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A Free Radical Approach to Cyclopentanone and Spirocyclic Systems: Development of a 1,5 Allylic Abstraction-Cyclisation Sequence

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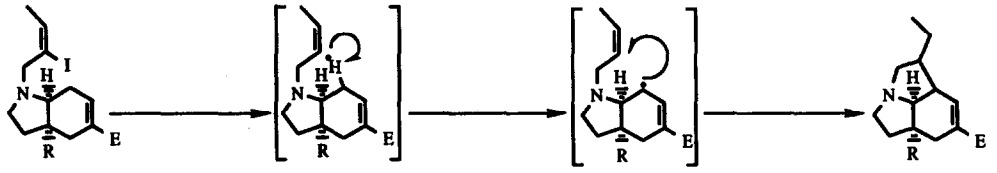
Abstract: A novel free radical approach to cyclopentanone and spirocyclic ring systems is described. This work illustrates the potential of the 1, 5 allylic abstraction-cyclisation reaction and demonstrates the application of the sequence to systems in which alternative radical cyclisation pathways can be envisaged.

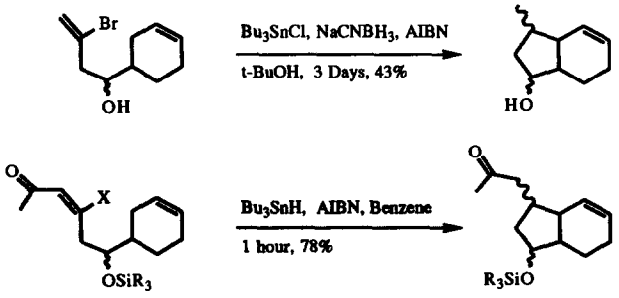
Organic chemists have witnessed a quite unprecedented increase in the use of free radicals for the construction of carbon-carbon bonds in recent years[1]. As part of our investigations into the development of new synthetic methodology based around novel free radical reactions we have developed a 1,5 allylic abstraction-cyclisation[2] approach which has been used in the construction of heterocyclic systems (scheme 1).



Reagents: Bu_3SnH, AIBN, Benzene, Δ (60-85%)

Scheme 1

We have also recently demonstrated that this strategy can be successfully employed in the construction of fused carbocyclic ring systems[3] and that the efficiency of the abstraction-cyclisation pathway can be enhanced by using carefully designed precursors (scheme 2).

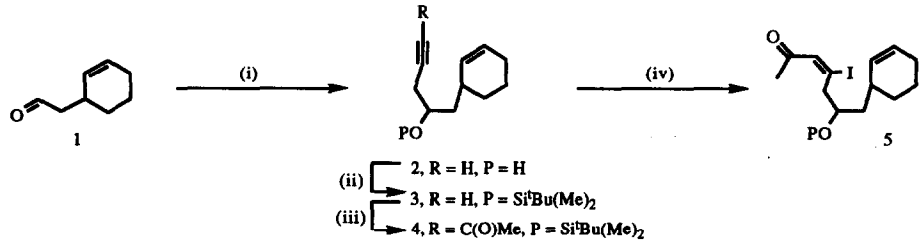


Scheme 2

In this current paper we further detail the scope of this process; we have found that the sequence can be successfully employed for the synthesis of functionalised spirocyclic and monocyclic systems. This report should serve to illustrate the considerable potential that this method has for synthetic purposes.

Results and Discussion

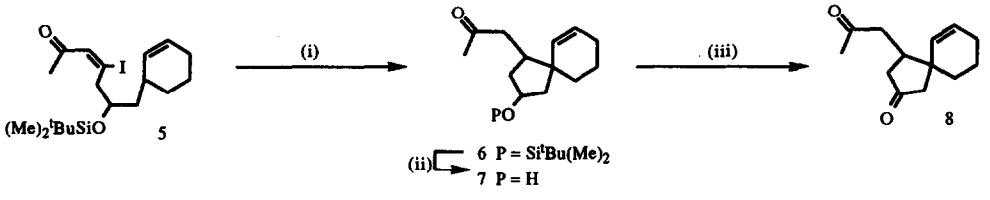
We wanted to investigate how the rearrangement sequence would compete with a 6-*exo*-trig cyclisation. The preparation of **5** from **1**[4] is shown in scheme 3; the alkenyl radical generated from **5** could undergo either rearrangement or 6-*exo*-trig cyclisation. We expected to observe some products resulting from the competing 6-*exo*-trig cyclisation thus the experiment would give some indication of the relative rates of rearrangement versus 6-*exo*-trig cyclisation.



Reagents; (i) Propargylmagnesium bromide, Et_2O, r.t., 64%; (ii) TBSOTf, 2,6-lutidine, 0 °C, 88%; (iii) n-BuLi, THF, $(CH_3CO)_2$ 0 -78°C to r.t., C, 38%; (iv) TMSI, CH_2Cl_2, - 78 °C 63% (ref 5).

Scheme 3

Initial experiments in which **5** (ca 0.1 mmoles) was treated with tri-*n*-butyltin hydride led us to isolate an inseparable mixture of the desired product **6** along with other unidentified products. We were delighted to find, however, that when the reaction was carried out on a larger scale (ca. 1 mmole) the only product isolated was the desired spirocyclic material **6** in 45% yield as a chromatographically inseparable mixture of four diastereoisomers. Deprotection and oxidation of **6** led us to isolate **8** as a chromatographically inseparable mixture of two diastereoisomers (scheme 4).

