,[22] one of the olefinic protons is not reported, and only 1 H for the CH_2O group. In a third reference,[23] a value δ 2.59 (1 H, dd, *J* 10.6 and 8.7, CH_AH_BO) is reported where we have δ 3.57 or 3.48 (and δ 3.56 or 3.50 in a 500 MHz spectrum taken of our other synthetic sample, see below). This appears to be a typographical error in the literature, since our values are more reasonable for a proton in this environment.

(±)-Lavandulyl 3,5-dinitrobenzoate

(±)-Lavandulol (133 mg, 0.86 mmol), 3,5-dinitrobenzoyl chloride (231 mg, 1.16 mmol), triethylamine (150 mg, 1.48 mmol) and DMAP (32 mg, 0.262 mmol) were stirred in dichloromethane (6 cm^3) at room temperature for 1 day. The mixture was diluted with dichloromethane (30 cm^3) and washed with hydrochloric acid (5%, 20 cm^3). The organic layer was dried ($MgSO_4$) and the solvent evaporated off under reduced pressure to give the benzoate (131 mg, 44%). Recrystallisation gave the pure ester (50 mg) mp 75–76 °C (from Me_2CO-light petroleum) (lit.[24] 73–75 °C); R_f(light petroleum–EtOAc, 9:1) 0.65; ν_{max}(neat)/cm^{-1} 3089 (vinyl =CH), 2925 and 2854 (aliphatic CH), 1724 (CO) 1646 and 1627 (C=C bond), 1461 (CH_2) and 1376 and 1340 (CMe_2); δ_H(250 MHz; $CDCl_3$) 9.21 (1 H, t, *J* 2.1, *p*-ArH), 9.12 (2 H, d, *J* 2.1, *o*-ArH), 5.10 (1 H, t, *J* 7.1, =C*H*CH_2), 4.89–4.87 (1 H, m, =CH_AH_B), 4.82 (1 H, br s, =CH_AH_B), 4.42 (2 H, d, *J* CH_2O), 2.61 (1 H, q, *J* 7.1, CH_2CHCH_2), 2.20 (2 H, t, *J* 9.3, =CHCH_2CH), 1.87 (3 H, s, =C$Me_A$$Me_B$), 1.76 (3 H, s, =C$Me_A$$Me_B$) and 1.69 [3 H, s, =C(CH)*Me*].

2-Methylene-5-methylhept-4-enoic acid

Ethyl 2-methylene-5-methylhept-4-enoate **16** (1.68 g, 10.0 mmol) and potassium hydroxide (1.68 g, 30.0 mmol) were refluxed in ethanol (9 cm^3) and water (1 cm^3) for 1.5 h. The solvent was evaporated off under reduced pressure and water (5 cm^3) and hydrochloric acid (1 mol dm^{-3}, 5 cm^3) were added to the residue. The mixture was extracted with ether (3 × 50 cm^3) and the extracts were dried ($MgSO_4$) and the solvent was evaporated off under reduced pressure. Column chromatography (SiO_2, light petroleum–EtOAc, 2:1) of the residue gave the *acid* (1.25 g, 89%); R_f(light petroleum–EtOAc, 1:1) 0.44; ν_{max}(neat)/cm^{-1} 3500–2400 (carboxylic OH), 2923 (aliphatic CH), 1694 (C=O), 1629 (C=C) and 1377 (Me); δ_H(250 MHz; $CDCl_3$) 11.79 (1 H, br s, OH), 6.28 (1 H, d, *J* 1.2, =CH_AH_B), 5.64 (1 H, m, =CH_AH_B), 5.17 (1 H, m, =C*H*CH_2), 2.98 (2 H, d, *J* 7.2, =CHCH_2), 1.73 (3 H, s, C$Me_A$$Me_B$) and 1.62 (3 H, s, C$Me_A$$Me_B$) (Found: M^+, 140.0840. $C_8H_{12}O_2$ requires *M*, 140.0837).

