Tetrahedron Vol. 48, No. 37, pp. 8031-8052, 1992
Printed in Great Britain

0040-4020/92 $5.00+.00
Pergamon Press Ltd

Construction of Bicyclic Systems *via* a Tandem Free Radical Cyclopropylcarbinyl Rearrangement-Cyclisation Strategy†

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(*Received in USA* 14 *July* 1992)

Abstract: Regio- and stereospecific construction of bicyclic systems may be achieved by directed Simmons-Smith cyclopropanation of an allylic alcohol possessing a suitably positioned unsaturated acceptor, followed by a tandem free radical cyclopropylcarbinyl rearrangement-cyclisation reaction.

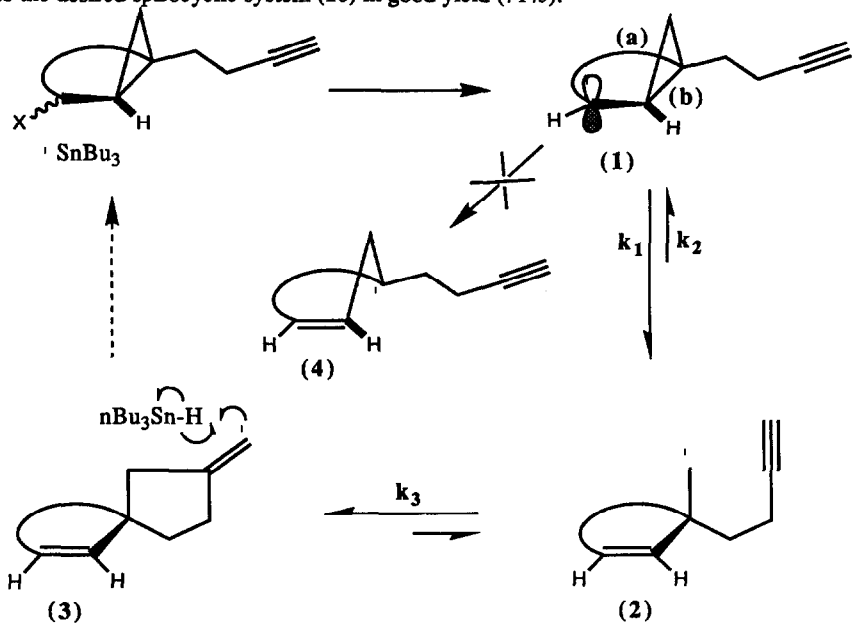
As part of our interest in developing preparatively useful free radical chain reactions based on cyclopropyl radical ring opening,[1,2] we have described our preliminary studies[3] of a tandem cyclopropylcarbinyl rearrangement-cyclisation strategy which was specifically targeted towards regiospecific generation of spirocyclic quaternary carbon centres. We now report, in full, on the application of this approach for the construction of a variety of bicyclic systems.

The essential design features of the system as illustrated for the particular case of a spiro-fused exomethylene cyclopentane (Scheme 1) were initially centred around kinetic considerations. Thus, the extremely rapid rate of cyclopropyl carbinyl radical ring opening ($k_1 = 1.3 \times 10^8\ M^{-1}s^{-1}$), when contrasted with the relatively slower rates of reclosure ($k_2 = 1 \times 10^3\ M^{-1}s^{-1}$) and 5-exo cyclisation to the alkyne acceptor ($k_3 = 2.8 \times 10^4\ M^{-1}s^{-1}$),[4] suggested to us that formation of the initial radical (**2**) would be followed, under controlled conditions involving slow addition of stannane, by a radical cascade *via* (**2**) without competing hydrogen atom abstraction until radical (**3**) had been formed. A second factor of equal importance, was the incorporation of the sequence into a rigid bicyclo [x.1.0] framework. In this respect, a considerable body of theoretical[5] and experimental[6] work is available to support the fact that, under kinetic control, stereoelectronically controlled cleavage of bond (**9**) to produce the higher energy primary radical is favoured over the thermodynamic alternative (**4**) [bond (b)]. Moreover, from earlier work on related epoxide ring opening in cyclic systems,[7] we anticipated that the relative stereochemistry of the C-X bond serving as the radical trigger was of no consequence, since conformational realignment to the situation depicted in (**2**) would be sufficiently rapid to preclude any undesired cleavage of bond (b), even in the case of a favourably disposed trans coplanar relationship.

The foregoing analysis was initially supported by construction of the spiro[4.5]decane (**10**). A suitable bicyclo[4.1.0] precursor (**8**) was readily assembled as shown in **Scheme (2)**. 1,2 addition of 4-lithio-1-trimethylsilylbut-1-yne[8] to the enol ether of dimedone[9] (**5**) gave, after acidic work-up, enone (**6**) in 80% yield. Subsequent reduction with diisobutylaluminum hydride (88%) followed by hydroxyl directed Simmons-Smith cyclopropanation[10] furnished alcohol (**8**) (66%). Finally, quantitative conversion to the thiocarbonyl

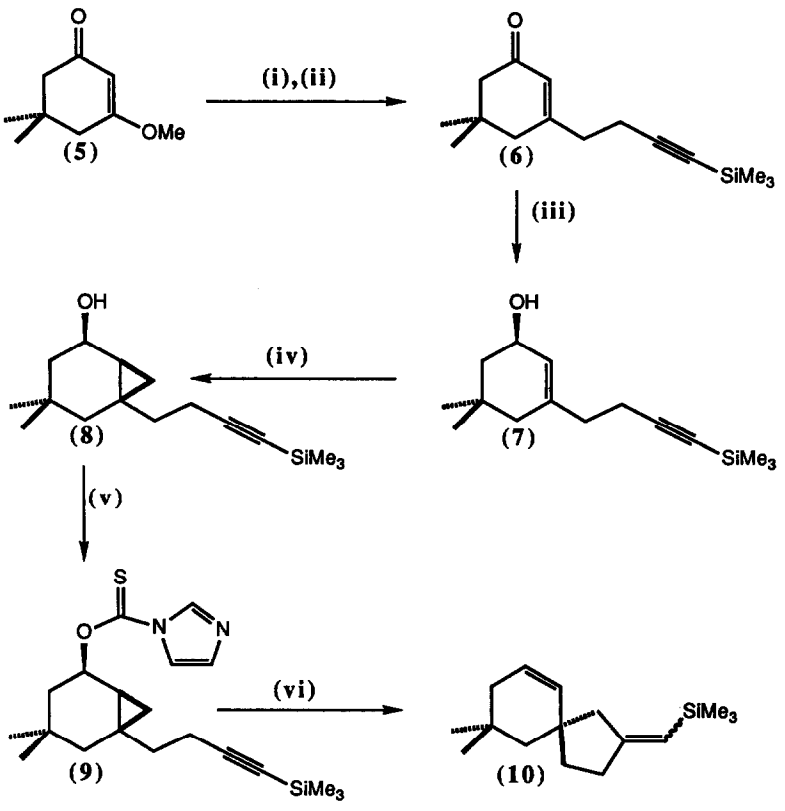
† Dedicated with respect to Professor C. W. Rees FRS on the occasion of his 65th birthday

imidazolide[11] derivative (**9**) yielded a suitable precursor for carbon centred radical generation. Slow addition of tri-n-butylstannane to a refluxing solution of (**9**) using azobisisobutyronitrile (AIBN) as initiator led smoothly to the desired spirocyclic system (**10**) in good yield (71%).



Scheme 1

Having confirmed the regiospecific nature and the kinetic and stereoelectronic features of the proposed sequence, we then wished to demonstrate that stereospecific integrity could be retained. Accordingly, we elected to prepare precursors (**14**) and (**19**) in which the additional methyl group serves as a stereochemical marker. This was carried out as shown in **Scheme** (**3**) by prior conversion of enone (**6**) to the methylated derivative (**11**) via alkylation of the kinetic lithium enolate. Problems were initially encountered in the reduction step since separation of the major allylic alcohol (**12**) from its epimer (**17**) proved to be troublesome. An experimentally convenient solution was found, however, through use of L-selectride,® since a simple aqueous work-up allowed isolation of (**12**) in pure form because of a substantial difference in hydrolysis of the precursor borate esters of (**12**) and (**17**). Clean inversion of configuration of the hydroxyl group in (**12**) was then achieved *via* Mitsunobu[12] reaction followed by a titanium tetraisopropoxide mediated solvolysis[13] of the intermediate benzoate ester (**16**). Allylic alcohols (**12**) and (**17**) were then separately subjected to the stereospecific cyclopropanation sequence and the resultant carbinols (**13**) and (**18**) transformed *via* reductive deoxygenation of their derived thiocarbonylimidazolides (**14**) and (**19**) to the respective spirocycles (**15**) (79%) and (**20**) (81%), which differ only in their relative orientation of the vinyl silane moiety with reference to the methyl group marker. The total absence of any stereochemical crossover in each series provides firm evidence that cleavage of the endocyclic bond to give (**21**) as a common intermediate was not occluding at any time during the reaction. The above examples in the spiro mode therefore present a solution to the challenging problem of stereospecific elaboration of quaternary centres.

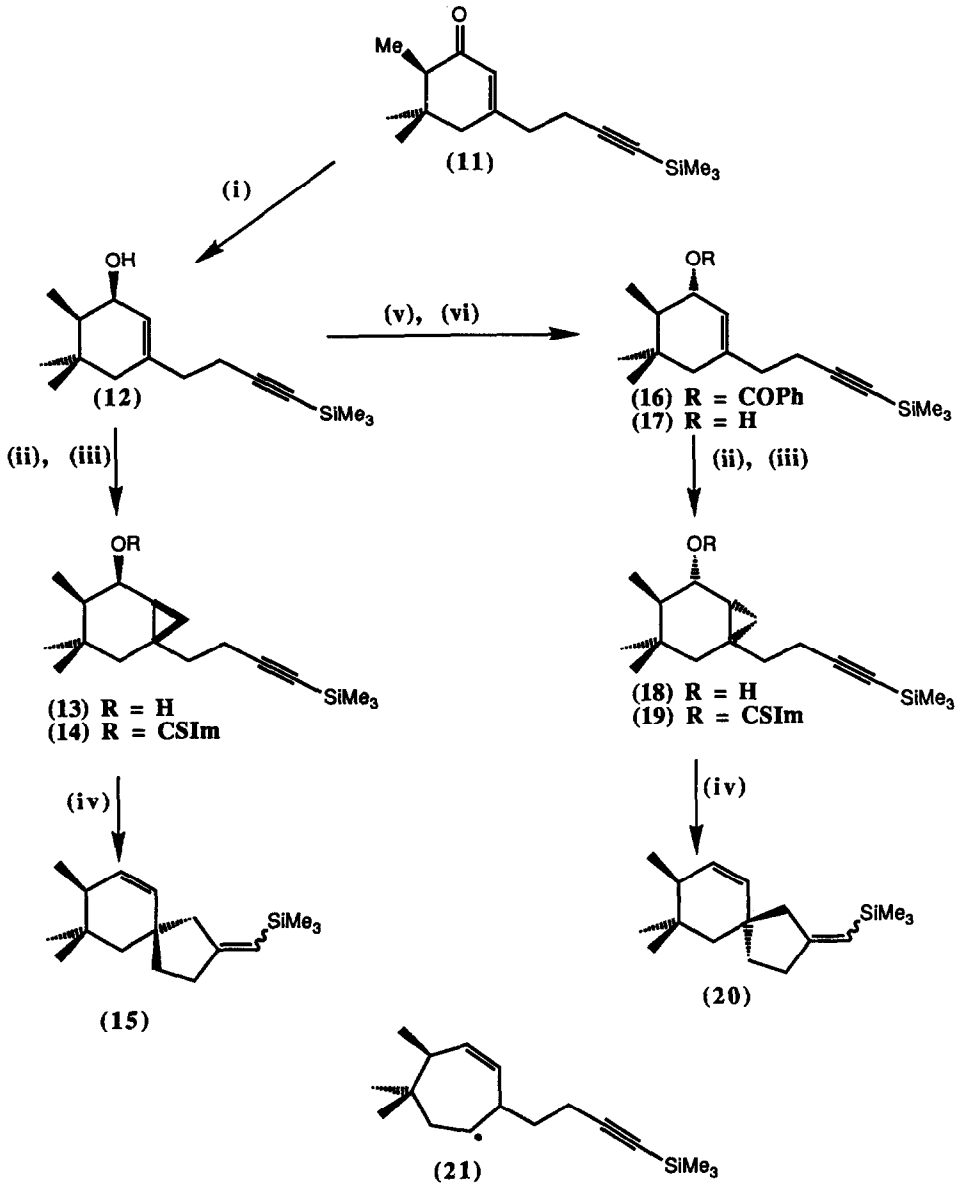


Reagents :(i) 4-lithio-1trimethylsilylbut-1-yne, pentane,THF(ii) H_3O^+ **(iii)** DIBAL, toluene **(iv)** Zn/Ag, CH_2I_2 **(v)** thiocarbonyldiimidazole, CH_2Cl_2 **(v)** Bu_3SnH,AIBN, benzene

Scheme 2

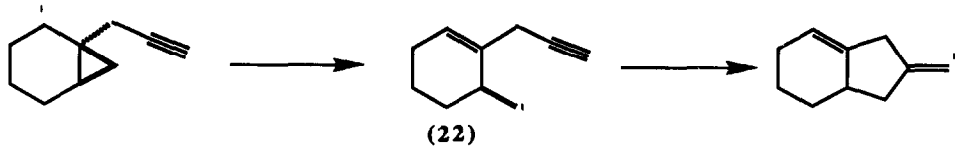
At this stage, it was also of interest to extend the range of connectivity patterns in this tandem rearrangement-cyclisation strategy and hence gain access to a variety of other bicyclic skeletons. Our attention was initially directed towards the possibility of generating the hydrindane nucleus possessing a double bond at the ring junction (**Scheme 4**).

