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Allylsilanes in Organic Synthesis; Double Asymmetric Induction in the Dihydroxylation of a Chiral Allylsilane.

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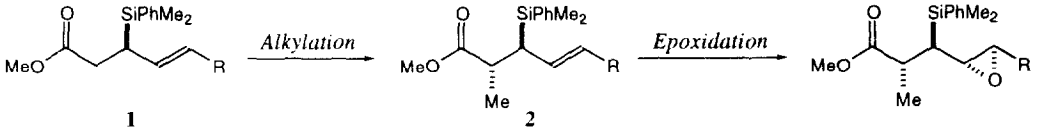
Dedicated to Emeritus Professor Hans Suschitzky, University of Salford, on the occasion of his 80th Birthday

Abstract: The diastereoselectivity of the dihydroxylation of ester-allylsilanes, particularly stereoisomers of methyl *E*-2-methyl-3-(phenyldimethylsilyl)hept-4-enoate, has been studied; the diastereoselectivity can be increased by using potassium ferricyanide as the stoichiometric oxidant and by double asymmetric induction using dihydroquinidine p-chlorobenzoate as catalyst. The major product of one of these reactions, (±)-(3*R*, 4*S*, 5*S*)-5-((1'*R*)-hydroxypropyl-3-methyl-4-(phenyldimethylsilyl)-dihydrofuran-2-one, was converted to a unit corresponding to one of the stereoisomers of the amino acid portion of the natural product baciphelacin.

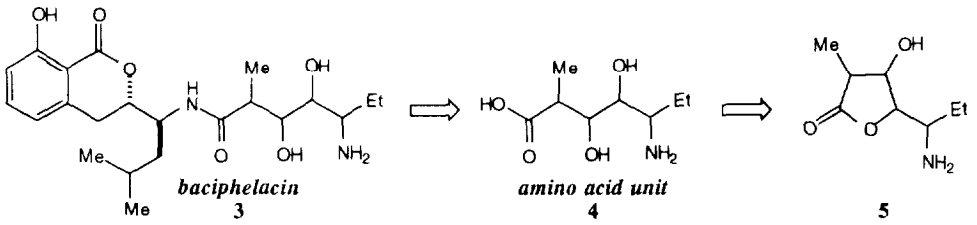
Chiral allylsilanes, particularly those which carry other functional groups such as **1** and **2** (Scheme 1), have considerable potential in stereoselective organic synthesis.[1,2,3] Much of this potential arises because of the ability of the silyl substituent to control the facial selectivity of reactions at adjacent double bonds as exemplified by the simple sequence illustrated in Scheme 1.[4] In this, the stereoselectivity of both the alkylation step and the epoxidation step is controlled by the silyl group, and in both steps the diastereoselectivity is very high (≥95:5).[5] As an extension to previous work on the epoxidation of systems such as **2** we recently communicated the results of a study investigating the dihydroxylation of this type of allylsilane using osmium tetroxide.[3d]



1 **2**

Scheme 1

One of the synthesis targets of our efforts in this area if the development of routes for the asymmetric synthesis of various stereoisomers of the dihydroxylated amino acid unit of baciphelacin **3** (Scheme 2), one of a number of 3,4-dihydroisocoumarin natural products with interesting biological properties.[6] Baciphelacin has been reported to possess antibiotic, antiviral, and antileukaemic activity, and although its overall structure and

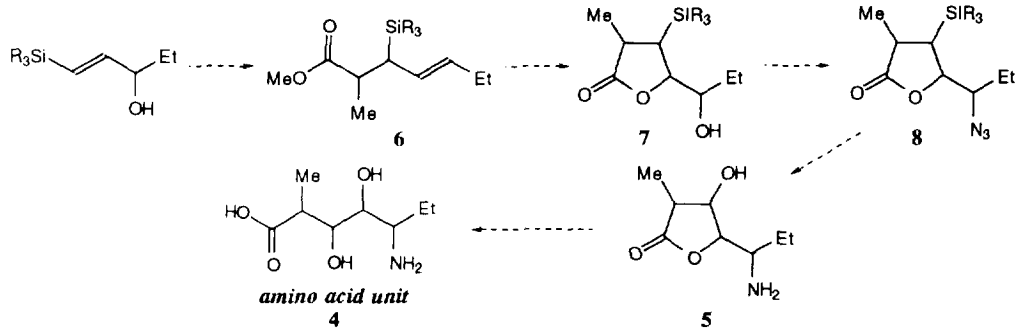


baciphelacin **3** ***amino acid unit*** **4** **5**

Scheme 2

the absolute configuration of the 2,3-dihydroisocoumarin unit have been determined, the stereochemistry of the amino acid portion **4** remains to be determined.

The lack of knowledge regarding the stereochemistry **4** imposes the need for flexibility in any synthetic route. The outline of one such route which, given various subsequent transformations, might provide access to the various possible isomers are outlined in Scheme 3. Methods are available for the enantioselective preparation of both diastereoisomers of allylsilane **6**[2a,b,3a,b,7] and various stereoisomers of **7** could be generated by oxidation of the double bond of **6** or its corresponding carboxylic acid. Conversion to **8** and further standard manipulation should then provide the desired systems.

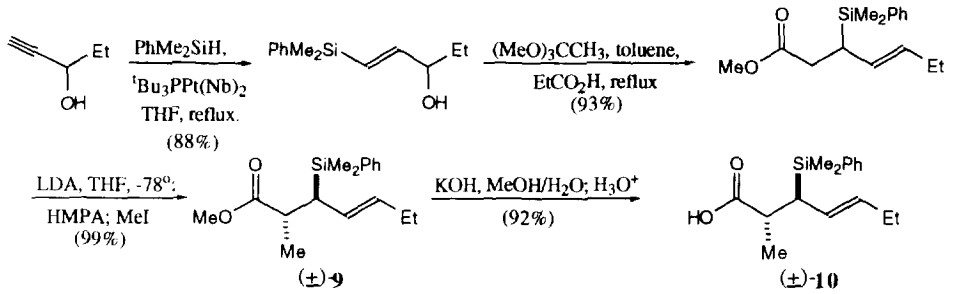


Scheme 3

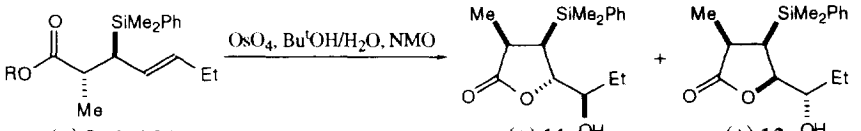
In this part of the project we were particularly interested in studying the dihydroxylation of allylsilanes such as **6**, with a view to studying the diastereoselectivity of this process. The dihydroxylation of allylsilanes is known to be less selective than epoxidation and other related reactions involving addition to the C-C double bond of the allylsilane.[8] The immediate aim of our work was to investigate the possibility of increasing the diastereoselectivity of this hydroxylation step.

Initial experiments were carried out on the racemic allylsilane **9** and the corresponding carboxylic acid, prepared as shown in Scheme 4. Hydrosilylation of pent-1-yn-3-ol catalyzed by the complex t-$Bu_3PPt(Nb)_2$ (Nb = norbornene) provided the vinylsilane regioselectively (13:1),[9] and the major regioisomer was subjected to the Johnson orthoester version of the Claisen rearrangement. Diastereoselective alkylation (97:3) of the resulting ester provided the desired ester-allylsilane (±)-**9**, hydrolysis of which gave acid (±)-**10**.

The two allylsilanes (±)-**9** and (±)-**10** were subjected to dihydroxylation with OsO_4 using *N*-methylmorpholine *N*-oxide as the co-oxidant. At room temperature both allylsilanes (±)-**9** and (±)-**10** underwent dihydroxylation with similar diastereoselectivity, lactones **11** and **12** being produced in ratios of



Scheme 4



(±)-**9** (R=Me)
(±)-**10** (R=H)
(±)-**11**
(±)-**12**

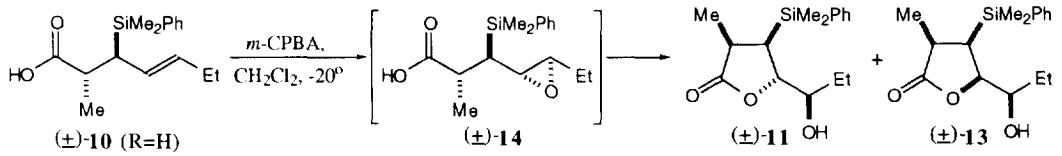
Substrate	Temp. (°C)	11:12[a]	Yield (%)[b]
(±)-**9**	Ambient	78:22	91
(±)-**10**	Ambient	74:26	95
(±)-**9**	0	87:13	93

[a]Estimated from 300 MHz ^{1}H nmr spectrum of crude product mixture.
[b]Isolated yield of **11** plus isolated yield of **12**.