N-Methyl-*N*-methoxy-2-methylene-5-methylhex-4-enamide

The acid (216 mg, 1.5 mmol), triethylamine (404 mg, 4 mmol), *N*,*O*-dimethylhydroxylamine hydrochloride (195 mg, 2 mmol) and DMAP (22 mg, 0.2 mmol) were mixed at 0 °C in dichloromethane (2 cm^3) and stirred for 30 min at room temperature. Dichloromethane (30 cm^3) was added, and the mixture was washed with hydrochloric acid (10%, 2 × 20 cm^3) and aqueous sodium hydrogen carbonate (10%, 2 × 20 cm^3). The organic extract was dried ($MgSO_4$), and the solvent was evaporated off under reduced pressure. Column chromatography (SiO_2, light petroleum–EtOAc, 10:1) of the residue gave the *amide* (138 mg, 50%); R_f(light petroleum–EtOAc, 9:1) 0.13; ν_{max}(neat)/cm^{-1} 2970 and 2932 (aliphatic CH), 1651 (CO), 1375 (Me), 997, 917

and 837 (vinyl CH); δ_H(250 MHz; $CDCl_3$) 5.31–5.09 (3 H, m, =C*H*CH_2 and =CH_2), 3.62 (3 H, s, OMe), 3.22 (3 H, s, NMe), 2.95 (2 H, d, *J* 7.2, =CHCH_2), 1.70 (3 H, s, =C*Me*$_A$Me$_B$) and 1.59 (3 H, s, =CMe$_A$*Me*$_B$) (Found: M^+, 183.1251. $C_{10}H_{17}NO$ requires *M* , 183.1259).

3-Methylene-6-methylhept-5-en-2-one 25

Methylmagnesium bromide (3.0 mol dm^{-3} in ether, 1.5 cm^3, 4.5 mmol) was added to the Weinreb amide (630 mg, 3.44 mmol) in THF (10 cm^3) at 0 °C, and the mixture was stirred at room temperature for 9 h. Aqueous ammonium chloride (saturated, 3 cm^3) was added, and the mixture was extracted with ether (3 × 30 cm^3). The combined extracts were dried ($MgSO_4$), and the solvent was evaporated off under reduced pressure. Chromatography of the residue gave the ketone (181 mg, 38%), identical with the sample described above, together with some starting material (290 mg, 46%).

2,6-Dimethyl-3-{[(*Z*)-2-methylbut-2-enyl]diphenylsilyl}methylhept-5-en-2-ol 30

Methylmagnesium bromide (3 mol dm^{-3} solution in ether, 1 cm^3, 3 mmol) was added to a stirred solution of the ester **17** (421 mg, 1 mmol) in dry ether (10 cm^3) and the mixture kept at room temperature under argon for 24 h. Saturated aqueous ammonium chloride (10 cm^3) was added dropwise to the solution at 0 °C, and the mixture was extracted with ether (2 × 30 cm^3). The combined ether layers were washed with water (20 cm^3) and brine (20 cm^3), dried ($MgSO_4$) and the ether evaporated off under reduced pressure. Chromatography of the residue (SiO_2, light petroleum–EtOAc, 10:1) gave the *alcohol* (326 mg, 80%); R_f(light petroleum–EtOAc, 10:1) 0.37; ν_{max}(neat)/cm^{-1} 3463 (OH), 3068 (=CH), 2968 and 2914 (aliphatic CH), 1662 and 1589 (aromatic C=C bond), 1377 (Me) and 1110 (C–O); δ_H(500 MHz; $CDCl_3$) 7.58–7.56 (4 H, m, *m*-ArH), 7.37–7.34 (6 H, m, *o*- and *p*-ArH), 5.05–4.94 (2 H, m, =C*H*CH_2 and =C*H*Me), 2.13 (1 H, d, *J* 14.7, SiC*H*$_A$H$_B$CMe=), 2.11 (1 H, d, *J* 14.7, SiCH$_A$*H*$_B$CMe=), 2.09 (1 H, m, =CHC*H*$_A$H$_B$CH), 1.86 (1 H, m, =CHCH$_A$*H*$_B$CH), 1.72 (1 H, m, CH_2C*H*CCH_2), 1.60 (3 H, s, CH_2C*Me*=), 1.51–1.50 (7 H, m, OH and Me_2C=), 1.35 (1 H, dd, *J* 15.0 and 3.7, CHC*H*$_A$H$_B$Si), 1.30 (3 H, d, *J* 7.0, =CH*Me*), 1.13 [3 H, s, C(OH)*Me*$_A$Me$_B$], 1.11 [3 H, s, C(OH)Me$_A$*Me*$_B$] and 1.07 (1 H, dd, *J* 15.0 and 9.1, CHCH$_A$-*H*$_B$Si); δ_C(250 MHz; $CDCl_3$) 136.39+, 135.27−, 135.24−, 134.56−, 134.47−, 132.83+, 132.07+, 129.17−, 127.65−, 124.52−, 117.74−, 74.80+, 45.33−, 31.98+, 27.09−, 26.62−, 26.37−, 25.76−, 19.87+, 17.85−, 14.73+ and 13.77– (Found: M^+ + Na, 429.2590. $C_{27}H_{38}SiO$ requires *M* + Na, 429.2596).