In this case, and in contrast to the majority of alicyclic radical cyclisations, consideration of the ring opened homoallylic radical intermediate (**22**) reveals that the subsequent 5-exo dig cyclisation involves the presence of an sp^2 carbon centre in the linking chain. We therefore anticipated, both on grounds of angle strain and optimal transition state geometry, that such a cyclisation might well be difficult to achieve. A suitable substrate (**28**) was prepared from the readily accessible dimedone derivative (**23**) as shown in **Scheme 5**, using the previously established protocol and with the addition of the electron withdrawing carbomethoxy group at the acetylenic terminus in order to favour the cyclisation step.



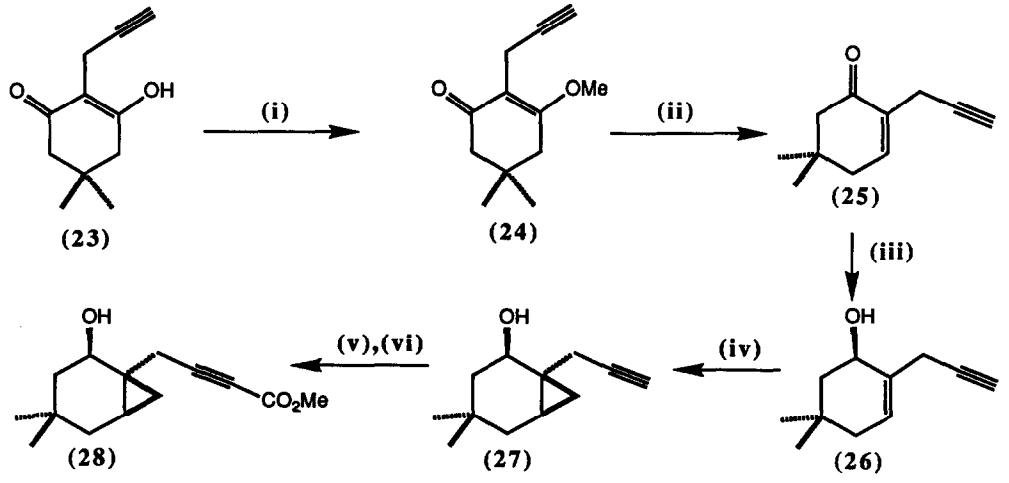
Reagents : (i) L-Selectride® THF (ii) Zn/Ag, CH_2I_2 (iii) thiocarbonyldiimidazole, CH_2Cl_2 (iv) Bu_3SnH,AIBN, benzene (v) DEAD, Ph_3P (vi) $Ti(O^iPr)_4$, MeOH

Scheme 3



(22)

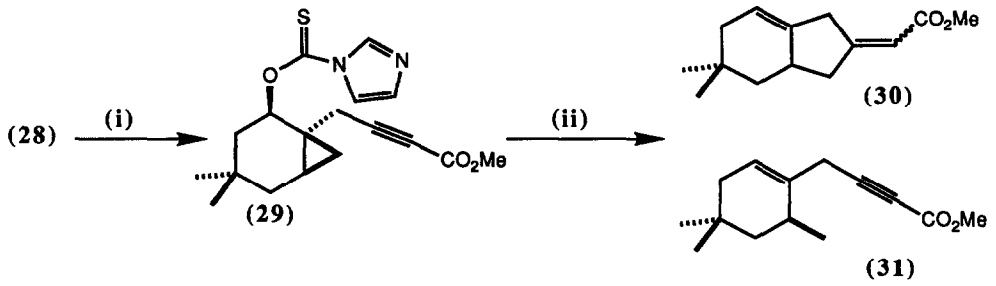
Scheme 4



Reagents : (i) Trimethylorthoformate, H_2SO_4, MeOH (ii) DIBAL then H_3O^+ (iii) DIBAL, toluene (iv) Zn/Ag, CH_2I_2 (v) TMSCl, Et_3N (vi) Methyl chloroformate, acid work up

Scheme 5

The subsequent formation of the thiocarbonylimidazolide derivative and radical deoxygenation proved to be considerably more complex than in the spirocyclic series (**Scheme 6**). As expected, reaction of the neopentylic alcohol (**28**) with thiocarbonylimidazole was very slow, requiring 36 hours at 40°C for completion. However, examination of the n.m.r. spectrum revealed a 1:1 mixture of two very similar compounds with all resonances doubled up except for the methine proton at C-2, which resonated at δ 4.37 in one compound and δ 6.28 in the other. Free radical deoxygenation using this substance and a slow addition of stannane over a 3 hour period did, however, allow the isolation of the desired bicyclo[4.3.0]nonene derivative (**30**) in 30% yield as a 1:1 mixture of the two geometrical isomers of the α,β unsaturated ester. A shorter addition time of only 1 hour led to mixtures of (**30**), and the previously absent ring opened but uncyclised product (**31**) (**30:31** 70:30) (**Scheme 6**).



Reagents : (i) thiocarbonyldiimidazole, CH_2Cl_2 (ii) Bu_3SnH, benzene

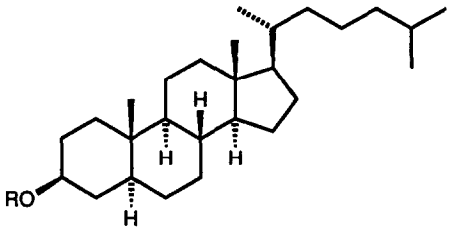
Scheme 6

In order to rationalise the relatively low yield of products, we then returned to the problematical nature of the thiocarbonylimidazolide (**29**). A simple control experiment established that hydrolysis of the thiocarbonylimidazolide derivative of 3β-cholestanol[11] (**33**) using dilute aq. hydrochloric acid led to quantitative recovery of the starting alcohol (**32**). When the above procedure was repeated on the 'abnormal' thiocarbonylimidazolide (**29**), however, alcohol (**28**) was not recovered, and the spectral properties were clearly indicative of the unstable thiol (**34**) along with its corresponding disulfide as a single diastereomer. On the basis of nmr coupling constant comparisons with the corresponding alcohol (**28**) and the failure of the thiol to undergo a facile Michael addition to the acetylenic ester, we consider that the relative stereochemistry involves replacement of oxygen by sulfur with retention as shown in (**34**). The combined yield of thiol and disulfide amounted to 81%, thereby inferring that both components of the 1:1 mixture (**29**) hydrolysed to give thiol with some subsequent air oxidation accounting for the presence of disulfide. Considering the implications of this result, the thiocarbonylimidazolide derivative (**35**) of the terminal acetylene was also prepared. In this case, reaction was considerably faster and the nmr spectrum of the product displayed the characteristic signal at δ 4.42 for a normal adduct, although small traces of the second derivative could be detected.

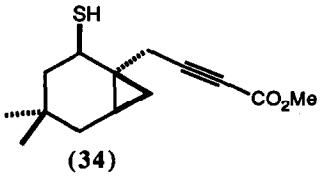
Remarkably, however, in sharp contrast to the straightforward behaviour of the cholestanyl derivative (**33**), acid hydrolysis of (**35**) also yielded thiol (**36**) in 77% yield. While it is apparent that this phenomenon is worthy of further investigation in its own right, it is clear that the hydrolytic rearrangement does not involve a fully developed carbocation or radical since the cyclopropane remains intact. The thermodynamically favoured thiocarbonyl-carbonyl interconversion has, of course, been shown to proceed *via* a four centre transition state with retention of configuration in a number of cases and also to be subject to acid catalysis.[14] In the present cases, we offer the speculative suggestion that a π-stacking interaction between the imidazole and the acetylene moieties as in (**37**), or in a subsequent tetrahedral intermediate such as (**38**), may be responsible for the increased facility of these intramolecular 1,3-shifts.

From the standpoint of radical deoxygenation, however, we conclude that the forcing conditions required in the reaction of alcohol (**28**) with thiocarbonyldiimidazole most probably resulted in the formation of the desired derivative (**29**) accompanied by an equal amount of the rearranged isomer (**39**), and consequently to a low

yield in the rearrangement-cyclisation. Since completion of our work in the hydrindane series, Clive[15] has shown that cyclopropylcarbinyl alcohols may be transformed into their corresponding phenylselenides, and this approach could therefore provide an alternative solution for generation of the initial carbon centred radical.



(32) R =H
(33) R = CSIm



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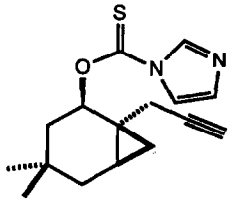

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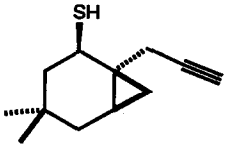

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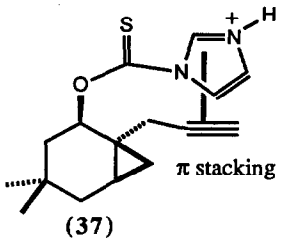

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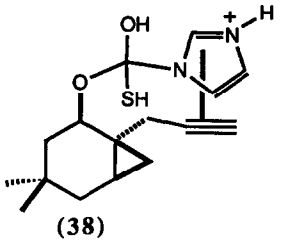

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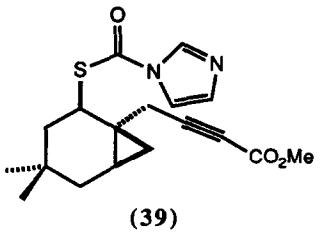
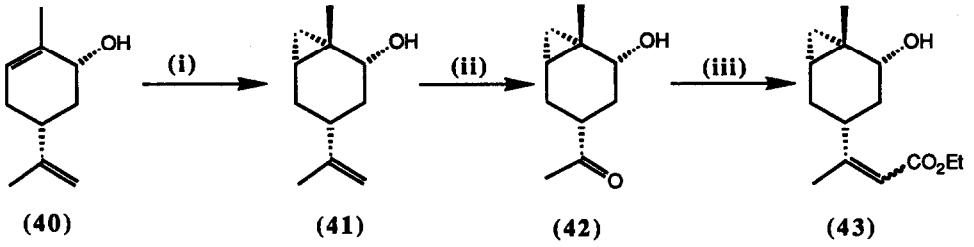


(39)

We then decided to study the construction of bridged bicyclic systems using the ring opened cyclopropyl carbinyl trigger. In this case, a necessary prerequisite is that the cyclopropane and the radicophilic acceptor alkene be disposed in a cis relationship. A suitable precursor was therefore prepared from (-) cis carveol[16] **(40)** as shown in **Scheme 7.** Once again, in order to favour the final 5-exo trig cyclisation, activation of the pendant alkenic side chain by a carboethoxy group was incorporated into substrate **(43)** using ozonolysis (90%) followed by Wadsworth-Emmons reaction (61%) **(43)** was obtained as a 5:1 mixture of E and Z isomers which were then transformed in essentially quantitative yield to the thiocarbonylimidazolide derivative **(44).** In this case, no problems of thiocarbonyl-carbonyl interconversion were noted, despite a similar steric environment around the hydroxyl group.

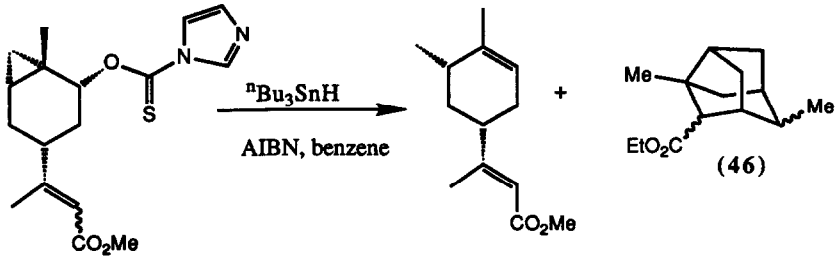


(40) (41) (42) (43)

Reagents : (i) Zn/Ag, CH_2I_2 (ii) O_3, MeOH (iii) NaH, Triethylphosphonoacetate, DME

Scheme 7

The radical reaction was carried out initially by adding 1.5 equivalents of tri-n-butylstannane over a three hour period. A t.l.c. analysis of the reaction revealed the presence of two major products in equimolar amounts. The more polar of these was assigned the structure of the ring opened but uncyclised compound (45) on the basis of the proton nmr spectrum (two alkenic protons at 5.02 and 5.64 and two allylic methyl groups at δ 2.16 and 2.10) and an infrared exhibiting characteristic α,β-unsaturated ester stretches at 1713 and 1639 cm^{-1}. The less polar product showed a saturated ester stretch at 1729 cm^{-1}, but any possibility that a bicyclic compound was present could be immediately discounted by ^{13}C and ^{1}H nmr which were notable for the complete absence of any alkenic centres. Three different types of methyl group, corresponding to the ester, and those attached to a tertiary and secondary carbon atom could be assigned and this, when taken in conjunction with the mass spectral data, is consistent with the formulation of the tricyclic structure (46) as a mixture of diastereomers. The overall conversion to (46) was then improved by an even slower addition of stannane over a 6 hour period ((45):(46), 1:2).