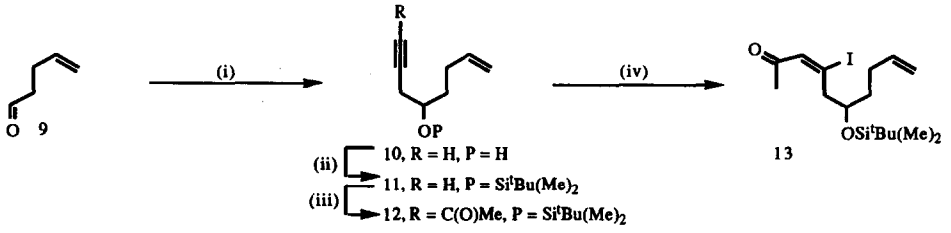


Reagents; (i) Bu_3SnH, AIBN, Benzene, Δ, 1 hr., 45%; (ii) HF, MeCN, H_2O, r.t., 97%; (iii) PDC, CH_2Cl_2, r.t., 62%;

Scheme 4

The successful isolation of the desired product **6** from this reaction demonstrated that allylic abstraction would successfully compete with a 6-*exo*-trig cyclisation and that it could be used to synthesise

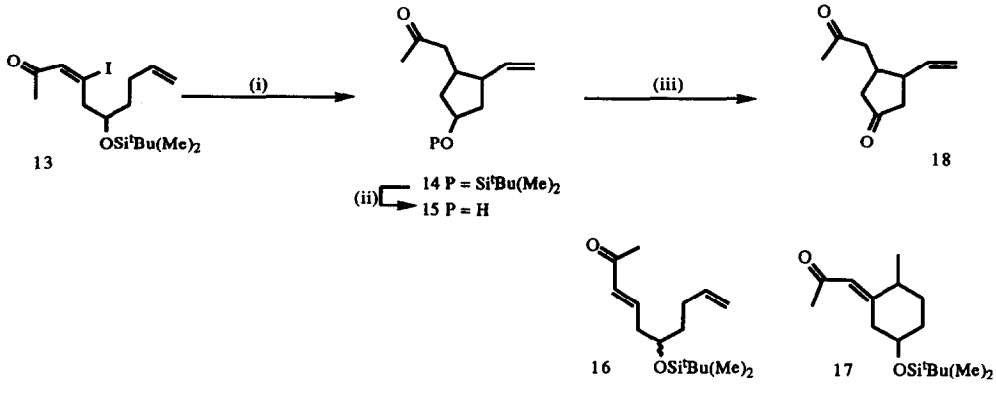
functionalised spirocyclic systems which may be of use in target synthesis. We were interested in designing an experiment which would allow the direct comparison of the rearrangement with a 6-*exo*-trig cyclisation in an acyclic system[6]. Thus precursor **13** was synthesised from **9** [7] in an unoptimised sequence analogous to that used for previous precursors (scheme 5).



Reagents; (i) Propargylmagnesium bromide, Et_2O, r.t., 53%; (ii) TBSCl, DMAP, Imidazole, DMF, 60 °C, 77%; (iii) n-BuLi, THF, CH_3COCl,-78°C to r.t., , 19%; (iv) TMSI, CH_2Cl_2, - 78 °C 65%;

Scheme 5

Treatment of precursor **13** with tri-*n*-butyltin hydride led us to isolate the desired cyclopentane **14** as the major product 46% yield[8] as an inseparable mixture of four diastereoisomers, two additional minor products **16** and **17** resulted from direct reduction or 6-*exo*-trig cyclisation. Deprotection and oxidation of **14** led us to isolate the 3, 4-disubstituted cyclopentanone **18** as an inseparable mixture of two diastereoisomers in reasonable yield (scheme 6).



Reagents; (i) Bu_3SnH, AIBN, Benzene, Δ, 1 hr., 46%; (ii) HF, MeCN, H_2O, r.t., 77%; (iii) PDC, CH_2Cl_2, r.t., 56%;

Scheme 6

The results presented here show that this sequence is viable for the production of spirocyclic and cyclopentane precursors. Whilst we have gained some insight into the relative rates of abstraction versus 6-*exo*-trig cyclisation[6] further investigations are required to probe the nature of the slow step in the sequence i.e abstraction or cyclisation.

Conclusions

We have shown that the 1,5 allylic abstraction-cyclisation sequence is a useful new cyclisation procedure and allows the synthesis of a variety of functionalised intermediates which should be useful in synthesis. With improved routes to the desired precursors and optimisation of individual cyclisations, using either slow addition techniques or more efficient radical reagents, this method should represent a useful synthetic tool for the synthesis of cyclopentanoid structures. Further studies are in progress and will be reported in due course.

Experimental

^1H NMR spectra were recorded in $CDCl_3$ (unless otherwise stated) using a Jeol GSX 270 or a Bruker AM-360 nmr spectrometer. ^{13}C NMR spectra were recorded in $CDCl_3$ (unless otherwise stated) at 67.5 MHz on a Jeol GSX 270 or at 90.1 MHz on a Bruker AM-360 spectrometer. Where appropriate tetramethylsilane was used as a standard. Infra-red spectra were recorded on a Perkin-Elmer 298 spectrometer. Mass spectra were recorded, using either a VG Micromass ZAB-E or a VG Analytical 70-250 instruments. Unless otherwise stated all reactions were carried out under an atmosphere of nitrogen using flame dried or oven dried apparatus. Column chromatography was carried out using Merck Kieselgel 9385 (230-400 mesh). Diethyl ether and tetrahydrofuran solvents were distilled from sodium-benzophenone ketyl; dichloromethane, acetonitrile, benzene, dimethylformamide, toluene and triethylamine from calcium hydride. Petrol refers to petroleum ether b.p. 40-60°C which was distilled prior to use. Other solvents and reagents were purified by standard procedures as necessary. Analytical thin layer chromatography was performed using pre-coated glass-backed plates (Merck Kieselgel 60 F_{254}) and visualised by ultra-violet light, vanillin, potassium permanganate or iodine as appropriate. Coupling constants are measured in Hertz.