1,1-Diphenyl-1-sila-2-oxa-3,3-dimethyl-4-(3-methylbut2-enyl)-cyclopentane 32

Hydrogen chloride (25% in MeOH, 2–3 drops) was added to a stirred solution of the alcohol (200 mg, 49.2 mmol) in dichloromethane (5 cm^3) at room temperature. After 1 min the solvent was evaporated off under reduced pressure. Chromatography of the residue (SiO_2, light petroleum–EtOAc, 20:1) gave the *silyl ether* (133 mg, 80%); R_f(light petroleum–EtOAc; 10:1) 0.71; ν_{max}(neat)/cm^{-1} 3067 (=CH), 2967 and 2927 (aliphatic CH), 1590 (aromatic C=C), 1379 (Me) and 1118 (Si–Ph); δ_H(400 MHz; $CDCl_3$) 7.64–7.57 (4 H, m, *m*-ArH), 7.43–7.35 (6 H, m, *o*- and *p*-ArH), 5.15 (1 H, br s, =CH), 2.25–1.86 (3 H, m, =CHCH_2C*H*), 1.70 (3 H, s, *Me*$_A$Me$_B$C=), 1.61 (3 H, s, Me$_A$*Me*$_B$-C=), 1.48–1.43 (4 H, m, SiC*H*$_A$H$_B$ and C*Me*$_A$Me$_B$), 1.17 (3 H, s, CMe$_A$*Me*$_B$) and 0.99 (1 H, t, *J* 12.5, SiCH$_A$*H*$_B$); δ_C(400 MHz; $CDCl_3$) 135.7+, 135.5+, 134.6−, 134.5−, 132.0+, 130.0−, 129.9−, 127.9−, 127.8−, 123.5−, 82.6+, 49.5−, 32.2+, 29.6−, 25.9−, 24.2−, 17.9– and 12.3+; *m*/*z* (EI) 336 (60%, M^+), 321 (71%, M − Me), 278 (75%, M − 58) and 258 (100%, M − C_6H_6) (Found: M^+, 336.1908. $C_{22}H_{28}OSiF$ requires *M*, 336.1909).

