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ON THE STEREOSELECTIVITY OF REACTIONS BETWEEN α-METHYLBUT-2-ENYLSTANNANES AND ALDEHYDES

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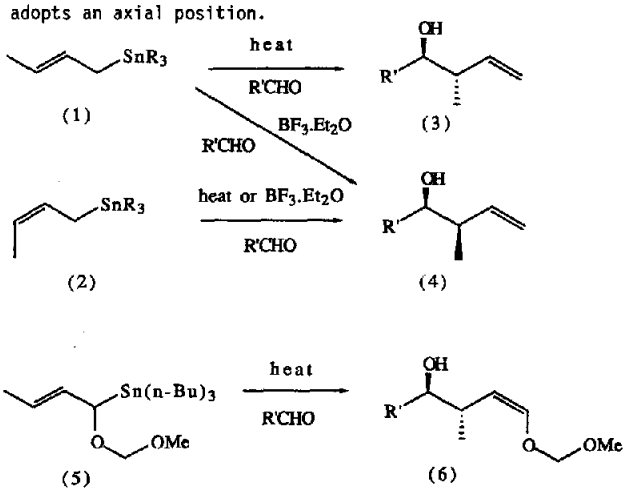
α-Methylbut-2-enylstannanes (7) - (9) react stereoselectively on heating with aldehydes to form anti-5-hydroxy-4-methyl-Z-pent-2-enes (16) and (17). In the presence of $BF_3.Et_2O$, the major products are the corresponding syn-5-hydroxy-4-methyl-E-pent-2-enes (22) and (23).

The chemistry of allylstannanes is being widely studied because of their use as reagents in organic synthesis.[1] But-2-enylstannanes (1) and (2) have been found to react stereoselectively with aldehydes on heating, and at lower temperatures in the presence of Lewis acid catalysts. However the stereoselectivities of these reactions are different. At -78°C, in the presence of $BF_3.Et_2O$, both E- and Z-but-2-enylstannanes (1) and (2) react with aldehydes to give the syn-adducts (4) via open-chain transition state processes.[2] In contrast, on heating with aldehydes in the absence of a catalyst, E-stannanes (1) give rise to the anti-adducts (3), whereas Z-stannanes (2) form the syn-adducts (4).[3] Chair-like, six- membered ring, transition states have been used to explain the stereoselectivities of these latter reactions. The α-alkoxybut-2-enylstannanes (5) react with aromatic and secondary aliphatic aldehydes on heating to give the anti-cis-enol ether products (6);[4] the stereoselectivity of these reactions again being explained in terms of chair-like, six-membered ring transition states in which the α-alkoxy substitutent adopts an axial position.



With these observations in mind, it was of interest to examine the stereochemistry of reactions between other α-substituted but-2-enylstannanes and aldehydes under both thermal and Lewis acid catalysed conditions. We now report the synthesis and aldehyde addition chemistry of the α-methylbut-2-enylstannanes (7), (8), and (9).[5]

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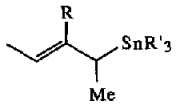
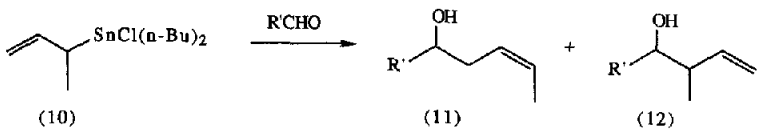
At the onset of this work, the α-methylbut-2-enyl(tri-n-butyl)stannane (7) was a known compound and its $BF_3.Et_2O$ catalysed reaction with propanal had been used in a synthesis of (±)-syn-4-methylheptan-3-ol.[6] The generation of the reactive α-methylpropenylstannane (10) in the presence of aldehydes giving rise to adducts (11) and (12) had also been described.[7]



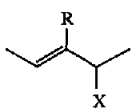
(7) R = H, R' = n-Bu
(8) R = H, R' = Ph
(9) R = Me, R' = n-Bu



(10) (11) (12)

