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The Intramolecular Silyl-Modified Sakurai (ISMS) Reaction. Synthetic Studies Towards Ambruticine¶

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¶ Dedicated with deep respect to Professor L Ghosez on the occasion of his 60th birthday.

Abstract: *The ISMS reaction has been used to efficiently construct the right-hand portion 3 of the antifungal antibiotic ambruticine 1.*

The antifungal antibiotic ambruticine **1**, isolated by Warner-Lambert scientists in 1977, possesses not only unique biological properties[2] but also a complex architectural framework which has stimulated considerable synthetic interest amongst research groups worldwide.[3] These efforts culminated in the elegant total synthesis of the natural product by Kende in 1990.[4]

Our own interest in ambruticine stems from the recognition that subunits **2** and **3**, which comprise the left- and right-hand portions of the natural product, respectively, are polysubstituted tetrahydropyran derivatives (Figure 1).

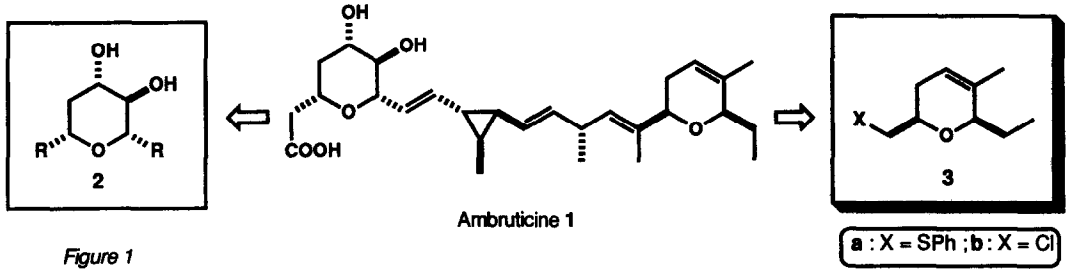
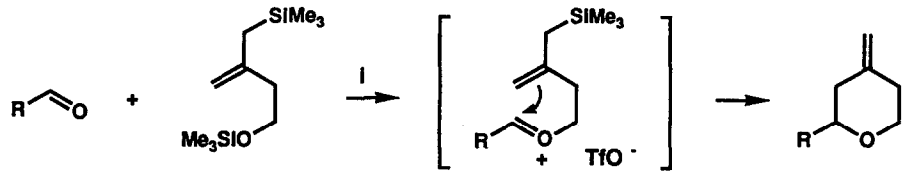


Figure 1

These oxygen-containing heterocycles are readily accessible *via* the Intramolecular Silyl-Modified Sakurai (ISMS) condensation.[5] This novel methodology consists of the coupling between a carbonyl compound and a silyl ether, containing a judiciously positioned allylsilane moiety. A small amount of a Lewis acid such as trimethylsilyl triflate is required (Figure 2) to catalyse the process. The reaction involves the initial formation of an oxonium cation **6**,[6] by condensation between the carbonyl derivative **4** and the silyl ether **5**, followed by intramolecular interception of the electron-deficient function by the nucleophilic allylsilane

residue. The *exo*-methylene tetrahydropyrans **7** are produced in high yields and may be manipulated further, providing an efficient entry into spiroketal-containing pheromones.[7]

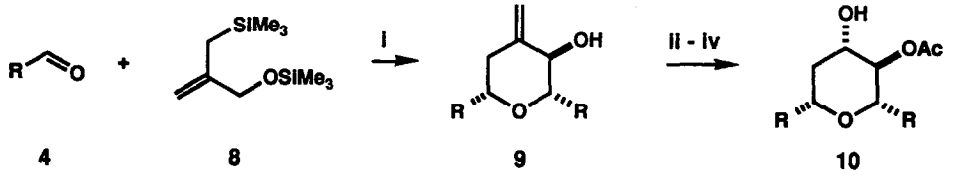


4 5 6 7

Figure 2

I = Me_3SiOTf cat., CCl_4, 20°C

A modification of the ISMS protocol allowed a particularly short preparation of model compounds for the western subunit of ambruticine 1.[8] Thus, employing Trost's reagent **8**[9] as the annelating agent, a triple condensation took place and the pyran derivative **9** was obtained in a single step. Cleavage of the exocyclic double bond, followed by stereoselective reduction, produced the diastereomerically pure *anti*-hydroxy-acetate **10** featuring the correct functionalities and relative stereochemistries of the left-hand portion of **1** (Figure 3).

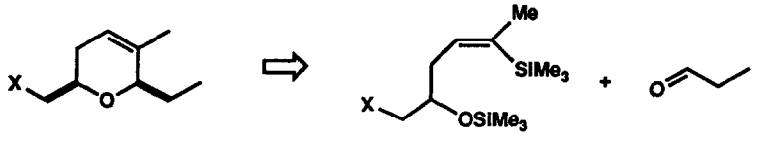


4 8 9 10

Figure 3

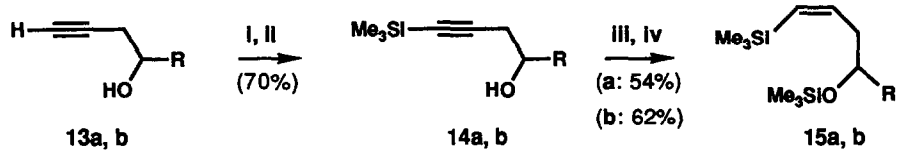
I = $BF_3.Et_2O$, CH_2Cl_2, -78°C to 20°C; II = O_3, Me_2S; III = AcCl, Py; Iv = $NaBH_4$, $CeCl_3$, THF, -78°C.

In this Article, we report our results on the ISMS condensation of vinyl silanes[10] with aldehydes and acetals which have led to the stereocontrolled synthesis of the eastern fragments **3a** and **3b**. Antithetic analysis of subunit **3**, using the ISMS retron, clearly reveals vinylsilane **11** as the preferred condensation partner (Figure 4). Alternative ISMS-based disconnections were considered but judged less appealing.



3 *Figure 4* 11 12

Before embarking on the total synthesis of fragment **3**, a few model studies were conducted to test the feasibility of this approach. We initially selected the reagents **15a** and **15b**, readily available from commercial acetylenic alcohols **13a** and **13b**, as our annelating reagents and studied their reactions with various aldehydes and acetals (Figure 5).



13a, b **14a, b** **15a, b**

a : R = H;
b : R = Me

Figure 5

I = 2 eqs BuLi, 2 eqs Me_3SiCl, -78°C to 20°C; II = 10% H_2SO_4
III = 3 eqs Dibal, ether, reflux; Iv = Me_3SiCl, Et_3N, CH_2Cl_2.

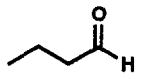
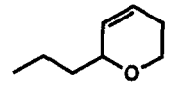
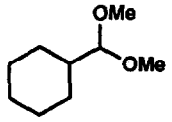
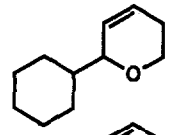
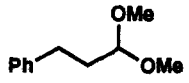
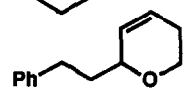
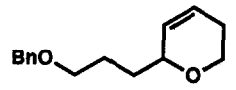
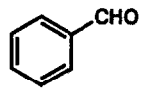
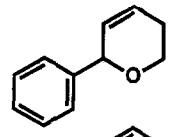
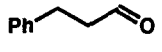
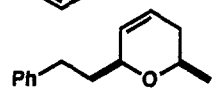
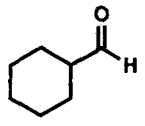
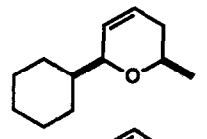
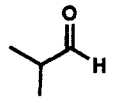
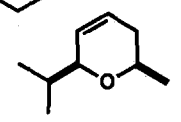
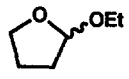
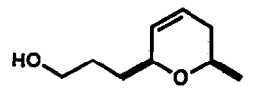
Double deprotonation of *homo*-propargylic alcohols **13a** and **13b** with *n*-butyl lithium generated the corresponding dianions which were quenched by the addition of an excess of trimethylsilyl chloride.[11] Based upon the elegant work of Overman[6b, 10] and our own observations,[12] Z-vinylsilanes **15a** and **15b** were targeted and a Lindlar hydrogenation appeared an ideal solution. However, despite all our efforts, a mixture of *E*- and *Z*-vinylsilane isomers was constantly produced.[13] A *Z*/*E* ratio of 8:1 was eventually obtained by carefully-controlled hydrogenation of **13a**. The situation deteriorated even further in the case of **13b**, for which catalytic hydrogenation led to a disappointing *Z*/*E* ratio of 2:1.

