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THE STEREOCHEMISTRY OF THE INTRAMOLECULAR ELECTROPHILIC ATTACK OF AN ALDEHYDE ON A CARBON-TIN BOND†

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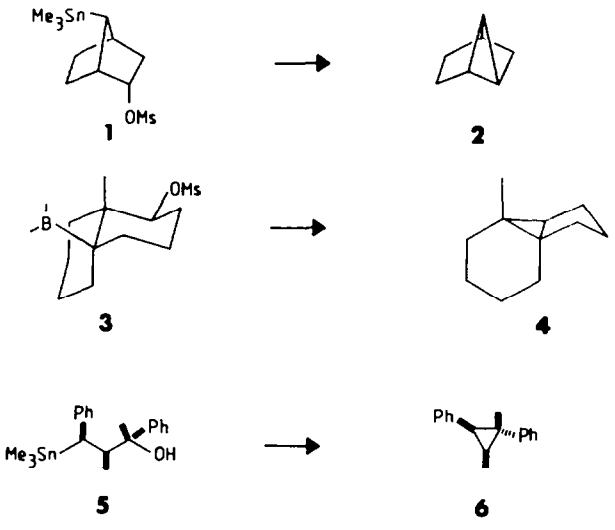
Abstract-The cyclopentane-forming reaction (20 - 43) of (4RS,5SR)-2,2,4-trimethyl-5-trimethylstannylhexanal takes place with retention of configuration at the carbon atom undergoing electrophilic substitution, in contrast to similar cyclopropane-forming reactions (e.g. 47 - 48), which take place with inversion of configuration. The hydride transfer (24 - 45) of the 4RS,5RS diastereoisomeric hexanal takes place from a conformation with hydride anti to the stannyl group. In the case of reactions which might have formed four-membered rings, fragmentation takes place (16 - 28 and 17 - 30). The presence of a phenyl ring on the carbon carrying the stannyl group interferes with the reactions designed to test the stereochemistry of the S_E2 reaction, diverting the reaction to the formation of tetralins (10 - 26 and 34 - 38) or benzcycloheptenes (34 - 37).

The stereochemistry of electrophilic substitution at saturated carbon takes place sometimes with retention of configuration and sometimes with inversion of configuration. It is clearly of interest to understand what factors affect whether retention or inversion shall be observed. The factor most obviously of importance is the nature of the electrophile, bromo-demetallation, for example, taking place quite frequently with inversion of configuration, and proto-demetallation taking place almost always with retention of configuration.[1] Organometallic carbon nucleophiles generally react with carbon electrophiles with retention of configuration,[2] but the number of known examples is still quite small, largely because it has been difficult to prepare organometallic carbon nucleophiles in a stereodefined state. The only examples in which a carbon electrophile induces inversion of configuration are those reactions in which a three membered ring is being formed, when inversion of configuration has been observed both at the nucleophilic and at the electrophilic carbon atoms. Thus it has been known for some years that the cyclopropane-forming reactions (1 - 2)[3] and (3 - 4)[4] follow this pattern, and in the former case it is known that the other three stereoisomers do not cyclise. More recently, we have shown that open-chain 3-stannylalcohols regularly cyclise (5 - 6) with clean inversion of configuration at the tin-bearing carbon (and usually with a high degree of inversion of configuration at the oxygen-bearing carbon too).[5] Thus we showed that this type of reaction can properly be called stereospecific in the Zimmerman sense,[6] and more recently still, Johnson and Kadow[7] have supplied even more examples, extending considerably the scope of this cyclopropane synthesis. Nevertheless, there remains the anomaly that in this reaction a carbon-

†No reprints available.

Dedicated to Professor R.A. Raphael for his 65th birthday.

tin bond is attacked by a carbon electrophile with inversion of configuration, whereas all other known reactions of carbon-metal bonds with carbon electrophiles take place with retention of configuration.



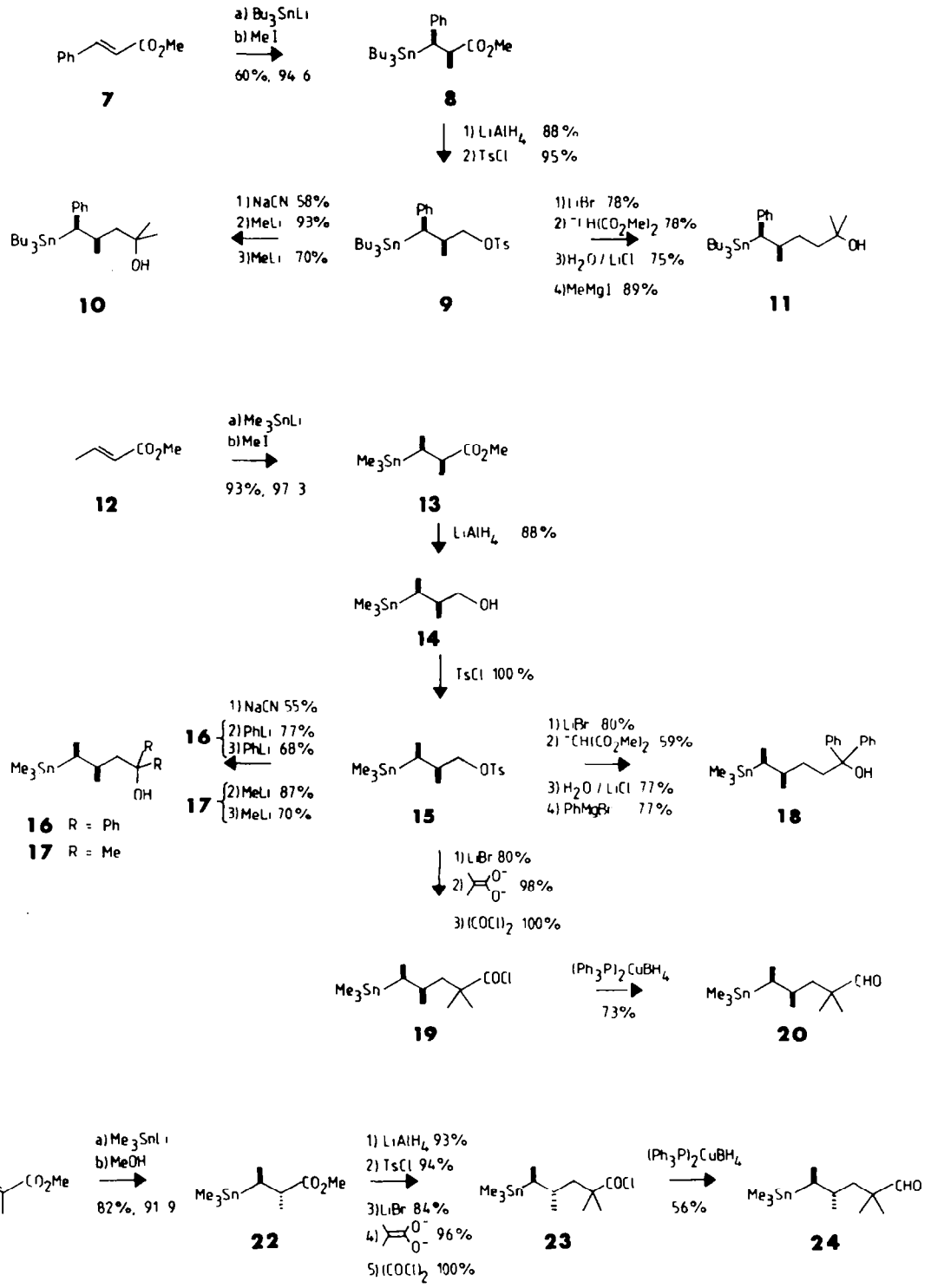
To address this problem, we have studied comparable reactions which might form four-membered rings and five-membered rings. We met a number of problems in this work, but eventually secured one reaction (Scheme 7), in which a five-membered ring was formed cleanly with a high degree of retention of configuration at the tin-bearing carbon.

We report this work in full now, having reported only the successful reaction in a preliminary communication.[8] The unusual inversion of configuration found in cyclopropane-formation remains anomalous. It is perhaps relevant that the reverse reaction, the electrophilic opening of cyclopropanes, takes place sometimes with inversion and sometimes with retention of configuration at the carbon atom undergoing the electrophilic attack.[9]

RESULTS AND DISCUSSION

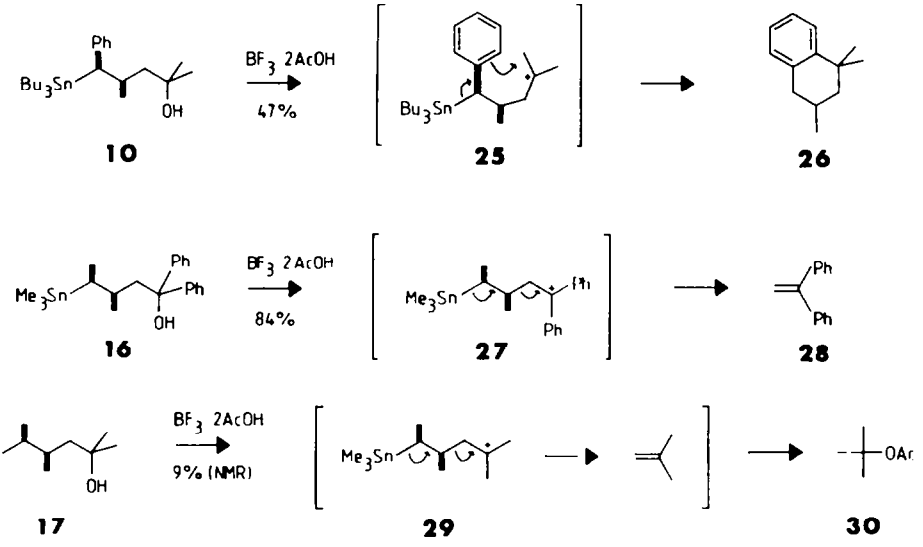
Synthesis and Attempted Cyclisations. The key to all our work is the highly diastereoselective alkylation of β-stannyl enolates,[5] typifed by the reaction (7 - 8). This reaction has given us easy access to stereodefined tin-containing compounds, and is based on our earlier observation of similar diastereoselectivity with β-silyl enolates.[10] More recently, this high diastereoselectivity in the tin series has been confirmed by McGarvey and Williams.[11] Using this type of reaction, we prepared the tertiary alcohols (10, 11, 16, 17, and 18), the acid chlorides (19 and 23), and the aldehydes (20 and 24), as shown in Scheme 1. In each case, we tried to cyclise these products, and our results are summarised in Schemes 2, 4 and 7. The reactions in Schemes 2 and 4 failed to give us the information we sought.

We tried to form cyclobutanes first (Scheme 2). The alcohol (10) cyclised, but by attack on the ortho position of the benzene ring (25), giving the tetralin (26). We proved the structure of this product by an alternative synthesis, described in the experimental section. The tertiary alohol (16) underwent fragmentation (27), with formation of α-phenylstyrene (28) in good yield. The alcohol (17) also underwent fragmentation (29), as judged by the appearence in the ^{1}H-NMR

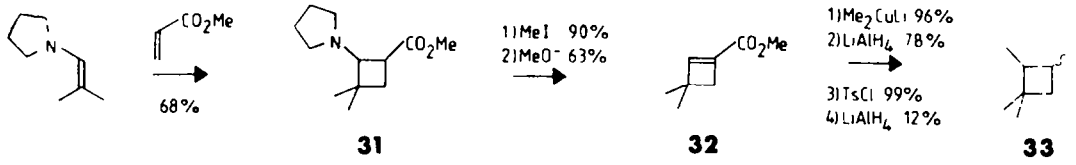

a) Bu_3SnLi
b) MeI
60%, 94 6
7
8
1) $LiAlH_4$ 88%
2) TsCl 95%
1) NaCN 58%
2) MeLi 93%
3) MeLi 70%
10
9
1) LiBr 78%
2) $^-CH(CO_2Me)_2$ 78%
3) H_2O / LiCl 75%
4) MeMgI 89%
11
a) Me_3SnLi
b) MeI
93%, 97 3
12
13
$LiAlH_4$ 88%
14
TsCl 100 %
1) NaCN 55%
16 {2) PhLi 77%, 3) PhLi 68%
17 {2) MeLi 87%, 3) MeLi 70%
16 R = Ph
17 R = Me
15
1) LiBr 80%
2) $^-CH(CO_2Me)_2$ 59%
3) H_2O / LiCl 77%
4) PhMgBr 77%
18
1) LiBr 80%
2) 98%
3) $(COCl)_2$ 100%
19
$(Ph_3P)_2CuBH_4$
73%
20
a) Me_3SnLi
b) MeOH
82%, 91 9
21
22
1) $LiAlH_4$ 93%
2) TsCl 94%
3) LiBr 84%
4) 96%
5) $(COCl)_2$ 100%
23
$(Ph_3P)_2CuBH_4$
56%
24

Scheme 1

spectrum of the signals of t-butyl acetate (30). In this case, we synthesised a mixture of the cyclobutane stereoisomers (33), by the route shown in Scheme 3, and examined the crude reaction mixture by GLC for traces of these products. There was no sign of them.