[[(1-[Methyl-(2-cyclohexenyl)]]]-3-butynyloxy](1,1-dimethylethyl)dimethylsilane) **3**.- Propargyl bromide (6.7ml, 89 mmoles) was added to a stirred solution of magnesium turnings (2.15g, 89.6 mmoles) and mercuric chloride (10mg, 0.037 mmoles) in ether (200ml) at a rate which maintained a steady reflux. After the addition was complete the reaction mixture was stirred at room temperature for one hour. 2-(2-Cyclohexenyl)-acetaldehyde **1** (3.72g, 30 mmoles) was added dropwise to the reaction mixture which was then allowed to stir at room temperature overnight. The mixture was poured into saturated ammonium chloride solution (100ml) and the organic layer separated. The aqueous layer was extracted with ether (3 x 50ml) and the organic layers were combined, washed with saturated sodium bicarbonate solution (3 x 50ml), water (3 x 50ml) and dried over magnesium sulphate. Filtration and removal of the solvent *in vacuo* gave the crude product. Purification was carried out by distillation (100°C, 0.3mm Hg) to give *the eneynol* **2** (3.16g, 64%) as an inseparable mixture of diastereoisomers. *The eneynol* **2** (3.05g, 18.6 mmoles) was added dropwise to a stirred solution of t-butyldimethylsilyl trifluoromethanesulphonate (8.5ml, 36.3 mmoles) in 2,6-lutidine (6.5ml, 55.2 mmoles) at 0°C. After the addition was complete the reaction mixture was allowed to warm to room temperature and the mixture was poured into dilute hydrochloric acid solution (30ml, 5%). The aqueous layer was extracted with ether (3 x 50ml) and the organic layers were washed with saturated sodium bicarbonate solution (6 x 30ml), water (3 x 50ml) and dried over magnesium sulphate. Filtration and removal of the solvent *in vacuo* gave the crude product. Purification was carried out by chromatography using petrol : ether (100 : 1 then 60 : 1) as eluant to give *the silane* **3** (4.56g, 88%) as an inseparable mixture of diastereoisomers.

ν_{max} (CH_2Cl_2) 3300, 2920, 2115 and 1645 cm^{-1}; δ_H (270 MHz) 5.6 (2H, m, C<u>H</u>), 3.95 (1H, m, C<u>H</u>OSi), 2.3 (2H, m, C<u>H</u>$_2$), 2.0 (4H, s), 1.4-1.9 (5H), 1.2 (1H, m), 0.9 (9H, m, t-<u>Bu</u>Si), 0.1 (6H, m, <u>Me</u>$_2$Si); δ_C (67.5 MHz); 132.6 (<u>C</u>H) , 131.2 (<u>C</u>H), 127.2 (<u>C</u>H), 127.0 (<u>C</u>H), 81.6 (C<u>C</u>H), 70.25 (<u>C</u>CH), 70.2 (<u>C</u>CH), 68.8 (<u>C</u>HOSi), 66.8 (<u>C</u>HOSi), 43.8 (<u>C</u>H$_2$CCH), 43.4 (<u>C</u>H$_2$CCH), 31.4 (<u>C</u>H), 30.1 (<u>C</u>H$_2$), 28.7 (<u>C</u>H$_2$), 28.2 (<u>C</u>H$_2$), 27.95, 26.1 (<u>C</u>H$_3$), 26.0 (<u>C</u>H$_3$), 25.8 (<u>C</u>H$_3$), 25.5 (<u>C</u>H$_2$), 25.45 (<u>C</u>H$_2$), 21.6 (<u>C</u>H$_2$), 21.23 (<u>C</u>H$_2$), 18.2 (<u>C</u>H$_3$), 4.1 (<u>C</u>H$_3$), -4.5 (<u>C</u>H$_3$), -4.6 (<u>C</u>H$_3$); HRMS found 278.2075 C_{17} H_{30}OSi requires $[M]^+$, 278.2066