Scheme 5

78:22 and 74:26 respectively (Scheme 5). This level of diastereoselectivity, which is typical for the dihydroxylation of allylsilanes, could be increased somewhat by carrying out the reaction of (±)-**9**, at 0°, but at lower temperatures the rate of dihydroxylation became too slow to be useful. A similar increase in diastereoselectivity was observed when potassium ferricyanide was used as the co-oxidant (see reactions of (+)-**9**).[10]

Lactone (±)-**11** is also the major product when carboxylic acid (±)-**10** is treated with *meta*-chloroperbenzoic acid (*m*-CPBA), and by analogy with previous work[3a] the other lactone product is tentatively assigned structure (±)-**13** (Scheme 6), as allylsilanes such as (±)-**10** have been shown to give essentially one epoxide diastereoisomer under these conditions.[3c] Lactone (±)-**13** is the 'expected' product, whereas lactone (±)-**11** presumably arises through the intermediacy of a β-silyl carbonium ion as proposed in our earlier studies of the epoxidation of this type of functionalized allylsilane.[3a]

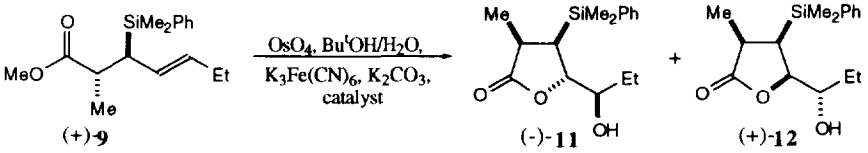


(±)-**10** (R=H)
(±)-**14**
(±)-**11**
(±)-**13**
11:**13** = 60:40

Scheme 6

In order to investigate the possibility of increasing the dihydroxylation diastereoselectivity by taking advantage of 'double asymmetric induction', reactions of allylsilane (+)-**9** (e.e. ≥ 95%) were investigated.[11] This allylsilane was prepared by the same route as for the racemate, except that the allylic alcohol was subjected to Sharpless kinetic resolution which gave a product of ≥95% e.e. (estimated by analysis of the Mosher's esters).

For these initial studies Sharpless' asymmetric dihydroxylation catalysts dihydroquinidine and dihydroquinine 4-chlorobenzoate were employed, with potassium ferricyanide as co-oxidant.[12] The results of these experiments are presented in Scheme 7. Using potassium ferricyanide as co-oxidant without catalyst results in increased diastereoselectivity (compared to NMO at the same temperature), and using the 'matched' catalyst increases this even further. The 'mismatched' catalyst derived from dihydroquinine slightly favours lactone (+)-**12**, previously the minor lactone under all dihydroxylation conditions. While the effects of these



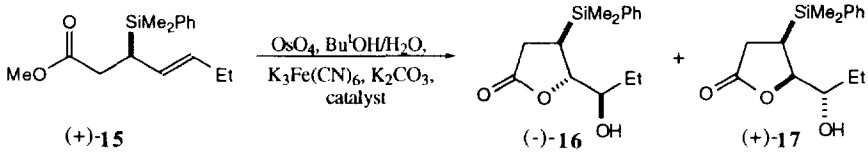
Catalyst[a]	11:12[b]	Yield (%)[c]
none	85:15	91
Dihydroquinidine	91:9	93
Dihydroquinine	43:57	94

[a]Used as 4-chlorobenzoates [b]Estimated from 300 MHz ^{1}H nmr spectrum of crude product mixture. [c]Isolated yield of **11** plus isolated yield of **12**.

Scheme 7

asymmetric dihydroxylation catalysts are not dramatic, they do allow for significant improvement in the diastereoselectivity in the 'matched case', and much higher yield of the 'minor' diastereoisomeric lactone (+)-**12** for the 'mismatched' case.

Following the above observations, it became of interest to investigate the effect of these asymmetric catalysts in the dihydroxylation of an allylsilane which shows essentially no diastereoselectivity in their absence. The immediate precursor to (+)-**9**, allylsilane (+)-**15** is just such a case. Dihydroxylation of (+)-**15** using potassium ferricyanide as co-oxidant and no catalyst gave essentially a 1:1 mixture of lactones (-)-**16** and (+)-**17** (Scheme 8). The product ratio could be altered to favour either of these lactones simply by incorporation of the appropriate asymmetric catalyst in the reaction mixture. In this way both these diastereoisomeric lactones can be separated by chromatography and obtained in synthetically useful yields. In particular, lactone (+)-**17** which corresponds to dihydroxylation '*syn*' to the silicon is easily available in reasonable yield.

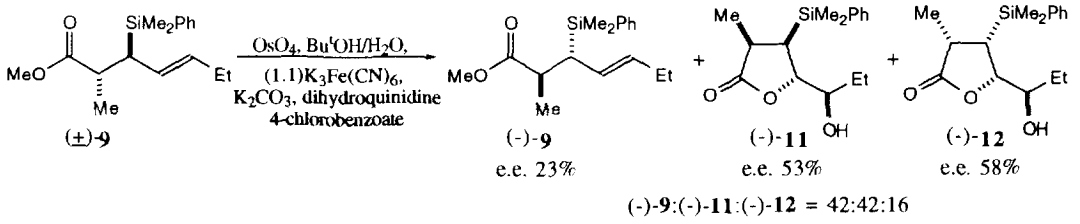


Catalyst[a]	16:17[b]	Yield (%)[c]
none	57:43	80
Dihydroquinidine	87:13	80
Dihydroquinine	13:87	81

[a]Used as 4-chlorobenzoates [b]Estimated from 300 MHz ^{1}H nmr spectrum of crude product mixture. [c]Isolated yield of **16** plus isolated yield of **17**.

Scheme 8

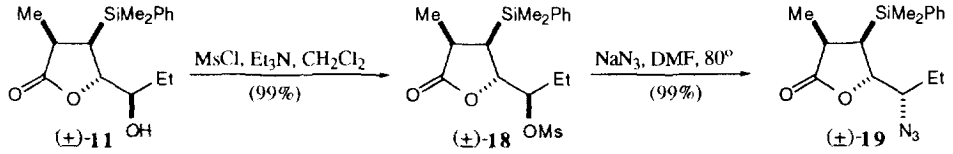
Although these asymmetric catalysts provide useful increases in the diastereoselectivity of dihydroxylation of enantiomerically enriched allylsilanes, we did not achieve a high level of kinetic resolution. The results of an attempted kinetic resolution of (±)-**9** are shown in Scheme 9. The reaction was carried out to approximately 55 percent completion by limiting the amount of potassium ferricyanide, in the presence of the dihydroquinidine catalyst, and the enantiomeric excesses estimated from the optical rotations of the isolated products. Similar



Scheme 9

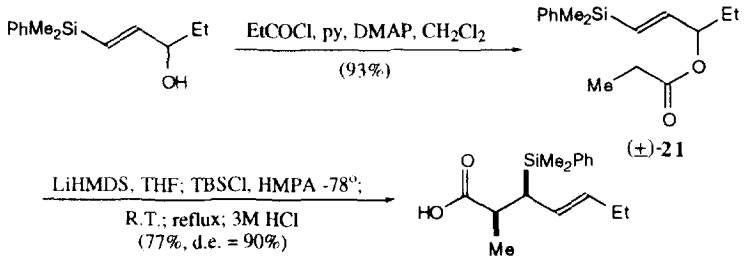
results were obtained using the dihydroquinine catalyst except that the absolute configurations of the products were opposite.

Given that one of the aims of this work is to provide access to compounds which might serve as precursors to the amino acid unit of the natural product baciphelacin, the conversion of lactone (±)-**11** into such a compound was investigated (Scheme 10). Following conversion to mesylate (±)-**18**, azide displacement was successfully accomplished by reaction with sodium azide in DMF at 90°. Under these conditions the displacement took place cleanly and in high yield to give azide (±)-**19**.



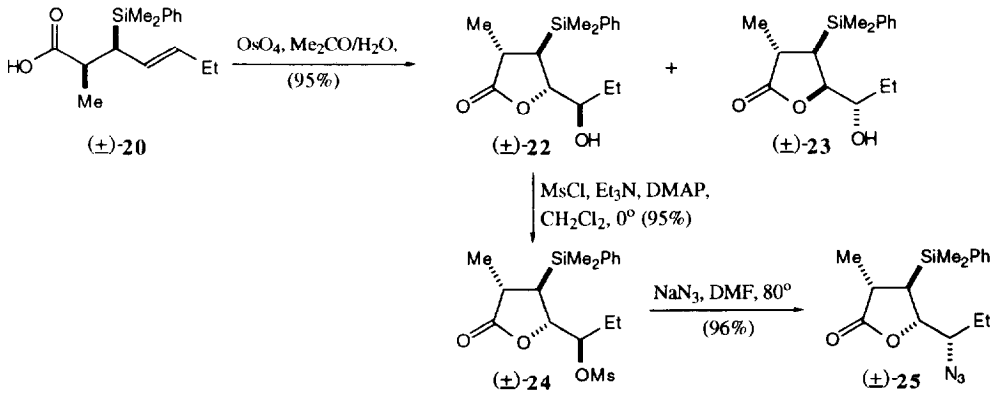
Scheme 10

An azide-lactone such as (±)-**19** could serve as a unit to represent the amino acid portion of baciphelacin, and in order to investigate the generality of this approach the sequence was also carried out using the *syn*-allylsilane (±)-**20** (Scheme 11). This *syn*-allylsilane could be prepared either by kinetic protonation of the enolate of (±)-**9** (see experimental) or by enolate Claisen rearrangement[7c] of propionate (±)-**21** (Scheme 11) (d.e.'s were estimated by careful ^{1}H nmr measurements on samples of the esters). As the Claisen rearrangement gave much higher diastereoselectivity this method was the method of choice.