Scheme 2



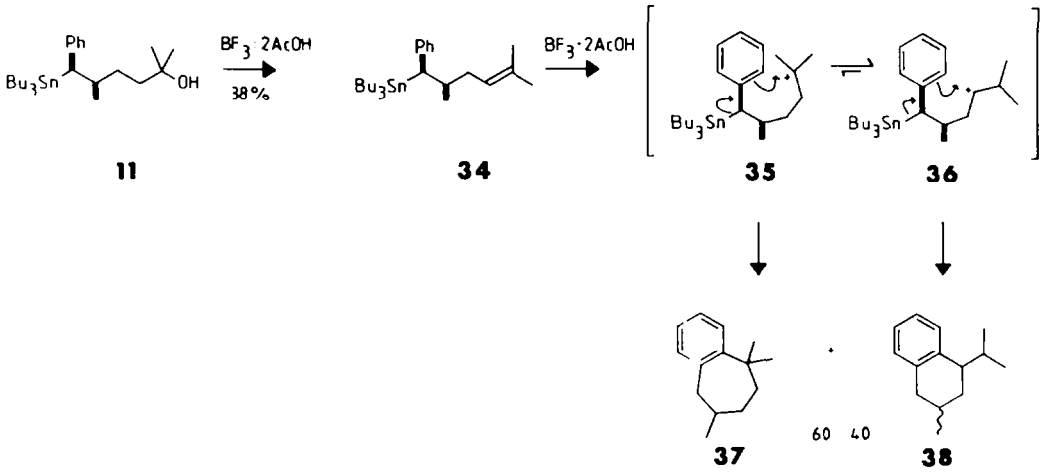
Scheme 3

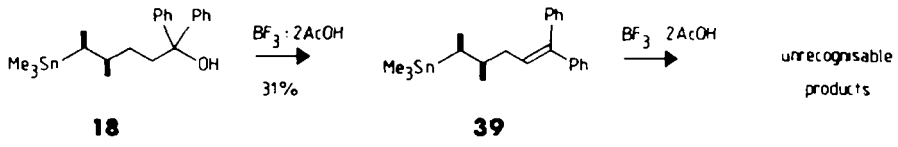
Having failed to get cyclobutanes, we tried to prepare cyclopentanes (Scheme 4), knowing that 5-membered ring formation at least had precedent.[12] The alcohol (11) initially underwent dehydration with formation of the alkene (34), but longer treatment with acid gave cyclisation to a mixture of the benzcycloheptene (37) and the tetralin (38). We proved the structures of these compounds by an alternative synthesis (Scheme 5). These compounds have obviously come from attack of carbonium ions on the benzene ring instead of at the tin-bearing carbon, the two products arising presumably by seven-membered ring formation from a high concentration of the less reactive tertiary cation (35), and six-membered ring formation from a low concentration of the more reactive secondary cation (36)in equilibrium with it. The proportion of benzcycloheptene (37) to tetralin (38) was 60:40 when they were prepared by way of the tin-containing alkene (34) and 25:75 when they were prepared from the alkene (41).

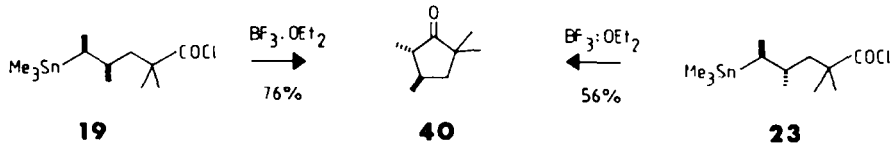
To avoid the problem of cyclisation onto the ring, we prepared the alcohol (18). On treatment with acid, it gave the alkene (39), but further treatment with acid gave only unrecognisable products.

The acid chlorides (19) and (23) each cyclised cleanly, but to give the same ketone (40), which we also made independently (Scheme 6). Since 40 is an enolisab-

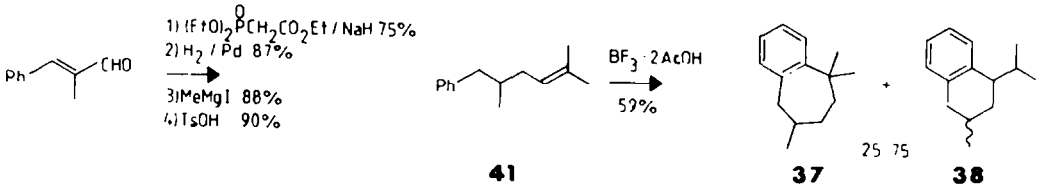
le ketone, we cannot tell whether this is a non-stereospecific reaction, or whether it is stereospecific, but with the less stable cis product isomerising to the more stable trans product. All attempts to make the cis ketone failed.







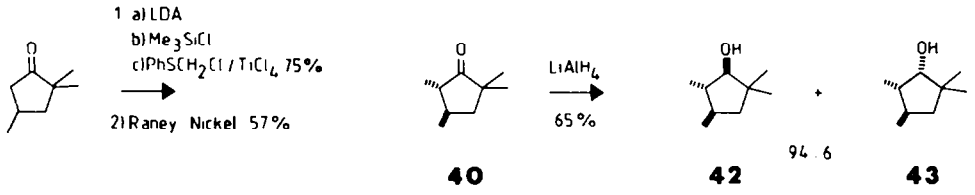
Scheme 4



Scheme 5

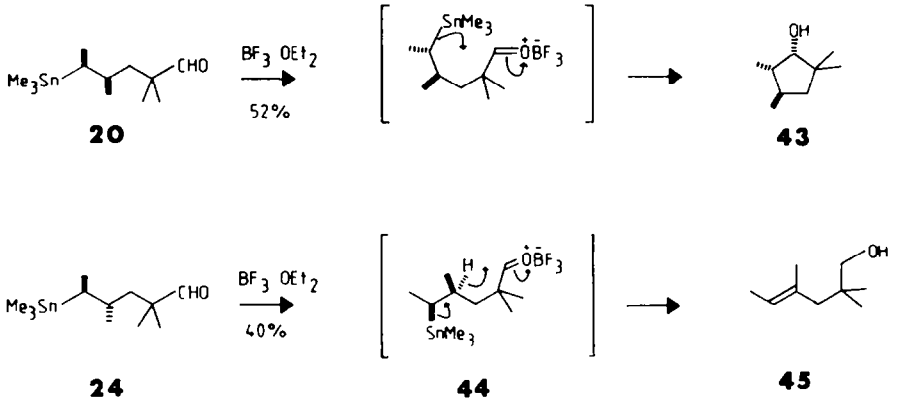
Finally, the aldehyde (20) cyclised mainly (9:1) to the alcohol (43). Since this alcohol is most unlikely to have equilibrated at C-5 in these reaction conditions, the reaction clearly took place with retention of configuration at C-5. The minor alcohol was probably one of the 4,5-cis isomers, but we were unable to prove this. The byproduct was not the alcohol (42) merely epimeric at C-1, since we made this alcohol by reduction of the ketone (40)(Scheme 6) and it was clearly different. However, we were not able to show that this reaction is stereospecific in the Zimmerman sense: the isomeric aldehyde (24) failed to cyclise, giving

instead the product (45) of stereospecifically anti hydride transfer (44, arrows), a reaction which has precedent,[13] although we believe this to be the first example showing the stereochemistry. We speculate that the failure to cyclise is due, at least in part, to the higher energy of the cis-4,5-dimethyl product, which would have been formed by a stereospecific cyclisation taking place with retention of configuration.



40 42 43

Scheme 6

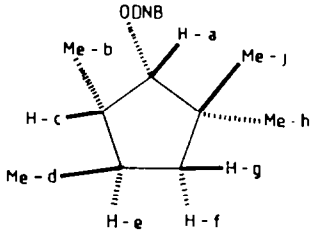


20 43

24 44 45

Scheme 7

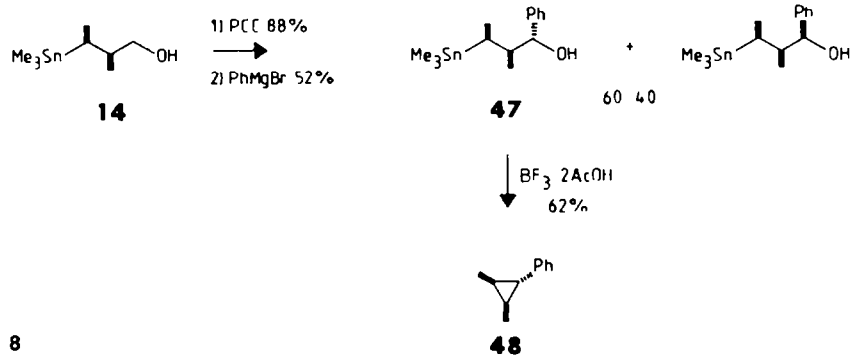
Proof of Stereochemistry of Starting Materials and Products. We carried out an elaborate series of nuclear Overhauser enhancement (NOE) experiments using difference spectra, in order to establish the configuration of the three centres in the key product (43). In particular we used the alcohol (43) itself, and its 3,5-dinitrobenzoate (46). To illustrate the argument as succinctly as we can, we shall describe here only the experiments on the 3,5-dinitrobenzoate (46). The downfield methyl doublet gave an NOE only to the downfield double doublet, whereas the



46

upfield methyl doublet gave an NOE to both the double doublets. This identified the downfield methyl doublet as b, and the upfield methyl double doublet as d. The carbinol proton H-a gave an NOE to the downfield methyl singlet and to the upfield double doublet (and the reverse in both cases). This identified the downfield methyl singlet as j, and established that H-a and H-g are cis. This is supported by an NOE from the downfield methyl singlet (j) to the upfield double doublet (g)

The stereochemical relationships of the key substituents then follow from the positive NOE's from (i) H-a to the upfield doublet (d) (and its reverse), and (ii) from the downfield double doublet (f) to the doublet (b) (and its reverse). NOE experiments on the alcohol (43) (see experimental section) support the assignment of stereochemistry.



Scheme 8

The stereochemistry of the alkene group in the product (45) was proved by an NOE experiment (see experimental). The stereochemistry of the starting material (13) was proved by cyclisation of the alcohol (47) to the cyclopropane (48) (Scheme 8), a reaction that goes reliably with inversion of configuration at the tin-bearing carbon.[5]

EXPERIMENTAL

For tin containing compounds only the peaks corresponding to the ^{120}Sn isotope are recorded in the mass spectra, and ^{35}Cl for chlorine containing compounds. Column chromatography was performed using Merck 40-63μ silica gel. THF was freshly distilled from lithium aluminium hydride, dichloromethane from phosphorus pentoxide, and ether was distilled from phosphorus pentoxide and stored over sodium wire. Other solvents were distilled before use. Light petroleum refers to the fraction b.p. 60 - 80 °C unless otherwise specified.

(2RS,3RS) Methyl 2-Methyl-3-phenyl-3-tributylstannylpropanoate (8).- Methyl cinnamate (7) (6.16 g, 38 mmol) in THF (25 ml) was added dropwise over 20 min to a stirred solution of tributyltin-lithium[14] (38 mmol) in THF (60 ml) at -78 °C. After a further 30 min, methyl iodide (14.2 g, 100 mmol) was added, and the solution warmed to room temperature. Water (100 ml) and light petroleum (75 ml) were added, the mixture separated, and the aqueous layer extracted with light petroleum (2 x 75 ml). The combined organic layers were washed with water and brine, dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography, eluting with light petroleum-ethyl acetate (30:1, v/v), to give the (2RS,3RS)- ester[5] (8) (9.86 g, 56%) and the (2RS,3SR)-ester[5] (0.60 g, 4%).

Method for Lithium Aluminium Hydride Reductions.- Typically, the ester (10 mmol) in dry ether (15 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (0.38 g) in dry ether (20 ml) at 0 °C. After stirring for 1 h, saturated ammonium chloride solution (10 ml) was added, the mixture filtered and separated, and the organic layer washed with brine, dried (Na_2SO_4), and evaporated in vacuo.

(2RS,3RS)-2-Methyl-3-phenyl-3-tributylstannyl-1-propanol.- This was made by the above method using the ester (8) (5.00 g, 10.71 mmol) and purified by flash chromatography, eluting with light petroleum-ethyl acetate (7:1, v/v), to give the alcohol (4.13 g, 88%) as an oil. R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.28, ν max.(film) 3 320 (OH), 1 599 and 1 498 cm^{-1} (Ph), δ ($CDCl_3$) 7.3-7.0 (5 H, m, Ph), 3.8-3.4 (2 H, m, CH_2O), 2.5-2.2 (2 H, m, CH's), 1.6-0.4 (31 H, m, remaining H's), m/z 440 (7%, M^+), 383 (100, M - Bu), 291(38, Bu_3Sn), 235 (71, Bu_2SnH), 179 (52, $BuSnH_2$).

Method for Tosylations.- Typically, the alcohol (8 mmol) in dry pyridine (15 ml) was added to a stirred solution of p-toluene sulphonyl chloride (8.5 mmol) in dry pyridine (15 ml) at 0 °C, and stirred overnight at room temperature. Ether (50 ml) and dilute hydrochloric acid (100 ml) were added, the mixture separated, and the aqueous layer extracted with ether (2 x 30 ml). The combined organic layers

were washed with dilute hydrochloric acid, sodium hydrogencarbonate solution, water, and brine, dried (Na_2SO_4) and evaporated *in vacuo*.