RESULTS AND DISCUSSION

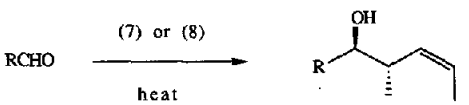
The α-methylbut-2-enylstannanes (7) and (8) were prepared by treatment of 4-chloropent-2-ene (13) with tri-n-butyl- and triphenyl-tin lithium respectively. The 2,3-dimethylbut-2-enylstannane (9) was similarly obtained from 4-chloro-3-methyl-pent-2-ene (14) which was prepared from tiglic aldehyde by treatment with methylmagnesium bromide, and the alcohol (15) so obtained converted into chloride (14) using thionyl chloride. The tri-n-butylstannanes (7) and (9) were non-polar oils purified by distillation; the triphenylstannane (8) was a crystalline solid purified by flash chromatography and recrystallisation from pentane.



(13) R = H, X = Cl
(14) R = Me, X = Cl
(15) R = Me, X = OH

Structures were assigned to the stannanes on the basis of spectroscopic data. The crystalline triphenylstannane (8) was obtained as a single stereoisomer with respect to the double-bond (^{1}H n.m.r.). However the (tri-n-butyl)-(E)-but-2-enylstannanes (7) and (9) did contain small amounts, ca. 10%, of the corresponding (Z)-isomers.

Reactions between the stannanes (7) and (8) and aromatic and secondary aliphatic aldehydes were carried out using a small excess of the stannane at temperatures between 80 - 150°C, neat for the stannane (7), or with a small amount of toluene as diluent for the stannane (8). Moderate to good yields of products were isolated, with the reaction conditions required depending upon the reactivity of the aldehyde towards nucleophilic attack, see Table. Reactions under thermal conditions using primary aliphatic aldehydes were not investigated because analogous reactions with the α-alkoxystannane (5) had been found to be complicated by competing aldol condensation of the aldehyde.[4] However the reaction between isopropyl glyoxylate, a reactive primary aldehyde which cannot undergo an aldol condensation, and the stannane (7), was found to be moderately efficient giving a 50% yield of adduct (16f) after 18h at 90°C.



(16)

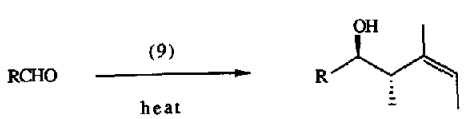
(a) R = Ph; (b) R = p-$O_2NC_6H_4$; (c) R = p-ClC_6H_4; (d) R = cyclohexyl;
(e) R = i-Pr; (f) R = i-PrO_2C; (g) R = PhCH=CH

In all cases the reactions were highly stereoselective giving, after flash chromatography, the anti-Z-alkenes (16), containing less than 1% of any other isomer as judged by 300 MHz. n.m.r. Examination of the crude reaction mixture from the reaction with benzaldehyde confirmed that essentially just the one stereoisomer had been formed.

TABLE

Aldehyde RCHO R	Stannane	Reaction Conditions Temp. °C	Time h	Product	Chromatographed Yield %
Ph	(7)	150	18	(16a)	72
p-$O_2NC_6H_4$	(7)	80	18	(16b)	87
p-ClC_6H_4	(7)	110	18	(16c)	70
cyclohexyl	(7)	150	18	(16d)	62
i-Pr	(7)	150	18	(16e)	55
i-PrO_2C	(7)	90	18	(16f)	50
Ph	(8)	150	18	(16a)	74
p-$O_2NC_6H_4$	(8)	80	18	(16b)	80
PhCH=CH	(8)	150	18	(16g)	67
Ph	(9)	150	18	(17a)	89
p-$O_2NC_6H_4$	(9)	80	18	(17b)	69
i-Pr	(9)	150	18	(17c)	50

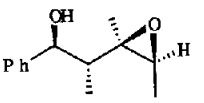
Reactions involving the stannane (9) were carried out under similar conditions to those required for stannane (7). Again product formation was highly stereoselective. In each case a single product, >98% isomerically pure as judged by 300 Mz. n.m.r., was isolated after flash chromatography and identified as the corresponding anti-Z-alkene (17). Qualitatively the trimethylallylstannane (9) was found to be ca. 10 times more reactive than the stannane (7).