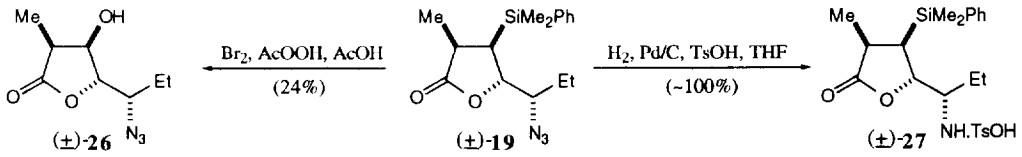
Scheme 11

Dihydroxylation of acid (±)-**20** using NMO as the co-oxidant at room temperature gave a mixture of diastereoisomeric lactones (±)-**22** and (±)-**23** (78:22) (Scheme 12). The major lactone was separated and converted to mesylate (±)-**24**, which underwent smooth displacement with azide under the same conditions used for the diastereoisomeric mesylate (±)-**18**.



Scheme 12

The two remaining transformations, conversion of the silyl substituent into hydroxyl,[13] and of the azide into an amino group were then studied using azide (±)-**19** (Scheme 13). Conversion of the phenyldimethylsilyl group into an hydroxyl group was slow, and provided only a low yield of the desired compound, but the reaction appeared to give the desired material (±)-**26**. Reduction of the azide to the amine could be achieved without lactam formation by reduction in the presence of an equivalent of *p*-toluenesulphonic acid (TsOH) which gave the salt (±)-**27** in good yield.



Scheme 13

In conclusion the work reported here shows that in appropriate cases it is possible to control, to some extent, the level of diastereoselectivity in the dihydroxylation of enantiomerically pure allylsilanes by the use of the simple Sharpless catalysts dihydroquinidine and dihydroquinine 4-chlorobenzoate. Moreover exploratory chemistry using lactone (±)-**11** has shown that it should be possible to apply this chemistry to the synthesis of the amino acid unit of baciphelacin, and we are actively pursuing this, and other applications of the allylsilane chemistry described herein.

Acknowledgement: We thank the SERC and Wellcome for a CASE studentship (R.A.W.).

Experimental

Infra-red absorption spectra were recorded on a Perkin-Elmer 1710 Fourier-transform spectrophotometer. The spectra were recorded either as a thin film (liquid and oil samples) or Nujol mull (solid samples). High field ^{1}H n.m.r. spectra were recorded on a Bruker AC-300 (300 MHz) in deuteriochloroform unless otherwise stated. Chemical shifts are quoted in δ and followed by the integration value, the signal multiplicity, J value(s) and proton assignment. The following abbreviations have been used to describe the signal multiplicity: br(broad), s(singlet), d(doublet), t(triplet), q(quartet), m(multiplet). Low resolution mass spectra (E.I. and C.I.) were recorded on a Finnigan 4500 and high resolution mass spectra (E.I., C.I. and F.A.B.) were measured on a Kratos concept. Capillary gas-chromatography was carried out on a Perkin-Elmer 8320 instrument using an SGE vitreous silica column (25QC2/BP1 0.25). Melting points were determined using an

"Electrothermal" apparatus and are uncorrected. Elemental analysis were carried out by the analytical chemistry department, Wellcome Research Ltd., Beckenham, Kent. Optical rotations were measured using an AA-10 monochromatic 589 nm polarimeter (Optical Activity Ltd.). Concentrations are expressed in grams per 100 ml of solvent. Thin layer chromatography was performed using Whatman or Macherey-Nagel glass-backed plates. The plates were visualised by use of ultraviolet light, iodide or one of the following reagents: ethanolic phosphomolybdic acid, ethanolic vanillin, aqueous potassium permanganate or ethanolic ninhydrin. Silica gel (particle sizes 0.040-0.063 mm) supplied by E.M. Merck was employed for flash chromatography using the procedure of Still, Khan and Mitra. Diethyl ether ("ether") and tetrahydrofuran were distilled from sodium/benzophenone ketyl immediately prior to use. Dichloromethane was distilled from calcium hydride prior to use. Chloroform, toluene, benzene, acetonitrile, dimethyl sulphoxide, dimethylformamide, triethylamine and diisopropylamine were distilled from calcium hydride and stored over 4Å molecular sieves. Pyridine was distilled from calcium hydride and stored over potassium hydroxide pellets. Methanol and ethanol ('Analar' grade) were routinely dried by standing over 3Å molecular sieves overnight. Reactions were routinely carried out under an argon or nitrogen atmosphere. *n*-Butyl lithium (~ 1.5M in hexane) was supplied by Lithco Corporation and was standardised by titration using diphenylacetic acid as indicator.

(±)-*E*-1-(Phenyldimethylsilyl)pent-1-en-3-ol. A mixture of pent-1-yn-3-ol (Lancaster, 10 g, 119 mmol) and phenyldimethylsilane (15.5 g, 112.3 mmol) in dry THF (100 ml) was treated with *bis*(2,5-norbornene) tris(*tert*-butyl)phosphine-platinum(0) (2 mg, 3.44 μmol) and the mixture refluxed with stirring for 18 hours. G.C. after this time showed a 13:1 mixture of regioisomers and no starting material. The solvent was removed *in vacuo* and the resulting liquid separated by flash chromatography (eluting with 5% ethyl acetate/petrol) to give the regioisomer (±)-2-(phenyldimethylsilyl)pent-1-en-3-ol, 1.67 g, 7% [R_f ~ 0.48 (9% ethyl acetate/petrol)]; δ_H 0.42 (3H, s, Si-CH_3); 0.44 (3H, s, Si-CH_3); 0.84 (3H, t, J = 7.4 Hz, H-5); 1.4-1.6 (3H, m, H-4a, H-4b, OH); 4.17 (1H, br t, J = 6.0 Hz, H-3); 5.49 (1H, d, J = 2.4 Hz, H-1a); 5.87-5.88 (1H, m, H-1b); 7.3-7.6 (5H, m, Ph); ν_{max} (thin film); 3400 cm^{-1} (br, OH); m/z (C.I., NH_3); 238 ($M + NH_4^+$); high resolution measured at 238.1636; $C_{13}H_{20}OSi + NH_4$ requires 238.1627 (~ 4 p.p.m. error).

Further elution from the flash chromatography column gave the desired product. This was further purified by Kugelrohr distillation (b.p. 150°C/0.1 torr) to give a colourless liquid, 21.73 g, 88% [R_f ~ 0.42 (9% ethyl acetate/petrol)]; δ_H 0.34 (6H, s, 2 x Si-CH_3); 0.92 (3H, t, J = 7.4 Hz, H-5); 1.50-1.60 (3H, m, H-4a, H-4b, -OH); 4.09 (1H, br q, J = 5.3 Hz, H-3); 5.97 (1H, dd, J = 18.7, 1.0 Hz, H-1); 6.11 (1H, dd, J = 18.7, 5.3 Hz, H-2); 7.3-7.6 (5H, m); ν_{max} (thin film); 3368 cm^{-1} (br, OH); m/z (C.I., NH_3); 238 ($M + NH_4^+$); high resolution measured at 238.1628; $C_{13}H_{20}OSi + NH_4$ requires 238.1627 (< 1 p.p.m. error).

(-)-(*R*)-*E*-1-(Phenyldimethylsilyl)pent-1-3-ol. Titanium tetraisopropoxide (4.14 ml, 13.8 mmol) was added to a stirred mixture of L-(+)-diethyl tartrate (3.57 ml, 20.8 mmol) and dried 4Å molecular sieves (20 g) in dry dichloromethane (140 ml) at -20°C. A solution of racemic alcohol (3.05 g, 13.9 mmol) in dry dichloromethane (20 ml) was then added and the mixture then stirred for a further 20 minutes before addition of *tert*-butylhydroperoxide (3.80 ml of a 5.48 M solution in dichloromethane, 20.83 mmol). The mixture was then stirred at -20°C for a further 48 hours after which time G.C. showed a 1:1 mixture of alcohol and epoxy alcohol. Dimethyl sulphide (2.59 g, 41.7 mmol) was then added and the mixture stirred for a further hour before pouring into acetone (250 ml) and water (4 ml). This mixture was stirred for 1 hour before further addition of water (4 ml) after which stirring was continued for a further hour. The mixture was filtered through Celite before concentration *in vacuo* to give a pale yellow oil. This was dissolved in ether (30 ml) and stirred

vigorously with 1M sodium hydroxide solution (30 ml) for 1 hour. The organic layer was separated, dried ($MgSO_4$) and concentrated *in vacuo* to give a yellow oil. This was purified by flash chromatography (eluting with 7% ethyl acetate/petrol) to give the desired compound which was purified by Kugelrohr distillation (b.p. 150°C/0.1 torr), 1.26 g, 41% (82% of theory), $[\alpha]_D$ = -1.82 (c = 2.4, $CHCl_3$), other data as reported above.