After considerable experimentation, it was eventually found that hydroalumination of **14b**, obtained by selective, acid-catalysed (10% H_2SO_4), removal of the silyl ether protecting group, using excess Dibal, followed by protonation of the resulting vinylalane, gave the desired Z-vinylsilane in isomerically pure form.[14] Silylation of the hydroxyl function finally afforded **15b** in 62% yield.

With ready access to these annelating agents established, the ISMS reaction was attempted with several aldehydes and acetals. The results are collected in Table 1 and deserve a few comments.

Both aliphatic and aromatic aldehydes prove to be efficient substrates, reacting smoothly with **15a** and **15b** to provide the desired dihydropyran derivatives in good to excellent yields (Entries 1, 4 - 8). Acetals also undergo the ISMS cyclisation with yields similar to the corresponding aldehyde (Entries 2, 3 and 9). Interestingly, a single isomeric dihydropyran is obtained when reagent **15b** is employed in the ISMS condensation. The *syn*-relative stereochemistry of the two substituents at C_{18}-C_{22} (ambruticine numbering) is attributed to this isomer by comparison of our spectroscopic data with those reported by Kende[4] and Hoffman.[10b] In addition, cyclisation using reagent **15b** consistently gives better yields of dihydropyran derivatives than reagent **15a**. Finally, incorporation of an unprotected oxygenated side-chain could be readily accomplished using 2-ethoxy-tetrahydrofuran (Entry 9).[15]

Table 1. ISMS Cyclisation of Vinyl Silanes **15a** and **15b**

Entry	Substrate	Reagent	Product	Yields[a]
1		15a		73%
2		15a		76%
3		15a		60%
4		15a		78%
5		15a		66%
6		15b		89%
7		15b		87%
8		15b		61%
9		15b		69%[b,c]

a : all yields are for isolated, pure compounds; **b** : 2eqs of substrate were used in this reaction; **c** : an aqueous acidic work-up was employed to remove traces of silyl ether.

With these encouraging results in hand, a final model study was performed and reagent **16** was expediently synthesised in three steps from acetylenic alcohol **14b** (hydroalumination with Dibal, reaction of the resulting vinylalane with excess methyl lithium/methyl iodide[16] and then O-silylation). ISMS reaction between vinylsilane **16** and dihydrocinnamaldehyde **17** gave the trisubstituted dihydropyran **18** as a single isomer in 80% yield (Figure 6).

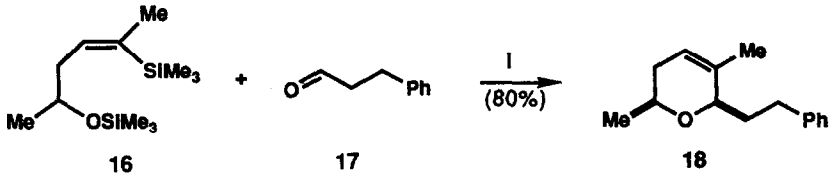
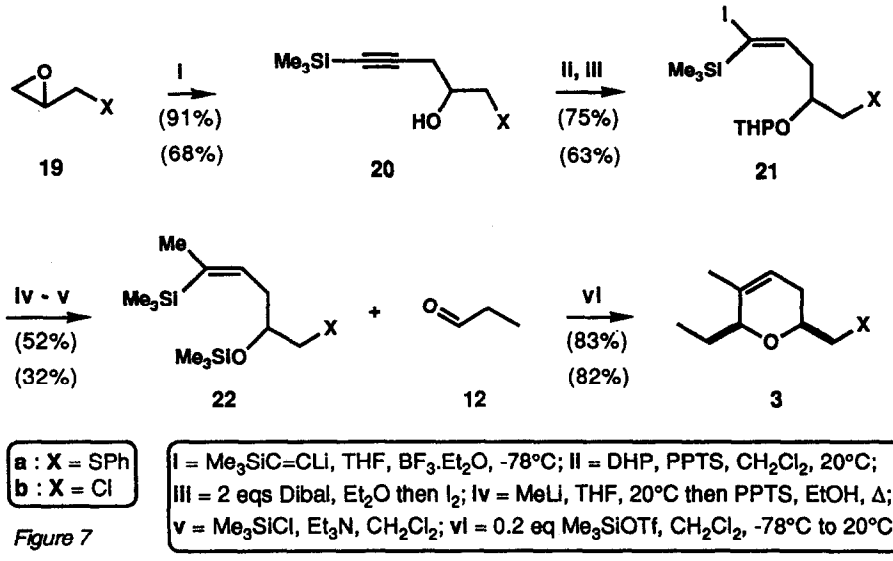


Figure 6

I = 0.2 eqs Me_3SiOTf, CH_2Cl_2, -78°C to 20°C

Having successfully established the basic methodology, the synthesis of target molecules **3a** and **3b** was subsequently investigated (Figure 7).[17] Access to **3a** started with readily available epoxide **19a**[18] which was opened regioselectively using 1-lithio-2-trimethylsilyl acetylene, giving the alcohol **20a** in 91% yield. Protection of the hydroxyl function followed by hydroalumination of the carbon-carbon triple bond and *in situ* reaction of the vinylalane with iodine generated the configurationally pure *E*-vinylsilane **21a** (75% overall yield).[19, 20]



a : X = SPh
b : X = Cl

I = $Me_3SiC{\equiv}CLi$, THF, $BF_3.Et_2O$, -78°C; II = DHP, PPTS, CH_2Cl_2, 20°C;
III = 2 eqs Dibal, Et_2O then I_2; IV = MeLi, THF, 20°C then PPTS, EtOH, Δ;
V = Me_3SiCl, Et_3N, CH_2Cl_2; VI = 0.2 eq Me_3SiOTf, CH_2Cl_2, -78°C to 20°C.

Figure 7

Addition of 2 eqs methyl lithium effected a one-pot transmetallation/alkylation sequence, replacing stereospecifically the iodine atom by a methyl group.[21] Deprotection and silylation finally gave annelating agent **22a**. A similar sequence of reactions successfully produced the chlorine-containing analogue **22b** (Figure 7).

The TMSOTf-catalysed ISMS reaction between vinylsilane **22a** and propionaldehyde **12** proceeded smoothly, affording the desired dihydropyran **3a** (X = SPh) in 83% yield, whilst condensation between chloride **22b** and propionaldehyde gave **3b** (X = Cl) in 82% yield. Oxidation finally produced the sulphone **3a** (X = SO_2Ph).

In summary, a short and stereocontrolled synthesis of the eastern subunit of ambruticine has been achieved using, as the key-step, the ISMS methodology. Model studies have already paved the way towards the western fragment of the natural product. Further studies directed at the total synthesis of ambruticine are currently underway in our laboratories and the results of these investigations will be reported in due course.

Acknowledgements :

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Experimental Section

General Methods. All the reactions were carried out under anhydrous conditions and in an atmosphere of argon unless otherwise stated. Melting points were obtained using a Leitz microhotstage and are uncorrected. NMR spectra were recorded on Varian XL-200, Gemini 200 and 300 and Brucker 250 MHz instruments. Chemical shifts are expressed as parts per million (δ) downfield from tetramethylsilane or calibrated from $CHCl_3$ in the case of silyl-containing compounds. Mass spectra were obtained using a Varian Matt 445 instrument, with electron impact (70eV) and chemical ionisation (100eV, ionisation gas, isobutane). IR spectra were taken with a Nicolet 500 FT instrument. Thin layer chromatography was performed on Merck 0.2 mm aluminium-backed TLC plates and visualised using ultra-violet light followed by development with alkaline $KMnO_4$ solution. Column chromatography was performed using Merck silica gel 60 (230-400 mesh) under pressure. Microanalyses were provided by the analytical department, University College, London.