(2RS,3RS)-2-Methyl-3-phenyl-3-tributylstannyl-1-propyl p-Toluenesulphonate (9).- This was made by the general method using the above alcohol (3.55 g, 8.09 mmol) to give the tosylate (9)(4.55 g, 95%) as an oil. R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.29, $\nu_{max.}$(film) 1 599 and 1 495 (Ph), 1 370 and 1 195 cm^{-1} (SO_2-O), δ(CDCl3) 7.79 (2 H, d, J 8.4 Hz, ArH, H's o to Me), 7.33 (2 H, d, J 8.4 Hz, ArH, H's m to Me), 7.25-6.8 (5 H, m, Ph), 4.02 (1 H, dd, J 4.3 and 8.6 Hz, CH_AH_B), 3.78 (1 H, dd, J 7.0 and 8.6 Hz, CH_AH_B), 2.44 (3 H, s, $ArCH_3$), 2.6-2.3 (2 H, m, CH's), 1.10 (3 H, d, J 7.0 Hz, $CHCH_3$), 1.6-0.4 (27 H, m, Bu_3Sn), m/z 594 (1%, M^+), 537 (3, M - Bu), 291 (27, Bu_3Sn), 235 (17, Bu_2SnH), 178 (21, $BuSnH_2$), 132 (100, $C_{10}H_{12}$), 117 (72, C_9H_9).

(3RS,4RS)-3-Methyl-4-phenyl-4-tributylstannylbutanenitrile.- The tosylate (9)(0.92 g, 1.55 mmol) in dimethyl sulphoxide (DMSO) (2 ml) was added dropwise over 30 min to a stirred solution of sodium cyanide (0.10 g) in DMSO (5 ml) at 60 °C. The temperature was raised to 70 °C and the mixture stirred for 2 h. After cooling to room temperature, water (20 ml) and ether (15 ml) were added, the mixture separated, and the aqueous layer extracted with ether (2 x 15 ml). The combined organic layers were washed with water and brine, dried (Na_2SO_4), evaporated *in vacuo*, and purified by flash chromatography, eluting with light petroleum-ethyl acetate (20:1, v/v), to give the nitrile (0.39 g, 58%) as an oil. R_F (light petroleum: ethyl acetate, 5:1 v/v) 0.56, $\nu_{max.}$(film) 2 255 (C≡N), 1 600 and 1 498 cm^{-1} (Ph), δ (CDCl3) 7.3-6.9 (5 H, m, Ph), 2.7-2.2 (4 H, m, CH's and CH_2), 1.10 (3 H, d, J 7.0 Hz, $CHCH_3$), 1.6-0.4 (27 H, m, Bu_3Sn), m/z 449 (12%, M^+), 392 (12, M - Bu), 291 (100, Bu_3Sn), 235 (43, Bu_2SnH), 179 (55, $BuSnH_2$).

Reaction of Nitriles with Lithium Reagents.- These were performed by the method of van Leusen.[15] Typically, the lithium reagent (0.7 mmol) in ether was added dropwise to a solution of the nitrile (0.6 mmol) in dry ether (10 ml) at 0 °C. After 30 min water (5 ml) was added, the mixture separated, and the aqueous layer extracted with ether (2 x 5 ml). The combined organic layers were evaporated *in vacuo*, hydrochloric acid (5 ml, 6N) and acetone (5 ml) added, and the mixture refluxed for 15 min. After cooling to room temperature, the mixture was diluted with water (25 ml), and extracted with ether (3 x 15 ml). The combined organic layers were washed with sodium hydrogencarbonate solution, water, and brine, dried (Na_2SO_4), and evaporated *in vacuo*.

(4RS,5RS)-4-Methyl-5-phenyl-5-tributylstannyl-2-pentanone.- This was made by the general method using the above nitrile (0.28 g, 0.63 mmol) and methyl-lithium to give the ketone (0.27 g, 93%) as an oil. R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.55, $\nu_{max.}$(film) 1 715 (C=O), 1 598 and 1 498 cm^{-1} (Ph), δ(CDCl3) 7.3-6.9 (5 H, m, Ph), 2.8-2.2 (4 H, m, CH's and CH_2), 2.14 (3 H, s, $COCH_3$), 1.6-0.4 (30 H, m, remaining H's), m/z 466 (5%, M^+), 409 (22, M - Bu), 291 (100, Bu_3Sn), 235 (99, Bu_2SnH), 179 (80, $BuSnH_2$).

(4RS,5RS)-2,4-Dimethyl-5-phenyl-5-tributylstannyl-2-pentanol (10).- Methyl-lithium (0.3 ml of a 1.5 M solution in ether) was added to a stirred solution of the above ketone (0.13 g, 0.28 mmol) in dry ether (5 ml) at 0 °C. After 1 h water (10 ml) and ether (10 ml) were added, the mixture separated, and the aqueous layer extracted with ether (2 x 10 ml). The combined organic layers were washed with water and brine, dried (Na_2SO_4), evaporated *in vacuo*, and purified by preparative thin layer chromatography, eluting with light petroleum-ethyl acetate (3:1, v/v), to give the alcohol (10)(93 mg, 70%) as an oil. R_F (light petroleum-ethyl acetate, 3:1 v/v) 0.50, $\nu_{max.}$(film) 3 350 (OH), 1 600 and 1 499 cm^{-1} (Ph), δ (CDCl3) 7.3-6.9 (5 H, m, Ph), 2.5-2.3 (2 H, m, CH's), 1.27 (6 H, s, CMe_2), 1.9-0.4 (33 H, m, remaining H's), m/z 482 (9%, M^+), 425 (32, M - Bu), 407 [11, M - (Bu + H_2O)], 291 (100, Bu_3Sn), 235 (67, Bu_2SnH), 179 (61, $BuSnH_2$).

Conversion of Tosylates to Bromides.- Typically, the tosylate (1.0 mmol) was refluxed in acetone (20 ml) with lithium bromide (5 mmol) for 5 h. The solution was cooled, water (50 ml) added and the mixture extracted with ether (3 x 25 ml). The combined organic layers were washed with water and brine, dried (Na_2SO_4), evaporated *in vacuo*, and purified by flash chromatography, eluting with light petroleum, to give the bromide.

(1RS,2RS)-3-Bromo-2-methyl-1-phenyl-1-propyltributylstannane.- This was made in the above way using the tosylate (9)(0.70 g, 1.18 mmol) to give the bromide (0.46 g, 78%) as an oil. R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.74, $\nu_{max.}$(film) 1 599 and 1 497 cm^{-1} (Ph), δ(CDCl3) 7.3-6.9 (5 H, m, Ph), 3.59 (1 H, dd, J 3.5 and 9.7 Hz, CH_AH_BBr), 3.30 (1 H, dd, J 6.0 and 9.7 Hz, CH_AH_BBr), 2.7-2.3 (2 H, m, CH's), 1.4-0.6 (30 H, m, remaining H's), m/z 447/445 (6%, M - Bu), 291 (100, Bu_3Sn), 235 (60, Bu_2SnH).

Addition of Sodium Dimethyl Malonate to Bromides.- Typically, dimethyl malonate (10 mmol) was added to 25 ml of a 2M solution of sodium methoxide in methanol. The mixture was refluxed for 5 min, the bromide (0.8 mmol) in methanol (2 ml) added,

and the refluxing continued for 10 h. The solution was cooled, ammonium chloride solution (50 ml) was added, and the mixture extracted with ether (3 x 20 ml). The combined organic layers were washed with water and brine, dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography, eluting with light petroleum-ethyl acetate (20:1, v/v).

(2RS,3RS) Dimethyl (2-Methyl-3-phenyl-3-tributylstannyl-1-propyl)-propandioate.- The above bromide (0.44 g, 0.88 mmol) gave the diester (0.28 g, 78%) as an oil, R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.33, $\nu_{max.}$(film) 1 755 and 1 740 (C=O), 1 598 and 1 495 cm^{-1} (Ph), δ ($CDCl_3$) 7.3-6.8 (5 H, m, Ph), 3.75 (3 H, s, OMe), 3.73 (3 H, s, OMe), 3.53 (1 H, dd, J 4.7 and 9.8 Hz, CHCO), 2.40 (1 H, d, J 9.2 Hz, SnCH), 2.4-0.6 (33 H, m, remaining H's), m/z 554 (12%, M^+), 493 (89, M - Bu), 291 (100, Bu_3Sn), 235 (98, Bu_2SnH).

Decarbomethoxylations.- These were performed by the method of Krapcho.[16] Typically, the diester (1 mmol), water (1 mmol), and lithium chloride (2 mmol) were refluxed in DMSO (10 ml) for 10 min. Water (25 ml) was added to the cooled solution and the mixture extracted with ether (3 x 20 ml). The combined organic layers were washed with water and brine, dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography, eluting with light petroleum-ethyl acetate (30:1, v/v).

(4RS,5RS)-Methyl 4-Methyl-5-phenyl-5-tributylstannylpentanoate.- The above diester (0.64 g, 1.16 mmol) was decarbomethoxylated to give the ester (0.43 g, 75%) as an oil. R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.57, $\nu_{max.}$(film) 1 741 (C=O), 1 599 and 1 494 cm^{-1} (Ph), δ ($CDCl_3$) 7.2-6.8 (5 H, m, Ph), 3.68 (3 H, s, OMe), 2.5-2.2 (3 H, m, SnCH and CH_2CO), 2.1-0.6 (33 H, m, remaining H's), m/z 361 (1%, M - $C_{10}H_{15}$), 291 (100, Bu_3Sn), 235 (71, Bu_2SnH).

Method for Reaction of Esters with Grignard Reagents.- Typically, the ester (10 mmol) in dry ether (15 ml) was added dropwise to a refluxing solution of the Grignard reagent (25 mmol) in dry ether (30 ml). After refluxing for 2 h the solution was cooled and saturated ammonium chloride solution (30 ml) was carefully added. The mixture was separated, and the aqueous layer extracted with ether (2 x 20 ml). The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated in vacuo.

(5RS,6RS)-2,5-Dimethyl-6-phenyl-6-tributylstannyl-2-hexanol (11).- The above ester (0.18 g, 0.36 mmol) was treated with methyl magnesium iodide and the product purified by flash chromatography, eluting with light petroleum-ethyl acetate (9:1, v/v), to give the alcohol (11) (0.16 g, 89%) as an oil. R_F (light petroleum: ethyl acetate, 5:1 v/v) 0.33, $\nu_{max.}$(film) 3 400 (OH), 1 600 and 1 496 cm^{-1} (Ph), δ ($CDCl_3$) 7.3-6.8 (5 H, m, Ph), 2.39 (1 H, d, J 10.7 Hz, SnCH), 1.23 (6 H, s, CMe_2), 2.3-0.6 (34 H, m, remaining H's), m/z 496 (26%, M^+), 439 (8, M - Bu), 291 (100, Bu_3Sn), 235 (51, Bu_2Sn).

(2RS,3SR)-Methyl 2-Methyl-3-trimethylstannylbutanoate (13).- This was made in the same way as the ester (8), using methyl crotonate (12) (3.05 g, 30.5 mmol), trimethyltin-lithium[17] (30.6 mmol), and methyl iodide (60 mmol), to give the (2RS,3SR)-ester (13) (7.67 g, 90%) as an oil (Found: C, 38.9; H, 7.05. $C_9H_{20}O_2Sn$ requires C, 38.8; H, 7.20%), R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.55, $\nu_{max.}$(film) 1 735 cm^{-1} (C=O), δ ($CDCl_3$) 3.65 (3 H, s, OMe), 2.64 (1 H, dq, J 4.5 and 7.1 Hz, CHCO), 1.33 (1 H, dq, J 4.5 and 7.5 Hz, SnCH), 1.15 (3 H, d, J 7.1 Hz, $COCHCH_3$), 1.13 (3 H, d, J 7.5 Hz, $SnCHCH_3$), 0.05 (9 H, s, Me_3Sn), m/z 265 (100%, M - Me), 165 (71, Me_3Sn),

and the (2RS,3RS)-ester (22) (0.24 g, 3%) as an oil, R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.52, $\nu_{max.}$(film) 1 740 cm^{-1} (C=O), δ ($CDCl_3$) 3.69 (3 H, s, OMe), 2.58 (1 H, quintet J 7.2 Hz, CHCO), 1.51 (1 H, quintet, J 7.2 Hz, SnCH), 1.15 (3 H, d, J 7.2 Hz, $COCHCH_3$), 1.11 (3 H, d, J 7.2 Hz, $SnCHCH_3$), 0.05 (9 H, s, Me_3Sn), m/z 265 (60%, M - Me), 165 (100, Me_3Sn).

(2RS,3SR)-2-Methyl-3-trimethylstannyl-1-butanol (14).- The ester (13) (3.84 g, 13.8 mmol) was reduced with lithium aluminium hydride and purified by flash chromatography, eluting with light petroleum-ethyl acetate (7:1, v/v), to give the alcohol (14) (3.03 g, 88%) as an oil. (Found: C, 38.6; H, 8.05. $C_8H_{20}OSn$ requires C, 38.3; H, 8.05%), R_F (light petroleum-ethyl acetate, 3:1 v/v) 0.41, $\nu_{max.}$(film) 3 350 cm^{-1} (OH), δ ($CDCl_3$) 3.7-3.3 (2 H, m, CH_2O), 2.1-1.6 (1 H, m, $CHCH_2$), 1.4-1.0 (1 H, m, SnCH), 1.15 (3 H, d, J 5.7 Hz, $SnCHCH_3$), 0.94 (3 H, d, J 6.8 Hz, CH_2CHCH_3), 0.05 (9 H, s, Me_3Sn), m/z 237 (60%, M - Me), 165 (100, Me_3Sn).