Further elution from the flash chromatography column gave (1*S*,2*S*,3*S*)-1,2-epoxy-1-(phenyldimethylsilyl)pentan-3-ol, 1.19 g, 36% (72% of theory) as a pale yellow oil [R_f ~ 0.32 (9% ethyl acetate/petrol)]; δ_H 0.32 (3H, s, Si-CH_3); 0.35 (3H, s, Si-CH_3); 0.96 (3H, t, J = 7.5 Hz, H-5); 1.40-1.65 (2H, m, H-4a, H-4b); 2.11 (1H, br s, -OH); 2.53 (1H, d, J = 3.5 Hz, H-1); 2.86 (1H, t, J = 3.5 Hz, H-2); 3.72-3.77 (1H, m, H-3); 7.3-7.6 (5H, m, Ph); ν_{max} (thin film); 3436 cm^{-1} (br, OH); m/z (C.I., NH_3); 254 (M + NH_4^+); high resolution measured at 254.1581; $C_{13}H_{20}O_2Si$ + NH_4 requires 254.1576 (~ 2 p.p.m. error).

(3*R*)-*E*-1-(Phenyldimethylsilyl)pent-1-en-3-ol, (*R*)-Mosher's ester. A solution of the above (*R*)-allylic alcohol (10 mg, 43.10 μmol), triethylamine (8.7 mg, 86.21 μmol) and 4-dimethylaminopyridine (~ 1 mg, catalytic amount) in dry dichloromethane (0.5 ml) was treated with a solution of (*R*)-Mosher's acid chloride (22 mg, 86.21 μmol) in dry dichloromethane (0.2 ml). After stirring at room temperature for 1 hour the reaction mixture was diluted with water (5 ml) and dichloromethane (5 ml) and the organic layer separated. After washing with 1M hydrochloric acid (10 ml) and saturated sodium bicarbonate solution (10 ml) the organic phase was dried ($MgSO_4$) and concentrated *in vacuo* to give the product as a pale yellow oil, 19 mg, ~100% [R_f ~ 0.7 (5% ethyl acetate/petrol)]; δ_H 0.07 (3H, s, Si-CH_3); 0.32 (3H, s, Si-CH_3); 0.82 (3H, t, J = 7.3 Hz, H-5); 1.62-1.72 (2H, H-4a, H-4b); 3.49 (3H, s with slight splitting, -OCH_3); 5.42 (1H, apparent dt, J = 5.7, 6.4 Hz, H-3); 5.99 (1H, dd, J = 18.7, 5.7 Hz, H-2); 6.09 (1H, d, J = 18.7 Hz, H-1); 7.3-7.5 (10H, m, 2 x Ph); ν_{max} (thin film); 1748 cm^{-1} (CO_2R); m/z (C.I., NH_3); 454 (M + NH_4); high resolution measured at 454.2036; $C_{23}H_{27}O_3Si$ + NH_4 requires 454.2025 (~ 2 p.p.m. error).

(3*S*)-*E*-1-(Phenyldimethylsilyl)pent-1-en-3-ol, (*R*)-Mosher's ester. This was prepared in an identical manner to the (*R*,*R*) diastereoisomer. Yield 20 mg, ~100% [R_f ~ 0.70 (5% ethyl acetate/petrol)]; δ_H 0.28 (3H, s, Si-CH_3); 0.29 (3H, s, Si-CH_3); 0.92 (3H, t, J = 7.5 Hz, H-5); 1.66-1.74 (2H, m, H-4a, H-4b); 3.55 (3H, s with slight further splitting, -OCH_3); 5.39 (1H, dt, J = 4.6, 6.6 Hz, H-3); 5.85 (1H, dd, J = 18.6, 4.6 Hz, H-2); 5.96 (1H, d, J = 18.6, H-1); 7.3-7.5 (10H, m, 2 x Ph); ν_{max} (thin film); 1746 cm^{-1} (CO_2R); m/z (C.I., NH_3); 454 (M + NH_4^+); high resolution measured at 454.2005; $C_{23}H_{27}F_3O_3Si$ + NH_4 requires 454.2025 (~ 4.5 p.p.m. error).

(+)-Methyl (*R*)-*E*-3-(phenyldimethylsilyl)hept-4-enoate, (+)-15. A mixture of the above (3*R*)-alcohol (1.00 g, 4.55 mmol), trimethylorthoacetate (0.82 g, 6.82 mmol) and propionic acid (3 drops, catalyst) in dry toluene (20 ml) was heated to reflux for 30 minutes. The apparatus was then rearranged to allow for removal of volatiles by distillation and the volume of the reaction mixture reduced to ~ 10 ml. A further portion of trimethylorthoacetate (0.82 g, 6.82 mmol) and propionic acid (1 drop) in dry toluene (10 ml) was then added and the distillation continued. This process of distillation followed by addition was repeated a further 3 times until T.L.C. showed no remaining starting material. After cooling the reaction mixture was washed with saturated sodium bicarbonate solution (20 ml), dried ($MgSO_4$) and concentrated *in vacuo* to give a colourless oil. This was purified by flash chromatography (eluting with 2.5% ethyl acetate/petrol) to give the product as a colourless liquid, 1.17 g, 93% R_f ~ 0.39 (9% ethyl acetate/petrol)]; δ_H 0.27 (6H, s, 2 x Si-CH_3); 0.91 (3H, t, J = 7.5 Hz, H-7); 1.92-2.00 (2H, m, H-2a, H-2b); 2.1-2.4 (3H, m, H-3, H-6a, H-6b); 3.56 (3H, s, -CO_2CH_3); 5.20-5.35 (2H, m, H-4, H-5); 7.3-7.5 (5H, m, Ph); ν_{max} (thin film); 1741 cm^{-1} (CO_2Me); m/z

(C.I., NH_3); 294 ($M + NH_4^+$); 277 ($M + H^+$); high resolution measured at 294.1885; $C_{16}H_{24}O_2Si + NH_4^+$ requires 294.1889 (~ 1 p.p.m. error); $[\alpha]_D$ = + 6.91 (c = 2.17, $CHCl_3$).

(+)-Methyl (2*R*,3*S*)-*E*-2-methyl-3-(phenyldimethylsilyl)hept-4-enoate (+)-9. A solution of allylsilane (+)-**15** (0.98 g, 3.55 mmol) in dry THF (10 ml) was added dropwise to a solution of LDA (17.8 mmol, generated from diisopropylamine, 2.16 g, 21.3 mmol and *n*-butyllithium, 11.83 ml of a 1.5M solution in hexanes) in dry THF (20 ml) at -78°C. The mixture was stirred at -78°C for 20 minutes before dropwise addition of freshly distilled HMPA (2.55 g, 14.2 mmol) and then for a further 20 minutes before dropwise addition of methyl iodide (5.04 g, 35.51 mmol). After slowly warming to 0°C the reaction mixture was quenched by addition of saturated ammonium chloride solution (100 ml). The mixture was then extracted with light petrol (2 x 40 ml), these extracts being washed with 1M hydrochloric acid (80 ml) before drying ($MgSO_4$) and concentration to give a dark brown oil. This was purified by filtering through a pad of flash silica eluting with light petrol. Concentration then gave the product as a colourless oil, 1.02 g, 99% [R_f ~ 0.25 (2.5% ethyl acetate/petrol)]; δ_H 0.24 (3H, s, Si-CH_3); 0.29 (3H, s, Si-CH_3); 0.91 (3H, t, J = 7.6 Hz, H-7); 1.04 (3H, d, J = 7.1 Hz, C2-Me); 1.92-2.02 (2H, m, H-6a, H-6b); 2.10 (1H, dd, J = 10.5, 7.4 Hz, H-3); 2.52 (1H, dq, J = 6.9, 7.4 Hz, H-2); 3.42 (3H, s, -CO_2Me); 5.14 (1H, br dd, J = 15.1, 10.5 Hz, H-4); 5.30 (1H, dt, J = 15.1, 6.3 Hz, H-5); 7.3-7.5 (5H, m, Ph); ν_{max} (thin film); 1738 cm^{-1} (CO_2Me); m/z (C.I., NH_3); 308 ($M + NH_4^+$); 291 ($M + H^+$); high resolution measured at 308.2057; $C_{17}H_{26}O_2Si + NH_4$ requires 308.2046 (~ 3.5 p.p.m. error); $[\alpha]_D$ = + 19.3 (c = 3.62, $CHCl_3$).

(±) (2*R,3*S**)-*E*-2-Methyl-3-(phenyldimethylsilyl)hept-4-enoic acid (±)-10**. A mixture of methyl ester (±)-9 (500 mg, 1.72 mmol) and potassium hydroxide (292 mg, 5.20 mmol) in methanol/water (4:1, 5 ml) was stirred at room temperature for 72 hours before addition of 1M hydrochloric acid to pH 1. The mixture was then diluted with water (15 ml) and extracted with ether (2 x 20 ml). The combined ether extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give a pale yellow oil. This was purified by flash chromatography (eluting with 10% ethyl acetate/petrol) to give the acid as a colourless oil, 438 mg, 92% [R_f ~ 0.35 (10% ethyl acetate/petrol)]; δ_H 0.27 (3H, s, Si-CH_3); 0.30 (3H, s, Si-CH_3); 0.90 (3H, t, J = 7.5 Hz, H-7); 1.05 (3H, d, J = 6.9 Hz, C2-Me); 1.91-1.99 (2H, m, H-6a, H-6b); 2.12 (1H, dd, J = 10.5, 6.9 Hz, H-3); 2.52 (1H, apparent quintet, J = 6.9 Hz, H-2); 5.17 (1H, br dd, J = 15.1, 10.5 Hz, H-4); 5.32 (1H, dt, J = 15.1, 6.5 Hz, H-5); 7.3-7.5 (5H, m, Ph); ν_{max} (thin film); 3200-2800 cm^{-1} (br, OH); 1705 cm^{-1} (CO_2H); m/z (C.I., NH_3); 294 ($M + NH_4^+$); high resolution measured at 294.1875; $C_{16}H_{24}O_2Si + NH_4^+$ requires 294.1889 (~ 5 p.p.m. error).