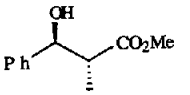
(17)

(a) R = Ph; (b) R = p-$O_2NC_6H_4$; (c) R = i-Pr

Structures were assigned to the products (16) and (17) on the basis of spectroscopic data and chemical correlation, with the cis double-bond geometry of the disubstituted alkenes (16) being established by the ^1H n.m.r. coupling constant across the double-bond, $J_{3,4}$ = 11 Hz. This stereochemistry was confirmed by n.O.e. data, i.e. for the benzaldehyde adducts (16a) irradiation of H(5) caused enhancements of the peaks due to H(2) and H(1) of 5.1 and 1.8% respectively, but had no effect on H(3). The Z-double-bond geometry assigned to the trisubstituted alkenes (17) was established by n.O.e. data which were obtained on the epoxide (18). This was prepared stereoselectively from the alkene (17a) by treatment with t-BuOOH - $VO(acac)_2$.[8] For epoxide (18) irradiation of 3-CH_3 and H(5) caused 9.8% and 14.6% enhancements of the peaks due to H(4) and H(2), respectively, so establishing the indicated stereochemistry.



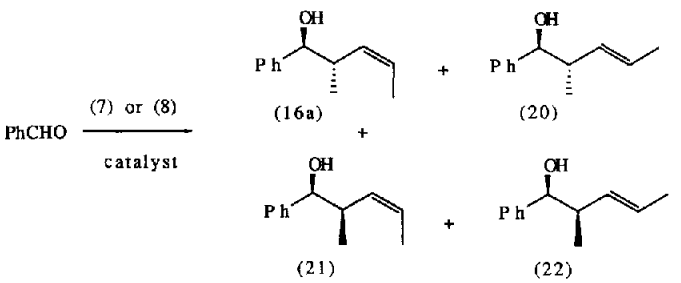
(18)

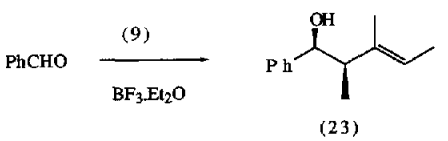


(19)

The anti-stereochemistry of adducts (16) and (17) at C(1) and C(2) was assigned by analogy with the literature,[3,4] and was confirmed for the benzaldehyde adduct (16a) by ozonolysis with a dimethyl sulphide work-up, oxidation, and esterification which gave the hydroxypropanoate (19) (53% overall), identical with an authentic sample.[9]

Lewis acid catalysed reactions of stannanes (7) - (8) with benzaldehyde were also investigated. These reactions were less stereoselective than the thermal, uncatalysed reactions had been, and the results were not always reproducible. The best results were obtained with $BF_3.Et_2O$ as catalyst at -78°C, which with the triphenylstannane (8), gave a mixture of syn- and anti-, cis- and trans-products, (16a), (20) - (22), containing predominantly the syn-E-isomer (22); ratio (16a) : (20) : (21) : (22) = 6 : 6 : 15: 73; yield 62%. The tri-n-butylstannane gave a slightly better yield, 77% but was a little less selective, perhaps due to its isomeric purity, (16a) : (20) : (21) : (22) = 13 : 7: 21: 59, respectively in this case. Amongst the other catalysts investigated, $SnCl_2$, $ZnCl_2$, $ZnBr_2$ and $FeCl_3$ (at 20°C), and $SnCl_4$ (at -78°C), gave similar distributions of products with the syn-E-product (22) predominating, whereas with $TiCl_4$ as catalyst, the anti-E-adduct (20) was the major product obtained using the tri-n-butylstannane (7), (16a) : (20) : (21) : (22) = 15 : 56: 14: 15, respectively (71%). The $BF_3.Et_2O$ catalysed reaction of the trimethylallylstannane (9) with benzaldehyde gave predominantly the syn-E-adduct (23) which accounted for ca. 75% of the product mixture, together with the other three diastereoisomers as minor components.