1-Trimethylsilyl-4-trimethylsilyloxy-butyne :- To a cold (-78°C) solution of 3-butyn-1-ol (4.0 g, 1.0 eq., 0.057 mol) in THF (100 mL) was added 55 mL of a 2.5 M hexane solution of n-BuLi (2.4 eq., 0.137 mol). The resulting slurry was stirred vigorously at -30°C for 30 minutes then cooled to -78°C before the addition of 16.0 mL chlorotrimethylsilane (2.2 eq., 0.125 mol). After stirring at room temperature for 1 hr, the reaction mixture was poured onto saturated aqueous $NaHCO_3$ (100 mL). The aqueous and organic layers were separated and the aqueous phase was extracted with Et_2O (3 x 50 mL). The combined organic extracts were dried over anhydrous K_2CO_3 and the solvents were removed *in vacuo* to give a pale yellow oil. Purification by distillation (bp 74-76°C, 0.5 mm Hg) gave 9.82 g (80%) of the title compound. IR (neat) ν_{max} = 2965, 2180, 1355, 1100, 840 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) : δ_H = 3.54 (2H, t, J = 7.0 Hz), 2.32 (2H, t, J = 7.0 Hz), 0.00 (18H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 103.90, 85.65, 61.20, 24.07, 0.00, -0.52. MS (EI) m/z = 214 (5), 199 (15), 169 (27), 147 (19), 103 (74), 73 (100).

Z-1-Trimethylsilyl-4-trimethylsilyloxy-butene ***15a*** :- A 100 mL round bottomed flask containing 6.0 g of *1-trimethylsilyl-4-trimethylsilyloxy butyne* (0.028 mol), 0.15 g of 5% palladium on calcium carbonate poisoned with lead, 0.15 mL of quinoline and 45 mL of hexane was evacuated and recharged with hydrogen three times. The reaction mixture was stirred under an atmosphere of hydrogen for 3 hrs, then filtered through a plug of silica using CH_2Cl_2 (50 mL) as the eluant. The solvents were removed *in vacuo* to give a clear oil. Distillation (bp 69-70°C, 0.45 mm Hg) gave 4.67 g (77%) of the title compound as an 8:1 mixture of *Z:E* olefin isomers. Data given for Z- isomer : IR (neat) ν_{max} = 2965, 2910, 1615, 1250, 1100, 840 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) : δ_H = 6.16 (1H, dt, *J* = 15.0, 7.5 Hz), 5.50 (1H, d, *J* = 15.0 Hz), 3.50 (2H, t, *J* = 6.8 Hz), 2.27 (2H, dt, *J* = 7.5, 6.8 Hz), 0.00 (18 H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 144.41, 131.26, 62.09, 36.67, 0.02, -0.65. MS (EI) *m/z* = 147 (48), 133 (19), 113 (10), 103 (64), 73 (100), 45 (19).

1-Trimethylsilyl-pentyn-4-ol ***14b*** :- Following the procedure given for the preparation of *1-trimethylsilyl-4-trimethylsilyloxy-butyne*, the dianion of 4-pentyn-2-ol (0.106 mol) was quenched using 0.234 mol of chlorotrimethylsilane. Aqueous 1.0 M H_2SO_4 work-up and purification by distillation gave the title compound **14b** in 70% yield (bp 47°C, 0.05 mm Hg). IR (neat) ν_{max} = 3350, 2960, 2900, 2175, 1250, 1025, 845 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) : δ_H = 3.90 (1H, m), 2.41 (1H, ABX, *J* = 16.6, 4.8 Hz), 2.30 (1H, ABX, *J* = 16.6, 6.4 Hz), 2.05 (1H, d, *J* = 4.4 Hz), 1.21 (3H, d, *J* = 6.2 Hz), 0.10 (9H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 103.17, 87.52, 66.19, 30.39, 22.14, -0.02. MS (EI) *m/z* = 141 (16), 117 (57), 112 (34), 97 (19), 75 (59), 73 (100).

Z-1-Trimethylsilyl-penten-4-ol :- To a cold (0°C) solution of alkyne **14b** (6.0 g, 1.0 eq., 0.039 mol) in Et_2O (60 mL) was added 115 mL of a 1.0 M hexane solution of diisobutylaluminium hydride (3.0 eq., 0.115 mol). The reaction mixture was heated at reflux for 24 hrs, cooled to 0°C, then poured onto 0.5 M aqueous HCl/ice (40 mL/40 g). The resulting slurry was filtered through celite®, washed with Et_2O (100 mL) and the aqueous phase extracted with Et_2O (3 x 30 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and the solvents removed *in vacuo* to leave a pale yellow oil. Flash column chromatography (silica gel, hexane-EtOAc, 5:1) gave 3.85 g (63%) of the title compound. IR (neat) ν_{max} = 3330, 2960, 2880, 1610, 1250, 835 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) : δ_H = 6.33 (1H, dt, *J* = 14.8, 7.4 Hz), 5.70 (1H, d, *J* = 14.8 Hz), 3.88 (1H, tq, *J* = 7.4, 6.0 Hz), 2.32 (2H, dd, *J* = 7.4, 7.4 Hz), 1.80 (1H, br s), 1.22 (3H, d, *J* = 6.0 Hz), 0.15 (9H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 144.18, 132.71, 67.47, 42.90, 22.86, 0.21. MS (EI) *m/z* = 157 (6), 143 (12), 125 (29), 117 (28), 99 (46), 75 (82), 73 (100). HRMS : Calcd mass for $C_8H_{18}OSi$: 158.1127. Found : 158.1125.

Z-1-Trimethylsilyl-4-trimethylsilyloxy-pentene **15b**:- To a cold (0°C) solution of *Z-1-trimethylsilyl-penten-4-ol* (0.40 g, 1.0 eq., 2.53 mmol) and chlorotrimethylsilane (0.30 g, 1.1 eq., 2.78 mmol) in CH_2Cl_2 (3 mL) was added 0.31 g triethylamine (1.2 eq., 3.04 mmol). The reaction mixture was stirred overnight at room temperature then poured onto saturated aqueous $NaHCO_3$ (15 mL). The aqueous phase was separated and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and the solvent removed *in vacuo*

to leave a brown oil. Distillation (bp 50°C, 0.1 mm Hg) gave 0.50 g (85%) of pure silyl ether **15b**. IR (neat) ν_{max} = 2945, 2860, 1590, 1250, 1130, 1075, 830 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) : δ_H = 6.27 (1H, dt, *J* = 14.0, 8.0 Hz), 5.55 (1H, dt, *J* = 14.0, 1.3 Hz), 3.79-3.83 (1H, m), 2.22-2.25 (2H, m), 1.12 (3H, d, *J* = 6.1 Hz), 0.10 (18H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 145.23, 130.82, 68.46, 43.23, 23.55, 0.18. MS (EI) *m/z* = 207 (29), 147 (22), 133 (11), 117 (92), 75 (20), 73 (100).