7-(2-Cyclohexenyl)-6-[((1,1-dimethylethyl)dimethylsilyl)oxy]-3-heptyn-2-one 4. n-Butyllithium (12ml, 19.2 mmoles) was added to a stirred cold solution (-78°C) of *the silane* **3** (3.82g, 13.7 mmoles) in THF (60ml) and stirred for five minutes. Acetic anhydride (5ml, 52.5mmoles) was added to the reaction mixture which was then allowed to warm to room temperature. The mixture was then poured into dilute hydrochloric acid solution (50ml, 2%) and extracted with ether. The organic layers were combined and washed with saturated sodium bicarbonate solution (8 x 50ml), water (3 x 50ml) and dried over sodium sulphate. Filtration and removal of the solvent *in vacuo* gave the crude product. Purification was carried out by chromatography using petrol : ether (50 : 1) as eluant to give *the silane* **3** (1.65g, 43%) and *the yneone* **4** (1.66g, 38%) both as inseparable mixtures of diastereoisomers. ν_{max} (CH_2Cl_2) 3005, 2920, 2200, 1670 and 1630 cm^{-1}; δ_H (360 MHz) 5.5 (2H, m, C<u>H</u>), 4.0 (1H, m, C<u>H</u>OSi), 2.5 (2H, m, CC<u>C</u>H$_2$), 2.35 (3H, m, C<u>H</u>$_3$CO), 2.2 (1H, m), 2.0 (2H, m), 1.65 (2H, m), 1.45 (3H, m), 1.25 (1H, m) 0.9 (9H, m, C<u>H</u>$_3$), 0.1 (6H, m, C<u>H</u>$_3$); δ_C (67.5 MHz); 169.0 (<u>C</u>O), 132 (<u>C</u>H), 130.9 (<u>C</u>H), 127.5 (<u>C</u>H), 127.3 (<u>C</u>H), 91.0 (COC<u>C</u>), 83.0 (CO<u>C</u>C), 82.5 (CO<u>C</u>C), 68.2 (<u>C</u>HOSi), 68.1 (<u>C</u>HOSi), 44.1 (CC<u>C</u>H$_2$), 43.8 (CC<u>C</u>H$_2$), 32.8 (<u>C</u>H$_3$CO), 31.4 (<u>C</u>H$_3$CO), 28.5 (<u>C</u>H$_2$), 28.3 (<u>C</u>H$_2$), 28.1 (<u>C</u>H$_2$), 26.5 (<u>C</u>H$_2$), 25.9 (<u>C</u>H$_3$), 25.8 (<u>C</u>H$_3$), 25.3 (<u>C</u>H$_2$), 22.8 (<u>C</u>H$_2$), 21.4 (<u>C</u>H$_2$), 21.1 (<u>C</u>H$_2$), 18.1 (<u>C</u>H$_3$), -4.3 (<u>C</u>H$_3$), -4.5 (<u>C</u>H$_3$), -4.6 (<u>C</u>H$_3$); HRMS found 320.2179 C_{19} $H_{32}O_2Si$ requires $[M]^+$, 320.2171.

(E)-7-(2-Cyclohexenyl)-6-[[(1,1-dimethylethyl)dimethylsilyl]oxy]]-4-iodo-3-hepten-2-one 5a and (Z)-7-(2-Cyclohexenyl)-6-[[(1,1-dimethylethyl)dimethylsilyl]oxy]]-4-iodo-3-hepten-2-one 5b. Iodotrimethylsilane (0.4ml, 2.38 mmoles) was added dropwise to a stirred cold solution (-78°C) of *the yneone* **4** (760mg, 2.375 mmoles) in dichloromethane (10ml) and stirred for ten minutes at -78°C. Water (10ml) was added and the reaction was allowed to warm to room temperature. The aqueous layer was extracted with dichloromethane (3 x 10ml) and the organic layers were combined and washed with saturated sodium bicarbonate solution (2 x 10ml), saturated sodium thiosulphate solution (2 x 10ml), brine (2 x 20ml) and dried over sodium sulphate. Filtration and removal of the solvent *in vacuo* gave the crude product. Purification was carried out by chromatography using petrol : ether (100 : 1, 80 : 1 then 50 : 1) as eluant to give *the iodide* **5a** (342mg, 32%) and *the iodide* **5b** (328mg, 31%) both as inseparable mixtures of diastereoisomers.

E-Isomer 5a ν_{max} (CH_2Cl_2) 3005, 2920, 1695 and 1585 cm^{-1}; δ_H (270 MHz) 7.1 (1H, s, C(O)C<u>H</u>), 5.6 (2H, m, C<u>H</u>), 4.1 (1H, m, C<u>H</u>OSi), 3.3 (2H, m, C(I)C<u>H</u>$_2$), 2.2 (3H, s, C<u>H</u>$_3$CO), 1.9 (2H, s), 1.7 (2H, m), 1.2-1.6 (5H) 0.9 (9H, s, C<u>H</u>$_3$), 0.1 (6H, m, C<u>H</u>$_3$); δ_C (67.5 MHz); 195.3 (<u>C</u>O), 140.6 (CO<u>C</u>H), 140.5(CO<u>C</u>H), 132.3 (<u>C</u>H), 131.5 (<u>C</u>H), 127.1 (<u>C</u>H), 125.7 (<u>C</u>I), 125.2 (<u>C</u>I), 70.9 (<u>C</u>HOSi), 48.6 (C(I)<u>C</u>H$_2$), 48.5 (C(I)<u>C</u>H$_2$), 43.8 (<u>C</u>H$_2$), 43.2 (<u>C</u>H$_2$), 31.6 (<u>C</u>H$_3$CO), 31.4 (<u>C</u>H$_3$CO), 31.3 (<u>C</u>H), 29.8