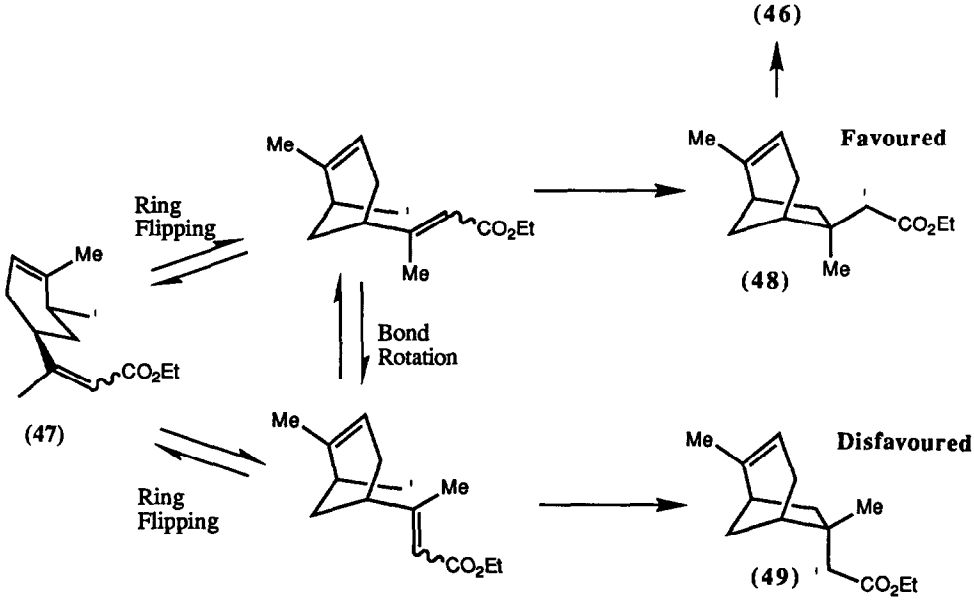


(44) (45) (46)

Scheme 8

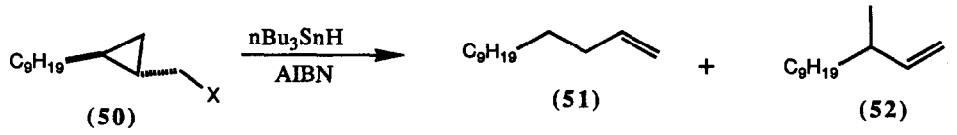
Consideration of the conformations involved in this radical rearrangement are particularly instructive (**Scheme 9**). Thus, formation of a bicyclic intermediate from the ring opened homoallylic radical (47) must first involve ring flipping to a higher energy diaxial conformer. The formation of monocyclic product (45) by competitive hydrogen atom abstraction from the stannane at this stage is therefore readily understood. The

failure to isolate bicyclic compounds, and the observed formation of the tricyclic skeleton are of greater interest, in as much as they imply that cyclisation proceeds via a preferred chair-like conformer (**48**) (with respect to the 5-hexenyl system) which is then favourably disposed to undergo a second 5-exo trig cyclisation onto the olefinic terminus initially formed at the homoallylic radical stage. Cyclisation via the alternative boat like transition state (**49**) can only lead to bicyclic products. These observations therefore support recent experimental and theoretical work by Beckwith and Schiesser[17] who concluded, in a simpler system, that the difference in transition state energies between the chair-like and boat-like conformations is 1 kcal mol^{-1}. In the present instance, the additional steric contraints imposed by the bridge in chair-like (**48**) may well make the energy difference even smaller.



Scheme 9

Although all of the foregoing examples have been argued on the basis of the necessity for the incorporation of the cyclopropylcarbinyl rearrangement within a bicyclo[x.1.0] framework, our attention was attracted by the work of Davies and Pereyre,[18] who studied the regioselectivity of ring opening of both cis and trans methyl substituted cyclopropylcarbinyl radicals. These authors noted that, while the cis disubstituted radical gave the expected ring opened secondary radical under kinetic control as a result of radical alignment to relieve an unfavourable steric interaction, the trans disubstituted system also displayed a curious kinetic preference for formation of the higher energy primary radical at lower temperatures (4:1, primary : secondary), despite the absence of any obvious steric restrictions on conformational alignment. As a prerequisite to application of a tandem sequence in a monocyclic system, it was therefore of interest to determine, in this latter case, if a similar degree of control could be produced on a preparative scale.



(50) (51) (52)

Scheme 10

Method (A-E)	Substrate (X)	Yield (%)	Product distribution (51) : (52)
A	Br	23%	98 : 2
A	Cl	89%	96 : 4
B	Br	81%	66 : 34
B	Cl	73%	67 : 33
B	OCSSMe	63%	73 : 27
C	Br	72%	62 : 38
C	Cl	28%	56 : 44
C	SePh	82%	60 : 40
D	Br	70%	60 : 40
D	Cl	76%	62 : 38
D	SePh	80%	63 : 37
D	OCSSMe	GC	58 : 42
E	Br	GC	51 : 49
E	Cl	GC	49 : 51
E	SePh	GC	47 : 53
E	OCSSMe	GC	52 : 48

Five different reduction methods were used: slow addition of tributylstannane to a refluxing benzene solution of the substrate (method A); slow addition of substrate to a refluxing benzene solution of tributylstannane (method B); neat substrate and tributylstannane (45°C) (method C, i.e. the conditions employed by Davies and Pereyre); slow addition of substrate to a concentrated refluxing solution of tributylstannane in benzene (method D); a solution of substrate and tributylstannane with hexaphenylditin/hν as initiator (-78°C to RT) (method E).

Table 1

To this end, we have made a brief study of regioselectivity in the case of the trans disubstituted 2-nonylcyclopropylmethyl system (**Scheme 10**). A suitable series of radical precursors were prepared from the corresponding alcohol ((**50**), X=OH), which was in turn available by Simmons-Smith cyclopropanation of E-2-dodecen-1-ol.[19] The results of this study are shown in the Table. While, as expected, a preparatively useful procedure for maximising the thermodynamic product (**51**) was obtained (Method A), a complementary method for the non-thermodynamic product (**52**) was not established even under high stannane concentrations (Methods B-E) which would mitigate against a subsequent tandem cyclisation. At best, under low temperature photolytic conditions (Method E), a 1:1 mixture of ring opened products is obtained. Since completion of our study, detailed rate data have been published[20] which reveal the rate difference between cleavage of the more and less substituted double bonds is very small indeed, and several convincing molecular orbital explanations

have been produced.[21] We have therefore concluded that the application in monocyclic systems would be limited to selected substrates with an inbuilt conformational bias. Nevertheless, in summary, the tandem free radical cyclopropylcarbinyl rearrangement-cyclisation under conditions of low stannane concentration provides a useful and flexible method for regio- and stereocontrolled elaboration of a variety of bicyclic systems.

EXPERIMENTAL

Melting points were determined on a Kofler-hot stage and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 983G grating infrared spectrometer as thin films or chloroform solutions. NMR spectra were obtained for solutions in d-chloroform with residual protic solvent or tetramethylsilane as internal standard, and were recorded on JEOL FX90Q (90 MHz), JEOL GSX-270 (270 MHz), Bruker WM-250 (250 MHz) or Bruker AM-500 (500 MHz) instruments. Mass spectra were obtained with VG micromass 7070B instrument. Microanalyses were performed by the Imperial College Chemistry Department Microanalytical Laboratory. Optical rotations were measured on an Optical Activity AA-1000 polarimeter. Ether, tetrahydrofuran, toluene and benzene were distilled from sodium-benzophenone ketyl under argon immediately prior to use. Dimethylformamide and dimethylsulphoxide were distilled from calcium hydride at reduced pressure, and stored over 4Å molecular sieves under an argon atmosphere. Pyridine was distilled from potassium hydroxide and stored over 4Å molecular sieves under an argon atmosphere. Dichloromethane was distilled from phosphorous pentoxide. Gas chromatography was carried out on a Perkin Elmer Sigma 3 machine with an Alltech 10 m x 0.53 mm bonded FSOT RSL-150 polydimethylsiloxane column, at a temperature of 90°C, using helium carrier gas at a flow pressure of 40 kPa. Tridecene and 3-methyl-dodec-1-ene recorded retention times of 3.5 minutes and 2.6 minutes respectively.

5,5-Dimethyl-3-(4-trimethylsilylbut-3-ynyl)cyclohex-2-enone(6). 4-Iodo-1-trimethylsilylbut-1-yne (10g, 40 mmol) was dissolved in anhydrous pentane and cooled to -78°C under argon. t-Butyllithium (26 ml, 44 mmol) was added dropwise over 10 minutes with stirring. After 1 hour, the solution of the lithio species was transferred *via* a lagged cannula to a vessel containing 3-methoxy-5,5 dimethyl-cyclohex-2-enone (8g, 52 mmol) in THF (250 ml) at -78°C under argon. After a further 1 hour of stirring, the mixture was allowed to warm up to room temperature. Distilled water (10 ml) was added followed by removal of solvents *in vacuo*. To the residue was added 2M HCl (200 ml) and THF (200 ml), and the homogeneous mixture was then stirred for 2 hours at room temperature. The mixture was then neutralised with aq. sodium bicarbonate and extracted with diethyl ether (3 x 150 ml). The combined organic phases were dried over magnesium sulphate before removal of solvents *in vacuo*. The resultant yellow oil was chromatographed (silica, 5% ether / petrol) to afford (**6**) (7.85g, 80%) as a colourless oil. ν_{max} 2958, 2176, 1670, 1628, 1250, 844 cm^{-1}; δ_H (270 MHz; $CDCl_3$) 0.109 (9H, s, $SiMe_3$), 1.02 (6H, s, gem Me), 2.20 (4H, m, C-2' -CH_2 and C-6 -CH_2), 2.40 (4H, m, C-6 -CH_2 and C-1' -CH_2), 5.89 (1H, m, =CH); m / z 247 ($m-H^+$), 192, 177, 146, 73.(Found C 72.40, H 9.80; $C_{15}H_{24}SiO$ requires C 72.52, H 9.74 %)

5,5 Dimethyl-3-(4-trimethylsilylbut-3-ynyl)cyclohex-2-en-1-ol (7). The enone (**6**) (6g, 24 mmol) was dissolved in anhydrous toluene (100 ml) and cooled in an ice / salt bath to -20°C under argon. DIBAL (1.5 M in toluene, 16 ml, 24 mmol) was added dropwise over 15 minutes. After stirring for a further 3 hours at -20°C, water (3 ml) was added dropwise and the reaction allowed to warm up to room temperature. Sodium sulphate (40g) was then added, and the mixture stirred overnight. The solid was filtered off and solvents removed *in vacuo*. The crude product was chromatographed (silica, 30% ether / petrol) to afford (**7**) (5.32g, 88%) as a colourless oil. ν_{max} 3324, 2954, 2176, 1249, 843 cm^{-1}; δ_H (250 MHz ; $CDCl_3$): 0.13 (9H, s, $SiMe_3$), 0.8 (3H, s, C-5 Me), 0.99 (3H, s, C-5 Me), 1.24 (1H, b, O-H), 1.70 - 1.93 (4H, m, C-4 allylic -CH_2 and C-6 CH_2), 2.17 (2H, m, C-1' allylic -CH_2), 2.32 (2H, t, J = 7 Hz C-2' propargylic -CH_2), 4.25 (1H, bm, HO-C-H), 5.47 (1H, m, C-2 alkenic CH). (Found : C 71.80, H 10.61; $C_{15}H_{26}OSi$ requires: C 71.93, H 10.46 %)

(1RS,5SR,6RS)-3,3-Dimethyl-1-(4-trimethylsilylbut-3-ynyl)bicyclo[4.1.0]heptan-5-ol

(8). Alcohol (7) (2g, 8 mmol) and diiodomethane (2.58ml, 32 mmol) were dissolved in anhydrous ether (50 ml) and added to freshly prepared zinc / silver couple (2g, 32 mmol). The mixture was refluxed under argon with vigorous stirring for 3 hours. After cooling to 0°C, saturated aq. ammonium chloride (30ml) was added dropwise. The aqueous and organic phases were separated and the aqueous phase extracted with ether (2 x 25ml). The combined organic phases were dried over $MgSO_4$ before removal of solvents *in vacuo*. The residue was chromatographed (silica, 40% ether / petrol)to afford (8) (1.39g, 66 %) as a colourless oil. ν_{max} (film) 3340, 2953, 2175, 1249, 1032, 841 cm^{-1};δ_H (270 MHz, $CDCl_3$): 0.14 (9H, s, $SiMe_3$), 0.27 (1H, t, J = 4.8Hz C-7 C-H), 0.48 (1H, dd, J = 4.8, 9 Hz, C-7 -CH), 0.71 (1H, m, C-2 H-C cis to cyclopropane), 0.84 (3H, s, C-3 Me), 0.87 (3H, s, C-3 Me), 1.16 - 1.27 (3H, m, C-1' -CH_2 and C-2 C-H trans to cyclopropane), 1.39 - 1.62 (3H, m, C-4 -CH_2 and O-H), 2.28 (2H, t, J = 7.8 Hz, C-2' CH_2), 4.27 (1H, m, C-5 -CH); m / z 264 (M^+), 249, 231 75, 73 .(Observed M^+ 249.1674; $C_{16}H_{28}SiO$ requires M^+ 249.1679.)