General procedure for the ISMS condensation of aldehydes with vinyl silanes:

2-Propyl-oxacyclohex-3-ene (Table 1, Entry 1):- To a cold (-78°C) solution of butyraldehyde (0.15 g, 1 eq., 2.1 mmol) and vinyl silane **15a** (0.48 g, 1.0 eq., 2.1 mmol) in 10 mL CH_2Cl_2 was added 0.090 g (0.4 mmol, 0.20 eq.) of TMSOTf. The reaction mixture was allowed to warm slowly (2 hrs) to 0°C before being poured onto saturated aqueous $NaHCO_3$ (10 mL). The aqueous layer was separated and then extracted with CH_2Cl_2 (3 x 10 mL). The organic phases were combined and dried over anhydrous K_2CO_3. The solvent was removed *in vacuo* and the crude product was purified by flash column chromatography (silica gel, hexane-EtOAc, 50:1) affording 0.19 g (73%) of the title compound as a colourless oil (bp 50 °C, 15 mm Hg). IR (neat) ν_{max} = 2965, 2930, 2870, 1685, 1470, 1180, 1080, 910 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) : δ_H = 5.68-5.80 (1H, m), 5.50-5.59 (1H, m), 3.83-4.40 (2H, m), 3.56 (1H, ddd, *J* = 11.0, 10.0, 4.0 Hz), 2.08-2.30 (1H, m), 1.74-1.90 (1H, m), 1.26-1.50 (4H, m), 0.80-0.90 (3H, m). ^{13}C NMR ($CDCl_3$) : δ_C = 130.54, 124.34, 73.53, 63.30, 37.41, 25.29, 18.36, 13.95. MS (EI) *m/z* = 126 (6), 125 (71), 115 (100), 71 (82), 70 (59), 43 (28).

2-Cyclohexyl-oxacyclohex-3-ene (Table 1, Entry 2):- Following the general procedure described for *2-propyl-oxacyclohex-3-ene*, 2.1 mmol of cyclohexanecarboxaldehyde dimethylacetal was treated with 2.1 mmol of vinyl silane **15a** in the presence of 0.4 mmol of TMSOTf. Aqueous work-up and purification by flash column chromatography afforded the title compound in 72 % yield as a colourless oil (bp 75 °C, 0.3 mm Hg). IR (neat) ν_{max} = 2925, 2860, 2800, 1655, 1450, 1180, 1075 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) : δ_H = 5.84-5.85 (1H, m), 5.65-5.67 (1H, m), 3.80-4.00 (2H, m), 3.62 (1H, ddd, *J* = 11.0, 10.0, 4.0 Hz), 2.23-2.25 (1H, m), 1.60-1.90 (6H, m), 1.44-1.46 (1H, m), 1.00-1.30 (5H, m). ^{13}C NMR ($CDCl_3$) : δ_C = 128.94, 124.99, 78.10, 63.67, 42.65, 28.64, 28.04, 26.51, 26.26, 25.48. MS (EI) *m/z* = 166 (13), 155 (11), 127 (9), 111 (12), 83 (100), 55 (25). HRMS : Calcd mass for $C_{11}H_{18}O$: 166.1358. Found : 166.1343.

2-(2-Phenylethyl)-oxacyclohex-3-ene (Table 1, Entry 3):- Following the general procedure described for *2-propyl-oxacyclohex-3ene*, 2.1 mmol of dihydrocinnamaldehyde dimethylacetal was treated with 2.1 mmol of vinyl silane **15a** in the presence of 0.4 mmol of TMSOTf. Aqueous work-up and purification by flash column chromatography afforded the title compound in 60% yield as a colourless oil (bp 125 °C, 0.3 mm Hg). IR (neat) ν_{max} = 030, 2955, 2850, 1610, 1500, 1455, 1090 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) : δ_H = 7.10-7.30 (5H, m), 5.80-5.83 (1H, m), 5.59 (1H, ddd, *J* = 10.4, 2.0, 2.0 Hz), 3.90-4.10 (2H, m), 3.63 (1H, ddd, *J* = 11.0, 10.0, 3.8 Hz), 2.72-2.74 (2H, m), 2.23-2.25 (1H, m), 1.78-1.82 (3H, m). ^{13}C NMR ($CDCl_3$) : δ_C = 142.07, 130.17, 128.33, 128.15, 125.56, 124.73, 72.83, 63.17, 36.88, 31.32, 25.21. MS (EI) *m/z* = 188 (100), 159 (6), 97 (3), 91(11), 83 (15). HRMS : Calcd mass for $C_{13}H_{16}O$: 188.1201. Found : 188.1206.

2-(3-Benzyloxypropyl)-oxacyclohex-3-ene (Table 1, Entry 4):- Following the general procedure described for *2-propyl-oxacyclohex-3-ene*, 6.0 mmol of 4-benzyloxybutyraldehyde was treated with 6.0 mmol of vinyl silane **15a** in the presence of 1.2 mmol of TMSOTf. Aqueous work-up and purification by distillation afforded the title compound in 78% yield as a colourless oil (bp 150 °C, 0.01 mm Hg). IR (neat) ν_{max} = 3025, 2930, 2860, 1640, 1450, 1350, 1080 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) : δ_H = 7.30-7.35 (5H, m), 5.78-5.90 (1H, m), 5.63 (1H, ddd, *J* = 10.2, 2.2, 2.2 Hz), 4.50 (2H, s), 4.03-4.17 (1H, m), 3.96 (1H, ddd, *J* = 11.0, 5.6, 2.4 Hz), 3.63 (1H, ddd, *J* = 11.0, 9.6, 4.0 Hz), 3.50 (2H, t, *J* = 6.0 Hz), 2.15-2.38 (1H, m), 1.55-2.0 (5H,m). ^{13}C NMR ($CDCl_3$) : δ_C = 138.61, 130.30, 128.25, 127.51, 127.38, 124.69, 73.45, 72.69, 70.19, 63.27, 31.77, 25.36, 25.24. MS (EI) *m/z* = 232 (4), 141 (11), 129 (100), 102 (21), 91 (14), 83 (13), 75 (13).

2-Phenyl-oxacyclohex-3-ene (Table 1, Entry 5):- Following the general procedure described for *2-propyl-oxacyclohex-3ene*, 3.0 mmol of benzaldehyde was treated with 3.0 mmol of vinyl silane **15a** in the presence of 0.60 mmol of TMSOTf. Aqueous work-up and purification by flash column chromatography afforded the title compound in 66% yield as a colourless oil. IR (neat) ν_{max} = 3030, 2925, 2860, 1690, 1630, 1265, 1080 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) : δ_H = 7.22-7.40 (5H, m), 5.86-6.02 (1H, m), 5.79 (1H, ddd, *J* = 11.2, 2.0, 2.0 Hz), 5.11-5.13 (1H, m), 3.98 (1H, ddd, *J* = 10.4, 5.6, 4.2 Hz), 3.78 (1H, ddd, *J* = 10.4, 8.8, 4.4 Hz), 1.95-2.40 (2H, m). ^{13}C NMR ($CDCl_3$) : δ_C = 141.32, 129.34, 128.31, 128.06, 127.70, 127.36, 125.15, 125.06, 75.93, 62.94, 24.98. MS (EI) *m/z* = 160 (100), 131 (23), 128 (33), 115 (20), 105 (93), 77 (45).

Syn-2-(2-phenylethyl)-6-methyl-oxacyclohex-3-ene (Table 1, Entry 6):- To a cold (-78°C) solution of dihydrocinnamaldehyde (0.28 g, 1.0 eq., 2.1 mmol) and vinyl silane **15b** (0.48 g, 1.0 eq., 2.1 mmol) in CH_2Cl_2 (10 mL) was added 0.08 mL of TMSOTf (0.2 eq., 0.42 mmol). The reaction mixture was allowed to warm slowly (2 hrs) to 0°C then poured onto saturated aqueous $NaHCO_3$. The aqueous layer was separated and then extracted with CH_2Cl_2 (3 x 10 mL). The organic extracts were combined and dried over anhydrous K_2CO_3. The solvent was removed *in vacuo* to give a yellow oil which was purified by flash column chromatography (hexane-EtOAc, 50:1) on silica gel to afford 0.38 g (89 %) of the title compound as a colourless oil. IR (neat) ν_{max} = 3025, 2975, 2930, 2830, 1660, 1610, 1490, 1455, 1185, 1090, 1070 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 7.10-7.30 (5H, m), 5.74-5.84 (1H, m), 5.50-5.62 (1H, m), 4.10-4.15 (1H, m), 3.67 (1H, dq, *J* = 13.0, 6.0 Hz), 2.70-2.78 (2H, m), 1.93-1.97 (2H, m), 1.80-1.85 (2H, m), 1.15 (3H, d, *J* = 6.0 Hz). ^{13}C NMR ($CDCl_3$) : δ_C = 142.34, 130.04, 128.50, 128.23, 125.61, 124.98, 73.87, 69.92, 37.10, 32.90, 31.18, 21.64. MS (EI) *m/z* = 202 (100), 143 (7), 133 (6), 105 (18), 97 (71), 91 (56), 79 (10), 69 (6). HRMS : Calcd mass for $C_{14}H_{18}O$: 202.1358. Found : 202.1374.