3-(Hydroxymethyl)-2,6-dimethylhept-5-en-2-ol 33

The silyl ether (189 mg, 0.56 mmol), potassium fluoride (98 mg, 1.68 mmol), potassium hydrogen carbonate (168.2 mg, 1.68 mmol) and hydrogen peroxide (30% in water, 188.5 mg, 1.68 mmol) were stirred in THF (5 cm^3) and methanol (5 cm^3) at room temperature for 20 min. The solvent was evaporated off under reduced pressure and the residue extracted with ether (2 × 50 cm^3). The combined ether extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography (SiO_2, light petroleum–EtOAc, 1:10) of the residue gave the diol[25] (68 mg, 70%); R_f(EtOAc) 0.49; ν_{max}(neat)/cm^{-1} 3327 (OH), 2971 and 2926 (aliphatic C–H), 1594 (C=C), 1380 (Me) and 1135 (C–O); δ_H(250 MHz; $CDCl_3$) 5.12 (1 H, t, *J* 7.2, =C*H*CH_2), 3.76–3.70 (2 H, m, CH_2O), 3.07 (1 H, br s, OH), 2.87 (1 H, br s, OH), 1.68 (3 H, s, *Me*$_A$Me$_B$C=), 1.63 (1 H, m, CH_2C*H*CH_2OH), 1.59 (3 H, s, Me$_A$*Me*$_B$C=), 1.30 [3 H, s, C(OH)*Me*$_A$Me$_B$] and 1.21 [3 H, s, C(OH)Me$_A$*Me*$_B$]; δ_C(250 MHz; $CDCl_3$) 132.8+, 123.0−, 74.7+, 63.4+, 50.0−, 29.8−, 26.1+, 25.7−, 25.1– and 17.7−; *m*/*z* (EI) 154 (17%, M − H_2O), 123 (100%, M − 49) and 81 (85%, M − 91).

3-[(*tert*-Butyldimethylsilyl)oxymethyl]-2,6-dimethylhept-5-en-2-ol

The diol **33** (65 mg, 0.38 mmol), *tert*-butyldimethylsilyl chloride (62 mg, 0.41 mmol), triethylamine (45.5 mg, 0.45 mmol) and 4-dimethylaminopyridine (10 mg, 0.082 mmol) were stirred in dichloromethane (50 cm^3) at room temperature for 48 h. The mixture was diluted with dichloromethane (2 × 50 cm^3), and the dichloromethane extracts were washed with hydrochloric acid (0.5 mol dm^{-3}, 20 cm^3) and dried ($MgSO_4$). The solvent was removed under reduced pressure, and chromatography of the residue gave the *silyl ether* (74 mg, 69%); R_f(light petroleum–EtOAc, 10:1) 0.42; ν_{max}(neat)/cm^{-1} 3462 (OH), 2958 and 2921 (aliphatic C–H) and 1255 (C–O); δ_H(250 MHz; $CDCl_3$) 5.07 (1 H, t, *J* 7.2, =C*H* CH_2), 4.21 (1 H, s, OH), 3.68 (1 H, dd, *J* 10.3 and 6.5, C*H*$_A$H$_B$OSi), 3.68 (1 H, dd, *J* 10.3 and 3.6, CH$_A$*H*$_B$OSi), 2.13–1.84 (2 H, m, =CHCH_2CH), 1.69 (3 H, s, *Me*$_A$Me$_B$C=), 1.60 (3 H, s, Me$_A$*Me*$_B$C=), 1.52 (1 H, m, CH_2C*H* CH_2OSi), 1.26 [3 H, s, *Me*$_A$Me$_B$C(OH)], 1.18 [3 H, s, Me$_A$*Me*$_B$-C(OH)], 0.88 (9 H, s, $SiCMe_3$) and 0.06 (6 H, s, $SiMe_2$); δ_C(250 MHz; $CDCl_3$) 132.61+, 123.29−, 73.23+, 63.85+, 49.33−, 29.32−, 25.83−, 25.75−, 25.62−, 25.42+, 17.96+, 17.82−, −5.79− and −5.82−.