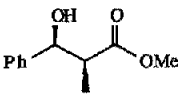




(23)

The products (16a), (20) - (22) were not separated, but were clearly distinguished by 300 Mz. ^1H n.m.r. with the protons at C(1) being particularly useful in this respect. Ozonolysis, oxidation, and diazomethane esterification of the mixture of products from the $BF_3.Et_2O$ catalysed reaction between stannane (8) and benzaldehyde, gave the syn-hydroxypropanoate (24) so showing that the major product had the syn-stereochemistry as expected by analogy with the literature.[2] The E-double-bond geometry of this major product was indicated by the vinylic coupling constant of 16 Hz. Since the anti-Z-product had already been identified from the thermal reactions, the other two products had to be the anti- E- and syn-Z-isomers (20) and (21). The major product from the $TiCl_4$ - tri-n-butylstannane reaction was not (22) yet was found to be an E-isomer by ^1H n.m.r., and was therefore identified as the anti-E-isomer.

The double-bond geometry of adduct (23) was established by n.O.e. studies on the epoxide (25) prepared stereoselectively using t-BuOOH - $VO(acac)_2$; in particular irradiation of 2-CH_3 and H(4) caused enhancements of the peaks due to H(4) and H(2) by 12% and by 7%, respectively. Ozonolysis of adduct (23) gave the hydroxyketone (26) which was distinctly different from the hydroxyketone (27) obtained by ozonolysis of the thermal adduct (17a). This synthesis of ketones (26) and (27) shows how addition of stannane (9) followed by ozonolysis can be used to prepare ketone aldol adducts stereoselectively.



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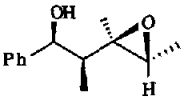

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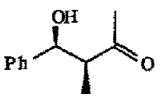

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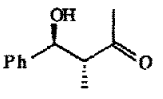
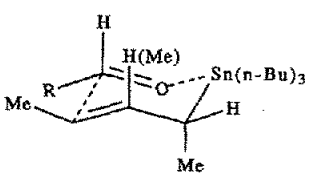


(27)

The stereoselectivity of the uncatalysed reactions between the stannanes (7) - (9) and aldehydes is consistent with the participation of six-membered, chair-like, cyclic transition states in which the α-methyl substituent adopts a pseudo-axial position, see Figure. The high stereoselectivities observed suggest that these reactions should find application in acyclic stereochemical control particularly for the formation of trisubstituted alkenes using the stannane (9), although widespread use of these reactions may be limited by the high temperatures required. Of note is the observation that the isomeric purity of the products from the tri-n-butylstannane (7) reactions was greater than that of the stannane itself which generally contained ca. 10% of its Z-double-bond isomer. The Z-stannane under thermal conditions would be expected to give rise to the formation of syn-products which were not observed. This suggests that the reactions of the Z-stannane are significantly slower than those of the E-stannane perhaps due to unfavourable 1,3-diaxial interactions between the axial α-methyl group and the vinylic methyl group in the transition states for these reactions.[10] Similar enhanced stereoselectivities were observed for thermal reactions of the trimethylallylstannane (9).

Figure



EXPERIMENTAL

I.r. spectra were measured on Perkin Elmer 297 and 1710 F.T. spectrometers, and ^1H n.m.r. spectra were recorded on a Bruker WH 300 spectrometer (300 MHz) in chloroform-d_1, unless otherwise stated. Mass spectra were recorded on VG Micromass 16F, 30F, and ZAB IF spectrometers using either electron impact (E.I.) or chemical ionization (C.I./NH_3) modes. Compounds containing Sn showed characteristic clusters of peaks in their mass spectra; only those corresponding to ^{120}Sn are given below. Melting points were determined on a Kofler Block apparatus, and are uncorrected.

Flash chromatography was carried out using Merck silica gel 60. All solvents were dried and distilled before use. Ether refers to diethyl ether throughout, and light petroleum to the fraction boiling between 40 and 60°C.