o-[(1RS,5SR,6RS)-3,3-Dimethyl-1-(4-trimethylsilylbut-3-ynyl)bicyclo[4.1.0]hept-5-yl]-1-imidazolethiocarboxylate (9). Alcohol (8) (500mg, 1.90 mmol) was dissolved in dry DCM (25 ml). N,N'-thiocarbonyldiimidazole (2g, 10.99 mmol) was added, and the mixture refluxed under argon for 5 hours. On cooling, the mixture was diluted with more DCM (25 ml) and then washed sequentially with water, dilute HCl, sat. $NaHCO_3$, water and brine before drying over Na_2SO_4. Removal of solvents *in vacuo* afforded (9) (710mg, quantitative yield) as a yellow oil. ν_{max} (film) 2955, 2175, 1688, 1215, 888, 843 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.14 (9H s, $SiMe_3$), 0.27 (1H, t, J = 4.8 Hz, C-7 C-H), 0.52 (1H, dd, J = 4.8, 9 Hz, C-7 - CH) 0.71 (1H, m, C-2 H-C cis to cyclopropane), 0.87 (3H, s, C-3 Me), 1.02 (3H, s, C-3 Me), 1.16 - 1.27 (3H, m, C-1' -CH_2 and C-2 C-H trans to cyclopropane), 1.39 - 1.62 (2H, m, C-4 -CH_2), 2.28 (2H, t, J = 7.8 Hz C-2' CH_2), 4.39 (1H, m, C-5 -CH), 7.06 (1H, m, imidazole CH), 7.44 (1H, m, imidazole CH), 8.17 (1H, m, imidazole CH).

(2EZ)-9,9-Dimethyl-2-[(trimethylsilyl)methylene]-spiro[4.5]dec-6-ene (10). Thiocarbonyl-imidazolide derivative (9) (700 mg, 1.86 mmol) was dissolved in dry degassed benzene (30 ml). The solution was brought to reflux under argon and a solution of tri-n-butyltinhydride (1ml, 3.7 mmol) and AIBN (50 mg) in benzene (4 ml) was added dropwise over 30 minutes. The mixture was then allowed to reflux overnight. On cooling, CCl_4 (5 ml) was added with stirring for 10 minutes. A dilute solution of iodine in ether was titrated in until a faint yellow colour persisted. After dilution with more ether (50 ml), the mixture was washed three times with 5% aqueous potassium fluoride and then dried over $MgSO_4$ before removal of solvents *in vacuo*. The residue was chromatographed (silica, pentane) to afford (10) (327 mg, 71%) as a colourless oil. ν_{max} (film): 2951, 1622, 1246, 872, 83 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.07 (4.5H, s, $SiMe_3$ of one isomer), 0.09 (4.5H, s, $SiMe_3$ of one isomer), 0.93 (1.5H, s, C-9 Me- of one isomer), 0.95 (3H, s, C-9 Me), 0.945 (1.5H, s, C-9 Me- of one isomer), 1.40 (1H, s, C-10 -CH_2 of one isomer), 1.41 (1H, s, C-10 -CH_2 of one isomer), 1.52 - 1.75 (2H, m, C-4 -CH_2), 1.78 (2H, m, C-8 allylic -CH_2), 2.24 - 2.46 (4H, m, C-1 & C-3 allylic -CH_2), 5.36 (1H, m, exocyclic C=CH), 5.53 (2H, m, C-6 & C-7 alkenic =CH); m / z 248 (M^+), 233, 192, 174, 73 .(Observed M^+: 248.1960; $C_{16}H_{28}Si$ requires 248.1960)

5,5,6-Trimethyl-3-(4-trimethylsilylbut-3-ynyl)cyclohex-2-enone (11). Diisopropylamine (1.58 ml, 11.24 mmol) was dissolved in dry THF (40 ml) and cooled to 0°C under argon. n-BuLi (4.50 ml of a 2.5M solution in hexanes, 11.24 mmol) was added dropwise and the mixture left to stir for 30 minutes. On cooling the solution of LDA to -78°C, enone (10) (2.5 g, 10 mmol in THF (3 ml) was added dropwise. After 1 hour at -78°C, the orange-red solution of the anion was transferred *via* cannula to a flask containing MeI (700 ml, 11.24 mmol) in THF (50 ml) at -78°C under argon. The mixture was stirred at -78°C for 30 minutes and then allowed to warm up to room temperature before addition of water (50 ml), followed by extraction with ether (3 x 30 ml). The combined organic extracts were washed sequentially with dilute aq. HCl, saturated aq. Na_2SO_4 aq. sodium thiosulphate, water, brine and then dried over $MgSO_4$. Removal of solvents *in vacuo* yielded a yellow oil which was chromatographed (silica, 10% ether / petrol) to afford (11) (2.03 g, 77%) as a colourless oil. ν_{max} (film) 2961, 2872, 2176, 1672, 1636, 1250, 843 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.11 (9H, s, $SiMe_3$), 0.87 (3H, s, C-5 Me), 1.04 (3H, s, C-5 Me), 1.04 (3H, d, J = 6.8 Hz, C-6 Me), 2.12-2.21

(3H, m, C-4 allylic -CH_2 & C-6 -CH), 2.38- 2.44 (4H, m, C-1' & allylic -CH_2, propargylic -CH_2), 5.84(1H, m, C-2 alkenic =CH); m / z 262 (M^+), 234, 177, 73. (Observed M^+: 262.1745; $C_{16}H_{26}SiO$ require : 262.1753)

(1RS,6RS)-5,5,6-trimethyl-3-(4-trimethylsilylbut-3-ynyl)-cyclohex-2-en-1-ol (12). Lithium tri-*iso*-butylborohydride (L-Selectride®) (3.8 ml of a 1M solution in THF, 3.74 mmol) was dissolved in THF (3ml) and cooled to -78°C under argon. Enone **(11)** (1 g, 3.75 mmol) dissolved in THF (1 ml) was added dropwise over 10 minutes. After stirring at -78°C for 2 hours, the cooling bath was removed and water (20 ml) was added with stirring for 20 minutes. The mixture was extracted with ether (4 x 5 ml) and the combined organic phases were dried over $MgSO_4$ before removal of solvents *in vacuo*. The residue was then chromatographed (silica, 30% ether / petrol) to afford **(12)** (695 mg, 69 %) as a white, low melting point waxy solid. ν_{max} 3341, 2960, 2878, 2175, 1671, 1249, 843 cm^{-1};δ_H (270 MHz, $CDCl_3$) 0.18 (9H, s, $SiMe_3$), 0.92 (3H, d, J = 8 Hz, C-6 Me), 0.975 (3H, s, C-5 Me), 0.98 (3H, s, C-5 Me), 1.28 (1H, d, 7.8 Hz, O-H), 1.59 (1H, m, C-6 -CH), 1.65 (1H, d, J=16 Hz, C-4 -CH), 1.88 (1H, d, J = 16 Hz, C-4 -CH), 2.18 (2H, t, J = 7 Hz, C-1' allylic -CH_2), 2.37 (2H, t, J=7 Hz, C-2' propargyl -CH_2), 4.29 (1H, bs, C-1 -CH), 5.42 (1H, m, C-2 alkenic -CH); m / z 264 (M^+), 249, 152, 73.(Found: C 72.56, H 10.95; $C_{16}H_{28}SiO$ requires: C 72.66, H 10.67 %)

(1RS,4SR,5SR,6RS)-3,3,4-trimethyl-1-(4-trimethylsilylbut-3-ynyl)-bicyclo[4.1.0]heptan-5-ol(13). Freshly prepared zinc / silver couple (660 mg, 10.9 mmol) was added to a solution of alcohol **(12)** (480 mg, 1.81 mmol) in dry ether (15 ml). The mixture was brought to reflux under argon with vigorous stirring. Diiodomethane (265 ml, 10.86 mmol) was added dropwise over 10 minutes, and the mixture refluxed for 3.5 hours. After cooling to 0°C, saturated aq. NH_4Cl (20 ml) was added dropwise. The phases were separated and the aqueous phase extracted with ether (2 x 10 ml). The combined organic phases were dried over $MgSO_4$ before removal of solvents *in vacuo*. The residue was chromatographed (silica, 30 % ether / petrol) to afford **(13)** (374 mg, 74%) as a colourless oil. ν_{max} (film)3374, 2960, 2912, 2866, 2174, 124, 1021, 842 cm^{-1}; δ_H (250 MHz, $CDCl_3$): 0.14 (9H, s, $SiMe_3$), 0.38 (1H, dd, J = 9, 4.8 Hz, C-7 cyclopropyl -CH into cyclohexane ring), 0.49 (1H, t, J = 4.8 Hz, C-7 cyclopropyl-CH out of cyclohexane ring), 0.77 (3H, J = 7.6 Hz, C-4 Me), 0.85 (3H, s, C-3 Me), 0.96 (3H, s, C-3 Me), 1.09 (1H, dt, J = 9, 4 Hz, C-6 ring fusion -CH), 1.20 - 1.33 (3H, m, C-2 -CH_2 & O-H), 1.48 - 1.80 (3H, m, C-1' -CH_2 & C-1' -CH), 2.30 (2H, m, C-2' propargyl -CH_2), 4.44 (1H, t, J = 6.5 Hz, C-5 C-1' -CH); m / z: 278 (M^+), 263, 245, 219, 75, 73. (Found: C 73.57, H 11.07; $C_{17}H_{30}SiO$ requires: 73.31, H 10.86%)

O-(1RS,4SR,5SR,6RS)-3,3,4-trimethyl-1-(4-trimethylsilylbut-3-ynyl)bicyclo[4.1.0]hept-5-yl]-1-imidazolethiocarboxylate (14). The alcohol **(13)** (250 mg, .9 mmol) and 1,1' thiocarbonyldiimidazole (1g, 5.6 mmol) were dissolved in dry DCM (20 ml) and refluxed under argon for 8 hours. After cooling, the mixture was diluted with more DCM (20 ml) and washed sequentially with water, dilute aq. HCl, aq. $NaHCO_3$, water and brine before drying over $MgSO_4$. Removal of solvents *in vacuo* afforded **(14)** as a yellow oil. ν_{max} (film) 2956, 2173, 1688, 1215, 841 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.13 (9H, s, $SiMe_3$), 0.48 (1H, t, J = 4.8 Hz, C-7 cyclopropyl -CH), 0.55 (1H, dd, J = 9, 4.8 Hz, C-7 cyclopropyl -CH,), 0.89 (3H, s, C-3 Me), 0.92 (3H, d, J = 7 Hz, C-4 Me-), 1.13 (3H, s, C-3 Me), 1.22- 1.42 (2H, m, C-2 -CH_2), 1.57- 1.85 (3H, m, C-1' -CH_2 & C-4 -CH), 2.31 (2H, m, C-2' propargyl -CH_2), 4.74 (1H, t, J = 6.6 Hz, C-5 -CH), 7.09 (1H, m, imidazole ring =CH), 7.49 (1H, m, imidazole ring =CH), 8.22 (1H, m, imidazole ring =CH).