(±)-(3*R,4*S**,5*S**)-5-((1'*R**)-Hydroxypropyl)-3-methyl-4-(phenyldimethylsilyl)-dihydrofuran-2-one (±)-11 and its 5*R**,1'*S** diastereoisomer (±)-12**

Method A: Osmium tetroxide (0.88 ml of a 0.5% w/v solution in *tert*-butanol, 17.3 μmol) was added to a stirred solution of allylsilane (±)-**9** (100 mg, 0.35 mmol) and *N*-methylmorpholine-*N*-oxide (61 mg, 0.52 mmol) in acetone/water (10:1, 3 ml) and the mixture stirred at room temperature for 18 hours. Sodium metabisulphite (~ 500 mg, excess) was then added and the mixture stirred at room temperature for a further 30 minutes before filtering and concentrating *in vacuo*. The residue was partitioned between EtOAc and 1M hydrochloric acid, the organic phase then being dried ($MgSO_4$) and concentrated *in vacuo* to give a 78:22 [(±)-**11**:(±)-**12**] mixture of diastereoisomers. Purification by flash chromatography (eluting with 15% ethyl acetate/petrol) gave the (3*R**,4*S**,5*R**,1'*S**) diastereoisomer, (±)-**12**, 20 mg, 20% [R_f ~ 0.49 (17% ethyl acetate/petrol)]; δ_H 0.43 (3H, s, Si-CH_3); 0.46 (3H, s, Si-CH_3); 0.79 (3H, t, J = 7.4 Hz, H-3'); 1.39 (3H, d, J

= 7.5 Hz, C3-Me); 1.48-1.59 (2H, m, H-2'a, H-2'b); 1.77 (1H, br d, J = 7.9 Hz, -OH); 2.46 (1H, dd, J = 10.9, 9.1 Hz, H-4); 2.80 (1H, dq, J = 9.1, 7.5 Hz, H-3); 3.44 (1H, br dt, J = 7.9, 6.8 Hz, H-1'); 4.45 (1H, dd, J = 10.9, 1.1 Hz, H-5); 7.3-7.5 (5H, m, Ph); ν_{max} (thin film); 3453 cm^{-1} (OH); 1764 cm^{-1} (γ-lactone); m/z (C.I., NH_3); 310 ($M + NH_4^+$); high resolution measured at 310.1825; $C_{16}H_{24}O_3Si + NH_4$ requires 310.1838 (~ 4 p.p.m. error).

Further elution from the flash chromatography column gave the (3*R**,4*S**,5*S**,1'*R**) isomer, (±)-**11**, 71 mg, 71% [R_f ~ 0.39 (17% ethyl acetate/petrol)]; δ_H 0.39 (3H, s, Si-CH_3); 0.41 (3H, s, Si-CH_3); 0.87 (3H, t, J = 7.4 Hz, H-3'); 1.18 (3H, d, J = 7.7 Hz, C3-Me); 1.45-1.55 (2H, m, H-2'a, H-2'b); 1.64 (1H, br s, -OH); 2.26 (1H, dd, J = 9.3, 7.8 Hz, H-4); 2.92 (1H, dq, J = 9.3, 7.7 Hz, H-3); 3.16 (1H, br dt, J = 6.7, 2.5 Hz, H-1'); 4.37 (1H, dd, J = 9.3, 2.5 Hz, H-5); 7.3-7.5 (5H, m, Ph); ν_{max} (thin film); 3450 cm^{-1} (OH); 1765 cm^{-1} (γ-lactone); m/z (C.I., NH_3); 310 ($M + NH_4^+$); high resolution measured at 310.1829; $C_{16}H_{24}O_3Si + NH_4$ requires 310.1838 (~ 3 p.p.m. error).

Method B: Performing the above reaction at 0°C for 72 hours under otherwise identical conditions gave a 87:13 ratio of (±)-**11**:(±)-**12** in a combined yield of 93%.

Method C: Performing the osmylation on the racemic allyl silane acid (±)-**10** (100 mg, 0.36 mmol) at room temperature gave a 74:26 ratio of (±)-**11**:(±)-**12** in a combined yield of 95%.

(-)-(3*R*,4*S*,5S)-5-((1'*R*)-Hydroxypropyl)-3-methyl-4-(phenyldimethylsilyl)-dihydrofuran-2-one (-)-11 and its (3*R*,4*S*,5*R*,1'*S*) diastereoisomer (+)-12. Osmium tetroxide (50 μl of a 2% w/v solution in *tert*-butanol, 4.31 μmol) was added to a vigorously stirred mixture of allylsilane ester (+)-**9** (100 mg, 0.35 mmol), potassium ferricyanide (341 mg, 1.03 mmol) and potassium carbonate (143 mg, 1.03 mmol) in *tert*-butanol/water (1:1, 5 ml) and the mixture then stirred for 18 hours before addition of sodium sulphite (~ 1 g, excess). After stirring for a further 30 minutes the mixture was concentrated to dryness *in vacuo*. The solid residue was then partitioned between ethyl acetate (15 ml) and 1M hydrochloric acid (25 ml), the organic phase being separated, dried ($MgSO_4$) and concentrated to give an 85:15 [(-)-**11**:(+)-**12**] ratio of products. these were separated by flash chromatography (eluting with 17% ethyl acetate/petrol) to give (+)-**12**, 14 mg, 13.5%; Spectral data as reported above; $[\alpha]_D$ = +20.6 (c = 2.52, $CHCl_3$).

Further elution from the flash chromatography column gave the (3*R*,4*S*,5*S*,1'*R*) diastereoisomer, (-)-**11**, 77 mg, 77%; Spectral data as reported above; $[\alpha]_D$ = -22.4 (c = 2.32, $CHCl_3$).

Performing the above reaction on an identical scale in the presence of dihydroquinidine 4-chlorobenzoate (80 mg, 0.17 mmol) gave the same two products in a ratio of 91:9 (93% combined yield), and using dihydroquinine 4-chlorobenzoate (80 mg, 0.17 mmol) gave a ratio of 43:57 (94% combined yield).

(±)-(3*R,4*S**,5*S**)-5-((1'*R**)-Hydroxypropyl)-3-methyl-4-(phenyldimethylsilyl)-dihydrofuran-2-one (±)-11 and its 5R* diastereoisomer (±)-13.** *meta*-Chloroperbenzoic acid (72 mg, 0.42 mmol) was added to a stirred and cooled (-20°C) solution of the acid (±)-**10** (77 mg, 0.28 mmol) in dry dichloromethane (1.5 ml). The mixture was stirred until all the mCPBA had dissolved and then transferred to a freezer (approx. -20°C). The mixture was left as this temperature for 4 days before diluting with dichloromethane (10 ml) and washing sequentially with saturated sodium metabisulphite solution (10 ml) and saturated sodium bicarbonate solution (10 ml), drying ($MgSO_4$) and concentrating *in vacuo* to give an inseparable 60:40 [(±)-**11**:(±)-**13**] mixture of γ-lactones, 74 mg, 81%.

3*R**,4*S**,5*R**,1'*R** Diastereoisomer ((±)-**13**) δ_H (estimated from mixture) 0.45 (3H, s, Si-CH_3); 0.47 (3H, s, Si-CH_3); 0.90 (3H, t, J = 7.4 Hz, H-3'); 1.31 (3H, d, J = 7.7 Hz, C3-Me); 1.35-1.55 (2H, m, H-2'a,

H-2'b); 2.33 (1H, dd, J = 8.9, 7.7 Hz, H-4); 2.70 (1H, br dq, J = 8.9, 7.7 Hz, H-3); 3.48-3.58 (1H, m, H-1'); 4.25 (1H, dd, J = 9.5, 7.5 Hz, H-5); 7.3-7.5 (5H, m, Ph). 3*R**,4*S**,5*S**,1'*R** Diastereoisomer ((±)-**11**) - see below for physical data.