(2RS,3SR)-2-Methyl-3-trimethylstannyl-1-butyl p-Toluenesulphonate (15).- The alcohol (14) (1.14 g, 4.55 mmol) gave the tosylate (15) (1.84 g, 100%) as an oil. (Found: C, 44.2; H, 6.55. $C_{15}H_{26}O_3SSn$ requires C, 44.5; H, 6.45%), R_F (light petroleum-ethyl acetate, 3:1 v/v) 0.50, $\nu_{max.}$(film) 1 600 and 1 499 (Ar), 1 375 and 1 200 cm^{-1} (SO_2-O), δ ($CDCl_3$) 7.78 (2 H, d, J 8.3 Hz, ArH, H's m to Me), 7.31 (2 H, d, J 8.3 Hz, ArH, H's o to Me), 3.94 (1 H, dd, J 5.7 and 11.6 Hz, CH_AH_B), 3.77 (1 H, dd, J 6.1 and 11.6 Hz, CH_AH_B), 2.43 (3 H, s, ArMe), 2.2-1.8 (1 H, m, $CHCH_2$), 1.30 (1 H, dq, J 5 and 7.4 Hz, SnCH), 1.02 (3 H, d, J 7.4 Hz, $SnCHCH_3$), 0.86 (3 H, d, J 6.8 Hz, CH_2CHCH_3), 0.01 (9 H, s, Me_3Sn), m/z 391 (5%, M - Me), 165

(100, Me_3Sn).

(3RS,4SR)-3-Methyl-4-trimethylstannylpentanenitrile.- This was made in the same way as the above nitrile using the tosylate (15)(1.70 g, 4.20 mmol) to give the nitrile (0.60 g, 55%) as an oil. (Found: C, 41.4; H, 7.60; N, 5.1. $C_9H_{19}NSn$ requires C, 41.6; H, 7.35; N, 5.4%), R_F (light petroleum-ethyl acetate, 3:1 v/v) 0.54, $\nu_{max.}$(film) 2 255 cm^{-1} (C≡N), δ ($CDCl_3$) 2.4-2.0 (3 H, m, CH_2CH), 1.5-1.2 (1 H, m, SnCH), 1.12 (3 H, d, J 6.6 Hz, $SnCHCH_3$), 1.07 (3 H, d, J 6.8 Hz, CH_2CHCH_3), 0.08 (9 H, s, Me_3Sn) m/z 246 (23%, M - Me), 165 (100, Me_3Sn).

(3RS,4SR)-3-Methyl-4-trimethylstannyl-1-phenyl-1-pentanone.- The above nitrile (0.30 g, 1.15 mmol) reacted with phenyl-lithium to give the ketone (0.30 g, 77%) which was purified by preparative thin layer chromatography, eluting with light petroleum-ethyl acetate (5:1, v/v). R_F (light petroleum-ethyl acetate, 3:1 v/v) 0.54, $\nu_{max.}$(film) 1 678 (C=O), 1 597 and 1 580 cm^{-1} (Ph), δ ($CDCl_3$) 8.0-7.8 (2 H, m, Ph), 7.6-7.2 (3 H, m, Ph), 3.05 (1 H, dd, J 4.5 and 14.0 Hz, CH_AH_B), 2.80 (1 H, dd, J 6.8 and 14.0 Hz, CH_AH_B), 1.7-1.3 (2 H, m, CH's), 1.19 (3 H, d, J 6.0 Hz, $SnCHCH_3$), 0.96 (3 H, d, J 6.5 Hz, CH_2CHCH_3), 0.08 (9 H, s, Me_3Sn), m/z 325 (34%, M - Me), 284 (87, M - C_4H_8), 269 (100, M - C_5H_{11}), 165 (47, Me_3Sn).

(3RS,4SR)-3-Methyl-4-trimethylstannyl-1,1-diphenyl-1-pentanol (16).- This was made in the same way as the alcohol (10) using the above ketone (0.20 g, 0.59 mmol) and phenyl-lithium to give the alcohol (16)(0.17 g, 68%) as an oil. (Found: C, 60.6; H, 7.40. $C_{21}H_{30}OSn$ requires C, 60.6; H, 7.25%), R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.43, $\nu_{max.}$(film) 3 480 (OH), 1 598 and 1 498 cm^{-1} (Ph), δ ($CDCl_3$) 7.4-7.1 (10 H, m, Ph's), 2.41 (1 H, dd, J 5 and 10 Hz, CH_AH_B), 2.12 (1 H, dd, J 7 and 10 Hz, CH_AH_B), 1.8-1.2 (2 H, m, CH's), 1.6 (1 H, s, OH), 1.07 (3 H, d, J 7 Hz, $SnCHCH_3$), 0.81 (3 H, d, J 7 Hz, CH_2CHCH_3), 0.00 (9 H, s, Me_3Sn), m/z 403 (10%, M - Me), 385 [49, M - (Me + H_2O)], 165 (100, Me_3Sn).

(4RS,5SR)-4-Methyl-5-trimethylstannyl-2-hexanone.- (3RS,4SR)-3-Methyl-4-trimethylstannylpentanenitrile (0.48 g, 1.84 mmol) was treated with with methyl-lithium and the product purified by flash chromatography, eluting with light petroleum-ethyl acetate (15:1, v/v), to give the ketone (0.44, 87%) as an oil. R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.48, $\nu_{max.}$(film) 1 711 cm^{-1} (C=O), δ ($CDCl_3$) 2.7-2.2 (2 H, m, CH_2), 2.11 (3 H, s, $COCH_3$), 1.8-1.5 (1 H, m, CH_2CH), 1.4-1.2 (1 H, m, SnCH), 1.11 (3 H, d, J 5.7 Hz, $SnCHCH_3$), 0.89 (3 H, d, J 6.7 Hz, CH_2CHCH_3), 0.05 (9 H, s, Me_3Sn), m/z 263 (17%, M - Me), 222 (47, M - C_4H_8), 207 (71, M - C_5H_{11}), 165 (100, Me_3Sn).

(4RS,5SR)-2,4-Dimethyl-5-trimethylstannyl-2-hexanol (17).- This was made in the same way as the alcohol (10) using the above ketone (0.43 g, 1.56 mmol) to give the alcohol (17)(0.32 g, 70%) as an oil. R_F (light petroleum-ethyl acetate, 3:1 v/v) 0.33, $\nu_{max.}$(film) 3 400 cm^{-1} (OH), δ ($CDCl_3$) 2.0-1.2 (4 H, m, $CHCHCH_2$), 1.6 (1 H, s, OH), 1.23 (6 H, s, CMe_2), 1.14 (3 H, d, J 5.7 Hz, $SnCHCH_3$), 1.01 (3 H, d, J 6.7 Hz, CH_2CHCH_3), 0.05 (9 H, s, Me_3Sn), m/z 279 (12%, M - Me), 261 [15, M - (Me + H_2O)], 165 (100, Me_3Sn).

(2RS,3SR)-1-Bromo-2-methyl-3-butyltrimethylstannane.- The tosylate (15)(1.00 g, 2.47 mmol) reacted with lithium bromide to give the bromide (0.62 g, 80%) as an oil. R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.71, $\nu_{max.}$(film) 3000-2900 cm^{-1} (CH), δ($CDCl_3$) 3.41 (1 H, dd, J 5.6 and 9.7 Hz, CH_AH_B), 3.22 (1 H, dd, J 7.6 and 9.7 Hz, CH_AH_B), 2.2-1.9 (1 H, m, $CHCH_2$), 1.6-1.3 (1 H, m, SnCH), 1.11 (3 H, d, J 7.1 Hz, $SnCHCH_3$), 1.04 (3 H, d, J 6.8 Hz, CH_2CHCH_3), 0.07 (9 H, s, Me_3Sn), m/z 234 (7%, M - HBr), 165 (100, Me_3Sn).

(2RS,3SR)-Dimethyl (2-Methyl-3-trimethylstannyl-1-butyl)-propandioate.- The above bromide (0.85 g, 2.71 mmol) reacted with sodium dimethyl malonate to give the diester (0.58 g, 59%) as an oil. R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.31, $\nu_{max.}$(film) 1 745 and 1 735 cm^{-1} (C=O), δ($CDCl_3$) 3.72 (6 H, s, OMe's), 3.43 (1 H, dd, J 6.3 and 7.8 Hz, CHCO), 1.8-1.5 (3 H, m, $CHCH_2$), 1.3-1.1 (1 H, m, SnCH), 1.08 (3 H, d, J 5.8 Hz, $SnCHCH_3$), 0.89 (3 H, d, J 6.2 Hz, CH_2CHCH_3), 0.05 (9 H, s, Me_3Sn), m/z 366 (1%, M^+), 351 (53, M - Me), 165 (100, Me_3Sn).

(4RS,5SR)-Methyl 4-Methyl-5-trimethylstannylhexanoate.- The diester above (0.40 g, 1.10 mmol) was decarbomethoxylated to give the ester (0.24 g, 77%) as an oil. R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.54, $\nu_{max.}$(film) 1 740 cm^{-1} (C=O), δ ($CDCl_3$) 3.66 (3 H, s, OMe), 2.31 (2 H, t, J 7 Hz, CH_2CO), 1.8-1.2 (4 H, m, CH_2CHCH), 1.11 (3 H, d, J 6 Hz, $SnCHCH_3$), 0.89 (3 H, d, J 6.4 Hz, CH_2CHCH_3), 0.04 (9 H, s, Me_3Sn), m/z 308 (6%, M^+), 293 (29, M - Me), 165 (100, Me_3Sn).

(4RS,5SR)-4-Methyl-5-trimethylstannyl-1,1-diphenyl-1-hexanol (18).- The above ester (174 mg, 0.57 mmol) reacted with phenyl magnesium bromide and the product was purified by flash chromatography, eluting with light petroleum-ethyl acetate (15:1, v/v), to give the alcohol (18)(186 mg, 77%) as an oil. R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.61, $\nu_{max.}$(film) 3 450 (OH), 1 601 and 1 499 cm^{-1} (Ph), δ ($CDCl_3$) 7.5-7.1 (10 H, m, Ph's), 2.4-2.1 (2 H, m, CH_2CO), 1.9 (1 H, s, OH), 1.6-1.0 (4 H, m, CH_2CHCH), 1.04 (3 H, d, J 6.4 Hz, $SnCHCH_3$), 0.89 (3 H, d, J 6.4 Hz,

CH_2CHCH_3), -0.05 (9 H, s, Me_3Sn), m/z 414 (1%, M - H_2O), 399 [29, M - (H_2O + Me)], 165 (100, Me_3Sn).

(4RS,5SR)-2,2,4-Trimethyl-5-trimethylstannylhexanoic acid.- This reaction was performed by a method similar to that of Cregar.[18] Isobutyric acid (3.5 g, 40 mmol) in tetrahydrofuran (THF) (30 ml) was added to a suspension of sodium hydride (2.6 g of a 50% suspension in oil, 56 mmol) in THF (50 ml) containing di-isopropylamine (4.0 g, 40 mmol) at 0 °C. The mixture was refluxed for 15 min, cooled to 0 °C, and n-butyl-lithium (25 ml of a 1.6M solution in hexanes, 40 mmol) added dropwise over 15 min. The mixture was stirred at 30 °C for 30 min, cooled to 0 °C, (2RS,3SR)-1-bromo-2-methyl-3-butyltrimethylstannane (2.50 g, 7.67 mmol) in THF (10 ml) added over 5 min, and then stirred at 30 °C for 5 h. Dilute hydrochloric acid (100 ml) was added, the mixture separated, and the aqueous layer extracted with ether (2 x 30 ml). The combined organic layers were washed with water and brine, dried (Na_2SO_4), evaporated in vacuo, and the residue pumped at 0.1 mmHg for 3 h until no isobutyric acid remained, then purified by flash chromatography, eluting with light petroleum-ethyl acetate-acetic acid (90:12:1, v/v), to give the acid (2.50 g, 98%) as an oil. R_F (light petroleum-ethyl acetate, 3:1 v/v) 0.45 (streak), $\nu_{max.}$(film) 3 200-2 400 (OH), 1 698 cm^{-1} (C=O), δ ($CDCl_3$) 12.5 (1 H, s, OH), 1.9-1.2 (4 H, m, $CHCHCH_2$), 1.21 (3 H, s, CMe_AMe_B), 1.18 (3 H, s, CMe_AMe_B), 1.11 (3 H, d, J 6 Hz, $SnCHCH_3$), 0.88 (3 H, d, J 6.5 Hz, CH_2CHCH_3), 0.04 (9 H, s, Me_3Sn), m/z 322 (9%, M^+), 307 (24, M - Me), 165 (100, Me_3Sn).

(4RS,5SR)-2,2,4-Trimethyl-5-trimethylstannylhexanoyl chloride (19).- Oxalyl chloride (0.17 g, 1.3 mmol) was added dropwise to a stirred solution of the above acid (337 mg, 0.93 mmol) in dry dichloromethane (5 ml) containing anhydrous potassium carbonate (100 mg). After 1 h, the solution was evaporated in vacuo, dichloromethane (5 ml) added, and the solution filtered and evaporated in vacuo to give the acid chloride (19)(357 mg, 100%) as an oil. $\nu_{max.}$(film) 1 805 cm^{-1} (C=O), δ ($CDCl_3$) 2.1-1.6 (3 H, m, CH_2CH), 1.30 (3 H, s, CMe_AMe_B), 1.28 (3 H, s, CMe_AMe_B), 1.4-1.2 (1 H, m, SnCH), 1.22 (3 H, d, J 6 Hz, $SnCHCH_3$), 1.01 (3 H, d, J 7.1 Hz, CH_2CHCH_3), 0.06 (9 H, s, Me_3Sn), m/z 325 (5%, M - Me), 185 (100, Me_2SnCl), 165 (81, Me_3Sn).