Lithium diisopropylamide (LDA) was prepared from equimolar quantities of n-butyl-lithium in hexane and diisopropylamine in tetrahydrofuran (THF) under an atmosphere of nitrogen at 0°C. Tri-n-butyl and triphenyl-tin lithium were similarly obtained from LDA and tri-n-butyl and triphenyl-tin hydrides respectively.

(E)-2-Chloropent-3-ene (13) was prepared from (E)-pent-3-en-2-ol[11] by treatment with freshly distilled thionyl chloride at 0°C and isolated by distillation (85%); b.p. 99°C (lit.[12] 96-97°C). (E)-3-Methylpent-3-en-2-ol (15) was prepared from tiglic aldehyde and methyl magnesium iodide. After an aqueous work-up, the (E)-3-methylpent-3-en-2-ol (15) was purified by distillation (67%); b.p. 139-140°C (lit.[13] 140-141°C). Conversion to the (E)-2-chloro-3-methylpent-3-ene (14) was again carried out using freshly distilled thionyl chloride at 0°C. Distillation of the product gave (E)-2-chloro-3-methylpent-3-ene (14) (45%), b.p. 120°C; δ_H 1.6-1.8 (9 H, overlapping m, 3 x CH_3), 4.62 (1 H, q, J 8 Hz, 2-H), and 5.60 (1 H, q, J 8 Hz, 4-H).

(E)-(Pent-3-en-2-yl)(tri-n-butyl)stannane (7).- Tri-n-butyltin lithium (9.57 mmol) in THF-hexane (25 ml) was cooled to -78°C and added via a cannula to a stirred solution of (E)-2-chloropent-3-ene(13) (1g, 9.57 mmol) in THF (5ml) at -78°C under an atmosphere of argon. The mixture was stirred for 2.5 h at -78°, and for 12h at 20°C. Water (25 ml) was added, and the mixture extracted with ether. After drying ($MgSO_4$), the ethereal extracts were concentrated under reduced pressure to leave an oil which was distilled to provide (E)-(pent-3-en-2-yl)(tri-n-butyl)stannane (7)[6] (2.55g, 74%), as a colourless oil, b.p. 108-120°C (1 mm. Hg), shown to contain ca. 10% of its (Z)-isomer by ^{1}H n.m.r.; $\upsilon_{max.}$ ($CHCl_3$) 960 cm^{-1}; δ_H(major isomer) 0.6-1.75 (33 H, complex m), 2.10 (1 H, m, 2-H), and 5.15 and 5.7 (each 1 H,m, vinylic H); m/z (E.I.) 313 (M^+ - 47, 10%).

(E)-(Pent-3-en-2-yl)(triphenyl)stannane (8).- Following the procedure outlined above, triphenyltin lithium (29 mmol) and (E)-2-chloropent-3-ene (13) (2.98g, 29 mmol) gave a yellow oil which was flash chromatographed using benzene-light petroleum (1:5) as eluant to give (E)-(Pent-3-en-2-yl)(triphenyl)-stannane (8) (3.0g, 25%) as white needles, m.p. 44-47°C (from n-pentane). (Found: C, 65.55; H, 5.8. $C_{23}H_{24}$ Sn requires C, 65.9; H, 5.75%); δ_H 1.51 (3 H, d, J 7 Hz, 1-CH_3), 1.66 (3 H, br. d, J 7 Hz, 5-CH_3), 2.83 (1 H, m, 2-H), 5.3 and 5.85 (each 1 H, m, vinylic H), and 7.3-7.6 (15 H, m, aromatic H).