($\underline{C}H_2$), 28.8 ($\underline{C}H_2$), 26.1 ($\underline{C}H_3$), 26 ($\underline{C}H_3$), 25.4 ($\underline{C}H_2$), 21.6 ($\underline{C}H_2$), 21.2 ($\underline{C}H_2$), 18.1 ($\underline{C}H_3$), -3.9 ($\underline{C}H_3$), 4.2 ($\underline{C}H_3$), -4.3 ($\underline{C}H_3$); **Z-Isomer 5b** ν_{max} (CH_2Cl_2) 3020, 2920, 1695 and 1590 cm^{-1}; δ_H (270 MHz) 6.7 (1H, s, COC$\underline{H}$), 5.5 (2H, m, C$\underline{H}$), 4.2 (1H, m, C$\underline{H}$OSi), 2.8 (2H, d, J 5.8, ClC$\underline{H}_2$), 2.2 (3H, s, C$\underline{H}_3$CO), 1.9 (2H, s), 1.65 (2H, m), 1.2-1.6 (5H), 0.9 (9H, s, C$\underline{H}_3$), 0.1 (6H, m, C$\underline{H}_3$); δ_C (67.5 MHz); 195.3 ($\underline{C}O$), 133.4 (CO$\underline{C}H$), 133.2 (CO$\underline{C}H$), 131.7 ($\underline{C}H$), 131.4 ($\underline{C}H$), 127.5 ($\underline{C}H$), 127.4 ($\underline{C}H$), 114 ($\underline{C}I$), 113.6 ($\underline{C}I$), 69 ($\underline{C}HOSi$), 68.9 ($\underline{C}HOSi$), 55.9 (C(I)$\underline{C}H_2$), 55.6 (C(I)$\underline{C}H_2$), 43.9 ($\underline{C}H_2$), 43.5 ($\underline{C}H_2$), 31.7 ($\underline{C}H_3$), 31.6 ($\underline{C}H$), 31.4 ($\underline{C}H$), 29.6 ($\underline{C}H_2$), 29.1 ($\underline{C}H_2$), 26 ($\underline{C}H_3$), 25.34 ($\underline{C}H_2$), 25.32 ($\underline{C}H_2$), 21.5 ($\underline{C}H_2$), 21.1 ($\underline{C}H_2$), 18.1 ($\underline{C}H_3$), -3.96 ($\underline{C}H$), -4.01 ($\underline{C}H_3$), -4.14 ($\underline{C}H_3$), -4.2 ($\underline{C}H_3$);

***[4-(2-Oxopropyl)spiro[4.5]dec-6-ene-2-one* 8**.- Tri-*n*-butyltin hydride (0.35ml, 1.26 mmoles) was added to a stirred refluxing solution of *the iodides* **5a** and **5b** (416mg, 0.93 mmoles), AIBN (30mg, 0.18 mmoles) in benzene (100ml) and stirred at reflux for four and a half hours. The mixture was allowed to cool to room temperature and the solvent was removed *in vacuo* to give the crude product which was dissolved in ethyl acetate (5ml) and water (2ml). Potassium fluoride dihydrate (150mg, 1.59 mmoles) was added and the reaction was stirred at room temperature overnight. The solution was filtered and the filtrate washed with ethyl acetate (50ml total). The organic layers were combined and dried over sodium sulphate. Filtration and removal of the solvent *in vacuo* gave the crude product. Purification was carried out by chromatography using petrol : ether (10 : 1) as eluant to give the crude *spiro ketone* (**6**) (134mg, 45%) as an inseparable mixture of diastereoisomers, which was used immediately. Aqueous hydrogen fluoride (1ml, 29 mmoles) was added dropwise to a stirred solution of *spiro ketone* **6** (130mg, 0.4 mmoles) in acetonitrile (5ml) at room temperature. As soon as the addition was complete the solution was neutralised with sodium bicarbonate. The reaction mixture was extracted with ether (5 x 10ml) and the organic layers were combined and dried over sodium sulphate. Removal of the solvent *in vacuo* and chromatography using petrol : ether (2 : 1 then 1 : 1) as eluant gave the crude *alcohol* **7** (81mg, 97%) which was used immediately. Pyridinium dichromate (170mg, 0.44 mmoles) was added to a stirred solution of the crude *alcohol* **7** (69mg, 0.33 mmoles) in dichloromethane (5ml) and the reaction mixture stirred at room temperature overnight. Petrol (10ml) was added and the reaction mixture was filtered and the filtrate was washed with portions of ether (100ml total). The solvent was removed *in vacuo* to give the crude product. Purification was carried out by chromatography using ether : petrol (1 : 1) as eluant to give *the diketone* **8** (42mg, 62%) as an inseparable mixture of diastereoisomers. ν_{max} (CH_2Cl_2) 3000, 2920, 1740, 1715 and 1650 cm^{-1}; δ_H (360 MHz) 5.8 (1H, m, C$\underline{H}$), 5.4 (1H, m, J 10 and 1.5, C$\underline{H}$), 2.2 (6H, m), 2.15 (3H, s, C$\underline{H}_3$CO), 1.3-2.1 (7H); δ_C (67.5 MHz); 217.1 ($\underline{C}O$), 207.8 ($\underline{C}O$), 207.6 ($\underline{C}O$), 133.1 ($\underline{C}H$), 130.2 ($\underline{C}H$), 129.3 ($\underline{C}H$), 129.2 ($\underline{C}H$), 53.6 ($\underline{C}H_2$), 52.6 ($\underline{C}H_2$), 44.7 ($\underline{C}H_2$), 43.9 ($\underline{C}H_2$), 43.1 (spiro $\underline{C}$), 43.0 (spiro $\underline{C}$), 42.9 ($\underline{C}H_2$), 42.0 ($\underline{C}H_2$), 41.7 ($\underline{C}H$), 40.4 ($\underline{C}H$), 34.6 ($\underline{C}H_2$), 30.5 ($\underline{C}H_3$CO), 30.4 ($\underline{C}H_3$CO), 27.2 ($\underline{C}H_2$), 25.1 ($\underline{C}H_2$), 25 ($\underline{C}H_2$), 20.4 ($\underline{C}H_2$), 19.2 ($\underline{C}H_2$); HRMS found 206.1307 $C_{13}H_{18}O_2$ requires $[M]^+$, 206.1307