(4RS,5SR)-2,2,4-Trimethyl-5-trimethylstannylhexanal (20).- This was made by the method of Fleet.[19] The acid chloride (19)(700 mg, 2.18 mmol) in acetone (2 ml) was added to a stirred suspension of a mixture of bis-triphenylphosphine copper(I) borohydride[19] (2.0 g, 3.3 mmol) and triphenylphosphine (1.70 g, 6.5 mmol) in acetone (50 ml). After 2 h the mixture was filtered and evaporated in vacuo. Light petroleum (5 ml) was added to the residue, the mixture filtered to remove triphenylphosphine, and left at 0 °C overnight. It was then filtered again, evaporated in vacuo and purified by flash chromatography, eluting with light petroleum-ethyl acetate (20:1, v/v), to give a mixture of triphenylphosphine and the aldehyde (20)(total 654 mg, 75% w/w aldehyde by NMR, 73%) as an oil. R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.56, $\nu_{max.}$(film) 1 735 cm^{-1} (C=O), δ($CDCl_3$) 9.47 (1 H, s, CHO), 1.8-1.2 ($CHCHCH_2$), 1.10 (3 H, d, J 6 Hz, $SnCHCH_3$), 1.04 (6 H, s, CMe_2), 0.83 (3 H, d, J 6.6 Hz, CH_2CHCH_3), 0.04 (9 H, s, Me_3Sn), m/z 306 (8%, M^+), 291 (22, M - Me), 165 (100, Me_3Sn).

(2RS,3RS)-Methyl 2-Methyl-3-trimethylstannylbutanoate (22).- This was made in the same way as its diastereoisomer using methyl tiglate (21)(2.78 g, 24.4 mmol) and trimethyltin-lithium (25 mmol), and quenching at -78 °C with methanol to give the (2RS,3RS)-ester (22)(5.06 g, 74%) and the (2RS,3SR)-ester (13)(0.51 g, 8%).

(2RS,3RS)-2-Methyl-3-trimethylstannyl-1-butanol.- This was made in the same way as its diastereoisomer, using the ester (22)(4.37 g, 15.7 mmol) to give the alcohol (3.65 g, 93%) as an oil. R_F (light petroleum-ethyl acetate, 3:1 v/v) 0.40 $\nu_{max.}$(film) 3 300 cm^{-1} (OH), δ($CDCl_3$) 3.48 (2 H, d, J 6 Hz, CH_2O), 1.9-1.6 (1 H, m, $CHCH_2$), 1.6 (1 H, s, OH), 1.4-1.1 (1 H, m, SnCH), 1.16 (3 H, d, J 6 Hz, $SnCHCH_3$), 0.91 (3 H, d, J 6.7 Hz, CH_2CHCH_3), 0.04 (9 H, s, Me_3Sn), m/z 237 (72%, M - Me), 165 (100, Me_3Sn).

(2RS,3RS)-2-Methyl-3-trimethylstannyl-1-butyl p-Toluenesulphonate.- This was made in the same way as its diastereoisomer, using the above alcohol (3.46 g, 13.8 mmol) to give the tosylate (5.29 g, 94%) as an oil. R_F (light petroleum-ethyl acetate, 3:1 v/v) 0.50, $\nu_{max.}$(film) 1 602 and 1 498 (Ar), 1 365 and 1 185 cm^{-1} (SO_2-O), δ ($CDCl_3$) 7.72 (2 H, d, J 8.3 Hz, ArH, H's m to Me), 7.32 (2 H, d, J 8.3 Hz, ArH, H's o to Me), 3.87 (2 H, d, J 6Hz, CH_2O), 2.43 (3 H, s, ArMe), 2.1-1.8 (1 H, m, $CHCH_2$), 1.4-1.1 (1 H, m, SnCH), 1.09 (3 H, d, J 5.8 Hz, $SnCHCH_3$), 0.88 (3 H, d, J 6.7 Hz, CH_2CHCH_3), 0.00 (9 H, s, Me_3Sn), m/z 391 (7%, M - Me), 165 (100, Me_3Sn).

(2RS,3RS)-1-Bromo-2-methyl-3-butyltrimethylstannane.- This was made in the same way as its diastereoisomer, using the above tosylate (5.15 g, 12.7 mmol), to give the bromide (3.34 g, 84%) as an oil. R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.75, $\nu_{max.}$(film) 3 000-2 900 cm^{-1} (CH), δ ($CDCl_3$) 3.39 (2 H, d, J 6 Hz, CH_2Br), 2.1-1.8 (1 H, m, $CHCH_2$), 1.6-1.3 (1 H, m, SnCH), 1.17 (3 H, d, J 6.1 Hz, $SnCHCH_3$), 1.02 (3 H, d, J 6.5 Hz, CH_2CHCH_3), 0.08 (9H, s, Me_3Sn), m/z 234 (4%, M - HBr),

231/229 (100, Me_2SnBr), 165 (45, Me_3Sn).

(4RS,5RS)-2,2,4-Trimethyl-5-trimethylstannylhexanoic acid.- This was made in the same way as its diastereoisomer, using the above bromide (1.00 g, 3.19 mmol) to give the acid (0.98 g, 96%) as an oil. R_F (light petroleum-ethyl acetate, 3:1 v/v) 0.43 (streak), $\nu_{max.}$(film) 3 400-2 400 (OH), 1 705 cm^{-1} (C=O), δ ($CDCl_3$) 9.3 (1 H, br s, OH), 1.9-1.2 (4 H, m, $CHCHCH_2$), 1.22 (3 H, d, J 6 Hz, $SnCHCH_3$), 1.20 (3 H, s, CMe_AMe_B), 1.18 (3 H, s, CMe_AMe_B), 0.88 (3 H, d, J 6 Hz, CH_2CHCH_3), 0.05 (9 H, s, Me_3Sn), m/z 322 (8%, M^+), 307 (25, M - Me), 165 (100, Me_3Sn).

(4RS,5RS)-2,2,4-Trimethyl-5-trimethylstannylhexanoyl chloride (23).- This was made in the same way as its diastereoisomer, using the above acid (344 mg, 1.07 mmol), to give the acid chloride (23) (364 mg, 100%) as an oil. $\nu_{max.}$(film) 1 810 cm^{-1} (C=O), δ ($CDCl_3$) 2.0-1.2 (4 H, m, $CHCHCH_2$), 1.30 (3 H, s, CMe_AMe_B), 1.29 (3 H, s, CMe_AMe_B), 1.16 (3 H, d, J 6 Hz, $SnCHCH_3$), 0.90 (3 H, d, J 6 Hz, CH_2CHCH_3), 0.07 (9H, s, Me_3Sn), m/z 325 (20%, M - Me), 185 (100, Me_2SnCl), 165 (100, Me_3Sn).

(4RS,5RS)-2,2,4-Trimethyl-5-trimethylstannylhexanal (24).- This was made in the same way as its diastereoisomer, using the acid chloride (22) (406 mg, 1.20 mmol) to give a mixture of triphenylphoshine and the aldehyde (24) (284 mg total, 71% w/w aldehyde by NMR, 56%). R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.54, $\nu_{max.}$(film) 1 735 cm^{-1} (C=O), δ ($CDCl_3$) 9.47 (1 H, s, CHO), 1.8-1.2 (4 H, m, $CHCHCH_2$), 1.14 (3 H, d, J 6 Hz, $SnCHCH_3$), 1.05 (3 H, s, CMe_AMe_B), 1.04 (3 H, s, CMe_AMe_B), 0.83 (3 H, d, J 6.5 Hz, CH_2CHCH_3), 0.06 (9 H, s, Me_3Sn), m/z 306 (11%, M^+), 291 (30, M - Me), 165 (100, Me_3Sn).

Reaction of Alcohols and Alkenes with Boron Trifluoride:Acetic Acid Complex.- Typically, boron trifluoride: acetic acid complex (1 equivalent with respect to boron trifluoride) was added to a stirred solution of the substrate (0.2 mmol) in chloroform (3 ml) at 0 °C. After 2 h, 10% sodium hydroxide solution (5 ml) and ether (10 ml) were added, the mixture separated, and the aqueous layer extracted with ether. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated in vacuo.

Cyclisation of Alcohol (10).- The alcohol (10) (82 mg, 0.17 mmol) was cyclised by the above method and purified by preparative thin layer chromatography, eluting with light petroleum, to give 1,2,3,4-tetrahydro-1,1,3-trimethylnaphthalene (26) (14 mg, 47%) as an oil. R_F (light petroleum) 0.48, $\nu_{max.}$ (film) 1 602 and 1 490 cm^{-1} (Ar), δ ($CDCl_3$) 7.4-7.0 (4 H, m, Ar), 2.81 (1 H, ddd, J 2.3, 3.6, and 16.2 Hz, $C=CCH_AH_B$, H_A trans to CHMe), 2.41 (1 H, dd, J 11.8 and 16.2 Hz, $C=CCH_AH_B$, H_B cis to CHMe), 2.1-1.9 (1 H, m, CHMe), 1.65 (1 H, dt, J 13.0 and 2.3 Hz, $CH_AH_BCMe_2$, H_A trans to CHMe), 1.37 (1 H, dd, J 7.0 and 13.0 Hz, $CH_AH_BCMe_2$, H_B cis to CHMe), 1.36 (3 H, s, CMe_AMe_B), 1.28 (3 H, s, CMe_AMe_B), 1.08 (3 H, d, J 6.4 Hz, $CHCH_3$) (Found: M^+, 174.142 3. $C_{13}H_{18}$ requires M, 174.140 8), m/z 174 (22%, M^+), 159 (100, M - Me), 117 (70, M - C_4H_9).

An authentic sample of the tetralin (26) was made in the following way. Methyl 3-methyl-4-phenylbutanoate[20] (2.60 g, 13.5 mmol) reacted with methyl magnesium iodide to give 2,4-dimethyl-5-phenyl-2-pentanol (2.20 g, 85%) as an oil, b.p. 79-81 °C/0.5 mmHg, $\nu_{max.}$(film) 3 380 (O-H), 1 603 and 1 491 cm^{-1} (Ph), δ ($CDCl_3$) 7.3-7.1 (5 H, m, Ph), 2.68 (1 H, dd, J 6.7 and 13.2 Hz, $PhCH_AH_B$), 2.41 (1 H, dd, J 7.4 and 13.2 Hz, $PhCH_AH_B$), 2.2-1.8 (1 H, m, $CHCH_3$), 1.57 {1 H, dd, J 4.0 and 16.8 Hz, $CH_AH_BC(OH)$}, 1.5 (1 H, s, OH), 1.35 {1 H, dd, J 6.8 and 16.8 Hz, $CH_AH_BC(OH)$}, 1.20 (6 H, s, CMe_2), 0.98 (3 H, d, J 6.4 Hz, $CHCH_3$) (Found: M - Me, 177.129 0. $C_{13}H_{20}O-CH_3$ requires M, 177.130 1), m/z 177 (4%, M - Me), 174 (3, M - H_2O), 118 (100, M - $C_4H_{10}O$). The alcohol (0.50 g, 2.6 mmol) was cyclised by refluxing it with p-toluenesulphonic acid (0.70 g) in toluene for 15 min. The solution was the cooled, washed with sodium hydroxide solution and brine, dried (Na_2SO_4), evaporated in vacuo, and distilled (Kugelrohr, 80 °C/4 mmHg) to give the tetralin (26) (0.38 g, 84%), identical (thin layer chromatography (TLC), infra-red (IR), and 250 MHz NMR) with that produced from the stannyl alcohol (10).

α-Phenylstyrene (28).- The alcohol (16) (0.14 g, 0.33 mmol) reacted with boron trifluoride: acetic acid complex to give the styrene[21] (28) (51 mg, 84%) as an oil. $\nu_{max.}$(film) 1 609 (C=C), 1 600 and 1 494 cm^{-1} (Ph), δ ($CDCl_3$) 7.33 (10 H, s, Ph's), 5.46 (2 H, s, CH_2).

Reaction of Alcohol (17) with Boron Trifluoride: Acetic Acid Complex.- Boron trifluoride:acetic acid complex (110 μl of a solution 40% w/w in boron trifluoride) was added to a stirred solution of the alcohol (17) (255 mg, 0.88 mmol) in deuterochloroform (2 ml) at -23 °C. After 45 min, the mixture was warmed to room temperature and 10% sodium hyroxide solution (2 ml) was added. The mixture was separated, the aqueous layer extracted with deuterochloroform (1 ml) and the combined organic layers washed with water and dried (Na_2SO_4) to give a solution of t-butyl acetate[22] (30) (0.08 mmol by comparison of NMR integrals with a known quantity of benzene, 9%). $\nu_{max.}$(film) 1 725 cm^{-1} (C=O), δ ($CDCl_3$) 1.96 (3 H, s, OMe), 1.43 (9 H, s, CMe_3).