(E)-(3-Methylpent-3-en-2-yl)(tri-n-butyl)stannane (9).- Following the procedure outlined above, tri-n-butyltin lithium (42 mmol) and (E)-2-chloro-3-methylpent-3-ene (14) (5g, 42 mmol) gave a yellow oil which was distilled to provide (E)-(3-methylpent-3-en-2-yl)(tri-n-butyl)stannane (9) (8.97g, 57%) as a colourless oil, b.p. 128°C (0.55 mmHg), shown to contain ca. 10% of its (Z)-isomer by ^{1}H n.m.r., $\upsilon_{max.}$ (film) 1650, 1460, 1375, 1070, 960, 870, and 810 cm^{-1}; δ_H 0.7-1.7 (36 H, complex m), 2.08 (1 H, m, 2-H), and 5.0 (1 H, m, 4-H); m/z (E.I.) 317 (M^+ - 57, 10%) and 291 (M^+ - 83, 60%).

(1RS, 2RS, 3Z)-2-Methyl-1-phenylpent-3-en-1-ol (16a).- A mixture of benzaldehyde (200 mg, 1.9 mmol) and the stannane (7) (1.35g, 3.8 mmol) was heated in a sealed tube at 150°C for 18h. Flash chromatography of the orange residue using ether-light petroleum (1:5) as eluant gave (1RS, 2RS, 3Z)-2-methyl-1-phenylpent-3-en-1-ol (16a) (240 mg, 72%), as a pale yellow oil; $\upsilon_{max.}$ ($CHCl_3$) 3550, 1600, 1450, 1018, 940, and 700 cm^{-1}; δ_H 0.79 (3 H, d, J 7 Hz, 2-CH_3), 1.67 (3 H, dd, J 2, 7 Hz, 5-CH_3), 2.20 (1 H, s, OH), 2.8 (1 H, m, 2-H), 4.28 (1 H, d, J 8 Hz, 1-H), 5.36 and 5.69 (each 1 H, m, vinylic H), and 7.26-7.36 (5 H, m, aromatic H); m/z (C.I./NH_3) 176(M^+).

Using stannane (8). A mixture of benzaldehyde (105 mg, 1 mmol), the stannane (8) (0.63g, 1.5 mmol), and anhydrous toluene (1 ml), was heated in a sealed tube at 150°C for 18 h. Flash chromatography of the residue gave the 2-methyl-1-phenylpent-3-en-1-ol (16a) (130 mg, 74%) as a pale yellow oil.

(1RS, 2RS, 3Z)-2-Methyl-1-(4-nitrophenyl)pent-3-en-1-ol (16b).- p-Nitrobenzaldehyde (60 mg, 0.39 mmol) and the stannane (7) (0.21g, 0.6 mmol) were dissolved in toluene (1 ml) and the solution heated at 80°C for 18 h. Concentration under reduced pressure gave an oil, which was flash chromatographed using ether-light petroleum (1:4) as eluant to give (1RS, 2RS, 3Z)-2-methyl-1-(4-nitrophenyl)pent-3-en-1-ol (16b) (76 mg, 87%) as a pale yellow oil; $\upsilon_{max.}$ (film) 3400, 1600, 1010, 840, and 700 cm^{-1}; δ_H 0.86 (3 H, d, J 7Hz, 2-CH_3), 1.62 (3 H, dd, J 2, 7 Hz, 5-CH_3), 2.40 (1 H, br. s, OH), 2.78 (1 H, m, 2-H), 4.44 (1 H, d, J 8 Hz, 1-H), 5.30 and 5.73 (each 1 H,m, vinylic H), and 7.52 and 8.20 (each 2 H, d, J 9 Hz, aromatic H); m/z (C.I./NH_3) 239 (M^+ + 18, 25%) and 174 (M^+ - 7, 100%).

Using stannane (8). Following the above procedure, the triphenylstannane (8) (315 mg, 0.75 mmol) and p-nitrobenzaldehyde (75 mg, 0.5 mmol) in toluene (1 ml) gave the 2-methyl-1-(4-nitrophenyl)pent-3-en-1-ol (16b) (87 mg, 80%) as a pale yellow oil.