(-)-(4*R*,5*S*)-5-((1'*S*)-Hydroxypropyl)-4-(phenyldimethylsilyl)dihydrofuran-2-one (-)-16 and its (+)-(4*R*,5*R*,1'*R*) diastereoisomer (+)-17. Osmium tetroxide (60 µl of a 2% w/v solution in *tert*-butanol, 4.53 µmol) was added to a stirred solution of allyl silane (+)-**15** (100 mg, 0.36 mmol), potassium ferricyanide (358 mg, 1.09 mmol) and potassium carbonate (150 mg, 1.09 mmol) in *tert*-butanol/water (1:1, 5.5 ml) and the mixture stirred at room temperature for 18 hours. Sodium metabisulphite (~ 500 mg) was then added and the mixture stirred at room temperature for 1 hour before concentrating to dryness. The solid residue was then partitioned between ethyl acetate (10 ml) and 1M hydrochloric acid (10 ml), the organic phase then being separated, dried ($MgSO_4$) and concentrated to give a 57:43 [(-)-**16**:(+)-**17**] mixture of lactones. This mixture was separated by flash chromatography (eluting with 20% ethyl acetate/petrol) to give (+)-**17** as a crystalline solid, m.p. 62-64°C, 38 mg, 37% [R_f ~ 0.60 (33% ethyl acetate/petrol)]; δ_H 0.38 (3H, s, Si-CH_3); 0.44 (3H, s, Si-CH_3); 0.79 (3H, t, J = 7.4 Hz, H-3'); 1.23 (1H, br s, -OH); 1.51 (2H, apparent quintet, J = 7.4 Hz, H-2'a, H-2'b); 2.20 (1H, ddd, J = 13.2, 9.2, 8.8 Hz, H-4); 2.36 (1H, dd, J = 17.0, 9.2 Hz, H-3a); 2.73 (1H, dd, J = 17.0, 13.2 Hz, H-3b); 3.42-3.51 (1H, br m, H-1'); 4.47 (1H, dd, J = 8.8, 1.1 Hz, H-5); 7.3-7.5 (5H, m, Ph); ν_{max} (nujol mull); 3399 cm^{-1} (OH); 1760 cm^{-1} (γ-lactone); m/z (C.I., NH_3); 278 (M + NH_4^+); high resolution measured at 296.1683; $C_{15}H_{22}O_3Si + NH_4^+$ requires 296.1682 (~ 1 p.p.m. error); $[\alpha]_D$ = + 27.0 (c = 2.08, $CHCl_3$).

Further elution from the flash chromatography column gave (+)-**16** , 43 mg, 43% as a colourless oil [R_f ~ 0.45 (33% ethyl acetate/petrol)]; δ_H 0.36 (6H, s, 2 x Si-CH_3); 0.88 (3H, t, J = 7.4 Hz, H-3'); 1.4-1.7 (3H, m, H-2'a, H-2'b, -OH); 2.16 (1H, ddd, J = 10.8, 10.1, 8.9 Hz, H-4); 2.35 (1H, dd, J = 17.7, 10.8 Hz, H-3a); 2.63 (1H, dd, J = 17.7, 10.1 Hz, H-3b); 3.08-3.17 (1H, m, H-1'); 4.28 (1H, dd, J = 8.9, 1.8 Hz, H-5); 7.3-7.5 (5H, m, Ph); ν_{max} (thin film); 3437 cm^{-1} (OH); 1769 cm^{-1} (γ-lactone); m/z (C.I., NH_3); 296 (M + NH_4^+); high resolution measured at 296.1694; $C_{15}H_{22}O_3Si + NH_4$ requires 296.1682 (~ 4 p.p.m. error); $[\alpha]_D$ = -27.1 (c = 2.14, $CHCl_3$).

Performing the reaction under otherwise identical conditions and scale except including dihydroquinidine 4-chlorobenzoate (84 mg, 0.181 mmol) gave the same two products in a ratio of 87:13 [(+)-**16**: (+)-**17**] in similar isolated yield. Using dihydroquinine 4-chlorobenzoate (84 mg, 0.181 mmol) a ratio of 13:87 [(+)-**16**: (+)-**17**] was obtained in a combined yield of 81%.

Kinetic Resolution of (±)-9. Osmium tetroxide (0.22 ml of a 0.5% w/v solution in *tert*-butanol, 4.31 µmol) was added to a stirred solution of racemic allylsilane (±)-**9** (100 mg, 0.35 mmol), dihydroquinidine 4-chlorobenzoate (80 mg, 0.17 mmol), potassium ferricyanide (125 mg, 0.38 mmol) and potassium carbonate (143 mg, 1.04 mmol) in *tert*-butanol/water (1:1, 5.2 ml) and the mixture stirred overnight at room temperature. The mixture was then concentrated *in vacuo* and the residue partitioned between water (10 ml) and ether (10 ml). The organic phase was then washed with 1M hydrochloric acid (2 x 20 ml) and saturated brine (10 ml) before drying ($MgSO_4$) and concentrating *in vacuo*. N.m.r. analysis of this residue showed a 42:42:16 mixture of starting material (**A**), γ-lactone arising from attack "*anti*" to silicon (**B**) and γ-lactone arising from attack "*syn*" to silicon (**C**). These were separated by flash chromatography to give:- (a) Recovered starting material (-)-**9**, (**A**) 36 mg, $[\alpha]_D$ = -4.36 (~ 23% e.e.); (b) Minor isomer (-)-**12** (**B**), 14.5 mg, $[\alpha]_D$ = -12.0° (c = 2.0, $CHCl_3$) (~ 58% e.e.); (c) Major isomer (-)-**11** (**C**), 32 mg, $[\alpha]_D$ = -11.8 (c = 2.2, $CHCl_3$) (~ 53% e.e.).

Carrying out the reaction under otherwise identical conditions except using dihydroquinine 4-chlorobenzoate in place of dihydroquinidine 4-chlorobenzoate gave a 45:37:18 mixture (**D**:**E**:**F**). Separation by flash chromatography afforded: (d) Recovered starting material (+)-**9** (**D**), 35 mg, $[\alpha]_D$ = + 3.3 (c = 3.5, $CHCl_3$) (~ 17% e.e.); (e) Minor γ-lactone diastereoisomer (+)-**12** (**E**), 13 mg, $[\alpha]_D$ = +10.8 (c = 2.6, $CHCl_3$) (~ 52% e.e.); (f) Major γ-lactone diastereoisomer (+)-**11** (**F**), 33 mg, $[\alpha]_D$ = +10.0 (c = 3.2, $CHCl_3$) (~ 45% e.e.).

(±)-(3*R,4*R**,5*S**)-5-((1'*R**)-(Methanesulphonyloxy)propyl)-3-methyl-4-(phenyldimethylsilyl)-dihydrofuran-2-one (±)-18.** Triethylamine (208 mg, 2.06 mmol) was added dropwise to a stirred and cooled (0°C) solution of racemic γ-lactone alcohol (±)-**11** (200 mg, 0.69 mmol) and methanesulphonyl chloride (157 mg, 1.37 mmol) in dry dichloromethane (3 ml). Stirring was continued at 0°C for 2 hours before addition of 1M hydrochloric acid (10 ml) and dichloromethane (10 ml). The mixture was separated and the organic phase washed with saturated sodium bicarbonate solution (20 ml), dried ($MgSO_4$) and concentrated *in vacuo* to give a pale yellow oil. This was purified by flash chromatography (eluting with 14% ethyl acetate/petrol) to give the product as a colourless oil, 253 mg, ~100% [R_f ~ 0.47 (17% ethyl acetate/petrol)]; δ_H 0.40 (3H, s, Si-CH_3); 0.44 (3H, s, Si-CH_3); 0.81 (3H, t, J = 7.4 Hz, H-3'); 1.22 (3H, d, J = 7.5 Hz, C3-Me); 1.48-1.72 (2H, m, H-2'a, H-2'b); 2.09 (1H, dd, J = 10.6, 3.6 Hz, H-4); 3.04 (3H, s, OSO_2CH_3); 3.06 (1H, dq, J = 10.6, 7.5 Hz, H-3); 4.28-4.35 (2H, m, H-5, H-1'); 7.3-7.5 (5H, m, Ph); ν_{max} (thin film); 1776 cm^{-1} (γ-lactone); m/z (C.I., NH_3); 388 ($M + NH_4^+$); high resolution measured at 388.1631; $C_{17}H_{26}O_5SSi + NH_4$ requires 388.1614 (~ 4 p.p.m. error).

(±)-(3*R,4*R**,5*S**)-5-((1'*S**)-Azidopropyl)-3-methyl-4-(phenyldimethylsilyl)-dihydrofuran-2-one (±)-19.** A mixture of γ-lactone mesylate (±)-**18** (550 mg, 1.49 mmol) and sodium azide (480 mg, 7.43 mmol) in dry DMF (15 ml) was heated to 80°C with stirring for 8 hours. The mixture was then cooled and poured into water (100 ml) before extraction with ether (2 x 25 ml). The combined ether extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give a pale yellow oil which was purified by flash chromatography (eluting with 7% ethyl acetate/petrol) to give the product as a colourless oil, 508 mg, 97% [R_f ~ 0.2 (7% ethyl acetate/petrol)]; δ_H 0.38 (3H, s, Si-CH_3); 0.41 (3H, s, Si-CH_3); 0.81 (3H, t, J = 7.3 Hz, H-3'); 1.20 (3H, d, J = 7.6 Hz, C3-Me); 1.20-1.40 (2H, m, H-2'a, H-2'b); 1.98 (1H, dd, J = 10.2, 3.6 Hz, H-4); 3.11 (1H, dq, J = 10.2, 7.6 Hz, H-3); 3.23 (1H, apparent dt, J = 9.2, 4.2 Hz, H-1'); 4.26 (1H, dd, J = 4.2, 3.8 Hz, H-5); 7.3-7.5 (5H, m, Ph); ν_{max} (thin film); 2104 cm^{-1} (N_3); 1776 cm^{-1} (γ-lactone); m/z (C.I., NH_3); 335 ($M + NH_4^+$); high resolution measured at 335.1916; $C_{16}H_{23}N_3O_2Si + NH_4$ requires 335.1903 (~ 4 p.p.m. error).