***7-Octen-1-yne-4-ol* 10**.- Propargyl bromide (12ml, 160 mmoles) was added to a stirred solution of magnesium turnings (3.8g, 0.156 moles) and mercuric chloride (10mg, 0.037 mmoles) in ether (150ml) at a rate which maintained a steady reflux. After the addition was complete the reaction mixture was stirred at room temperature for one hour. 4-Pentenal **9** (4.5g, 53.6 mmoles) was added dropwise to the reaction mixture and then allowed to stir at room temperature for one hour. The mixture was poured into saturated ammonium

chloride solution (100ml) and the organic layer separated. The aqueous layer was extracted with ether (3 x 50ml) and the organic layers were combined, washed with saturated sodium bicarbonate solution (3 x 50ml), water (3 x 50ml) and dried over magnesium sulphate. Filtration and removal of the solvent *in vacuo* gave the crude product. Purification was carried out by chromatography using petrol : ether (2 : 1) as eluant to give *the eneyneol* **10** (3.53g, 53%). ν_{max} (CH_2Cl_2) 3600, 3300, 3090, 2940, 2120 and 1640; δ_H (360 MHz) 5.8 (1H, m, J 17.1, 10.3 C<u>H</u>), 5.0 (2H, m, J 17.2, 10.2, C<u>H</u>$_2$), 3.8 (1H, m, C<u>H</u>OH), 2.15-2.6 (5H, m), 2.1 (1H, t, CC<u>H</u>), 1.6 (2H, m, C<u>H</u>$_2$); δ_C (67.5 MHz); 138.1 ($CH_2\underline{C}H$), 115.1 ($\underline{C}H_2$), 80.9 (C<u>C</u>H), 70.9 (<u>C</u>CH), 69.4 (<u>C</u>HOH), 35.3 ($CH\underline{C}H_2$), 29.9 ($CHC\underline{C}H_2$), 27.4 ($\underline{C}H_2$); HRMS found 142.1232 $C_8H_{16}NO$ requires, $[M+NH_4]^+$, 142.1232

[[1-(3-Butenyl)]-3-butynyloxy](1,1-dimethylethyl)dimethylsilane 11.- t-Butyldimethylsilyl chloride (7.25g, 47 mmoles) was added to a stirred solution of *the eneyneol* **10** (3.5g, 28.2 mmoles), imidazole (3.5mg, 51 mmoles) and N,N-dimethylaminopyridine (340mg, 2.76 mmoles) in DMF (8ml) and heated at 70°c overnight. The reaction mixture was allowed to cool to room temperature and poured into pentane (25ml), then extracted with pentane (3 x 25ml). The pentane layers were combined and washed with copper sulphate solution (4 x 10ml), brine (3 x 10ml), water (3 x 10ml) and dried over magnesium sulphate. Filtration and removal of the solvent *in vacuo* gave the crude product. Purification was carried out by chromatography using petrol as eluant to give *the silane* **11** (5.18g, 77%). ν_{max} (CH_2Cl_2) 3300, 3090, 2900, 2120, 1680 and 1640 cm^{-1}; δ_H (270 MHz) 5.9 (1H, m, J 17.0, 10.3, $CH_2C\underline{H}$), 5.0 (2H, m, J 17.1, 10.2, C<u>H</u>$_2$), 3.8 (1H, m, C<u>H</u>OSi), 2.39 (2H, m, C<u>H</u>$_2$), 2.01 (2H, m, C<u>H</u>$_2$), 2.0 (1H, t, C<u>H</u>), 1.6 (2H, m, C<u>H</u>$_2$), 0.9 (9H, m, C<u>H</u>$_3$), 0.1 (6H, m, C<u>H</u>$_3$); δ_C (67.5 MHz); 138.6 (<u>C</u>H$_2$), 114.6 (<u>C</u>H), 81.6 (<u>C</u>HC), 70.5 (<u>C</u>HOSi), 70.1 (<u>C</u>CH), 36 (<u>C</u>H$_2$), 29.5 ($CHC\underline{C}H_2$), 27.5 ($\underline{C}H_2$), 26 ($\underline{C}H_3$), 25.8 ($\underline{C}H_3$), 18.2 ($\underline{C}H_3$), -4.3 ($\underline{C}H_3$), -4.5 ($\underline{C}H_3$); HRMS found 239.1831 $C_{14}H_{27}OSi$ requires $[M+H]^+$, 239.1831