(1RS, 2RS, 3Z)-1-(4-Chlorophenyl)2-methylpent-3-en-1-ol (16c).- A mixture of p-chlorobenzaldehyde (148 mg, 1.04 mmol) and the stannane (7) (0.75g, 2 mmol) was stirred at 110°C for 18 h. Flash chromatography of the residue using ether-light petroleum (1:5) as eluant gave (1RS, 2RS, 3Z)-1-(4-chlorophenyl-2-methylpent-3-en-1-ol (16c) (220 mg, 70%) as a clear oil (Found: C, 68.45; H, 7.45. $C_{12}H_{15}ClO$ requires C,

68.4; H, 7.15%); $\upsilon_{max.}$ (film) 3420, 1600, 1490, 1400, 1088, 1012, 940, and 820 cm^{-1}; δ_H 0.80 (3 H, d, J 7 Hz, 2-CH_3), 1.67 (3 H, dd, J 2, 7 Hz, 5-CH_3), 2.28 (1 H, d, J 2 Hz, OH), 2.75 (1 H, m, 2-H), 4.27 (1 H, dd, J 2, 8 Hz, 1-H), 5.30 and 5.72 (each 1 H, m, vinylic H), and 7.25-7.37 (4 H, m, aromatic H); m/z (C.I./NH_3) 210 (M^+, 100%).

(1RS, 2SR, 3Z)-1-Cyclohexyl-2-methylpent-3-en-1-ol (16d).- A mixture of cyclohexanecarboxaldehyde (180 mg, 1.61 mmol) and the stannane (7) (1.15 g, 3.2 mmol) was heated in a sealed tube at 150° C for 18 h. Flash chromatography of the residue using ether-light petroleum (1:5) as eluent gave (1RS, 2SR, 3Z)-1-cyclohexyl-2-methylpent-3-en-1-ol (16d) (180 mg, 62%) as a clear oil; $\upsilon_{max.}$ (film) 3400, 3010, 1450, 990, and 980 cm^{-1}; δ_H 0.94 (3 H, d, J 7 Hz, 2-CH_3), 1.05-1.95 (12 H, complex m), 1.63 (3 H, dd, J 2, 7 Hz, 5-CH_3), 2.67 (1 H, m, 2-H), 3.09 (1 H, m, 1-H), and 5.30 and 5.58 (each 1 H, m, vinylic H); m/z (C.I./NH_3) 200 (M^+ + 18, 50%) and 165 (M^+ - 17, 100%).

(3RS, 4SR, 5Z)-2,4-Dimethylhept-5-en-3-ol (16e).- A mixture of 2-methylpropanal (440 mg, 6.1 mmol) and the stannane (7) (2.8 g, 7.82 mmol) was heated in a sealed tube at 150°C for 18 h. Flash chromatography of the residue using ethyl acetate-light petroleum (1:10) as eluant gave (3RS, 4SR, 5Z)-2,4-dimethylhept-5-en-3-ol (16e) (480 mg, 55%) as a colourless oil); $\upsilon_{max.}$ (film) 3450, 1460, 990, and 730 cm^{-1}; δ_H 1.00 (3 H, d, J 7 Hz, 4-CH_3), 1.05 (6 H, d, J 7 Hz, 2 x CH_3), 1.54 (1 H, br. s, OH), 1.66 (3 H, dd, J 2, 7 Hz, 7-CH_3), 1.77 (1 H, m, 2-H), 2.65 (1 H, m, 4-H), 3.10 (1 H, m, 3-H), and 5.3 and 5.59 (each 1 H, m, vinylic H); m/z (C.I./NH_3) 160 (M^+ + 18, 100%).