(±)-*E*-1-(Phenyldimethylsilyl)pent-1-en-3-ol propionate (±)-21. Propionyl chloride (1.34 g, 14.52 mmol) was added dropwise to a stirred solution of the racemic allylic alcohol (1.60 g, 7.26 mmol), pyridine (1.72 g, 21.78 mmol) and 4-dimethylaminopyridine (89 mg, 0.73 mmol) in dry dichloromethane (10 ml) at 0°C. The reaction mixture was then stirred at 0°C for 2 hours before careful addition of water (20 ml). The organic phase was then washed with 1M hydrochloric acid (2 x 20 ml) and saturated sodium bicarbonate solution (2 x 20 ml), dried ($MgSO_4$) and concentrated *in vacuo* to give a pale yellow oil. This was purified by Kugelrohr distillation (b.p. 150°C/1 torr) to give the product as a colourless liquid, 1.86 g, 93% [R_f ~ 0.4 (2.5% ethyl acetate/petrol)]; δ_H 0.33 (6H, s, 2 x Si-CH_3); 0.88 (3H, t, J = 7.5 Hz, H-5); 1.14 (3H, t, J = 7.5 Hz, H-3'); 1.59-1.68 (2H, m, H-4a, H-4b); 2.35 (2H, q, J = 7.5 Hz, H-2'); 5.22 (1H, dt, J = 4.0, 6.3 Hz, H-3); 5.94 (1H, d, J = 18.9 Hz, H-1); 6.02 (1H, dd, J = 18.9, 4.0 Hz, H-2); 7.3-7.5 (5H, m, Ph); ν_{max} (thin

film); 1738 cm^{-1} (CO_2R); m/z (C.I., NH_3); 294 ($M + NH_4^+$); high resolution measured at 294.1881; $C_{16}H_{24}O_2Si + NH_4^+$ requires 294.1889 (~ 3 p.p.m. error).

(±)-(2*S,3*S**)-*E*-2-Methyl-3-(phenyldimethylsilyl)-hept-4-enoic acid (±)-20.** Lithium *bis*(trimethylsilyl)amide (1.53 ml of a nominally 1M solution in THF, 1.53 mmol) was added dropwise to a stirred solution of propionate ester (±)-**21** (210 mg, 0.76 mmol) in dry THF (8 ml) at -78°C. The mixture was then stirred at -78°C for 10 minutes before addition of a solution of *tert*-butyldimethylsilyl chloride (230 mg, 1.53 mmol) in dry HMPA (1 ml). The mixture was then allowed to warm to room temperature over 2 hours before heating to reflux for 2 hours to complete the rearrangement. The mixture was then cooled to room temperature before addition of 3M hydrochloric acid (30 ml). After stirring vigorously at room temperature for 30 minutes the mixture was extracted with diethyl ether (2 x 20 ml). The combined ether extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give a pale yellow oil, which was purified by flash chromatography (gradient elution, petrol → 40% ethyl acetate/petrol) to give the product as a colourless oil, 162 mg, 77% [R_f ~ 0.32 (9% ethyl acetate/petrol)]; δ_H 0.28 (3H, s, Si-CH_3); 0.31 (3H, s, Si-CH_3); 0.90 (3H, t, J = 7.4 Hz, H-7); 1.04 (3H, d, J = 6.9 Hz, C2-Me); 1.9-2.0 (3H, m, H-3, H-6a, H-6b); 2.51-2.62 (1H, m, H-2); 5.28-5.31 (2H, m, H-4, H-5); 7.3-7.5 (5H, m, Ph); ν_{max} (thin film); 3300 cm^{-1} (br, OH); 1706 cm^{-1} (CO_2H); m/z (C.I., NH_3); 294 ($M + NH_4^+$); high resolution measured at 294.1887; $C_{16}H_{24}O_2Si + NH_4$ requires 294.1889 (~ 1 p.p.m. error).

(±)-Methyl (2*S,3*S**)-*E*-2-methyl-3-(phenyldimethylsilyl)hept-4-enoate**

Method A: A solution of carboxylic acid (±)-20 (150 mg, 0.54 mmol) in iodomethane (4 ml) was treated with silver oxide (2 g, excess) and the mixture stirred for 18 hours before filtering through Celite and concentrating to give the desired product as a pale yellow oil, 156 mg, 99% [R_f ~ 0.40 (2.5% ethyl acetate/petrol)]; δ_H 0.27 (3H, s, Si-CH_3); 0.29 (3H, s, Si-CH_3); 0.90 (3H, t, J = 7.5 Hz, H-7); 1.02 (3H, d, J = 7.1 Hz, C2-Me); 1.80-2.00 (3H, m, H-3, H-6a, H-6b); 2.57 (1H, apparent quintet, J = 7.1 Hz, H-2); 3.51 (3H, s, -CO_2Me); 5.20-5.34 (2H, m, H-4, H-5); 7.3-7.5 (5H, m, Ph); ν_{max} (thin film); 1739 cm^{-1} (CO_2Me); m/z (C.I., NH_3); 308 ($M + NH_4^+$); 291 ($M + H^+$); high resolution measured at 308.2052; $C_{17}H_{26}O_2Si + NH_4$ requires 308.2046 (~ 2 p.p.m. error).

Method B: A mixture of racemic allyl alcohol (500 mg, 2.27 mmol), trimethylorthopropionate (915 mg, 6.82 mmol) and propionic acid (2 drops) in dry toluene (10 ml) was heated under reflux for 36 hours. The mixture was allowed to cool before washing with saturated sodium bicarbonate solution (10 ml), drying ($MgSO_4$) and concentrating *in vacuo* to give the product as a 55:45 *syn:anti*) mixture of diastereoisomers 619 mg, 94%; Spectral data as reported above.

Method C: A solution of the *anti* allylsilane ester (±)-9 (100 mg, 0.35 mmol) in dry THF (1 ml) was added dropwise to a solution of LDA (1.38 mmol, generated from diisopropylamine, (209 mg, 2.07 mmol) and *n*-butyl lithium (0.92 ml of a 1.5 M solution in hexanes)) in dry THF (2.5 ml) at -78°C. The mixture was then allowed to stir at 0°C for 1 hour before re-cooling to -78°C and quenching by addition of a solution of *tert*-butanol (255 mg, 3.45 mmol) in dry THF (1 ml). Saturated ammonium chloride solution (10 ml) was then added and the mixture allowed to warm to room temperature. Extraction with ether (2 x 10 ml) followed by drying ($MgSO_4$) and concentration *in vacuo* gave a pale yellow oil which was purified by flash chromatography to give the product as an 88:12 *syn:anti* mixture of diastereoisomers, 75 mg, 75%; Spectral data as reported above.

(±)-(3*S,4*R**,5*S**)-5-((1'*R**)-Hydroxypropyl)-3-methyl-4-(phenyldimethylsilyl)-dihydrofuran-2-one (±)-23 and its (5*R**,1'*S**)-diastereoisomer (±)-22.** Osmium tetroxide (0.46 ml of a 1% w/v solution in *tert*-butanol, 25.4 μmol) was added to a stirred solution of racemic *syn* allylsilane acid (±)-**20** (100 mg, 0.36 mmol) and N-methylmorpholine-N-oxide (64 mg, 0.54 mmol) in acetone/water (10:1, 2 ml) and the mixture stirred at room temperature for 18 hours. Sodium metabisulphite (500 mg, excess) was then added and stirring continued for 1 hour before filtering through Celite and concentration *in vacuo*. The residue was partitioned between ethyl acetate (10 ml) and 1M hydrochloric acid (10 ml), the organic phase then being dried ($MgSO_4$) and concentrated *in vacuo* to give the crude product as a 78:22 mixture of diastereoisomers [(±)-**22**:(±)-**23**)]. These were separated by flash chromatography (eluting with 20% ethyl acetate/petrol) to give the (3*S**,4*R**,5*R**,1'*S**) diastereoisomer (±)-**23**, 22 mg, 21% [R_f ~ 0.49 (20% ethyl acetate/petrol)]; δ_H 0.41 (3H, s, Si-CH_3); 0.45 (3H, s, Si-CH_3); 0.72 (3H, t, J = 7.5 Hz, H-3'); 1.13 (3H, d, J = 7.2 Hz, C3-Me); 1.42-1.52 (2H, m, H-2'a, H-2'b); 1.61 (1H, br s, -OH); 1.87 (1H, dd, J = 12.7, 8.4 Hz, H-4); 2.90 (1H, dq, J = 12.7, 7.2 Hz, H-3); 3.41 (1H, apparent br q, J = 6.8 Hz, H-1'); 4.36 (1H, dd, J = 8.4, 0.5 Hz, H-5); 7.3-7.5 (5H, m, Ph); ν_{max} (nujol mull); 3437 cm^{-1} (br, OH); 1767 cm^{-1} (γ-lactone); m/z (C.I., NH_3); 310 (M + NH_4^+); high resolution measured at 310.1842; $C_{16}H_{24}O_3Si + NH_4$ requires 310.1838 (~ 1 p.p.m. error).