Syn-2-cyclohexyl-6-methyl-oxacyclohex-3-ene (Table 1, Entry 7):- Following the general procedure described for *Syn-2-(2-phenylethyl)-6-methyl-oxacyclohex-3-ene*, 2.1 mmol of cyclohexanecarboxaldehyde was treated with 2.1 mmol of vinyl silane **15b** in the presence of 0.4 mmol of TMSOTf. Aqueous work-up and purification by flash column chromatography afforded the title compound in 87% yield as a colourless oil. IR (neat) ν_{max} = 2930, 2850, 1660,

1450, 1180, 1070 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 5.71-5.80 (1H, m), 5.60 (1H, ddd, J = 6.6, 1.2, 1.2 Hz), 3.82-3.86 (1H, m), 3.60 (1H, dq, J = 8.2, 4.1 Hz), 1.80-1.90 (2H, m), 1.35-1.78 (7H, m), 0.95-1.30 (4H, m), 1.15 (3H, d, J = 4.1 Hz). ^{13}C NMR ($CDCl_3$) : δ_C = 128.59, 125.12, 79.05, 69.81, 42.78, 33.17, 28.39, 28.33, 26.69, 26.46, 26.31, 21.77. MS (EI) *m/z* = 180 (39), 136 (3), 125 (8), 97 (100), 79 (11), 67 (10), 55 (13). HRMS : Calcd mass for $C_{12}H_{20}O$: 180.1514. Found : 180.1477.

Syn-2-(isopropyl)-6-methyl-oxacyclohex-3-ene (Table 1, Entry 8):- Following the general procedure described for *syn-2-(2-phenylethyl)-6-methyl-oxacyclohex-3-ene* , 2.2 mmol of isobutyraldehyde was treated with 2.2 mmol of vinyl silane **15b** in the presence of 0.4 mmol of TMSOTf. Aqueous work-up and purification by flash column chromatography afforded the title compound in 61% yield as a colourless oil. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 5.74-5.86 (1H, m), 5.61 (1H, ddd, J = 15.0, 3.0, 3.0 Hz), 3.86-3.96 (1H, m), 3.64 (1H, qdd, J = 6.8, 6.8, 6.8 Hz), 1.66-1.94 (3H, m), 1.18 (3H, d, J = 6.8 Hz), 0.82-0.91 (6H, m). ^{13}C NMR ($CDCl_3$) : δ_C = 127.99, 125.50, 79.38, 69.68, 33.05, 32.52, 21.70, 17.93, 17.62. MS (EI) *m/z* = 140 (M^+, 24), 129 (43), 97 (35), 83 (36), 71 (53), 55 (53), 43 (100).

Syn-2-(3-hydroxypropyl)-6-methyl-oxacyclohex-3-ene (Table 1, Entry 9):- Following the general procedure described for *Syn-2-(2-phenylethyl)-6-methyl-oxacyclohex-3-ene* , 4.4 mmol of 2-ethoxytetrahydrofuran was treated with 2.2 mmol of vinyl silane **15b** in the presence of 0.4 mmol of TMSOTf. Aqueous work-up (1M HCl) and purification by flash column chromatography afforded the title compound in 69% yield as a colourless oil. IR (neat) ν_{max} = 395, 2940, 1680, 1360, 1100, 1070 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 5.75-5.88 (1H, m), 5.59 (1H, ddd, J = 15.1, 2.7, 2.7 Hz), 4.12-4.26 (1H, m), 3.55-3.82 (3H, m), 3.10 (1H, br s), 1.92-2.20 (2H, m), 1.55-1.81 (4H, m), 1.24 (3H, d, J = 9.0 Hz). ^{13}C NMR ($CDCl_3$) : δ_C = 129.66, 125.00, 74.74, 70.22, 62.78, 32.75, 32.55, 28.71, 21.40. MS (EI) *m/z* = 156 (18), 155 (9), 138 (29), 112 (46), 97 (100), 79 (43), 55 (42).

Z-2-Trimethylsilyl-hex-2-en-5-ol :- To a cold (0°C) mixture of 0.5 g alkyne **14b** (1.0 eq., 3.21 mmol) in Et_2O (5 mL) was added 9.6 mL of a 1.0 M hexane solution of diisobutylaluminium hydride (3.0 eq., 9.62 mmol). The reaction mixture was heated at reflux for 24 hrs, cooled to 0°C and 6.9 mL of a 1.4 M Et_2O solution of MeLi (3.0 eq., 9.62 mmol) was added. After stirring at room temperature for 30 minutes, 2.27 g of methyl iodide (5 eq., 0.016 mol) was introduced and the mixture stirred for another 48 hrs. The cold (0°C) reaction mixture was poured onto 0.5 M aqueous HCl/ice (10 mL/10 g), filtered through celite®, washed with Et_2O (30 mL), and the aqueous phase extracted with Et_2O (3 x 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and the solvents removed *in vacuo* to leave a yellow oil. Distillation (bp 60 °C, 1.0 mm Hg) gave 0.35 g (63%) of the title compound as a colourless oil. IR (neat) ν_{max} = 3360, 2965, 2900, 1610, 1245, 840 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) : δ_H = 5.96 (1H, tq, J = 8.0, 1.6 Hz), 3.78-3.83 (1H, m), 2.23 (2H, dd, J = 8.0, 8.0 Hz), 1.77 (3H, d, J = 1.6 Hz), 1.54 (1H, br s), 1.18 (3H, d, J = 6.0 Hz), 0.10 (9H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 138.72, 137.69, 67.83, 41.38, 24.90, 22.81, -0.09. MS (EI) *m/z* =173 (2), 157 (28), 117 (23), 113 (71), 97 (29), 75 (49), 73 (74), 72 (100).

Z-2-Trimethylsilyl-5-trimethylsilyloxy-hex-2-ene **16** :- Following the procedure given for the preparation of **15b**, 1.95 mmol of *Z-2-Trimethylsilyl-hex-2-en-5-ol* was treated with 2.14 mmol of chlorotrimethylsilane and 2.34 mmol of triethylamine. Aqueous work-up and purification by distillation furnished the title compound **16** in 72% yield (bp 95°C, 3 mm Hg). IR (neat) ν_{max} = 2955, 2890, 1615, 1250, 995, 840 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) : δ_H = 5.93 (1H, tq, *J* = 6.0, 1.6 Hz), 3.74-3.77 (1H, m), 2.18-2.21 (2H, m), 1.73 (3H, d, *J* = 1.6 Hz), 1.11 (3H, d, *J* = 6.0 Hz), 0.07 (18H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 138.89, 136.27, 68.92, 41.63, 24.84, 23.62, 0.22, -0.09. MS (EI) *m/z* = 244 (8), 229 (9), 147 (13), 117 (100), 73 (24).