6-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-9-decen-3-yne-2-one 12.- *n*-Butyllithium (8ml, 12.8 mmoles) was added to a stirred cold solution (-78°C) of *the silane* **11** (2.99g, 12.6 mmoles) in THF (60ml) and stirred for five minutes. Acetyl chloride (4.5ml, 63 mmoles) was added to the reaction mixture which was allowed to warm to room temperature. The mixture was poured into dilute hydrochloric acid solution (50ml) and extracted with ether (4 x 50ml). The organic layers were combined, washed with saturated sodium bicarbonate solution (6 x 50ml), brine (3 x 50ml) and dried over magnesium sulphate. Filtration and removal of the solvent *in vacuo* gave the crude mixture. An initial separation was carried out by chromatography using petrol as eluant to give **12** (658mg, 22%) and then the crude product. Purification was carried out by chromatography using petrol : ether (100 : 1, 80 : 1 then 50 : 1) as eluant to give *the eneyneone* **12** (680mg, 19%). ν_{max} (CH_2Cl_2) 3060, 2900, 2200, 1675 and 1640 cm^{-1}; δ_H (270 MHz) 5.8 (1H, m, J 17.2, 10.3, $CH_2C\underline{H}$), 5.0 (2H, m, J 17.3, 10.5, C<u>H</u>$_2$), 3.86 (1H, m, C<u>H</u>OSi), 2.5 (2H, d, J 6, (CC)C<u>H</u>$_2$), 2.3 (3H, s, $CH_3\underline{C}O$), 2.1 (2H, m, C<u>H</u>$_2$), 1.6 (2H, m, C<u>H</u>$_2$), 0.9 (9H, m, C<u>H</u>$_3$), 0.1 (6H, m, C<u>H</u>$_3$); δ_C (67.5 MHz); 184.6 (<u>C</u>O), 138.18 ($CH_2\underline{C}H$), 114.9 (<u>C</u>H$_2$), 91 (CO<u>C</u>C), 82.8 (CO<u>C</u>C), 69.8 (<u>C</u>HOSi), 36.2 ($CC\underline{C}H_2$), 32.8 ($\underline{C}H_3CO$), 29.4 ($CH\underline{C}H_2$), 27.9 ($\underline{C}H_2$), 25.8 ($\underline{C}H_3$), 18.1 ($\underline{C}H_3$), -4.4 ($\underline{C}H_3$), -4.5 ($\underline{C}H_3$); HRMS found 281.1937 $C_{16}H_{29}O_2Si$ requires $[M+H]^+$, 281.1936

(e)-6-[[(Dimethylethyl)dimethylsilyl]oxy]-4-iodo-3,9-decadien-2-one 13a and (z)-6-[[(Dimethylethyl)dimethylsilyl]oxy]-4-iodo-3,9-decadien-2-one 13b .- Iodotrimethylsilane (0.3ml, 2.0 mmoles) was added dropwise to a stirred cold solution (-78°C) of *the eneyneone* **12** (552mg, 1.97 mmoles) in dichloromethane (7ml) and stirred for ten minutes at -78°C. Water (10ml) was added and the reaction was allowed to warm to room temperature. The aqueous layer was extracted with dichloromethane (3 x 10ml) and the organic layers were combined and washed with saturated sodium bicarbonate solution (2 x 10ml), saturated sodium thiosulphate solution (2 x 10ml), brine (2 x 20ml) and dried over sodium sulphate. Filtration and removal of the solvent *in vacuo* gave the crude product. Purification was carried out by chromatography using petrol : ether (60 : 1, 50 : 1 then 30 : 1) as eluant to give *the iodide* **13a** (314mg, 39%) and *the iodide* **13b** (205mg, 25%).

E-Isomer-13a ν_{max} (CH_2Cl_2) 3070, 2900, 2250, 1690, 1645 and 1590 cm^{-1}; δ_H (270 MHz) 7.07 (1H, s, COC<u>H</u>), 5.8 (1H, m, J 17.1, 10.4, C<u>H</u>), 5.0 (2H, m, 17.1, 10.2, C<u>H</u>$_2$), 4.0 (1H, m, C<u>H</u>OSi), 3.3 (2H, m, J 12.3, C(I)C<u>H</u>$_2$), 2.2 (5H, m), 1.6 (2H, q, C<u>H</u>$_2$), 0.9 (9H, m, C<u>H</u>$_3$), 0.1 (6H, m, C<u>H</u>$_3$); δ_C (67.5 MHz); 195.3 (<u>C</u>O), 140.6 (CO<u>C</u>H), 138.6 (<u>C</u>H), 125.4 (<u>C</u>I), 114.7 (<u>C</u>H$_2$), 72.3 (<u>C</u>HOSi), 48.2 (C<u>C</u>H$_2$), 36 (<u>C</u>H$_2$), 31.3 (<u>C</u>H$_3$CO), 29.4 (<u>C</u>H$_2$), 26 (<u>C</u>H$_3$), 18.1 (<u>C</u>H$_3$), -4.0 (<u>C</u>H$_3$), -4.3 (<u>C</u>H$_3$); HRMS found 426.1325 $C_{16}H_{33}INO_2Si$ requires $[M+NH_4]^+$, 426.1325; **Z-Isomer-13b** ν_{max} (CH_2Cl_2) 3070, 2900, 2250, 1690, 1645 and 1590 cm^{-1}; δ_H (270 MHz) 6.75 (1H, s, COC<u>H</u>), 5.8 (1H, m, J 17.0, 10.3 C<u>H</u>), 5.0 (2H, m, 17.2, 10.2, C<u>H</u>$_2$), 4.05 (1H, m, C<u>H</u>OSi), 2.8 (2H, m, C(I)C<u>H</u>$_2$), 2.25 (3H, s, C<u>H</u>$_3$CO), 2.1 (2H, m, C<u>H</u>$_2$), 1.6 (2H, m, C<u>H</u>$_2$), 0.9 (9H, m, C<u>H</u>$_3$), 0.1 (6H, m, C<u>H</u>$_3$); δ_C (67.5 MHz); 196 (<u>C</u>O), 138.2 (CO<u>C</u>H), 133.4 (<u>C</u>H), 115 (<u>C</u>H$_2$), 113.7 (<u>C</u>I), 70.3 (<u>C</u>HOSi), 55.4 (C<u>C</u>H$_2$), 36.1 (<u>C</u>H$_2$), 31.6(<u>C</u>H$_3$CO), 29.3 (<u>C</u>H$_2$), 25.9 (<u>C</u>H$_3$), 18.1(<u>C</u>H$_3$), -4.1 (<u>C</u>H$_3$), -4.2 (<u>C</u>H$_3$); HRMS found 426.1325 $C_{16}H_{33}INO_2Si$ requires $[M+NH_4]^+$, 426.1325.