(2EZ,5RS,8SR)-8,9,9-trimethyl-2-[(trimethylsilyl)methylene]spiro[4.5]dec-6-ene (15). The thiocarbonylimidazolide derivative **(14)** (245 mg, 0.63 mmol) was dissolved in dry benzene (15 ml) and brought to reflux under argon. Tri-n-butyltinhydride (0.5 ml, 1.89 mmol) and AIBN (20 mg, 0.095 mmol) in benzene (2ml) were added dropwise to the refluxing solution over 1 hour. The mixture was then allowed to reflux overnight and then worked up as previously described. The residue was chromatographed (silica, pentane) to afford **(15)** (130 mg, 79%) as a colourless oil. ν_{max} (film) 2954, 1623, 1246, 872, 836 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.07 (4.5H, s, $SiMe_3$), 0.08 (4.5H, s, $SiMe_3$), 0.78 (1.5H, s, C-9 Me), 0.80 (1.5H, s,

C-9 Me), 0.87 (1.5H, d, J = 7.2 Hz, C-8 Me), 0.90 (1.5H, d, J = 7.2 Hz, C-8 Me), 0.93 (3H, s, C-9 Me), 1.26- 1.65 (4H, m, C-4 & C-10 -CH_2), 1.89- 1.93 (1H, m, C-8 allylic -CH), 2.14- 2.23 (4H, m, C-1 & C-3 allylic -CH_2), 5.28- 5.47 (3H, m, alkenic =CH at C-6 C-7 & C-1'); m / z 262 (M^+), 192, 163, 75, 73. (Observed M^+ 262.2121; $C_{17}H_{30}Si$ requires 262.2117)

Benzoic acid[(1RS,6SR) 5,5,6-trimethylsilylbut-3-ynyl)cyclohex-2-enyl]ester (16). Alcohol (**12**) (500 mg, 1.87 mmol) and triphenylphosphine (487 mg, 1.87 mmol) dissolved in dry ether (3 ml) were added dropwise to a solution of diethylazodicarboxylate (300 ml, 1.87 mmol)and benzoic acid (227 mg, 1.87 mmol) in ether (7 ml). After stirring overnight at room temperature overnight, the solid precipitate was filtered off and the filtrate was concentrated *in vacuo*. The residue was chromatographed (silica, 5% ether / petrol)to afford (**16**) (478 mg, 65%) as a white crystalline solid (m.p. 64- 65°C). ν_{max} ($CHCl_3$) 2961, 2175, 1713, 1268, 1111, 842 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.12 (9H, s, $SiMe_3$), 0.89 (3H, s, C-5 Me), 0.95 (3H, d, J = 7 Hz, C-6 Me), 1.02 (3H, s, C-5 Me), 1.77 (2H, m, C-4 allylic CH_2), 2.03 (1H, m, C-6 -CH), 2.16 (2H, m, C-1' allylic CH_2), 2.34 (2H, t, J = 7.1 Hz, C-2' propargyl -CH_2), 5.28 (1H, m, C-1 -CH), 5.49 (1H, bs, C-2 alkenic =H), 7.42 (2H, m, m- aromatics), 7.55 (1H, m, p- aromatic), 8.05 (2H, m, o-aromatics); m / z 368 (M^+), 353, 279, 263, 105. (Found: C 74.69, H 8.63 ; $C_{23}H_{32}SiO_2$ requires: C 74.95, H 8.74%)

(1RS,6SR)-5,5,6-trimethyl-3-(4-trimethylsilylbut-3-ynyl)-cyclohex-2-en-1-ol (17). Titanium(IV) *iso* - propoxide (760ml, 2.6 mmol) was added to ester (**16**) (950 mg, 2.6 mmol) dissolved in *iso*-propanol (50ml) and the solution was refluxed under argon of 8 hours. After cooling to room temperature, water (50 ml) was added followed by extraction with ether (3 x 25 ml). The combined organic extracts were dried over $MgSO_4$ before removal of solvents *in vacuo*. The residue was chromatographed (silica, 25 % ether / petrol) to afford (**17**) (470 mg, 69 %)as a low melting point waxy solid. ν_{max} (film)3315, 2960, 2891, 2177, 1250, 1017, 842 cm^{-1};δ_H (270 MHz, $CDCl_3$) 0.14 (9H, s, $SiMe_3$), 0.77 (3H, s, C-5 Me), 0.94 (3H, s, C-5 Me), 1.01 (3H, d, J = 6.8 Hz, C-6 Me), 1.20 - 1.29 (1H, s, O-H), 1.63 - 1.70 (2H, m, C-4 allylic -CH_2), 1.94 (1H, m, C-6 -CH), 2.16 (2H, m, C-1' allylic -CH_2), 2.33 (2H, t, J = 7 Hz, C-2' allylic -CH_2), 3.72 (1H, b, C-1 -CH), 5.44 (1H, br. s, alkenic =CH); m / z 264 (M^+), 249, 165, 152, 75, 73.(Observed M^+: 264.1909; $C_{16}H_{28}SiO$ requires 264.1909)

(1RS,4RS,5SR,6RS)-3,3,4-Trimethyl-1-(4-trimethylsilylbut-3-ynyl)bicyclo[4.1.0]heptan-5-ol(18). Freshly prepared zinc / silver couple (410 mg, 6.79 mmol) was added to a solution of alcohol (**17**) (300 mg, 1.10 mmol) in dry ether (10 ml). The mixture was brought to reflux under argon with vigorous stirring. Diiodomethane (160 ml, 6.79 mmol) was added dropwise over 10 minutes and the mixture was then refluxed for 2 hours. After cooling to 0°C, saturated aq. NH_4Cl (20 ml) was added dropwise. The phases were separated and the aqueous phase extracted with ether (2 x 10 ml). The combined organic phases were dried over $MgSO_4$ before removal of solvents *in vacuo*. The residue was chromatographed (silica, 35 % ether / petrol) to afford (**18**) (264 mg, 84%) as a colourless oil. ν_{max} (film) 3370, 2960, 2912, 2866, 2175, 1249, 1021, 843 cm^{-1};δ_H (270 MHz, $CDCl_3$) 0.13 (9H, s, $SiMe_3$), 0.28 (1H, t, J = 4.7 Hz, C- cyclopropyl -CH), 0.48 (1H, dd, J = 4.8, 9Hz, C-7 cyclopropyl -CH), 0.77 (3H, s, C-3 Me), 0.79 (3H, s, C-3 Me), 0.93 (3H, d, J = 7.2 Hz, C-4 Me), 1.12 (1H, d, J = 8 Hz, O-H), 1.20-1.65 (6H, m, C-1' & C-5 -CH_2; C-6 & C-3 -CH), 2.29 (2H, t, J = 7 Hz, C-2' propargyl -CH_2), 3.76 (1H, m, C-5 HO-CH); m / z 278 (M^+),263, 245, 219, 179, 75, 73 . (Observed M^+: 278.2069; $C_{17}H_{20}SiO$ requires 278.2066)

o-[(1RS,4RS,5SR,6RS)-3,3,4-trimethyl-1-(4-trimethylsilylbut-3-ynyl)bicyclo[4.1.0]hept-5-yl]-1-imidazolethiocarboxylate (19). Alcohol (**18**) (230 mg, 0.83 mmol) and 1, 1'-thiocarbonyldiimidazole (1g, 5.5 mmol) were dissolved in dry DCM (15 ml) and refluxed under argon for 5 hours. After cooling, the mixture was diluted with more DCM (15 ml) and washed sequentially with water, dilute aq. HCl, aq. $NaHCO_3$, water and brine before drying ($MgSO_4$). Removal of solvents *in vacuo* afforded (**19**) as a yellow oil. ν_{max} (film) 2960, 2174, 1688, 1466, 1363, 1292, 1269, 1214, 886, 843 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.12 (9H, s, $SiMe_3$), 0.24 (1H, t, J = 4.5 Hz, C-7 cyclopropyl - CH), 0.65 (1H, dd, J = 9, 4.5 Hz, C-7 cyclopropyl -CH), 0.84 (3H, s, C-3 Me), 0.91 (3H, s, C-3 Me), 0.99 (3H, d, J = 7 Hz, C-4 -CH_3), 1.08 (1H, m,C-6 -CH), 1.23- 1.70 (5H, m, C-2 C-1' -CH_2 & C-4 -CH), 2.28

(2H, m, C-2' propargyl -CH_2), 4.08 (1H,dd, C-5 -CH), 7.11 (1H, m, imidazole ring =CH), 7.53 (1H, m, imidazole ring =CH), 8.17 (1H, m, imidazole ring =CH).

(2EZ,5RS,8RS)-8,9,9-Trimethyl-2-[(trimethylsilyl)methylene]spiro[4.5]dec-6-ene (20). The thiocarbonylimidazolide derivative (**19**) (300 mg, 0.77 mmol) was dissolved in dry benzene (15 ml) and brought to reflux under argon. Tri-n-butyltinhydride (0.61 ml, 2.30 mmol) and AIBN (40 mg, 0.184 mmol) in benzene (2ml) was added dropwise to the refluxing solution over 1 hour. The mixture was then allowed to reflux overnight. and worked in the usual manner. The residue was chromatographed (silica, pentane) to afford (**20**) (130 mg, 79%) as a colourless oil. ν_{max}(film) 2955, 2900, 1646, 1462, 1247, 844 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.02 (4.5H, s, $SiMe_3$), 0.03 (4.5H, s, $SiMe_3$), 0.78 (1.5H, s, C-9 Me), 0.79 (1.5H, s, C-9 Me), 0.86 (1.5H, d, J=7Hz, C-8 Me), 0.88 (1.5H, d, J = 7Hz C-8 Me), 0.91 (3H, s, C-9 Me), 1.40-1.61 (4H, m, C-4 & C-10 -CH_2), 1.86 (1H, m, C-8 allylic -CH), 2.07- 2.23 (4H, m, C-1 & C-3 allylic -CH_2), 4.84 (.5H, m, C-1' =CH), 5.01 (.5H, m, C-1' =CH), 5.22 (0.5H, t, J = 3 Hz, C-6 =CH), 5.26 (0.5H, t, J = 3 Hz, C-6 =CH), 5.39 (0.5H, d, J = 3 Hz, C-7 =CH), 5.60 (0.5H, d, J = 3 Hz, C-7 =CH); m / z 262 (M^+), 247 192, 163, 75, 73. (Observed M^+ 262.2120 $C_{17}H_{30}Si$ requires 262.2117)

3-Methoxy-5,5-dimethyl-2-(prop-2-ynyl)-cyclohex-2-enone (24). To the dione (**23**) (5.75 g, 32 mmol) dissolved in methanol (250 ml) was added trimethylorthoformate (30 ml) and conc. H_2SO_4 (2 ml). The solution was then stirred at room temperature for 6 hours. Most of the methanol was then removed *in vacuo* and the residue neutralised to pH 7 with aq. $NaHCO_3$. The mixture was then extracted with chloroform (3 x 150 ml) and the combined organic phases dried over Na_2SO_4. Removal of solvents *in vacuo* gave a yellow solid. Recrystallisation (20 % ether / petrol) afforded (**24**) (5.27g, 85 %) as colourless needle-shaped crystals (m.p. 87- 88°C). ν_{max} (solvent: $CHCl_3$) 3306, 2555, 2117, 1369, 1076, 1617 cm^{-1};δ_H (90 MHz, $CDCl_3$), 1.06 (6H, s, C-5 gem Me), 1.7 (1H, t, J = 2.8 Hz, C-3' acetylenic CH), 2.22 (2H, s, C-6 -CH_2), 2.42 (2H, s, C-4 allylic -CH_2), 3.14 (2H, d, J = 2.8 Hz, C-1' allylic / propargylic -CH_2), 3.83 (3H, s, -OMe); m / z 192, 177, 149, 145, 135 121. (Found: C 74.92, H 8.42 ; $C_{12}H_{16}O_2$ requires: C 74.97, H 8.38%)

5,5-Dimethyl-2-(prop-2-ynyl)-cyclohex-2-enone (25). Ketone (**24**) (3.64 g, 18.96 mmol) was dissolved in toluene 50 ml) and cooled to 0°C under argon. DIBAL (19.04 ml of a 1.5M solution in toluene, 28.44 mmol) was added dropwise over 10 minutes. After stirring at 0°C for 2 hours, water (15 ml) was added dropwise followed by 2M HCl (10 ml) and the mixture stirred vigorously for 30 minutes. The phases were separated and the aqueous phase extracted with ether (2 x 15 ml). The combined organic extracts were washed with aq. $NaHCO_3$ and then dried over $MgSO_4$ before removal of solvents *in vacuo*. Chromatography (silica, 40% ether / petrol)afforded (**25**) (3.40 g, 96%)as a colourless oil. ν_{max} (film) 3290, 2957, 2121, 1673, 1378cm^{-1};δ_H (270 MHz, $CDCl_3$), 1.03 (6H, s, C-5 gem Me), 2.17 (1H, s, J = 2.7 Hz, C-3' acetylenic CH), 2.31 (4H, br. s, C-4 allylic & C-6 -CH_2), 3.17 (2H, m, C-1' allylic / propargylic -CH_2), 7.01 (1H, m, C-3 alkenic =CH). (Found: C 81.37, H 8.89; $C_{11}H_{14}O$ requires: C 81.44, H 8.70 %)

5,5-Dimethyl-2-(prop-2-ynyl)-cyclohex-2-en-1-ol (26). The enone (**25**) (2.80 g, 17.28 mmol) was dissolved in toluene (50 ml) and cooled to -78°C under argon. DIBAL (11.56 ml of a 1.5M solution in toluene, 17.28 mmol) was added dropwise over 1 minute. After stirring at -78°C for 3 hours, the reaction was worked up in the usual manner. The crude material was chromatographed (silica, 30% ether / petrol)to afford (**26**) (2.61g, 92 %) as a colourless oil. ν_{max} (film)3306, 2950, 2117, 1465, 1043 cm^{-1};δ_H (270 MHz, $CDCl_3$) 0.91 (3H, s, C-5 Me), 0.99 (3H, s, C-5 Me), 1.41 (1H, dd, J = 8.8, 12.7 Hz C-6 -CH), 1.58 (1H, br. d, J = 7 Hz, -O-H), 1.74 - 1.97 (3H, m, C-4 allylic -CH_2 & C-6 -CH), 2.12 (1H, t, J = 2.7 Hz, C-3' acetylenic CH), 3.08 (2H, m, C-1' allylic / propargylic -CH_2), 4.24 (1H, b, C-1 HO-CH), 5.7 (1H, m, C-3 alkenic =CH); m/z 164 (M^+), 125, 109, 79.(Found: C 80.32, H 10.08; $C_{11}H_{16}O$ requires C 80.44, H 9.82%)