Further elution from the flash chromatography column gave the (3*S**,4*R**,5*S**,1'*R**) diastereoisomer (±)-**22**, as a colourless oil, 78 mg, 74% [R_f ~ 0.34 (20% ethyl acetate/petrol)]; δ_H 0.38 (3H, s, Si-CH_3); 0.39 (3H, s, Si-CH_3); 0.84 (3H, t, J = 7.5 Hz, H-3'); 1.16 (3H, d, J = 7.0 Hz, C3-Me); 1.45-1.65 (3H, m, H-2'a, H-2'b, -OH); 1.82 (1H, dd, J = 11.8, 10.4 Hz, H-4); 2.47 (1H, dq, J = 11.8, 7.0 Hz, H-3); 2.91-3.01 (1H, br m, H-1'); 4.20 (1H, dd, J = 10.4, 1.2 Hz, H-5); 7.3-7.5 (5H, m, Ph); ν_{max} (thin film); 3437 cm^{-1} (br, OH); 1767 cm^{-1} (γ-lactone); m/z (C.I., NH_3); 310 (M + NH_4^+); high resolution measured at 310.1827; $C_{16}H_{24}O_3Si + NH_4$ requires 310.1838 (~ 3.5 p.p.m. error).

(±)-(3*S,4*R**,5*S**)-5-((1'*R**)-(Methanesulphonyloxy)propyl)-3-methyl-4-(phenyldimethylsilyl)-dihydrofuran-2-one (±)-24.** Triethylamine (572 mg, 5.65 mmol) was added dropwise to a stirred and cooled (0°C) solution of γ-lactone alcohol (±)-**22** (825 mg, 2.83 mmol) and methanesulphonyl chloride (356 mg, 3.11 mmol) in dry dichloromethane (10 ml). Stirring was continued for 30 minutes before washing the solution with 1M hydrochloric acid (20 ml) and saturated sodium bicarbonate solution (20 ml). The organic phase was then dried ($MgSO_4$) and concentrated *in vacuo* to give a pale yellow oil. This was purified by flash chromatography (eluting with 15% ethyl acetate/petrol) to give the product as a colourless oil, 1.01 g, 95% [R_f ~ 0.38 (20% ethyl acetate/petrol)]; δ_H 0.41 (3H, s, Si-CH_3); 0.43 (3H, s, Si-CH_3); 0.83 (3H, t, J = 7.5 Hz, H-3'); 1.17 (3H, d, J = 7.1 Hz, C3-Me); 1.74-1.83 (3H, m, H-2'a, H-2'b, H-4); 2.48 (1H, dq, J = 11.3, 7.1 Hz, H-3); 3.03 (3H, s, OSO_2CH_3); 4.18 (1H, td, J = 7.2, 1.6 Hz, H-1'); 4.31 (1H, dd, J = 10.0, 1.6 Hz, H-5); 7.3-7.5 (5H, m, Ph); ν_{max} (thin film); 1771 cm^{-1} (γ-lactone); m/z (C.I., NH_3); 388 (M + NH_4^+); high resolution measured at 388.1613 ; $C_{17}H_{26}O_5SSi + NH_4$ requires 388.1614 (< 1 p.p.m. error).

(±)-(3*S,4*R**,5*S**)-5-((1'*S**)-Azidopropyl)-3-methyl-4-(phenyldimethylsilyl)-dihydrofuran-2-one (±)-25.** A stirred mixture of γ-lactone mesylate (±)-**24** (955 mg, 2.58 mmol) and sodium azide (834 mg, 12.91 mmol) in dry DMF (25 ml) was heated to 80°C for 6 hours. The mixture was then poured into water (150 ml) and extracted with diethyl ether (2 x 25 ml). The combined ether extracts were dried ($MgSO_4$) and concentrated to give a pale yellow oil. This was purified by flash chromatography (eluting with 9% ethyl acetate/petrol) to give the product as a colourless oil, 789 mg, 96% [R_f ~ 0.33 (9% ethyl acetate/petrol)]; δ_H 0.39 (3H, s, Si-CH_3); 0.40 (3H, s, Si-CH_3); 0.91 (3H, t, J = 7.4 Hz, H-3'); 1.19 (3H, d, J = 7.2 Hz, C3-

Me); 1.32-1.43 (3H, m, H-4, H-2'a, H-2'b); 2.50 (1H, dq, J = 9.5, 7.2 Hz, H-3); 3.05 (1H, dt, J = 8.1, 5.1 Hz, H-1'); 4.32 (1H, dd, J = 8.1, 3.9 Hz, H-5); 7.3-7.5 (5H, m, Ph); ν_{max} (thin film); 2104 cm^{-1} (N_3); 1774 cm^{-1} (γ-lactone); m/z (C.I., NH_3); 335 ($M + NH_4^+$); high resolution measured at 335.1906; $C_{16}H_{23}N_3O_2Si + NH_4$ requires 335.1903 (~ 1 p.p.m. error).

(±)-(3*R,4*R**,5*S**)-5-((1'*S**)-Azidopropyl)-4-hydroxy-3-methyldihydrofuran-2-one (±)-26.** Potassium bromide (6 mg, 0.78 mmol) was added to a solution of silyl γ-lactone azide (±)-**19** (100 mg, 0.32 mmol) and sodium acetate (333 mg, 4.06 mmol) in acetic acid (3 ml). Peracetic acid (1.67 ml of a 32 wt. % solution in acetic acid, 6.22 mmol) was then added and the mixture stirred at room temperature for 24 hours. T.L.C. after this length of time showed starting material remaining, consequently extra portions of potassium bromide (47 mg, 0.32 mmol) and peracetic acid (1 ml of 32 wt. % solution in acetic acid, 3.72 mmol) were added and the mixture stirred for an additional 24 hours. The mixture was then poured into water (15 ml) and extracted with ether (2 x 15 ml). The combined ether extracts were washed with saturated sodium bicarbonate solution (2 x 20 ml), water (2 x 20 ml) and saturated sodium sulphite solution (2 x 20 ml) before drying ($MgSO_4$) and concentrating *in vacuo* to give a pale yellow oil. This was purified by flash chromatography (eluting with 33% ethyl acetate/petrol) to give the desired product as a colourless oil, 13 mg, 24% [R_f ~ 0.49 (33% ethyl acetate/petrol)]; δ_H 1.08 (3H, t, J = 7.4 Hz, H-3'); 1.24 (3H, d, J = 7.5 Hz, C3-Me); 1.59-1.83 (2H, m, H-2'a, H-2'b); 2.32 (1H, br s, disappears on D_2O shake, -OH); 2.84 (1H, dq, J = 7.0, 7.5 Hz, H-3); 3.52 (1H, dt, J = 5.1, 8.6 Hz, H-1'); 4.23 (1H, dd, J = 5.1, 1.8 Hz, H-5); 4.39 (1H, br d, sharpens with D_2O shake, J = 7.0 Hz, H-4); ν_{max} (thin film); 3454 cm^{-1} (br, -OH); 2106 cm^{-1} (N_3); 1768 cm^{-1} (γ-lactone).

(±)-(3*R,4*R**,5*S**)-5-((1'*S**)-Aminopropyl)-3-methyl-4-(phenyldimethylsilyl)-dihydrofuran-2-one, *p*-toluenesulphonic acid salt (±)-27.** A solution of γ-lactone azide (±)-**19** (20 mg, 63.1 μmol), *p*-toluene sulphonic acid monohydrate (12 mg, 63.1 μmol) and 5% palladium on charcoal (~ 10 mg) in dry THF (1 ml) was stirred vigorously under a hydrogen atmosphere for 8 hours. The mixture was then filtered through pre-washed Celite and concentrated to give the product as a colourless oil, 29 mg, ~100%; δ_H 0.32 (6H, s, 2 x Si-CH_3); 0.63 (3H, t, J = 7.2 Hz, H-3'); 1.02 (3H, d, J = 7.4 Hz, C3-Me); 1.2-1.4 (2H, m, H-2'a, H-2'b); 1.98 (1H, apparent t, J = 8.7 Hz, H-4); 2.33 (3H, s, Ar-CH_3); 2.81 (1H, dq, J = 8.7, 7.4 Hz, H-3); 2.97-3.01 (1H, br m, H-1'); 4.87 (1H, br d, J = 8.7 Hz, H-5); 7.11 (2H, d, J = 7.9 Hz, Ts); 7.2-7.4 (5H, m, Ph); 7.74 (2H, d, J = 7.9 Hz, Ts); ν_{max} (thin film); 3470 cm^{-1} (br, -NH_3^+); 1771 cm^{-1} (γ-lactone); m/z (F.A.B.); 292 (R-NH_3^+); high resolution measured at 292.1744; $C_{16}H_{26}NO_2Si$ requires 292.1733 (~ 4 p.p.m. error).

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