3-[[[3-[(1,1-dimethylethyl)dimethylsilyl]oxy](8-ethenyl)cyclopentyl]methyl]propan-2-one 14 6-[((1,1-dimethylethyl)dimethylsilyl)oxy]-3,9-decadien-2-one 16; 3-[[3-[[(1,1-Dimethylethyl)dimethylsilyl]oxy](6-methyl)cyclohexyl]methylenyl]propan-2-one 17.-[3-(2-Oxopropyl)-4-ethenyl]propan-2-one 18.- Tri-*n*-butyltin hydride (0.65ml , 2.2 mmoles) was added to a stirred refluxing solution of *the iodides* **13a** and **13b** (747mg, 1.83 mmoles), AIBN (50mg, 0.3 mmoles) in benzene (300ml) and stirred at reflux for six hours. The mixture was allowed to cool to room temperature and the solvent was removed *in vacuo* to give the crude product which was dissolved in ethyl acetate (5ml) and water (2ml). Potassium fluoride dihydrate (300mg, 3.12 mmoles) was added and the reaction was stirred at room temperature for forty eight hours. The solution was filtered and the filtrate washed with ethyl acetate (50ml total). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (5 x 10ml) and the organic layers were combined and dried over sodium sulphate. Filtration and removal of the solvent *in vacuo* gave the crude product. Partial separation was achieved by chromatography using petrol : ether (100 : 1) as eluant to give first *the ketone* **17** (34mg, 7%) (as an inseparable mixture of diastereoisomers contaminated with *the ketone* **14** then *the ketone* **14** (237mg, 46%) (as an inseparable mixture of diastereoisomers contaminated with both *the ketone* **17** and *the ketone* **16**) and finally *the ketone* **16** (41mg, 8%) contaminated with *the ketone* **14**. Aqueous hydrogen fluoride (1ml, 29 mmoles) was added dropwise to a stirred solution of *the ketone* **14** (66mg, 0.23 mmoles) in acetonitrile (5ml) at room

temperature. As soon as the addition was complete the solution was neutralised with sodium bicarbonate. The reaction mixture was extracted with ether (5 x 10ml) and the organic layers were combined and dried over sodium sulphate. Removal of the solvent *in vacuo* and chromatography using petrol : ether (10 : 1 5 : 1, then 1 : 1) as eluant gave the crude *ketoalcohol* **15** (30mg, 78%) which was used immediately. Pyridinium dichromate (104mg, 0.27 mmoles) was added to a stirred solution of the crude *keto alcohol* **15** (27mg, 0.16 mmoles) in dichloromethane (5ml) and the reaction mixture stirred at room temperature overnight. Petrol (10ml) was added and the reaction mixture was filtered and the filtrate was washed with portions of ether (100ml total). The solvent was removed *in vacuo* to give the crude product. Purification was carried out by chromatography using ether : petrol (1 : 1) as eluant to give *the diketone* **18** (15mg, 56%) as an inseparable mixture of diastereoisomers .

17-ν_{max} (CH_2Cl_2) 2920, 1685 and 1615 cm^{-1}; δ_H (270 MHz) 6.0 (1H, m), 4.0 (1H, m, C<u>H</u>OSi), 2.4 (3H, m), 2.1 (3H, m) 1.1-1.8 (4H, m), 0.8 (12H, s), 0.1 (6H, m, C<u>H</u>$_3$); m/z 283 (M^+); **16**-ν_{max} (CH_2Cl_2) 2920, 1715 (contaminant), 1660, 1645, and 1635 cm^{-1}; δ_H (270 MHz) 6.8 (1H, m, C<u>H</u>), 6.1 (1H, d, J 16, C<u>H</u>), 5.8 (1H, m, C<u>H</u>) 5.0 (2H, m, C<u>H</u>$_2$), 3.8 (1H, m, C<u>H</u>OSi), 2.2 (1H, s, should be 3H), 1.2-2.2 (6H), 0.9 (9H, s, C<u>H</u>$_3$), 0.1 (6H, s, C<u>H</u>$_3$); m/z 283 (M^+); **18**-ν_{max} (CH_2Cl_2) 3060, 2970, 1745, 1715 and 1645 cm^{-1}; δ_H (360 MHz) 5.7 (1H, m, C<u>H</u>), 5.2 (2H, m, C<u>H</u>$_2$), 3.1 (1H, m), 2.85 (1H, m).2.65 (1H, m) , 2.4 (4H, m), 2.2 (3H, s, C<u>H</u>$_3$), 1.75 (1H, m) ; δ_C (67.5 MHz); (ring CO not found), 207.5 (<u>C</u>O), 138.9 (<u>C</u>H), 136.7 (<u>C</u>H), 117 (<u>C</u>H$_2$), 47.3 (<u>C</u>H), 47 (<u>C</u>H$_2$), 45.1 (<u>C</u>H$_2$), 44.9 (<u>C</u>H$_2$), 44.8 (<u>C</u>H$_2$), 43.8 (<u>C</u>H$_2$), 42.7 (<u>C</u>H$_2$), 42.5 (<u>C</u>H), 37.6 (<u>C</u>H), 35 (<u>C</u>H), 30.5 (<u>C</u>H$_3$CO), 30.4 (<u>C</u>H$_3$CO); HRMS found 166.0999 $C_{10}H_{16}O_2$ requires $[M]^+$, 166.0994

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References and Notes

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8. In our intial letter we reported a *moderate* yield of 78% for this transformation, this should have been quoted as 43%.

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