(1RS,2SR,6SR)-4,4-Dimethyl-1-(prop-2-ynyl)bicyclo[4.1.0]heptan-2-ol (27). To zinc / silver couple (4.32g, c. 72 mmol) was added allylic alcohol (**26**) (2 g, 12 mmol) and diiodomethane (1.76 ml, 72 mmol) in dry ether (40 ml). The mixture was refluxed under argon with vigorous stirring for 2 hours. On cooling to 0°C, sat. ammonium chloride solution (40 ml) was added dropwise. The two phases were separated

and the aqueous phase extracted with ether (2 x 20 ml). The combined organic phases were dried over $MgSO_4$ before removal of solvents *in vacuo*. The residue was chromatographed (silica, 40% ether / petrol) to afford (**27**) (1.68 g, 77%) as a colourless oil. ν_{max} (film) 3306, 2950, 2117, 1465, 1043 cm^{-1};δ_H (270 MHz, $CDCl_3$) 0.31 (1H, t, J=5 Hz, C-7 cyclopropyl -CH), .62 (1H, dd, J = 5, 9 Hz, C-7 cyclopropyl -CH), 0.82 (1H, m, C-6 -CH), 0.84 (3H s, C-4 Me), 0.90 (3H, s, C-4 Me), 1.05-1.20 (2H, m, C-5 -CH_2), 1.50 - 1.72 (3H, m, C-3 -CH_2 & O-H), 2.02 (1H, t, J = 2.5 Hz, C-3' acetylenic CH), 2.14 (1H, dd, J = 2.5, 17 Hz, C-1' -CH), 2.57 (1H, dd, J = 2.5, 17 Hz, C-1' -CH) 4.26(1H, m, C-2 HO- CH); m / z 178 (M^+), 163,112, 82. (Found: C 80.77, H 10.47 ; $C_{12}H_{18}O$ reqiures C 80.85, H 10.18 %)

(1RS,2SR,6SR)-4,4-Dimethyl-1-[3-(methylacetate)prop-2-ynyl]-bicyclo[4.1.0]heptan-2-ol (28). Alcohol (**27**) (1.38 g, 7.7 mmol) and diisopropylamine (1.40 ml, 8.4 mmol) were dissolved in pyridine (20 ml) and DCM (20 ml), and the mixture was cooled to 0°C under argon. Freshly distilled chlorotrimethylsilane (2.07ml, 16.3 mmol) was added and the mixture stirred at room temperature overnight. After dilution with petrol (250 ml), the mixture was washed sequentially with sat. K_2HPO_4 solution (50 ml) and water (50 ml). The combined aq. washings were back washed with petrol (2 x 25 ml) and then the combined organic phases were washed with aq. $NaHCO_3$ (50 ml) before being dried over Na_2SO_4. After removal of solvents *in vacuo*, the silyl ether (1.86 g, 7.44 mmol) was dissolved in dry THF and cooled to -78° C under argon. n-BuLi (9.38 ml of a 1.6M solution in hexanes, 15 mmol) was added dropwise and the reaction was left to stir at -78° C for 30 minutes. Methyl chloroformate (2.4 ml, 20 mmol) was then added dropwise accompanied by the removal of the cooling bath and the reaction left to warm up to room temperature over 1 hour. 2M HCl (15 ml) was added with stirring for 20 minutes before neutralisation with aq.$NaHCO_3$. The mixture was extracted with ether (3 x 20 ml) and the combined organic phases were dried over $MgSO_4$ before removal of solvents *in vacuo*. The residue was chromatographed (silica, 40% ether / petrol to afford (**28**) (1.51g, 86%) as a white waxy solid (m.p. 69°C). ν_{max} (solvent: chloroform) 3376, 2951, 223, 1713, 1255 cm^{-1}; δ_H (270 MHz, $CDCl_3$), 0.33 (1H, t, J = 5 Hz, C-7 cyclopropyl -CH), 0.63 (1H, dd, J = 5, 9 Hz, C-7 cyclopropyl -CH) 0.76 (1H, m, C-6 -CH), 0.84 (3H, s, C-4 Me), 0.91 (3H, s, C-4 Me), 1.10- 1.21 (2H, m, C5 CH_2), 1.30 (1H, br. d, J = 9 Hz, O-H), 1.55 (1H, m, C-3 -CH), 1.68 (1H, m, C-3 -CH), 2.19 (1H, d, J = 17.5 Hz, C-1' propargyl -CH), 2.88 (1H, d, J = 17.5 Hz, C-1' propargyl -CH), 3.75 (3H, s, C3' Me-ester), 4.21 (1H, m, C-2 HO-CH). (Found: C 71.40, H 8.77; $C_{14}H_{20}O_3$ reqiures C 71.16, H 8.53 %)

Attempted preparation of o-[(1RS,2SR,6SR)-4,4-dimethyl-1-[3-(methylacetate)prop-2-ynyl]-bicyclo-[4.1.0]hept-2-yl]-1-imidazole thiocarboxylate (29). Alcohol (**28**) (200 mg, .85 mmol) and N,N-thiocarbonyldiimidazole (1g, 5.5mmol)were dissolved in dry DCM (25 ml) and refluxed under argon for 36 hours. After cooling, the mixture was diluted with more DCM (25 ml) and washed sequentially with water, dilute aq. HCl, aq. $NaHCO_3$, water and brine before drying over $MgSO_4$. Removal of solvents *in vacuo* afforded (**29**) and (**39**) (294 mg, quantitative yield) as a yellow oil. ν_{max} (film) 2999, 2237, 171, 1385, 1285, 1257, 970 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.38 (0.5H, t, J = 5 Hz, C-7 cyclopropyl -CH), 0.69 (0.5H, t, J = 5 Hz, C-7 -CH), 0.80 - 1.00 (2H, m, C-6 & C-7 cyclopropyl -CH), 0.85 (1.5H, s, C-4 gem Me), 0.89 (1.5H, s, C-4 0 gem OMe), 1.03 (1.5H, s, C-4 gem Me), 1.06 (1.5H, s, C-4 gem Me), 1.25 (2H, m, C-5 -CH_2), 1.83 (1.5H, m, C-3 -CH_2), 1.97 (0.5H, m, C-3 -CH_2), 2.21 (0.5H, d, J = 17 Hz, C-1' propargyl -CH), 2.38 (0.5H, d, J = 17 Hz, C-1' propargyl -CH), 2.59 (0.5H, d, J=17 Hz, C-1' propargyl -CH), 2.94 (0.5H, d, J = 17 Hz, C-1' propargyl -CH), 3.67 (1.5H, s, C-4' -OMe), 3.74 (1.5H, s, C-4' -OMe), 4.37 (0.5H, m, C-7 O-CH), 6.28 (0.5H, m, C-7 O-CH), 7.02 (0.5H, dd, J = 1.5, 0.9 Hz, imidazole N=CH), 7.09 (0.5H, dd, J = 1.5, 0.9 Hz, imidazole N=CH), 7.44 (0.5H, t, J = 1.5 Hz, imidazole), 7.64 (0.5H, t, J = 1.5 Hz, imidazole), 8.19 (0.5H, t, J = 0.9 Hz, imidazole), 8.34 (.5H, t, J = 0.9 Hz, imidazole).

(E,Z)-Methyl-(2,3,3a,4,5,6-hexahydro-5,5-dimethyl-1H-inden-2-ylidene) acetate. (30). The thiocarbonylimidazolide derivative (**29**) (260 mg, .75 mmol) was dissolved in dry benzene (15 ml) and brought to reflux under argon. Tri-n-butyltinhydride (0.225 ml, 0.90 mmol) and AIBN (15 mg, 0.08 mmol) in benzene (5ml) were added dropwise to the refluxing solution over 2 hours. The mixture was then allowed to reflux for 5 hours. On cooling, CCl_4 (5 ml) was added with stirring for 10 minutes before removal of solvents *in vacuo*. The residue was chromatographed (silica, 5% ether / petrol) to afford (**30**) (49 mg, 30 %) as a

colourless oil. ν_{max} (film)2949, 2239, 1713, 1656, 1208, 1123 cm^{-1}; δ_H (500 MHz, $CDCl_3$): 0-.91 (3H, s, C-4 gem Me), 0.97 (3H, s, C-4 gem Me), 1.68 (1H, m, C-5 homoallylic -CH_2), 1.76 (1H, m, C-5 homoallylic -CH_2), 1.89 (1H, m, C-5 allyli -CH_2), 2.15 (1H, m, C-5 allylic -CH_2), 2.44 (1.5H, m, C-6 allylic & C-7 allylic -CH), 2.72 (0.5H, dd, J = 7.6, 16 Hz, C-7 allylic -CH_2), 3.07 (0.5H, m, C-7 allylic -CH_2), 3.21 (0.5H, m, C-7 allylic -CH_2), 3.45 (2H, br. s, C-9 allylic), 3.68 (1.5H, s, C-2 -OMe), 3.69 (1.5H, s, C-2' -OMe), 5.40 (0.5H, m, C-2 alkenic -CH_2), 5.44 (0.5H, m, C-2 alkenic -CH_2), 5.77 (0.5H, m, C-1' alkenic -CH_2), 5.81 (.5H, m, C-1' alkenic -CH_2); m / z 220 (M^+), 205, 189, 164, 105. (Found: C 76.17, H 9.15; $C_{14}H_{20}O_2$ requires C 76.33, H 9.15 %)

o-[(1RS,2SR,6SR)-4,4-Dimethyl-1-(prop-2-ynyl)-1-imidazole thiocarboxylate (35). Alcohol **(26)** (50mg, 0.28 mmol) and 1,1'-thiocarbonyldiimidazole (300 mg, 1.65 mmol) were dissolved in dry DCM (8 ml) and refluxed under argon for 18 hours. After cooling, the mixture was diluted with more DCM (15 ml) and washed sequentially with water, dilute aq. HCl, aq. $NaHCO_3$, water and brine before drying over $MgSO_4$. Removal of solvents *in vacuo* afforded **(39)** (81 mg, quantiative yield) as a yellow oil. ν_{max} (film) 3122, 2951, 2118, 1688, 1216, 887 cm^{-1}; δ_H (270 MHz, $CDCl_3$), 0.30 (1H, t, J = 5 Hz C-7 cyclopropyl), 0.72 (1H, dd, J=9Hz, C-7 cyclopropyl), 0.84 (3H, s, C-4 gem Me), 1.03 (3H, s, C-4 gem Me), 1.12-1.26 (3H, m C-5 -CH_2 & C-6 -CH), 1.72 - 1.8 (2H, m, C-3 -CH_2), 1.93 (1H, dd, J = 17, 2.7 Hz, C-1 propargyl -CH), 2.02 (1H, t, J=2.7Hz, C-3' acetylenic CH), 2.82 1H, dd, J = 17, 2.7 Hz, C-1' propargyl -CH), 4.42 (1H, dd, J = 12.6 Hz, C-10 -CH), 7.04 (1H, dd, J = 1.5, 0.9 Hz imidazole), 7.42 (1H, t, J = 1.5 Hz, imidazole), 8.15 (1H, t, J = 0.9 Hz, imidazole).

(1RS,2SR,6SR)-4,4-Dimethyl-1-[3-(methylacetate)-prop-2-ynyl]-bicyclo[4.1.0]heptan-2-thiol (34) Thiocarbonylimidazolide derivative **(35)** (53 mg, 0.15 mmol) was dissolved in THF (2 ml) and this solution was added to 2M aq. HCl (2 ml). The resultant mixture was heated with stirring at 50°C for 3 hours. On cooling, the mixture was extracted with DCM (3 x 1 ml). The combined organic extracts were dried over $MgSO_4$ before removal of solvents *in vacuo* to afford a yellow oil, characterised as a mixture of **(34)** and its corresponding disulphide. ν_{max} (film) 2951, 2925, 2236, 1713, 1255, 1034 cm^{-1};δ_H (270 MHz, $CDCl_3$) 0.22 (1H, t , J=5.3Hz, C-7 cyclopropyl -CH) 0.62 (1H, dd, J = 9, 5.3 Hz, C-7 cyclopropyl -CH), 0.82 (3H, s, C-4 Me), 0.93 (3H, s, C-4 Me), 1.20 - 1.31 (2H, m, C-5 & C-6 -CH), 1.37 (1H, d, J = 8.8 Hz, C-5 -CH), 1.70 (2H, m, C-3 -CH_2), 2.04 (1H, d, J = 17.5 Hz, C-1' propargyl -CH), 3.13 (1H, d, J = 17.5 Hz, C-1' propargyl -CH), 3.35 (1H, m, C-2 S-C-H), 3.75 (3H, s, C-4' -OMe); m / z 502 (M^+ of disulphide), 470, 443, 431, 300, 284, 268, 252 (M^+ of thiol). (Observed M^+: 502.2200; $C_{28}H_{38}O_4S_2$ requires 502.2211)