Syn-2-(2-phenylethyl)-3-methyl-6-methyl-oxacyclohex-3-ene **18** :- Following the general procedure described for *Syn-2-(2-phenylethyl)-6-methyl-oxacyclohex-3-ene* , 1.39 mmol of dihydrocinnamaldehyde was treated with 1.39 mmol of vinyl silane **16** in the presence of 0.28 mmol of TMSOTf. Aqueous work-up and purification by flash column chromatography afforded the title compound **18** in 81% yield as a colourless oil. IR (neat) ν_{max} = 3045, 2980, 2940, 1605, 1450, 1435, 1380, 1120 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) : δ_H = 7.10-7.32 (5H, m), 5.50-5.80 (1H, m), 4.05-4.15 (1H, m), 3.53-3.71 (1H, m), 2.63-2.80 (2H, m), 1.68-2.12 (4H, m), 1.60 (3H, s), 1.24 (3H, d, *J* = 6.0 Hz). ^{13}C NMR ($CDCl_3$) : δ_C = 142.77, 135.08, 128.48, 128.33, 128.17, 125.58, 125.50, 120.95, 76.57, 69.52, 34.67, 33.15, 30.52, 21.51, 18.90. MS (EI) *m/z* = 216 (100), 201 (25), 111 (84), 91 (46), 81 (21). HRMS : Calcd mass for $C_{15}H_{20}O$: 216.1514. Found : 216.1532.

1-Thiophenyl-2-epoxy-propane **19a** :- To a cold (0°C) suspension of sodium hydride (1.2 eq., 0.022 mol) in THF (30 mL) was added 2.0 g of thiophenol (1.0 eq., 0.018 mol). After stirring at 0°C for 20 minutes, 1.86 g of epichlorohydrin **19b** (1.1 eq., 0.02 mol) was added and the resulting mixture stirred at room temperature for 3 hrs before being poured onto saturated aqueous $NaHCO_3$ (30 mL). The aqueous phase was separated and extracted with Et_2O (3 x 15 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and the solvents removed *in vacuo* to leave a clear colourless oil. Purification by flash column chromatography (silica gel, hexane-EtOAc, 50:1) gave 2.02 g (67%) of the title compound **19a** as a colourless oil. IR (neat) ν_{max} = 3060, 2980, 1580, 1480, 1435, 1025, 740 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 7.42 (2H, d, *J* = 7.2 Hz), 7.19-7.32 (3H, m), 3.12-3.20 (2H, m), 2.93 (1H, dd, *J* = 15.3, 7.3 Hz), 2.76 (1H, ddd, *J* = 4.9, 3.7, 0.9 Hz), 2.51 (1H, dd, *J* = 4.9, 2.4 Hz). ^{13}C NMR ($CDCl_3$) : δ_C = 135.15, 130.21, 128.93, 126.67, 50.93, 47.33, 36.53. MS (EI) *m/z* = 166 (100), 135 (14), 123 (69), 109 (23), 91 (10), 65 (11), 45 (16).

1-Thiophenyl-5-trimethylsilyl-pent-4-yn-2-ol **20a** :- To a cold (-78°C) solution of 8.5 g ethynyltrimethylsilane (1.2 eq., 0.087 mol) in THF (120 mL) was added 35 mL of a 2.5 M hexane solution of n-BuLi (1.2 eq., 0.087 mol). The solution was stirred at this temperature for 30 minutes, then 12.0 g of epoxide **19a** (1.0 eq., 0.072 mol) was added followed by 10.7 mL of BF_3OEt_2 (1.2 eq., 0.087 mol) at such a rate as to maintain the internal temperature below -65°C. The resulting solution was stirred at -78°C for 1 hr, then poured onto saturated aqueous NH_4Cl (200 mL). The layers were separated and the aqueous phase extracted with Et_2O (3 x 50 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and the solvent removed *in*

vacuo to leave a brown oil which was distilled at reduced pressure (bp 136-138°C, 0.06 mm Hg) to give 17.3 g (91%) of the title compound **20a** as a clear colourless oil. IR (neat) ν_{max} = 3400, 2955, 2180, 1580, 1480, 1250, 1120, 845 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) : δ_H = 7.15-7.45 (5H, m), 3.74-3.92 (1H, m), 3.29 (1H, ABX, *J* = 13.9, 4.4 Hz), 2.98 (1H, ABX, *J* = 13.9, 7.9 Hz), 2.44-2.66 (3H, m), 0.15 (9H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 135.20, 129.42, 129.00, 126.39, 102.16, 87.92, 68.01, 39.90, 27.18, -0.02. MS (EI) *m/z* = 264 (48), 246 (9), 173 (43), 157 (37), 135 (100), 123 (75), 109 (60), 73 (91). HRMS : Calcd mass for $C_{14}H_{20}OSSi$: 264.1004. Found : 264.1013.

1-Thiophenyl-5-trimethylsilyl-2-(2-tetrahydropyranyloxy)-pent-4-yne :- A mixture of 2.0 g of alcohol **20a** (1.0 eq., 7.58 mmol), 0.76 g of dihydropyran (1.2 eq., 9.09 mmol) and 0.19 g of pyridinium *p*-toluenesulphonate (0.1 eq., 0.76 g) in CH_2Cl_2 (10 mL) were stirred at room temperature for 24 hrs. The solution was diluted with Et_2O (100 mL) and the white precipitate that formed was removed by filtration. The filtrate was evaporated *in vacuo* to leave a pale yellow oil which was purified by flash column chromatography (hexane-EtOAc-Et_3N, 20:1:1) to give 2.4 g (92% yield) of the title compound as a colourless oil. IR (neat) ν_{max} = 2950, 2160, 1575, 1440, 1250, 1025, 840 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 7.13-7.40 (10H, m), 4.81 (1H, t, *J* = 3.6 Hz), 4.67 (1H, t, *J* = 3.6 Hz), 3.90-4.05 (4H, m), 3.41-3.53 (2H, m), 3.37 (1H, ABX, *J* = 14.7, 4.2 Hz), 3.29 (1H, ABX, *J* = 14.7, 4.2 Hz), 2.44-2.66 (3H, m), 1.45-1.86 (12H, m), 0.17 (18H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 136.53, 128.79, 128.69, 128.49, 125.74, 125.62, 103.39, 103.32, 103.12, 99.13, 97.83, 86.86, 86.69, 74.94, 73.71, 62.35, 37.82, 37.31, 30.50, 30.44, 26.51, 25.31, 24.48, 19.29, -0.03. MS (EI) *m/z* = 349 (6), 246 (31), 173 (6), 123 (18), 109 (13), 85 (100).

E-1-Iodo-5-thiophenyl-1-trimethylsilyl-4-tetrahydropyranyloxy-pentene ***21a***:- To an ice cold solution of 1.34 g *1-thiophenyl-5-trimethylsilyl-2-(2-tetrahydropyranyloxy)-pent-4-yne* (1.0 eq., 3.85 mmol) in Et_2O (5 mL) was added 7.7 mL of a 1.0 M hexane solution of diisobutylaluminium hydride (2.0 eq., 7.7 mmol). The resulting mixture was treated with a solution of 2.1 g iodine (2.1 eq., 8.1 mmol) in Et_2O (5 mL) at such a rate as to maintain the internal temperature below -65°C. The black solution was allowed to reach 0°C over 3 hr, poured onto aqueous ammonia (25 mL) and stirred vigorously for 30 minutes. The slurry was filtered through a pad of celite®, washed with Et_2O (3 x 10 mL), the phases separated and the aqueous layer extracted with Et_2O (3 x 10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and the solvent removed *in vacuo* to give a yellow oil. Purification by flash column chromatography (silica gel, hexane-EtOAc-Et_3N, 30:1:1) yielded 1.49 g (81%) of the title compound **21a** as a colourless oil. IR (neat) ν_{max} = 2945, 1595, 1440, 1245, 1025, 845 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 7.10-7.40 (12H, m), 4.73 (1H, t, *J* = 3.3 Hz), 4.62 (1H, t, *J* = 3.3 Hz), 3.73-4.0 (4H, m), 3.42-3.55 (3H, m), 3.39 (1H, ABX, *J* = 13.7, 3.8 Hz), 2.96-3.10 (2H, m), 2.94 (1H, ABX, *J* = 13.7, 8.4 Hz), 2.30-2.55 (4H, m), 1.44-1.80 (12H, m), 0.27 (18H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 152.04, 151.51, 136.22, 128.95, 128.86, 128.33, 126.03, 125.67, 109.58, 109.42, 99.25, 97.53, 75.53, 74.01, 62.84, 62.19, 39.82, 38.38, 37.59, 37.29, 30.74, 30.48, 25.28, 25.13, 19.65, 19.19, 1.09. MS (EI) *m/z* = 402 (9), 300 (25), 226 (21), 185 (15), 173 (23), 85 (100).