Methyl 3,3-Dimethyl-2-(1-pyrrolidinyl)-cyclobutanecarboxylate (31).- This was made by a method similar to that of Brannock.[23] 1-(2-Methyl-1-propenyl)-pyrrolidine[24] (35 g, 0.28 mol) was refluxed with methyl acrylate (25 g, 0.29 mol) in dry dioxan (50 ml) for 3 h. The mixture was cooled, the solvent removed in vacuo and the residue distilled to give the ester (31)(41 g, 68%) as an oil, essentially a single (presumably trans) diastereoisomer by ^{1}H-NMR, b.p. 80-82 °C/0.3 mmHg, ν max.(film) 1 730 cm^{-1} (C=O), δ ($CDCl_3$) 3.58 (3 H, s, OMe), 2.85 (1 H, q, J 8Hz, CHCO), 2.55 (1 H, d, J 8 Hz, NCH), 2.6-2.2 (4 H, m, NCH_2's), 1.8-1.5 (6 H, m, other CH_2's), 1.06 (3 H, s, CMe), 1.04 (3 H, s, CMe)(Found: M - OMe, 180.138 5. $C_{12}H_{21}NO_2$ - CH_3O requires M, 180.138 8), m/z 180 (10%, M - OMe) 155 (67, M - C_4H_8), 140 (100, M - C_4H_9N).

N-(1-Carbomethoxy-3,3-dimethyl-2-cyclobutyl) N-Methyl Pyrrolidinium Iodide.- The ester (31)(21 g, 0.1 mol) and methyl iodide (18 g, 126 mmol) were kept in dry ether (50 ml) at room temperature for 14 days. The mixture was then filtered to give the methiodide (32 g, 90%) as cubes, m.p. 156-157 °C (from ethanol)(Found: C, 44.1; H, 6.90; N, 4.0. $C_{13}H_{24}NO_2$ requires C, 44.2; H, 6.90; N, 4.0%), ν max.(nujol mull) 1 725 cm^{-1} (C=O), δ (d_6-DMSO) 4.14 (1 H, d, J 10.3 Hz, NCH), 3.67 (3 H, s, OMe), 3.8-3.3 (5 H, m, NCH_2's and CHCO), 3.01 (3 H, s, NMe), 2.2-1.7 (6 H, m, other CH_2's), 1.36 (3 H, s, CMe), 1.28 (3 H, s, CMe).

Methyl (3,3-Dimethyl-1-cyclobutene)carboxylate (32).- The methiodide (5.0 g, 14.2 mmol) in methanol (50 ml) was added to a gently stirred solution of sodium methoxide (100 ml of a 0.7M solution) with a layer of light petroleum (50 ml) floating above it. After 1 h the mixture was separated, water (150 ml) added to the methanol, and this extracted with light petroleum (2 x 50 ml). The combined petroleum layers were washed with water and brine, dried (Na_2SO_4), evaporated in vacuo, and distilled to give the ester[23] (32)(1.2 g, 63%) as an oil. B.p. 66-67 °C/ 26 mmHg (lit.[23], 56-62 °C/ 15 mmHg), ν max.(film) 1 710 (C=O), and 1 610 cm^{-1} (C=C), δ ($CDCl_3$) 6.80 (1 H, s, C=CH), 3.70 (3 H, s, OMe), 2.40 (2 H, s, CH_2), 1.20 (6 H, s, CMe_2).

Methyl 2,3,3-Trimethylcyclobutanecarboxylate.- Methyl-lithium (56 ml of a 1.5M solution in ether) was added to a stirred suspension of copper(I) iodide (8.2 g, 43 mmol) in dry ether (150 ml) at 0 °C. The solution was cooled to -78 °C and the unsaturated ester (27)(3.00 g, 21.4 mmol) in dry ether (300 ml) was added over 30 min. The solution was warmed to room temperature for 20 min, then cooled to -78 °C and saturated ammonium chloride solution (50 ml) was added. After warming to room temperature the mixture was separated and the aqueous layer extracted with ether (2 x 30 ml). The combined organic layers were washed with water and brine, dried (Na_2SO_4), and evaporated in vacuo to give the esters (3.1 g, 96%) as an oil. ν max.(film) 1 730 cm^{-1} (C=O), δ ($CDCl_3$) 3.61 (3 H, s, OMe), 2.6-2.0 (2 H, m, CH's), 1.9-1.6 (2 H, m, CH_2), 1.1-0.8 (9 H, m, CMe's)(Found: M - H, 155.107 8. $C_9H_{16}O_2$ - H requires M, 155.107 2), m/z 155 (27%, M - H), 125 (83, M - OMe), 101 (100, $C_5H_9O_2$).

2,3,3-Trimethylcyclobutylmethanol.- The above esters (2.30 g, 14.7 mmol) were reduced with lithium aluminium hydride and the product distilled to give the alcohols (1.50 g, 78%) as an oil, b.p. 91-94 °C/38 mmHg, ν max.(film) 3 340 cm^{-1} (OH), δ ($CDCl_3$) 2.8-2.5 (2 H, m, CH_2O), 2.3-1.3 (4 H, m, CH's and other CH_2), 1.2-0.9 (9 H, m, Me's)(Found: M - Me, 113.097 2. $C_8H_{16}O$ - CH_3 requires M, 113.096 6), m/z 113 (2%, M - Me), 110 (3, M - H_2O), 95 (47, M - (Me + H_2O), 70 (84, C_4H_{10}), 55 (100, C_4H_7).

2,3,3-Trimethylcyclobutylmethyl p-Toluenesulphonate.- The above alcohols (1.40 g, 10.9 mmol) gave the tosylates (3.0 g, 99%) as an oil. R_F (light petroleum-ethyl acetate, 3:1 v/v) 0.42, ν max.(film) 1 601 and 1 498, (Ar), 1 370 and 1 195 cm^{-1} (SO_2-O), δ ($CDCl_3$) 7.77 (2 H, d, J 8.3 Hz, ArH, H's m to Me), 7.31 (2 H, d, J 8.3 Hz, ArH, H's o to Me), 4.1-3.9 (2 H, m, CH_2O), 2.43 (3 H, s, ArMe), 2.1-1.1 (4 H, m, CH's and other CH_2), 1.1-0.8 (9 H, m, other Me's)(Found: M - C_4H_7, 227.073 5. $C_{15}H_{22}O_3S$ - C_4H_7 requires M, 227.072 2), m/z 227 (17%, M - C_4H_7), 173 (100, M - C_8H_{13}).

1,1,2,3-Tetramethylcyclobutane (33).- The above tosylates (1.00 g, 3.5 mmol) in THF (5 ml) were added to a refluxing suspension of lithium aluminium hydride (0.14 g) in THF (10 ml). After 2 h the solution was cooled to 0 °C , saturated ammonium chloride solution (20 ml) added, the mixture filtered , then extracted with dichloromethane (3 x 20 ml). The combined organic layers were washed successively with water (2 x 30 ml), concentrated sulphuric acid (2 x 25 ml), water, sodium hydrogencarbonate solution, water, and brine. The solvent was then removed by distillation and the product distilled (Kugelrohr, 100 °C) to give the cyclobutanes (33)(0.24 g of a mixture with dichloromethane, 50 mg product by NMR, 12%). νmax.(film) 3 000-2 900 cm^{-1} (CH), δ($CDCl_3$) 2.3-1.2 (4 H, m, $CHCHCH_2$), 1.1-0.8 (12 H, m, Me's)(Found: M^+, 112.125 4. C_8H_{16} requires M, 112.125 2), m/z 112 (5%, M^+), 70 (61, C_5H_{10}), 56 (100, C_4H_8).

(5RS,6RS)-2,5-Dimethyl-6-phenyl-6-tributylstannyl-2-hexene (34).- The alcohol (11)(181 mg, 0.37 mmol) was treated with with boron trifluoride:acetic acid complex

(1 equivalent with respect to boron trifluoride) at 0 °C for 15 min in dichloromethane (3 ml), worked up as previously, and the product purified by preparative thin layer chromatography, eluting with light petroleum, to give the alkene (34) (58 mg, 38%) as an oil. R_F (light petroleum: ethyl acetate, 5:1 v/v) 0.74, $\nu_{max.}$(film) 1 599 and 1 491 (Ph), and 800 cm^{-1} (C=CH), δ ($CDCl_3$) 7.2-6.9 (5 H, m, Ph), 5.16 (1 H, t, J 5.1 Hz, C=CH), 2.37 (1 H, d, J 10.7 Hz, SnCH), 2.3-2.1 (2 H, m, CH_2CH=C), 2.0-1.8 (1 H, m, $CHCH_3$), 1.72 (3 H, s, C=CMe), 1.61 (3 H, s, C=CMe), 1.4-1.2 (12 H, m, $CH_2CH_2CH_2Sn$'s), 0.83 (9 H, t, J 7.0 Hz, CH_3CH_2's), 0.78 (3 H, d, J 6.5 Hz, CH_3CH), 0.72 (6 H, t, J 7.2 Hz, CH_2Sn's), m/z 421 (48%, M - Bu), 291 (95, Bu_3Sn), 235 (100, Bu_2SnH).

Cyclisation of the alcohol (11).- The alcohol (11) (169 mg, 0.34 mmol) was treated with boron trifluoride:acetic acid complex (3 equivalents with respect to boron trifluoride) for 1 h at room temperature, worked up as previously, and the product purified by preparative thin layer chromatography, eluting with light petroleum, to give a mixture of 6,7,8,9-tetrahydro-5,5,8-trimethyl-5H-benzocycloheptene (37) and 1,2,3,4-tetrahydro-3-methyl-1-(2-propyl)-naphthalene (38) (57 mg, 89%, in a ratio of 60:40 by NMR) as an oil. R_F (light petroleum) 0.43, $\nu_{max.}$(film) 1 601 and 1 495 cm^{-1} (Ar), δ ($CDCl_3$) (benzcycloheptene) 7.4-7.0 (4 H, m, Ar), 2.92 (1 H, dd, J 9.5 and 14.5 Hz, $ArCH_AH_B$), 2.74 (1 H, d, J 14.5 Hz, $ArCH_AH_B$), 2.0-1.5 (5 H, m, $CHCH_2CH_2$), 1.40 (3 H, s, CMe_AMe_B), 1.34 (3 H, s, CMe_AMe_B), 0.98 (3 H, d, J 6.4 Hz, $CHCH_3$), δ ($CDCl_3$) (tetralin) 7.4-7.0 (4 H, m, Ar), 3.0-2.9 (1 H, m, ArCH), 2.69 (1 H, dt, J 15.2 and 3.3 Hz, $ArCH_AH_B$), 2.46 (1 H, dseptet, J 4.0 and 6.9 Hz, $CHMe_2$), 2.32 (1 H, dd, J 15.2 and 12.0 Hz, $ArCH_AH_B$), 1.9-1.6 (3 H, m, $CHCH_3$ and other CH_2), 1.08 (3 H, d, J 6.9 Hz, CMe_AMe_B), 1.06 (3 H, d, J 6.9 Hz, CMe_AMe_B), 0.64 (3 H, d, J 6.8 Hz, CH_2CHCH_3) (although there were other minor peaks in the NMR the tetralin appeared to consist of essentially a single diastereoisomer) (Found: M^+, 188.155 2. $C_{14}H_{20}$ requires M, 188.156 5), m/z 188 (29%, M^+), 175 (52, M - Me), 145 (100, M - C_3H_7).

(4RS,5SR)-4-Methyl-5-trimethylstannyl-1,1-diphenyl-1-hexene (39).- The alcohol (18) (87 mg, 0.20 mmol) reacted with boron trifluoride:acetic acid complex and the product was purified by preparative thin layer chromatography, eluting with light petroleum to give the alkene (39) (26 mg, 31%) as an oil. R_F (light petroleum) 0.31, $\nu_{max.}$(film) 1 599 and 1 499 (Ph), and 790 cm^{-1} (C=CH), δ ($CDCl_3$) 7.5-7.1 (10 H, m, Ph's), 6.09 (1 H, t, J 7 Hz, C=CH), 2.3-1.9 (2 H, m, CH_2C=C), 1.6-1.2 (2 H, m, CH's), 1.04 (3 H, d, J 6.5 Hz, $SnCHCH_3$), 0.90 (3 H, d, J 6.2 Hz, CH_2CHCH_3), -0.04 (9 H, s, Me_3Sn), m/z 399 (7%, M - Me), 165 (100, Me_3Sn).

Reaction of Acid Chlorides and Aldehydes with Boron Trifluoride Etherate.- Typically, the substrate (1 mmol) and boron trifluoride etherate (1 mmol) were stirred in dry dichloromethane (2 ml) for 4 h at room temperature. The solution was then diluted with dichloromethane and washed with sodium hydrogencarbonate solution, water, and brine, dried (Na_2SO_4), and evaporated in vacuo.

Cyclisation of Acid Chloride (19).- The acid chloride (18) (357 mg, 0.93 mmol) was treated with boron trifluoride etherate and the product purified by distillation (Kugelrohr, 170 °C) to give trans-2,2,4,5-tetramethylcyclopentanone[25] (40) (111 mg, 76%) as an oil. $\nu_{max.}$(film) 1 745 cm^{-1} (C=O), δ ($CDCl_3$) 1.91 (1 H, dd, J 5.7 and 12.4 Hz, CH_AH_B), 1.8-1.6 (2 H, m, CH's), 1.29 (1 H, dd, J 12, 12.4 Hz, CH_AH_B), 1.11 (3 H, d, J 6.0 Hz, $CHCH_3$), 1.07 (3 H, s, CMe_AMe_B), 1.06 (3 H, d, J 6.6 Hz, other $CHCH_3$), 0.96 (3 H, s, CMe_AMe_B) (Found: M^+, 140.119 8. $C_8H_{16}O$ requires M, 140.120 1), m/z 140 (17%, M^+), 125 (10, M - Me), 83 (58, C_6H_{11}), 56 (100, C_3H_4O).