(1RS,2SR,6SR)-4,4-Dimethyl-1-(prop-2-ynyl)-bicyclo[4.1.0]heptan-2-thiol (36). Thiocarbonylimidazolide derivative **(39)** (81 mg, 0.28 mmol) was dissolved in THF (4 ml) and this solution was added to 2M aq. HCl (4 ml). The resultant mixture was heated at 50°C with stirring for 30 minutes. On cooling, the mixture was extracted with DCM (3 x 2.5 ml). The combined organic extracts were dried over $MgSO_4$ before removal of solvents *in vacuo* to afford **(36)** as a yellow oil. ν_{max} (film) 3302, 2950, 2922, 2117, 1460, 637 cm^{-1}; δ_H (270MHz, $CDCl_3$) 0.017 (1H, t, J = 5.3 Hz, C-7 cyclopropyl -CH), 0.60 (1H, dd, J = 9, 5.3 Hz, C-7 cyclopropyl -CH), 0.82 (3H, s, C- Me), 0.93 (3H, s, C-4 Me), 1.10-1.25 (3H, C-5 & C-6 -CH & S-H), 1.37 (1H, d, J=8.5Hz, C-5 -CH), 1.74 (2H, m, C-3 -CH_2), 1.86 (1H, dd, J = 17.5, 2.7 Hz, C-1' propargyl -CH), 1.96 (1H, t, J= 2.7 Hz, C-3' acetylenic CH), 2.96 (1H, dd, J = 17.5, 2.7 Hz, C-1' propargyl -CH), 3.42 (1H, m, C-2 S-C-H); m/z 194, 181, 161, 105, 98. (Observed M^+: 194.1130; $C_{12}H_{18}S$ requires 194.1129)

(1S,2R,4R,6R)-1-methyl-4-isoropenylbicyclo[4.1.0]heptan-2-ol (41). To zinc / silver couple (19.68g, c. 324 mmol) was added diiodomethane (14 ml, 162 mmol) in dry ether (100 ml). The mixture was refluxed under argon with vigorous stirring for 40 minutes. (-)-cis carveol **(40)** (10 g, 66 mmol) was added dropwise and refluxing continued for a further 2.5 hours. On cooling to 0°C, sat. ammonium chloride solution (100 ml) was added dropwise. The two phases were separated and the aqueous phase extracted with ether (2 x 50 ml). The combined organic phases were dried over $MgSO_4$ before removal of solvents *in vacuo*. The

residue was chromatographed (silica, 30% ether / petrol)to afford **(41)** (9.06 g, 83%) as a white waxy solid; $[\alpha]_D^{20}$ = 40.2° (c = 1.0, $CHCl_3$). ν_{max} (Solvent: chloroform) 3591, 3451, 2935, 1640, 1033, 894 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.33 (1H, t, J = 5 Hz, C-7 cyclopropyl -CH), 0.44 1H, dd, J = 5, 9 Hz, C-7 cyclopropyl -CH), 0.84 (1H, m, C-5 -CH), 0.96 (1H, m, C-6 -CH), 1.18 (3H, s, C-1 Me), 1.43 (2H, m, O-H, C-5 -CH), 1.67 (3H, m, C-1' allylic Me), 1.69- 1.95 (2H, m, C-3 -CH_2), 2.05 (1H, m, C-4 allylic =CH), 3.91 (1H, m, C-2 -CH), 4.63 (2H, m, C-2' alkenic =CH_2); m / z 166 (M^+), 148, 107, 98, 69 (Found: C 79.41, H 11.13; $C_{11}H_{18}O$ requires: C 79.47, H 11.13%)

(1S,2R,4R,6R)-4-Acetyl-1-methylbicyclo[4.1.0]heptan-2-ol (42). Alcohol **(41)** (5 g, 30 mmol) was dissolved in methanol (200 ml), cooled to -78°C and a stream of O_2 / O_3 was passed through the solution for 8 hours. After the solution had been purged of O_3 with a stream of O_2 only, triphenylphosphine (11.36 g, 43mmol) was added and the mixture stirred at room temperature overnight. Solvents were removed *in vacuo* and the residue chromatographed (silica, 50 % ether / petrol) to afford **(42)** (5.95 g, 90%) as a colourless oil; $[\alpha]_D^{20}$ = -60.2° (c = 1.0, $CHCl_3$).ν_{max} (film) 3399, 2945, 1702, 1039 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.36 (1H, t, J = 5 Hz, C-7 cyclopropyl -CH), 0.49 (1H, dd, J = 5, 8.8 Hz, C-7 cyclopropyl -CH), 0.83 - 1.05 (2H, m, C-5 & C-6 -CH), 1.98 (1H, ddt, J = 2.2, 5.5, 5.7 Hz, C-4 -CH), 2.11 (3H, C-2' Me), 2.17 (1H, m, C-3 -CH), 2.31 (1H, m, C-3 -CH), 4.93 (1H, m, C-2 -CH; m / z 168 (M^+), 107, 71, 43.(Found: C 71.24, H 9.66; $C_{10}H_{16}O_2$ requires C 71.39, H 9.59%)

(1S,2R,4R(2EZ),6R)-1-methyl-4-(isopropenyl-2-ethylester)-bicyclo[4.1.0]hept an-2-ol (43). DME (20 ml)was added to sodium hydride (260 mg of a 60% dispersion in oil, 6.53 mmol) under argon. Triethylphosphonoacetate (1.3 ml, 6.53 mmol) was added dropwise with stirring over 20 minutes and after a further 40 minutes, alcohol **(42)** (1 g, 5.97 mmol) was added. The mixture was then stirred at room temperature for 1 hour and at reflux for 1.5 hours. On cooling, water (150 ml) was added and the mixture was extracted with ether (3 x 50 ml). The combined organic extracts were dried over $MgSO_4$ before removal of solvents *in vacuo*. The residue was chromatographed (silica, 40% ether / petrol) to afford **(43)** (863 mg, 61 %) as a low melting point white waxy solid. ν_{max}, film) 3411, 2934, 1710, 1639, 1212, 1150, 1038 cm^{-1}; δ_H (270 MHz, $CDCl_3$), 0.25 ($^1/_6$H, dd, J = 5, 9.1 Hz, C-7 cyclopropyl -CH of Z isomer), 0.34 ($^5/_6$H, t, J = 5Hz, C-7 cyclopropyl -CH of E isomer), 0.42 ($^5/_6$H, dd, J = 5, 9.1 Hz, C-7 cyclopropyl -CH E isomer), 0.52 ($^1/_6$H, t, J=5Hz, C-7 cyclopropyl -CH of Z isomer), 0.80 - 1.10 (3H, m, C-5 -CH_2 & C-6 -CH), 1.15 (3H, s, C-1 Me), 1.21 (3H, t, J = 7 Hz, C-5' Me), 1.72 (1H, m, C-4 -CH), 1.82 (1H, b, O-H), 1.84 - 2.05 (2H, m, C-3 -CH_2), 2.04 ($^5/_6$H,J = 1Hz, C-1' allylic Me- of E isomer), 2.08 ($^1/_6$H, d,J = 1Hz, C-1' allylic Me- of Z isomer), 3.87 ($^5/_6$H, m, C-2 -CH of E isomer), 3.97 ($^1/_6$H, m C-2 -CH of Z isomer), 4.09 (2H, q, J = 7 Hz, C-4' -CH_2), 5.56 ($^5/_6$H, m, C-2' =CH of E isomer), 5.62 ($^1/_6$H, m, C-2'=CH of Z isomer); (Found: C 70.27, H 9.29: $C_{14}H_{23}O_3$ requires: C 70.56, H 9.30 %)

o-[(1S,2R,4R(2EZ),6R)-1-methyl-4-(isopropenyl-2-ethylester)-bicyclo[4.1.0]hept-2yl]1-imidazole thiocarboxylate (44). Alcohol **(43)** (500 mg, 2.1 mmol) and N,N-thiocarbonyl-diimidazole (1.5 g, 8.2 mmol) were dissolved in dry DCM (25 ml) and refluxed under argon for 18 hours. After cooling, the mixture was diluted with more DCM (25 ml) and washed sequentially with water, dilute aq. HCl, aq. $NaHCO_3$, water and brine before drying over $MgSO_4$. Removal of solvent *in vacuo* afforded **(44)** (660 mg, 91 %). ν_{max} (film) 3122, 2940, 2876, 1688, 1638, 1465, 1363, 1270, 1215, 1150, 886 cm^{-1} ;δ_H (270 MHz, $CDCl_3$): 0.41 ($^5/_6$H, t, J=5Hz, C-7 cyclopropyl -CH of E isomer), 0.50 ($^2/_6$H m, C-7 cyclopropyl -CH_2 of Z isomer), 0.64 ($^5/_6$, dd, J=5, 9.1 Hz , C-7 cyclopropyl -CH of E isomer), 0.80 - 1.15 (3H, m, C-5 -CH_2 & C-6 -CH), 1.23 (3H, s, C-1 Me), 1.25 (3H, t, J = 7.1 Hz, C-5' Me), 1.80 - 2.05 (3H, m, C- -CH_2 & C-4-CH), 2.10 ($^5/_6$H, d, J = 1Hz, C-1' allylic Me of E isomer), 2.16 ($^1/_6$H, d, J = 1Hz, C-1' allylic Me of Z isomer), 4.11 (1H, m, C-2 -CH of E isomer), 4.12 (2H, q, J = 7.1 Hz, C-4' -CH_2), 5.59 ($^5/_6$H, m, C-2' =CH of E isomer), 5.60 ($^1/_6$H, m, C-2' =CH of Z isomer); 7.09 (1H, dd, J = 1.5, 1 Hz, imidazole N=CH), 7.46 ($^5/_6$H, pt, J = 1.5, imidazole N=CH of E isomer), 7.48 ($^1/_6$H, pt, J = 1.5, imidazole N=CH of Z isomer), 8.19 ($^5/_6$H, pt, J = 1 Hz, imidazole N=CH of E isomer), 8.21 ($^1/_6$H, pt, J = 1 Hz, imidazole N=CH of Z isomer).

(4R(2E),6R)-1,6-Dimethyl-4-(isopropenyl-2-ethylester)cyclohex-1-ene (45) and 7,9-

Dimethyl-6-ethylester-tricyclo[3.3.1.0^{3,7}]nonanes (46) The thiocarbonyl-imidazolide derivative (**69**) (650 mg, 1.86mmol) dissolved in dry benzene (20 ml) and brought to reflux under argon. Tri-n-butyltinhydride (540 ml, 2 mmol) and AIBN (42 mg, 0.25 mmol) in benzene (10 ml) was added dropwise via a syringe pump to the refluxing solution over 6 hours. The mixture was then allowed to reflux for 6 hours. On cooling, CCl_4 (5 ml) was added with stirring for 10 minutes before removal of solvents *in vacuo*. The residue was chromatographed (silica, 5% ether / petrol to afford two major products. (**45**) (95 mg, 23 %). ν_{max} (film) 2926, 1713, 1639, 1443, 1367, 1148 cm^{-1}; δ_H (270 MHz, $CDCl_3$), 0.80- 1.10 (2H, m, -CH_2), 1.15 (2H, d, J = 6Hz, Me), 1.21 (3H, t, J = 7 Hz Me-CH_2-C(O)O), 1.45 - 2.05 (4H, m, 3 allylic protons & Me-C-H), 2.11 (3H, br. s, allylic Me), 2.17 (3H, br. s, allylic Me), 4.09 (2H, q, J = 7 Hz, Me-CH_2-C(O)O), 5.02 (1H, m, alkenic =CH), 5.64 (1H, m, alkenic =CH of α, β unsat. ester); m / z 222, 176, 149, 134, 94, 79. (Observed M$^+$ 222.1625; $C_{14}H_{22}O_2$ requires 222.1620); and (**46**) (198 mg, 48%). ν_{max} 2934, 2868, 1729, 1455, 1377, 1174 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 0.88, 0.99, 1.02 (3H, d, J = 5 Hz, C-9 Me), 1.25 (3H, t, J = 7 Hz, Me-CH_2-C(O)O), 1.26 (3H, s, Me), 1.4-2.7 (11H, m), 4.08 (2H, m, Me-CH_2-C(O)O); m / z 222, 207, 193, 176, 149, 93. (Observed M$^+$ 222.1623; $C_{14}H_{22}O_2$ requires 222.1621)

Preparation of (1R*, 2R*)-2-nonylcyclopropane-methanol (50, X=OH). Zinc powder (13.0 g, 199 mmol) was added to a stirred solution of silver acetate (250 mg, 1.50 mmol) in acetic acid (100 ml) at 80°C. The mixture was stirred for 2 minutes and the solvent decanted. The zinc-silver couple thus formed was washed with acetic acid (50 ml) and several portions of ether (each 100 ml) until no smell of acetic acid remained. Freshly distilled ether (120 ml) and diiodomethane (9.0 ml, 112 mmol) were slowly added to the couple and the mixture heated to reflux. A solution of the allylic alcohol (72) (6.65 g, 36.1 mmol) in ether (30 ml) was then added and the mixture vigorously stirred at reflux for 2.5 hours until no starting material remained. Saturated aqueous NH_4Cl solution was then added dropwise very cautiously to quench the reaction mixture. The solution was decanted from the zinc (washed with 50 ml of ether), the organic layer separated and the aqueous phase extracted again with ether (150 ml). The combined organic layers were washed with brine (100 ml), dried over Na_2SO_4, filtered and the solvent removed *in vacuo*. Column chromatography (15-30% ether / petrol, silica) yielded (**50, X=OH**) (5.26 g, 73%) as a colourless oil. ν_{max} (film) 3330 (br s), 3062, 2922, 2852, 1465, 1031 cm^{-1}; δH (270 MHz, $CDCl_3$) 3.41 (2H, m, 2 x H-α), 1.62 (1H, br s, OH), 1.37-1.11 (16H, m, CH_2 envelope), 0.86 (3H, t, J=6.6 Hz, CH_3), 0.80 (1H, m), 0.56 (1H, m), 0.37-0.24 (2H, m) (total 4H, cyclopropyl H's); m/z 198 (M$^+$), 180 (M$^+$-H_2O), 157, 97, 83. Found: C 78.56, H, 13.37%; $C_{13}H_{26}O$ requires: C 78.72, H 13.21%.