Z-1-Thiophenyl-5-trimethylsilyl-hex-4-en-2-ol :- To a cold (-78°C) solution of 1.47 g of iodide **21a** (1.0 eq., 3.09 mmol) in THF was added 2.9 mL of a 1.6 M Et_2O solution of MeLi (1.5 eq., 4.63 mmol). The resulting mixture was allowed to reach room temperature and was stirred for another 20 hrs before being poured onto aqueous ammonia (20 mL). The aqueous layer was extracted with Et_2O (3 x 15 mL) and the combined organic layers were concentrated *in vacuo* to give a brown oil which was taken up in EtOH-H_2O (9:1, 10 mL). This solution was treated with 0.08 g of pyridinium *p*-toluenesulphonate (0.1 eq., 0.31 mmol) and heated at 65°C for 12 hrs. The cold (0°C) reaction mixture was poured onto saturated aqueous $NaHCO_3$ (20 mL), the aqueous phase separated and extracted with Et_2O (3 x 15 mL). The combined organic layers were dried over anhydrous $MgSO_4$ and the solvents removed *in vacuo* to leave a brown oil which was purified by flash column chromatography (silica gel, hexane-EtOAc, 20:1) to afford 0.49 g (57%) of the title compound as a colourless oil (bp 125 °C, 3 x 10^{-4} mm Hg). IR (neat) ν_{max} = 3420, 2955, 1615, 1575, 1435, 1245, 840 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 7.05-7.28 (5H, m), 5.85 (1H, tq, *J* = 7.4, 1.7 Hz), 3.55-3.65 (1H, m), 3.03 (1H, ABX, *J* = 13.7, 3.8 Hz), 2.76 (1H, ABX, *J* = 13.7, 8.4 Hz), 2.21-2.30 (3H, m), 1.66 (3H, s), 0.00 (9H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 138.88, 136.64, 135.27, 129.70, 128.96, 126.40, 69.48, 41.22, 38.11, 24.89, -0.17. MS (EI) *m/z* = 280 (16), 262 (100), 153 (38), 135 (77), 123 (39), 109 (17), 73 (17). HRMS : Calcd mass for $C_{16}H_{24}OSSi$: 281.1395. Found : 281.1332.

Z-1-Thiophenyl-5-trimethylsilyl-2-trimethylsilyloxy-hex-4-ene **22a** :- Following the procedure described for the preparation of *Z-1-trimethylsilyl-4-trimethylsilyloxy-pentene* **15b**, 1.75 mmol of *Z-1-thiophenyl-5-trimethylsilyl-hex-4-en-2-ol* was treated with 2.10 mmol of chlorotrimethylsilane and 2.28 mmol of triethylamine. Aqueous work-up and purification by distillation furnished the title compound **22a** in 91% yield (bp 150°C, 0.05 mm Hg). IR (neat) ν_{max} = 2975, 2905, 1630, 1590, 1255, 1090, 840 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 7.13-7.37 (5H, m), 5.96 (1H, t, *J* = 6.4 Hz), 3.77-3.88 (1H, m), 3.00 (2H, d, *J* = 5.8 Hz), 2.42-2.53 (1H, m), 2.24-2.38 (1H, m), 1.78 (3H, s), 0.14 (9H, s), 0.10 (9H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 137.87, 137.23, 137.11, 128.79, 125.67, 71.87, 40.65, 38.83, 24.86, 0.33, -0.14. MS (EI) *m/z* = 352 (5), 337 (3), 262 (52), 225 (66), 147 (24), 135 (84), 73 (100).

Syn-2-methylthiophenyl-5-methyl-6-ethyl-oxacyclohex-4-ene **3a** :- Following the general procedure described for *Syn-2-(2-phenylethyl)-6-methyl-oxacyclohex-3-ene*, 0.88 mmol of propionaldehyde was treated with 0.88 mmol of vinyl silane **22a** in the presence of 0.18 mmol of TMSOTf. Aqueous work-up and purification by flash column chromatography afforded the title compound **3a** in 83% yield as a colourless oil. IR (neat) ν_{max} = 2950, 2895, 1625, 1255, 1100, 840 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 7.12-7.39 (5H, m), 5.50-5.55 (1H, m), 4.02-4.08 (1H, m), 3.61-3.69 (1H, m), 3.18 (1H, ABX, *J* = 13.2, 6.4 Hz), 2.96 (1H, ABX, *J* = 13.2, 6.2 Hz), 1.92-2.15 (2H, m), 1.68-1.80 (1H, m), 1.58 (3H, s), 1.43-1.58 (1H, m), 0.89 (3H, t, *J* = 7.3 Hz). ^{13}C NMR ($CDCl_3$) : δ_C = 137.05, 135.45, 128.96, 128.70, 125.67, 120.08, 78.41, 72.43, 39.00, 30.72, 25.51, 18.82, 8.39. MS (EI) *m/z* = 248 (85), 162 (27), 125 (43), 124 (100), 109 (43), 81 (36), 57 (36).HRMS : Calcd mass for $C_{15}H_{20}OS$: 248.1235. Found : 248.1211.

1-Chloro-5-trimethylsilyl-pent-4-yn-2-ol **20b** :- Following the procedure described for the preparation of *1-thiophenyl-5-trimethylsilyl-pent-4-yn-2-ol* **20a**, 0.085 mol of the lithium anion of ethynyltrimethylsilane was treated with 0.077 mol of epichlorohydrin in the presence of 0.085 mol of $BF_3.OEt_2$. Aqueous work-up and purification by flash column chromatography afforded the title compound **20b** in 68% yield as a colourless oil. IR (neat) ν_{max} = 3400, 2955, 2870, 2170, 1430, 1250, 1035, 845 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 3.93-4.03 (1H, m), 3.72 (1H, ABX_1, J = 11.1, 4.5 Hz), 3.63 (1H, ABX_1, J = 11.1, 6.1 Hz), 2.62 (1H, ABX_2, J = 17.0, 5.8 Hz), 2.55 (1H, ABX_2, J = 17.0, 6.6 Hz), 2.44 (1H, d, J = 5.9 Hz), 0.16 (9H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 101.15, 88.24, 69.55, 48.23, 25.69, -0.08. MS (EI) *m/z* = 191 (4), 175 (5), 151 (20), 112 (38), 95 (38), 93 (71), 73 (100). HRMS : Calcd mass for $C_7H_{12}ClOSi$ (M-CH_3): 175.0346. Found : 175.0370. Anal. calcd for $C_8H_{15}ClOSi$: C, 50.38; H, 7.93. Found : C, 50.04; H, 7.81.

1-Chloro-5-trimethylsilyl-2-(2-tetrahydropyranyloxy)-pent-4-yne :- Following the procedure described for the preparation of *1-thiophenyl-5-trimethylsilyl-2-(2-tetrahydropyranyloxy)-pent-4-yne*, 0.033 mmol of alcohol **20b** was treated with 0.050 mmol of dihydropyran in the presence of 3.32 mmol of pyridinium *p*-toluenesulphonate. Aqueous work-up and purification by distillation furnished the title compound (1:1 mixture of diastereomers) in 97% yield as a colourless oil (bp 150 °C, 1.5 mm Hg). IR (neat) ν_{max} = 2950, 2170, 1255, 1035, 845 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 4.76-4.83 (1H, m), 3.89-4.03 (2H, m), 3.45-3.78 (3H, m), 2.45-2.72 (2H, m), 1.47-1.85 (6H, m), 0.14 (9H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 102.40, 102.36, 98.48, 98.07, 86.95, 74.74, 74.39, 62.49, 62.27, 46.45, 45.35, 30.48, 30.36, 25.25, 24.71, 23.27, 19.27, 19.06, -0.11. MS (EI) *m/z* = 275 (100), 263 (28), 191 (25), 171 (26), 139 (20), 91 (47). Anal. calcd for $C_{13}H_{23}ClO_2Si$: C, 56.81; H, 8.43. Found : C, 56.80; H, 8.51.