3-[(*tert*-Butyldimethylsilyl)oxymethyl]-2,6-dimethylhepta-1,5-diene

The silyl ether (170 mg, 0.59 mmol), *N*,*N*-dimethylformamide (86.15 mg, 1.18 mmol), phosphorus trichloride (162 mg, 1.18 mmol) and pyridine (93.3 mg, 1.18 mmol) were stirred in THF (10 cm^3) at room temperature for 1 h. The solvent was removed under reduced pressure, and the residue was chromatographed to give the silyl ether[26] (37.6 mg, 24%); R_f(light petroleum–EtOAc 20:1) 0.84; ν_{max}(neat)/cm^{-1} 2927 and 2856 (aliphatic C–H), 1646 (C=C) and 1109 (C–O); δ_H(250 Mz; $CDCl_3$) 5.07 (1 H, br s, =C*H*CH_2), **4.78** (1 H, br s, =C*H*$_A$H$_B$), **4.69** (1 H, br s, =CH$_A$*H*$_B$), 3.56 (1 H, dd, *J* 9.9 and 6.4, C*H*$_A$H$_B$OSi), 3.50 (1 H, dd, *J* 9.9 and 6.1, CH$_A$*H*$_B$OSi), 2.31–1.94 (3 H, m, =CHCH_2C*H*), 1.67 (6 H, s, =CMe_2), 1.57 (3 H, s, =C*Me*CH_2), 0.88 (9 H, s, $SiCMe_3$) and 0.02 (6 H, s, $SiMe_2$); δ_C(250 MHz; $CDCl_3$) 146.3+, 132.0+, 122.7−, 111.6+, 65.6+, 49.8−, 28.3+, 25.9−, 25.8−, 20.6−, 18.3+, 17.9− and −**5.4**−. The literature values for the numbers in bold in the ^{1}H NMR spectrum are 5.77 and 5.68. This is probably a typographical error in the literature, since the values above are more reasonable. The literature values for the number in bold in the ^{13}C NMR spectrum are −5.23 and −5.21.

(±)-Lavandulol 1

The silyl ether (37 mg, 0.138 mmol) and tetrabutylammonium fluoride (1.0 mol dm^{-3} solution in THF, 0.15 cm^3, 0.15 mmol)

were stirred in THF (10 cm^3) at room temperature for 5 h. The solvent was removed under reduced pressure and the residue chromatographed to give (±)-lavandulol (17.3 mg, 67%); R_f(light petroleum–EtOAc, 15:1) 0.15; δ_H(500 MHz; $CDCl_3$) 5.10 (1 H, t, *J* 7.0, =C*H*CH_2), 4.90 (1 H, s, =CH_AH_B), 4.81 (1 H, s, =CH_AH_B), 3.56 (1 H, dd, *J* 5.0 and 10.6, CH_AH_BO), 3.50 (1 H, dd, *J* 8.7 and 10.6, CH_AH_BO), 2.28 (1 H, m, CH_2CH CMe=), 2.14–2.01 (2 H, m, =CHCH_2CHC), 1.70 (3 H, s, $Me_A$$Me_B$C=), 1.69 [3 H, s, $Me_A$$Me_B$C=], 1.61 (3 H, s, CH*Me*C=) and 1.44 (1 H, br s, OH), identical (^{1}H NMR) with the sample described above.

Chloro(diphenyl)methallylsilane 35

Phenyllithium (1.8 mol dm^{-3} in cyclohexane–Et_2O, 7:3, 55.6 cm^3, 100.1 mmol) and trichloromethallylsilane[14] (11.3 g, 50 mmol) in ether (100 cm^3) were stirred at −78 °C for 2 h. The solution was warmed up to room temperature, the precipitate was filtered off, and the solvent was removed under reduced pressure. Distillation of the residue gave the *silane* (7.62 g, 56%, bp 121–124 °C/0.25 mmHg); ν_{max}(neat)/cm^{-1} 3072 (vinyl CH), 3027 (aromatic CH), 2970 and 2915 (aliphatic CH), 1640, 1590 and 1487 (aromatic C=C) and 1116 (Si–Ph); δ_H(250 MHz; $CDCl_3$) 7.70–7.66 (2 H, m, *m*-ArH), 7.50–7.38 (3 H, m, *o*- and *p*-ArH), 4.73 (1 H, s, =CH_AH_B), 4.63 (1 H, s, =CH_AH_B), 2.38 (2 H, s, $SiCH_2$) and 1.64 (3 H, s, Me); δ_C(250 MHz; $CDCl_3$) 140.0+, 134.5−, 133.4+, 130.6−, 128.1−, 112.1+, 28.0+ and 25.2– (Found: M^+, 272.0788. $C_{16}H_{17}SiCl$ requires, *M*, 272.0788).

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