Preparation of (1R*, 2R*)-1-chloromethyl-2-nonylcyclopropane (50, X=Cl). Alcohol (73) (936 mg, 4.73 mmol), triphenylphosphine (1.60 g, 6.10 mmol) and distilled carbon tetrachloride (15 ml) were refluxed under argon for 20 hours. After cooling to room temperature, petrol (20 ml) was added and the mixture filtered through a silica plug. Removal of the solvent *in vacuo* followed by column chromatography (petrol, silica) yielded (**50, X=Cl**) (920 mg, 90%) as a clear oil; ν_{max} (film) 3066, 2926, 2853, 1463, 1405, 1377, 1262, 1194, 1028, 862, 703 cm^{-1}; δ_H (270 MHz, $CDCl_3$) 3.47 (1H, dd, J=11.0, 7.3 Hz, H-1'), 3.38 (1H, dd, J=11.0, 7.8 Hz, H-1'), 1.26 (16H, m, CH_2 envelope), 0.91 (1H, m, cyclopropyl H), 0.88 (3H, t, J=6.6 Hz, terminal CH_3), 0.70 (1H, m), 0.47 (2H, m) [total 3H, cyclopropyl H's]; m/z 218 / 216 (M$^+$), 190 / 188 (M$^+$-H_2O), 180 (M$^+$-HCl), 176 / 174, 97, 83. Found: C 72.20, H, 11.91%; $C_{13}H_{25}Cl$ requires: C 72.02, H, 11.62%.

Preparation of (1R*, 2R*)-1-bromomethyl-2-nonylcyclopropane (50, X=Br). Alcohol (73) (2.19 g, 11.1 mmol) and triphenylphosphine (3.10 g, 11.8 mmol) were stirred together in dry distilled dimethylformamide (25 ml). Bromine was added dropwise until 2 drops produced a stable orange coloration. The reaction mixture was poured into cold water and extracted with pentane (3 x 100 ml). The combined organic extracts were washed with water (100 ml), brine (100 ml), dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. Column chromatography (petrol, silica) yielded (**50, X=Br**) (2.40 g, 83%) as a straw-coloured oil. ν_{max} (film) 3066, 2995, 2923, 2853, 1463, 1437, 1376, 1219, 1027 cm^{-1}; δH (270 MHz, $CDCl_3$) 3.37 (1H, dd, J=10.0, 7.6 Hz, H-1'), 3.29 (1H, dd, J=10.1, 8.0 Hz, H-1'), 1.37-1.13 (16H, m,

CH_2 envelope), 1.01 (1H, m, cyclopropyl H), 0.88 (3H, t, J=6.7 Hz, CH_3), 0.71 (1H, m), 0.51 (2H, m) [total 3H, cyclopropyl H's]; m/z 262 / 260 (M^+), 125, 111, 97, 83. Observed (M^+): 260.1140; $C_{13}H_{25}Br$ requires 260.1147.

Preparation of (1R*, 2R*)-2-nonyl-1-phenylselenomethylcyclopropane (50, X=SePh). Alcohol (73) (530 mg, 2.68 mmol), tributylphosphine (1.70 g, 8.40 mmol) and N-(phenylseleno)phthalimide (1.66 g, 5.53 mmol) in dry distilled THF (20 ml) were refluxed under argon for 18 hours. The reaction mixture was added to saturated $NaHCO_3$ solution (25 ml) and extracted with dichloromethane (2 x 50 ml). The combined organic layers were dried over $MgSO_4$ and the solvent removed *in vacuo*. Column chromatography (30-40 petrol, silica - columned twice to remove all traces of diphenyl diselenide) yielded **(50, X=SePh)** (389 mg, 43 %) as a pale yellow oil. ν_{max} (film) 3059, 2922, 2851, 1576, 1475, 1201, 1023, 734, 690 cm^{-1}; δH (270 MHz, $CDCl_3$) 7.53-7.47 (2H, m, Ph), 7.28-7.20 (3H, m, Ph), 2.91 (1H, dd, J=11.7, 7.1 Hz, H-1'), 2.84 (1H, dd, J=12.0, 7.6 Hz, H-1'), 1.33-1.11 (16H, m, CH_2 envelope), 0.88 (3H, t, J=6.6 Hz, terminal CH_3), 0.79 (1H, m), 0.57 (1H, m), 0.36 (2H, m) [total 4H, cyclopropyl H's]; m/z 338 (M^+), 158, 97, 83, 69. Observed (M^+): 338.1512; $C_{19}H_{30}Se$ requires 338.1513.

Preparation of S-methyl O-[(1R*, 2R*)-2-nonylcycloprop-1-yl]methyl dithiocarbonate (50, X=OCSSMe). Sodium hydride (60% dispersion in oil, 420 mg, 10.5 mmol) and a spatula tip of imidazole were stirred under argon in dry, freshly distilled tetrahydrofuran (10 ml). A solution of the alcohol (460 mg, 2.32 mmol) in dry tetrahydrofuran (20 ml) was added and the solution refluxed for 2 hours. Carbon disulphide (2.00 ml, 33.4 mmol) was carefully added and the solution refluxed for 0.5 hours. Finally, iodomethane (2.00 ml, 32.1 mmol) was added and the solution stirred under reflux for a further 2.5 hours. After cooling to room temperature, acetic acid (4 ml) then water (20 ml) were added. The mixture was extracted with dichloromethane (3 x 30 ml) and the combined organic extracts washed with saturated aqueous $NaHCO_3$ solution (30 ml), brine (30 ml) and dried over $MgSO_4$. After removal of the solvent *in vacuo*, column chromatography (petrol, silica) yielded **(50, X=OCSSMe)** (567 mg, 85%) as a yellow oil. ν_{max} (film) 3066, 2996, 2922, 2851, 1462, 1218, 1057 cm^{-1}; δH (270 MHz, $CDCl_3$) 4.48 (1H, dd, J=11.4, 7.2 Hz, H-1'), 4.39 (1H, dd, J=11.3, 7.7 Hz, H-1'), 2.55 (3H, s, SCH_3), 1.35-1.13 (16H, m, CH_2 envelope), 1.01 (1H, m, cyclopropyl H), 0.88 (3H, t, J=6.5 Hz, terminal CH_3), 0.73 (1H, m, cyclopropyl H), 0.50 (1H, dt, J=8.5, 4.6 Hz, H-3"), 0.42 (1H, dt, J=8.0, 5.1 Hz, H-3"); m/z 288 (M^+), 273 (M^+-Me), 241 (M^+-SMe), 97, 83, 69. Observed (M^+): 288.1581; $C_{15}H_{28}OS_2$ requires 288.1582.

Preparation of 3-methyldodec-1-ene (52). To a stirred suspension of methyltriphenylphosphonium bromide (4.31 g, 12.1 mmol) in ether (100 ml) at 0°C was added butyllithium (2.5 M in hexanes, 5.40 ml, 12.1 mmol). The reaction mixture was stirred for 30 minutes (with the formation of a bright yellow coloration) and a solution of the aldehyde (85) (2.50 g, 13.6 mmol) in ether (10 ml) was added dropwise *via* cannula. After stirring for 1 hour, the solution was allowed to warm to room temperature and stirred, at room temperature, for 2 hours. The solution was diluted with petrol (200 ml) and filtered through a silica pad. Column chromatography (petrol, silica) yielded **(52)** (1.45 g, 59%) as a colourless oil. ν_{max} (film) 3076, 2957, 2924, 2854, 1821, 1638, 1465, 1374, 993, 909 cm^{-1}; δH (270 MHz, $CDCl_3$) 5.70 (1H, ddd, J=17.7, 9.8, 7.6 Hz, H-2), 4.94 (1H, ddd, J=17.3, 2.1, 1.1 Hz, H-1), 4.89 (1H, ddd, J=10.2, 1.9, 1.0 Hz, H-1), 2.10 (1H, m, H-3), 1.35-1.01 (16H, CH_2 envelope), 0.98 (3H, d, J=6.8 Hz, C-3-CH_3), 0.88 (3H, m, terminal CH_3); m/z, 182 (M^+), 153 (M^+-Et), 126, 111, 97, 83. Observed (M^+): 182.2031; $C_{13}H_{26}$ requires 182.2035.

Tri-n-butylstannane reductions of (50)

Method A (typical experiment).

To a refluxing solution of precursor (0.55 mmol) in dry, freshly distilled benzene (20.0 ml) was added *via* syringe pump a degassed solution of tributylstannane (0.300 ml, 1.12 mmol) and AIBN (35 mg, 0.18 mmol) in benzene (2.0 ml) over 1 hour. After refluxing for a further 12 hours, carbon tetrachloride (5 ml) was added to the cooled solution, followed by a solution of iodine in ether, until a yellow colouration persisted. A solution of saturated aqueous potassium fluoride (20 ml) was added, and the mixture stirred for several hours. Separation of the organic phase was followed by extraction of the aqueous layer with ether (30 ml). The

combined organic extracts were dried over $MgSO_4$ and the solvent cautiously removed in vacuo at 0°C. GC analysis of the product distribution was carried out directly after column chromatography (30-40 petrol, $AgNO_3$ impregnated silica).

Method B (typical experiment).

To a refluxing solution of tributylstannane (0.920 ml, 3.42 mmol) in dry, freshly distilled benzene (1.0 ml), was added via syringe pump a degassed solution of precursor (0.52 mmol) and AIBN (40 mg, 0.24 mmol) in benzene (2.0 ml) over a period of 15 hours. After refluxing for a further 4 hours, carbon tetrachloride (5 ml) was added to the cooled solution, followed by a solution of iodine in ether, until a yellow colouration persisted. A solution of saturated aqueous potassium fluoride (20 ml) was added, and the mixture stirred for several hours. Separation of the organic phase was followed by extraction of the aqueous layer with ether (30 ml). The combined organic extracts were dried over $MgSO_4$ and the solvent cautiously removed in vacuo at 0°C. GC analysis of the product distribution was either carried out at this stage or directly after column chromatography (30-40 petrol, $AgNO_3$ impregnated silica).

Method C (typical experiment).

A mixture of precursor (0.388 mmol), tributylstannane (0.125 ml, 0.465 mmol) and a spatula tip of AIBN were heated without solvent at 45°C under argon overnight. After cooling to room temperature, carbon tetrachloride (3 ml) was added, followed by a solution of iodine in ether until a yellow colouration persisted. A solution of saturated aqueous potassium fluoride (10 ml) was added and the mixture stirred for several hours. Separation of the organic phase was followed by extraction of the aqueous layer with ether (20 ml). The combined organic extracts were dried over $MgSO_4$, filtered, and the solvent cautiously removed in vacuo at 0°C. GC analysis of the product distribution was either carried out at this stage or directly after column chromatography (30-40 petrol, $AgNO_3$ impregnated silica).

Method D (typical experiment).

A solution of tributylstannane (900 ml, 3.35 mmol) in dry, freshly distilled benzene (1.0 ml) was thoroughly degassed with argon and stirred at 45°C under argon. To this solution was added *via* syringe pump a degassed solution of precursor (0.520 mmol) and AIBN (25 mg, 0.15 mmol) in benzene (2.0 ml) over a period of 15 hours. After heating at 45°C for a further 6 hours, carbon tetrachloride (5 ml) was added, followed by a solution of iodine in ether until a yellow colouration persisted. A solution of saturated aqueous potassium fluoride (20ml) was added and the mixture stirred for several hours. Separation of the organic phase was followed by extraction of the aqueous layer with ether (30 ml). The combined organic extracts were dried over $MgSO_4$ and the solvent cautiously removed in vacuo at 0°C. GC analysis of the product distribution was either carried out at this stage or directly after column chromatography (30-40 petrol, $AgNO_3$ impregnated silica).

Method E (typical experiment).

A solution of precursor (0.33 mmol), tributylstannane (0.500 ml, 1.86 mmol) and bistriphenyltin (50 mg, 0.071 mmol) in dry, freshly distilled toluene (0.50 ml) was thoroughly degassed with argon. The reaction mixture was cooled to -78°C under argon and was irradiated overnight (from above at an angle of 45°, d = 10 cm) using a 600 W tungsten lamp, thus allowing the reaction mixture to warm gradually to room temperature, over 6-8 hours. Carbon tetrachloride (5 ml) was added, followed by a solution of iodine in ether until a yellow colouration persisted. A solution of saturated aqueous potassium fluoride (20 ml) was added and the mixture stirred for several hours. Separation of the organic phase was followed by extraction of the aqueous layer with ether (30 ml). The combined organic extracts were dried over $MgSO_4$ and the solvent cautiously removed in vacuo at 0°C. GC analysis of the product distribution was then carried out.

Acknowledgement : We are grateful to the SERC and Quest International for the provision of studentships (to R.A.B and J.D.H) under the CASE scheme.

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