E-1-Iodo-5-chloro-1-trimethylsilyl-4-(2-tetrahydropyranyloxy)-pentene **21b** :- Following the procedure described for the preparation of **21a**, 0.032 mmol of *1-chloro-5-trimethylsilyl-2-(2-tetrahydropyranyloxy)-pent-4-yne* was treated with 0.064 mmol of diisobutylaluminium hydride, followed by 0.067 mol of iodine. Aqueous work-up and purification by flash column chromatography furnished the title compound **21b** (1:1 mixture of diastereomers) in 65% yield as a colourless oil. IR (neat) ν_{max} = 2945, 1590, 1255, 1125, 1035, 845 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$) : δ_H = 7.21 (1H, t, J = 7.6 Hz), 7.13 (1H, t, J = 7.6 Hz), 4.75 (1H, t, J = 3.6 Hz), 4.64 (1H, t, J = 3.6 Hz), 3.40-3.95 (10H, m), 2.30-2.55 (4H, m), 1.43-1.85 (12H, m), 0.25 (18H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 152.29, 150.82, 110.24, 110.03, 99.54, 97.34, 97.32, 76.41, 74.15, 62.87, 62.29, 46.45, 45.22, 38.31, 37.23, 30.77, 30.50, 25.37, 25.29, 19.56, 19.13, 1.10. MS (EI) *m/z* = 402 (4), 311 (25), 300 (12), 185 (9), 173 (13), 85 (100). Anal. calcd for $C_{13}H_{24}ClIO_2Si$: C, 30.15; H, 5.06. Found : C, 30.41; H, 4.92.

Z-1-Chloro-5-trimethylsilyl-hex-4-en-2-ol :- Following the procedure described for the preparation of *Z-1-thiophenyl-5-trimethylsilyl-hex-4-en-2-ol*, 0.021 mol of vinyl iodide **21b** was treated with 0.031 mol of MeLi, followed by THP deprotection with 2.06 mmol of pyridinium *p*-toluenesulphonate. Aqueous work-up and purification by flash column chromatography furnished the title compound in 34% yield as a colourless oil. IR (neat) ν_{max} = 3380, 2945, 2880,

1615, 1255, 1060, 840 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 5.93 (1H, tq, *J* = 7.5, 1.6 Hz), 3.77-3.87 (1H, m), 3.62 (1H, ABX, *J* = 11.1, 3.6 Hz), 3.48 (1H, ABX, *J* = 11.1, 6.8 Hz), 2.28-2.45 (2H, m), 2.18 (1H, d, *J* = 4.6 Hz), 1.77 (3H, s), 0.12 (9H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 139.39, 135.78, 71.36, 49.54, 36.40, 24.85, -0.26. MS (EI) *m/z* = 206 (3), 191 (42), 95 (52), 93 (63), 81 (64), 75 (70), 73 (100). HRMS : Calcd mass for $C_9H_{19}ClOSi$: 206.0894. Found : 206.0891.

Z-1-Chloro-5-trimethylsilyl-2-trimethylsilyloxy-hex-4-ene **22b** :- Following the procedure for the preparation of **22a**, 7.05 mmol of alcohol *Z-1-chloro-5-trimethylsilyl-hex-4-en-2-ol* was treated with 8.46 mmol of chlorotrimethylsilane and 9.17 mmol of triethylamine. Aqueous work-up and purification by distillation furnished the title compound **22b** in 94% yield (bp 125°C, 0.1 mm Hg). IR (neat) ν_{max} = 2970, 2940, 2845, 1595, 1480, 1440, 1120, 1055, 735 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 5.92 (1H, tq, *J* = 7.4, 1.5 Hz), 3.76-3.84 (1H, m), 3.43 (1H, ABX, *J* = 11.0, 5.3 Hz), 3.40 (1H, ABX, *J* = 11.0, 6.1 Hz), 2.35-2.46 (1H, m), 2.19-2.31 (1H, m), 1.77 (3H, q, *J* = 1.5 Hz), 0.13 (18H, s). ^{13}C NMR ($CDCl_3$) : δ_C = 137.13, 73.00, 48.66, 37.35, 24.83, 0.31, -0.14. MS (EI) *m/z* = 278 (3), 229 (6), 153 (43), 151 (100), 81 (9), 73 (68).

Syn-2-chloromethyl-5-methyl-6-ethyl-oxacyclohex-3-ene **3b** :- Following the general procedure described for *Syn-2-(2-phenylethyl)-6-methyl-oxacyclohex-3-ene* , 5.91 mmol of propionaldehyde was treated with 5.91 mmol of vinyl silane **22b** in the presence of 1.18 mmol of TMSOTf. Aqueous work-up and purification by distillation afforded the title compound **3b** in 81 % yield as a colourless oil (bp 150 °C at 15 mm Hg). IR (neat) ν_{max} = 2970, 2940, 1680, 1435, 1105, 1050 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 5.52-5.57 (1H, m), 4.08-4.13 (1H, m), 3.65-3.78 (1H, m), 3.58 (1H, ABX, *J* = 11.0, 6.0 Hz), 3.49 (1H, ABX, *J* =11.0, 5.4 Hz), 2.01-2.05 (2H, m), 1.70-1.85 (1H, m), 1.60 (3H, s), 1.45-1.60 (1H, m), 0.89 (3H, t, *J* = 7.3 Hz). ^{13}C NMR ($CDCl_3$) : δ_C = 135.36, 119.63, 78.35, 73.18, 47.00, 28.95, 25.46, 18.80, 8.21. MS (EI) *m/z* = 174 (80), 159 (53), 145 (100), 97 (34), 81 (57), 57 (47). HRMS : Calcd mass for $C_9H_{15}ClO$: 174.0811. Found : 174.0792.

Syn-2-methylphenylsulphonyl-5-methyl-6-ethyl-oxacyclohex-4-ene **3a** (X = SO_2Ph):- To a cold (-78°C) solution of 0.177 g of sulphide **3a** (1.0 eq., 0.714 mmol) in CH_2Cl_2 (5 mL) was added a solution of mCPBA (2.0 eq., 1.43 mmol) in CH_2Cl_2 (5mL). The reaction mixture was allowed to warm to 0°C over 90 minutes and was stirred at this temperature for a further 90 minutes before being poured onto saturated aqueous $NaHCO_3$ (30 mL). The aqueous phase was separated and extracted with CH_2Cl_2 (3 x 15 mL). The combined organic extracts were dried over anhydrous K_2CO_3 and the solvent removed *in vacuo* to leave a colourless oil. Purification by flash column chromatography gave 74 mg (37%) of the title compound **3a** (X = SO_2Ph) as a white solid (mp 96-97°C). IR (neat) ν_{max} = 2980, 2925, 1580, 1445, 1280, 1145, 745 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) : δ_H = 7.90-7.95 (2H, m), 7.51-7.67 (3H, m), 5.46-5.50 (1H, m), 3.95-4.04 (1H, m), 3.78-3.85 (1H, m), 3.46 (1H, ABX, *J* = 14.6, 8.0 Hz), 3.21 (1H, ABX, *J* = 14.6, 3.5 Hz), 1.97-2.04 (2H, m), 1.53 (3H, m), 1.20-1.46 (2H, m), 0.56 (3H, t, *J* = 7.3 Hz). ^{13}C NMR ($CDCl_3$) : δ_C = 140.28, 135.41, 133.32, 128.87, 128.00, 119.36, 78.08, 68.27, 61.63, 30.82, 25.20, 18.74, 8.16. MS (EI) *m/z* = 280 (100), 251 (23), 139 (82), 125 (39), 121 (35), 109 (96), 95 (25), 81 (64), 77 (47). Anal. Calcd for $C_{15}H_{20}O_3S$: C, 64.26; H, 7.19. Found : C, 63.83; H, 7.60.

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