Cyclisation of the acid chloride (23).- The acid chloride (23) (300 mg, 0.88 mmol) was cyclised in the same way as its diastereoisomer, to give trans-2,2,4,5-tetramethylcyclopentanone (40) (69 mg, 56%), identical (IR, 250 MHz NMR) with that from the acid chloride (19).

(E,E)-Ethyl 4-Methyl-5-phenyl-2,4-pentadienoate.-Triethylphosphonoacetate (9.0 g, 40 mmol) in dry ether (20 ml) was added dropwise to a stirred suspension of sodium hydride (1.6 g, 68 mmol, washed with light petroleum before use) in dry ether (30 ml). After 15 min α-methylcinnamaldehyde (5.9 g, 40 mmol) in dry ether (30 ml) was added dropwise, and the mixture stirred for 5 min. Water (50 ml) was added, the mixture separated, and the aqueous layer extracted with ether (2 x 25 ml). The combined organic layers were washed with water and brine, dried (Na_2SO_4), evaporated in vacuo, and distilled to give the ester[26] (6.54 g, 75%) as an oil, b.p. 106-110 °C/0.2 mmHg, $\nu_{max.}$(film) 1 710 (C=O), 1 614 (C=C), 1 589 and 1 500 cm-1 (Ph), δ ($CDCl_3$) 7.48 (1 H, dd, J 1 and 15.6 Hz, CH=CHCO), 7.4-7.1 (5 H, m, Ph), 6.8 (1 H, broad s, PhCH), 5.95 (1 H, dd, J 0.5 and 15.6 Hz, CHCO), 4.22 (2 H, q, J 7.1 Hz, OCH_2), 2.01 (3 H, d, J 1.3 Hz, CCH_3), 1.29 (3 H, t, J 7.1 Hz, CH_2CH_3).

Ethyl 4-Methyl-5-phenylpentanoate.- The above ester (3.0 g, 13.9 mmol) in ethanol (40 ml) was hydrogenated over palladium (0.06 g, 10% w/w on carbon) for 3 h until the theoretical amount of hydrogen had been taken up. The mixture was then filtered, the solvent removed in vacuo, and the residue distilled to give the ester (2.65 g, 87%) as an oil, b.p. 96-98 °C/0.2 mmHg, R_F (light petroleum-ethyl acetate,

5:1 v/v) 0.49, $\nu_{max.}$(film) 1 738 (C=O), 1 601 and 1 499 cm^{-1} (Ph), δ ($CDCl_3$) 7.3-7.0 (5 H, m, Ph), 4.11 (2 H, q, J 7.1 Hz, OCH_2), 2.8-2.3 (4 H, m, $PhCH_2$ and CH_2CO), 1.9-1.5 (3 H, m, $CHCH_2$), 1.24 (3 H, t, J 7.1 Hz, CH_2CH_3), 0.87 (3 H, d, J 6.2 Hz, $CHCH_3$)(Found: M^+, 220.148 1. $C_{14}H_{20}O_2$ requires M, 220.146 3), m/z 220 (6%, M^+), 174 (45, M - EtOH), 91 (100, $PhCH_2$).

2,5-Dimethyl-6-phenyl-2-hexanol.- The above ester (1.84 g, 8.36 mmol) was treated with methyl magnesium iodide, and the product distilled to give the alcohol (1.52 g, 88%) as an oil, b.p. 109-110 °C/0.3 mmHg, R_F (light petroleum: ethyl acetate, 5:1 v/v) 0.21, $\nu_{max.}$(film) 3 300 (OH), 1 601 and 1 599 cm^{-1} (Ph), δ ($CDCl_3$) 7.3-7.0 (5 H, m, Ph), 2.69 (1 H, dd, J 5.6 and 13.1 Hz, $PhCH_AH_B$), 2.35 (1 H, dd, J 7.6 and 13.1 Hz, $PhCH_AH_B$), 1.9-1.1 (5 H, m, CH_2CH_2CH), 1.33 (1 H, s, OH), 1.19 (6 H, s, CMe_2), 0.86 (3 H, d, J 6.3 Hz, $CHCH_3$)(Found M - Me, 191.144 0. $C_{14}H_{22}O$ - CH_3 requires M, 191.143 6), m/z 191 (9%, M - Me), 188 (68, M - H_2O), 91 (100, $PhCH_2$), 59 (88, C_3H_7O).

2,5-Dimethyl-6-phenyl-2-hexene (41).- In an attempt to cyclise it, the above alcohol (0.50 g, 2.43 mmol) was refluxed in toluene (15 ml) with p-toluenesulphonic acid (0.50 g) for 20 min. The solution was cooled, diluted with ether (30 ml), and washed successively with water, sodium hydrogencarbonate solution, water, and brine, dried (Na_2SO_4), and evaporated in vacuo to give the alkene (41)(0.41 g, 90%) as an oil. R_F (light petroleum) 0.43, $\nu_{max.}$(film) 1 670 (C=C), 1 602 and 1 499 cm^{-1} (Ph), δ($CDCl_3$) 7.3-7.0 (5 H, m, Ph), 5.2 (1 H, t with other fine coupling, J 7 Hz, C=CH), 2.63 (1 H, dd, J 5.8 and 13.4 Hz, $PhCH_AH_B$), 2.34 (1 H, dd, J 7.3 and 13.4 Hz, $PhCH_AH_B$), 2.1-1.8 (3 H, m, $CHCH_2$), 1.71 (3 H, broad s, C=CMe), 1.58 (3 H, broad s, C=CMe), 0.85 (3 H, d, J 6.3 Hz, $CHCH_3$)(Found: M^+, 188.154 8. $C_{14}H_{20}$ requires M, 188.155 5), m/z 188 (31%, M^+), 91 (100, $PhCH_2$).

Cyclisation of the Alkene (41).- The alkene (41)(0.34 g, 1.8 mmol) was treated with boron trifluoride acetic:acid complex and the product purified by flash chromatography, eluting with light petroleum, to give a mixture of the the benzcycloheptene (37) and the tetralin (38)(223 mg, 59%, in a ratio of 25:75 by NMR). The product coeluted by TLC with that from the stannyl alcohol (11), had a similar IR spectrum and the same peaks, but in different ratio, in the 250 MHz NMR and the mass spectrum.

Cyclisation of the aldehyde (20)- A mixture of the aldehyde (20) and triphenylphosphine (133 mg total, 100 mg aldehyde, 0.33 mmol) was treated with boron trifluoride etherate, and the product purified by flash chromatography, eluting with light petroleum (b.p. 30 - 40 °C): ether, 5:1 v/v, to give (1α,4β,5α)-2,2,4,5-tetramethylcyclopentanol (43)(24 mg, 52%) as an oil. R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.26, $\nu_{max.}$(film) 3 400 cm^{-1} (OH), δ ($CDCl_3$) 3.18 (1 H, d, J 9.3 Hz, CHO), 2.10 (1 H, dddq, J 8.1, 8.3, 9.3, and 7.2 Hz, $CHCH_2$), 1.88 (1 H, tq, J 9.3, 7.0 Hz, CHCHO), 1.73 (1 H, dd, J 8.1 and 13.0 Hz, CH_AH_B), 1.4 (1 H, s, OH), 1.01 (1 H, dd J 8.3 and 13.0 Hz, CH_AH_B), 1.00 (3 H, s, CMe_AMe_B), 0.97 (3 H, d, J 7.0 Hz, CH_3CHCHO), 0.87 (3 H, s, CMe_AMe_B), 0.83 (3 H, d, J 7.2 Hz, $CHCHCH_2$)(Found: M^+: 142.135 2. $C_9H_{18}O$ requires M, 142.135 7), m/z 142 (12%, M^+), 109 {18, M - (Me + H_2O)}, 83 (100, C_6H_{11}). The assignment and coupling constants of the two methine multiplets and the methyl doublets are derived from separately decoupling the methyl doublets and observing the methine signals. Positive NOE's that help determine relative stereochemistry were: (i) from H-a (using the convention adopted for 46) to the downfield methyl singlet, (ii) from H-e to the upfield methyl singlet, (iii) from H-c to the downfield methyl singlet, and (iv) from the methyl doublet (b) to the upfield methyl singlet. From these we can conclude that (i) the downfield singlet is j, (ii) that H-e is cis to the methyl group (h), i.e. that methyl group (d) is trans to the hydroxyl group, (iii) that H-c is cis to methyl group (j), i.e. that the C-5 methyl group is cis to the hydroxyl group, and (iv) the last NOE confirms that methyl group (b) is cis to methyl singlet (h), i.e. cis to the hydroxyl group. As well as these positive NOE's, there is a distinct negative NOE from each methyl doublet to the other, indicative of a linear three-spin system,[27] confirming the trans relationship of these methyl groups. In addition to the signals reported in the NMR there was a doublet δ 3.34 (J 8 Hz). The ratio of the integral of this signal to the one at δ 3.18 was 1:9. We presume this signal arises from one of the 4,5-cis isomers but cannot prove this.

Reaction of the Aldehyde (24) with Boron Trifluoride Etherate.- The aldehyde (24) and triphenylphosphine (260mg total, 185 mg aldehyde, 0.61 mmol) were treated with boron trifluoride etherate and the product purified by flash chromatography, eluting with light petroleum (b.p. 30 - 40 °C): ether, 5:1 v/v, to give E-2,2,4-trimethyl-4-hexen-1-ol (45)(35 mg, 40%) as an oil, R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.23, $\nu_{max.}$(film) 3 300 (OH), 1 630 cm^{-1} (C=C), δ ($CDCl_3$) 5.24 (1 H, q, J 7 Hz, C=CH), 3.31 (2 H, s, CH_2O), 1.96 (2 H, s, $C=CCH_2$), 1.66 (3 H, s, $C=CCH_3$), 1.58 (3 H, d, J 7 Hz, $C=CHCH_3$), 1.4 (1 H, s, OH), 0.88 (6 H, s, CMe_2)(Found M^+, 142.135 1. $C_9H_{18}O$ requires M, 142.135 7), m/z 142 (3%, M^+), 72 (58, C_4H_8O), 55 (100, C_4H_7). Irradiation of the signal at 5.24 ppm gave a positive NOE to the singlet at 1.96 ppm and no NOE to the singlet at 1.66 ppm, proving the geometry of the double bond.

(1'α,4'β,5'α)-2',2',4',5'-Tetramethyl-1'-cyclopentyl 3,5-Dinitrobenzoate (46).- 3,5-Dinitrobenzoyl chloride (8.5 mg, 0.037 mmol) in dry dichloromethane (0.5 ml) was added to a stirred solution of the alcohol (43)(5 mg, 0.036 mmol), triethylamine (4 mg) and 4-dimethylaminopyridine (1 mg) in dry dichloromethane (3 ml). After 5 h, the solution was diluted with dichloromethane, washed with dilute hydrochloric acid, sodium hydrogencarbonate solution, water and brine, dried (Na_2SO_4), and evaporated in vacuo to give the benzoate (46)(10 mg, 85%) as cubes, m.p. 100-101 °C (from pentane)(Found: C, 57.2; H, 6.05; N, 8.1. $C_{16}H_{20}N_2O_6$ requires C, 57.1; H, 6.00; N, 8.3%), R_F (light petroleum: ethyl acetate, 5:1 v/v) 0.45, $\nu_{max.}$($CHCl_3$) 1 725 (C=O), 1 500 (Ar), 1 550 and 1 350 cm^{-1} (NO_2), δ($CDCl_3$) 9.23 (1 H, t, J 2.1 Hz, ArH), 9.15 (2 H, d, J 2.1 Hz, ArH), 4.94 (1 H, d, J 7.6 Hz, CHO), 2.4-2.2 (2 H, m, CH's), 1.86 (1 H, dd, J 8 and 13 Hz, CH_AH_B), 1.30 (1 H, dd, J 7 and 13 Hz, CH_AH_B), 1.11 (3 H, s, CMe_AMe_B), 1.06 (3 H, s, CMe_AMe_B), 0.99 (3 H, d, J 6.7 Hz, $CHCH_3$), 0.95 (3 H, d, J 6.7 Hz, $CHCH_3$)(Found: M - NO, 306.132 8. $C_{16}H_{20}N_2O_6$ - NO requires M, 306.134 1), m/z 306 (7%, M - NO), 83 (100, C_6H_{11}). NOE experiments on this compound were conducted in a mixture of $CDCl_3$ and C_6D_6 (60:40 v/v) as this gave optimum signal separation. In that solvent the spectrum had the following signals: δ 8.83 (2 H, d, J 2 Hz, ArH), 8.70 (1 H, t, J 2 Hz, ArH), 4.93 (1 H, d, J 7.3 Hz, H-a), 2.3-2.1 (2 H, m, H-e and H-c), 1.70 (1 H, dd, J 7.4 and 13.0 Hz, H-f), 1.18 (1 H, dd, J 5.2 and 13.0 Hz, H-g), 1.10 (3 H, s, Me-j), 1.00 (3 H, s, Me-h), 0.95 (3 H, d, J 6.2 Hz, Me-b), 0.86 (3 H, d, J 6.3 Hz, Me-d).

trans 2,2,4-Trimethyl-5-phenylthiomethylcyclopentanone.- This was made by the method of Paterson.[28] 2,2,4-Trimethylcyclopentanone[29] (3.00 g, 23.8 mmol) in THF (10 ml) was added to a solution of lithium di-isopropylamide (36 mmol) in THF (150 ml) at -78 °C. After 1 h chlorotrimethylsilane (5.4 g, 50 mmol) was added, the solution brought to room temperature, pentane (100 ml) added, and the mixture filtered and evaporated in vacuo. Pentane (50 ml) was added to the residue, the mixture filtered and evaporated, and then this process repeated. The resultant oil was dissolved in dichloromethane (50 ml), chloromethyl phenyl sulphide (5.26 g, 41 mmol) added, and the solution cooled to -23 °C. Titanium tetrachloride (5.00 g, 26 mmol) in dichloromethane (20 ml) was added dropwise, then the black solution stirred for 2h. It was then poured into saturated sodium hydrogencarbonate solution, extracted with ether (3 x 50 ml), and the organic layers washed with water and brine, dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography, eluting with light petroleum-ethyl acetate (12:1, v/v), to give the ketone (4.41 g, 75%) as an oil. R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.43, $\nu_{max.}$(film) 1 745 (C=O), and 1 580 cm^{-1} (Ph), δ($CDCl_3$) 7.4-7.1 (5 H, m, Ph), 3.33 (1 H, dd, J 4.2 and 13.2 Hz, SCH_AH_B), 3.10 (1 H, dd, J 5.3 and 13.2 Hz, SCH_AH_B), 2.2-1.5 (4 H, m, $CHCHCH_2$), 1.15 (3 H, d, J 5.8 Hz, $CHCH_3$), 1.08 (3 H, s, CMe_AMe_B), 0.99 (3 H, s, CMe_AMe_B)(Found: M^+, 248.121 8. $C_{15}H_{20}OS$ requires M, 248.123 5), m/z 248 (23%, M^+), 69 (50, C_5H_9), 55 (100, C_4H_7).

Desulphurisation of 2,2,4-trimethyl-5-phenylthiomethylcyclopentanone.- The ketone (2.50 g, 10.1 mmol) was stirred with Raney nickel (approx. 12 g) in acetone: ethanol (100ml, 10:1 v/v) for 3 h. The mixture was then filtered and most of the solvent removed by distillation. Water (50 ml) was added, and the mixture extracted with ether (3 x 30 ml). The combined organic layers were washed with water and brine, dried (Na_2SO_4), evaporated in vacuo, and the residue distilled (Kugelrohr, 170 °C) to give the ketone (40)(0.80 g, 57%), identical (IR, 250 MHz NMR) with that from the acid chlorides (19) and (23).

Reduction of the ketone (40).- The ketone (40)(50 mg, 0.36 mmol) in dry ether (1 ml) was added to a stirred suspension of lithium aluminium hydride (15 mg, 0.39 mmol) in dry ether (3 ml) at 0 °C. After 1 h dry methyl formate (0.5 ml) was carefully added. (Destroying excess lithium aluminium hydride this way prevents possible epimerisation of any remaining starting material followed by reduction during the work up.) After 10 min, water (5 ml) was added, the mixture separated, and the aqueous layer extracted with ether (2 x 5 ml). The combined organic layers were washed with water and brine, dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography, eluting with light petroleum (b.p. 30 - 40 °C): ether, 5:1 v/v, to give a mixture of (1α,4α,5β)-2,2,4,5-tetramethylcyclopentanol (42) and the (1α,4β,5α)-isomer (43)(33 mg, 65%) in a ratio of 94:6 by NMR. The minor isomer had signals in the 250 MHz NMR identical with those of the alcohol produced by cyclisation of the aldehyde (20). Major isomer - R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.26, $\nu_{max.}$(film) 3 400 cm^{-1} (OH), δ ($CDCl_3$) 3.14 (1 H, d, J 8.9 Hz, CHO), 1.65 (1 H, dd, J 7.9 and 12.7 Hz, CH_AH_B), 1.4-1.2 (2 H, m, CH's), 1.13 (1 H, dd, J 8.4 and 12.7 Hz, CH_AH_B), 1.02 (3 H, d, J 6.2 Hz, $CHCH_3$), 1.00 (3 H, s, CMe_AMe_B), 0.94 (3 H, d, J 6.2 Hz, $CHCH_3$), 0.91 (3 H, s, CMe_AMe_B)(Found: M^+, 142.137 0. $C_9H_{18}O$ requires M, 142.135 7), m/z 142 (23%, M^+), 109 (12, M - (H_2O + Me)}, 83 (100, C_6H_{11}).

(2RS,3SR)-2-Methyl-3-trimethylstannylbutanal.- Pyridinium chlorochromate (3.73 g, 17 mmol) was stirred in dichloromethane (40 ml) for 15 min then a solution of the alcohol (14) (2.70 g, 10.8 mmol) in dichloromethane (10 ml) was added. After a further 3 h the solution was filtered through silica gel and evaporated in vacuo to give the aldehyde (2.34 g, 88%) as an oil. R_F (light petroleum-ethyl acetate, 5:1

v/v) 0.50 $\nu_{max.}$(film) 1 730 cm^{-1} (C=O), δ ($CDCl_3$) 9.63 (1 H, d, J 1.2 Hz, CHO), 2.7-2.4 (1 H, m, CHCO), 1.6-1.4 (1 H, m, SnCH), 1.11 (3 H, d, J 7 Hz, $SnCHCH_3$), 1.09 (3 H, d, J 7 Hz, CH_2CHCH_3), 0.08 (9 H, s, Me_3Sn), m/z 250 (2%, M^+), 235 (5, M - Me), 205 (100, M - C_3H_9), 165 (22, Me_3Sn).

2-Methyl-3-trimethylstannyl-1-phenyl-1-butanol.- The above aldehyde (0.37 g, 1.49 mmol) in dry ether (5 ml) was added to a stirred solution of phenyl magnesium bromide (2.25 mmol) in dry ether (10 ml) at 0 °C. After 1 h, saturated ammonium chloride solution (10 ml) was added, the mixture separated, and the aqueous layer extracted with ether (2 x 10 ml). The combined organic layers were washed with water and brine, dried (Na_2SO_4), evaporated in vacuo, and purified by flash chromatography, eluting with light petroleum-ethyl acetate (20:1, v/v), to give the (1RS,2RS,3SR)-alcohol (47)(152 mg, 31%) as an oil, R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.52, $\nu_{max.}$ 3 400 (OH), 1 600 and 1 498 cm^{-1} (Ph), δ ($CDCl_3$) 7.4-7.2 (5 H, m, Ph), 4.70 (1 H, d, J 5.2 Hz, CHO), 2.1-1.9 (1 H, m, CHCHO), 1.7 (1 H, s, OH), 1.4-1.2 (1 H, m, SnCH), 1.2 (3 H, d, J 6Hz, $SnCHCH_3$), 0.94 (3 H, d, J 6.8 Hz, other CH_3), 0.05 (9 H, s, Me_3Sn), m/z 328 (1%, M^+), 313 (10, M - Me), 295 [3, M - (Me + H_2O)], 165 (100, Me_3Sn), and the (1SR,2RS,3SR)-alcohol (102 mg, 21%) as an oil, R_F (light petroleum-ethyl acetate, 5:1 v/v) 0.49, $\nu_{max.}$(film) 3 400 (OH), 1 600 and 1 500 cm-1 (Ph), δ ($CDCl_3$) 7.3-7.2 (5 H, m, Ph), 4.39 (1 H, d, J 9 Hz, CHO), 2.1-1.5 (2 H, m, CH's), 1.7 (1 H, s, OH), 1.2 (3 H, d, J 7 Hz, $SnCHCH_3$), 0.63 (3 H, d, J 7 Hz, other CH_3), 0.06 (9 H, s, Me_3Sn), m/z 313 (13%, M - Me), 295 [2, M - (Me + H_2O)], 165 (100, Me_3Sn). The relative stereochemistry of the isomers at the hydroxyl-bearing carbon is assumed on the basis that the cyclisation of the major isomer (see below) goes with inversion at that centre [5].

(1α,2β,3β)-1,2-Dimethyl-3-phenylcyclopropane(48).- Thealcohol (47)(120 mg)(0.37 mmol) was treated with boron trifluoride:acetic acid complex in dichloromethane (5 ml) for 20 min at 0 °C then worked up as usual. The product was purified by flash chromatography, eluting with light petroleum (b.p. 30 - 40 °C) to give the cyclopropane[30] (48)(33 mg, 62%) as an oil. $\nu_{max.}$(film) 1 605, 1 585, and 1 500 cm^{-1} (Ph), δ ($CDCl_3$) 7.3-7.1 (5 H, m, Ph), 1.16 (9 H, s, other H's).

REFERENCES

1. For example: D.E. Applequist and G.N. Churmny, J. Am. Chem. Soc., 1967, **89**, 875; W.H. Glaze, C.M. Selman, A. Leroy Ball, and L.E. Bray, J. Organomet. Chem., 1969, **34**, 641; J.M. Fukuto and P.R. Jensen, Acc. Chem. Res., 1983, **16**, 177; H.A. Olszowy and W. Kitching, J. Org. Chem., 1982, **47**, 5231; see also ref. 2
2. For example: W.C. Still and C. Sreekumar, J. Am. Chem. Soc., 1980, **102**, 1201; J.S. Sawyer, T.L. MacDonald, and G.J. McGarvey, J. Am. Chem. Soc., 1984, **106**, 3376; H.M. Walborsky, F.J.Impastato, and A.E. Young, J. Am. Chem. Soc., 1963, **86**, 3283
3. D.D. Davis and H.T. Johnson, J. Am. Chem. Soc., 1974, **96**, 7576
4. J.A. Marshall and J.H. Babler, J. Chem. Soc., Chem. Commun., 1968, 993. See also H.L. Goering and S.L. Trenbeath, J. Am. Chem. Soc., 1976, **98**, 5016
5. I. Fleming and C.J. Urch, J. Organomet. Chem., 1985, **285**, 173
6. H.E. Zimmerman, L. Singer, and B.S. Thyagarajan, J. Am. Chem. Soc., 1959, **81**, 108, footnote 16
7. J.F. Kadow and C.R. Johnson, Tetrahedron Lett., 1984, 5255
8. I. Fleming and M. Rowley, Tetrahedron Lett., 1985, 3857
9. C.H. De Puy, Acc. Chem. Res., 1968, **1**, 40
10. I. Fleming, J.H.M. Hill, D.J. Parker, and D. Waterson, J. Chem. Soc., Chem. Commun., 1985, 318
11. G.J. McGarvey and J.M. Williams, J. Am. Chem. Soc., 1985, **107**, 1435
12. T.L. McDonald and S. Mahalingham, J. Am. Chem. Soc., 1980, **102**, 2113
13. E. Murayama, M. Uematsu, H. Nishio, and T. Sato, Tetrahedron Lett., 1984, 313
14. W.C. Still, J. Am. Chem. Soc., 1978, **100**, 1481
15. A.M. van Leusen and D. van Leusen, Synth. Commun., 1978, **8**, 397
16. A.P. Krapcho, J.F. Weimaster, J.M. Eldridge, E.G.E. Jahngen, A.J. Lovey, and W.P. Stephens, J. Org. Chem., 1978, **43**, 138
17. W.C. Still, J. Am. Chem. Soc., 1977, **99**, 4836
18. P.L. Cregar, Org. Synth., 1970, **50**, 58
19. G.W.J. Fleet and P.J.C. Harding, Tetrahedron Lett., 1979, 975
20. K.B. Wiberg and T.W. Hutton, J. Am. Chem. Soc., 1956, **78**, 1640
21. R. van der Linde, O. Korver, P.K. Korver, P.J. van der Haak, J.V. Veenland, and Th.J. de Boer, Spectrochim. Acta., 1965, **21**, 1893; A. Jung and M. Brini, Bull. Soc. Chim. Fr., 1965, 587
22. Aldrich Library of NMR Spectra, Edition II, Vol I, 1983, C.J. Pouchert (Ed.)
23. K.C. Brannock, R.D. Burpitt, W.V. Goodlett, and J.G. Thweat, J. Org. Chem., 1964, **29**, 813
24. E. Benzing, Angew. Chem., 1959, **71**, 521
25. J.C. Bardham and R.N. Adhyo, J. Chem. Soc., 1956, 2179
26. Y. Koyama, N. Kyomura, J. Ohishi, and S. Yamagishi, Yakugaku Zasshi, 1975, **95**, 1210
27. J.H. Noggle and R.E. Schirmer, The Nuclear Overhauser Effect, Academic Press, London, 1971, p.57

28. I. Paterson and I. Fleming, Tetrahedron Lett., 1979, 995
29. H.O. House, R.W. Giese, K. Kronberger, J.P. Kaplan, and J.F. Simeone, J. Am. Chem. Soc., 1970, 92, 2800
30. C.P. Casey, S.W. Polichnowski, A.J. Shusterman, and C.R. Jones, J. Am. Chem. Soc., 1979, 101, 7282

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