Isopropyl (2RS, 3RS, 4Z)-2-Hydroxy-3-methylhex-4-enoate (16f).- A mixture of isopropyl glyoxalate (112 mg, 0.96 mmol) and the stannane (7) (0.69 g, 1.94 mmol) was heated at 90°C for 18h. Flash chromatography of the residue using ether-light petroleum (1:5) as eluant gave isopropyl (2RS, 3RS, 4Z)-2-hydroxy-3-methylhex-4-enoate (16f) (89 mg, 50%) as a clear oil; $\upsilon_{max.}$ (film) 3400, 1730, 1580, 1010, 870, and 740 cm^{-1}; δ_H 1.09 (3 H, d, J 7 Hz, 3-CH_3), 1.25 and 1.28 (each 3 H, d, J 6 Hz, 2 x CH_3), 1.61 (3 H, dd, J 2, 7 Hz, 6-CH_3), 2.84 (1 H, d, J 6 Hz, OH), 2.97 (1 H, m, 3-H), 4.04 (1 H, dd, J 3, 6 Hz, 2-H), 5.06 (1 H, septet, J 6 Hz, 2'-H), and 5.37 and 5.50 (each 1 H, m, vinylic H); m/z (C.I./NH_3) 204 (M^+ + 18, 100%) and 187 (M^+ + 1, 60%).

(3RS, 4SR, 1E, 5Z)-4-Methyl-1-phenylhepta-1,5-dien-3-ol (16g).- A solution of cinnamaldehyde (75 mg, 0.57 mmol) and the triphenylstannane (8) (356 mg, 0.85 mmol) in anhydrous toluene (2 ml) was heated in a sealed tube at 150°C for 18 h. Flash chromatography of the residue using ether-light petroleum (1:5) as eluant gave (3RS, 4SR, 1E, 5Z)-4-methyl-1-phenylhepta-1,5-dien-3-ol (16g) (76 mg, 67%) as a clear oil; $\upsilon_{max.}$ (film) 3390, 3080, 3060, 3020, 1670, 1625, 1600, 1580, 1490, 1449, 965, 750, and 690 cm^{-1}; δ_H 1.03 (3 H, d, J 7 Hz, 4-CH_3), 1.72 (3 H, dd, J 2, 7 Hz, 7-CH_3), 2.17 (1 H, br. s, OH), 2.73 (1 H, m, 4-H), 4.02 (1 H, t, J 7 Hz, 3-H), 5.33 and 5.68 (each 1 H, m, vinylic H), 6.25 (1 H, dd, J 7 15 Hz, 2-H), 6.63 (1 H, d, J 15 Hz, 1-H), and 7.25-7.45 (5 H, m, aromatic H); m/z (C.I./NH_3) 201 (M^+ - 1, 40%) and 185 (M^+ - 17, 100%).

(1RS, 2RS, 3Z)-2,3-Dimethyl-1-phenylpent-3-en-1-ol (17a).- A mixture of benzaldehyde (190 mg, 1.79 mmol) and the stannane (9) (1 g, 2.55 mmol) was heated in a sealed tube at 150°C for 18h. Flash chromatography of the residue using ethyl acetate-light petroleum (1:8) as eluant gave (1RS, 2RS, 3Z)-2,3-dimethyl-1-phenylpent-3-en-1-ol (17a) (304 mg, 89%) as a clear oil (Found: C, 82.5; H, 9.75. $C_{13}H_{18}O$ requires C, 82.05; H, 9.55%); $\upsilon_{max.}$ (film) 3420, 3020, 1600, 1435, 1370, 1187, 1007, 910, 800, 730, and 695 cm^{-1}; δ_H 0.77 (3 H, d, J 7 Hz, 2-CH_3), 1.73-1.78 (6 H, m, 3-CH_3 + 5-CH_3), 2.25 (1 H, d, J 2 Hz, OH), 2.97 (1 H, m, 2-H), 4.38 (1 H, dd, J 2, 10 Hz, 1-H), 5.59 (1 H, q, J 6 Hz, 4-H), and 7.28-7.42 (5 H, m, aromatic H); m/z (C.I./NH_3) 190 (M^+, 40%) and 173 (M^+ - 17, 100%).

(1RS, 2RS,3Z)-2,3-Dimethyl-1-(4-nitrophenyl)pent-3-en-1-ol (17b).- A mixture of p-nitrobenzaldehyde (150 mg, 0.99 mmol) and the stannane (9) (0.55 g, 1.45 mmol) was heated at 80°C for 18 h. Flash chromatography of the residue using ether-light petroleum (1:3) as eluant gave (1RS, 2RS, 3Z)-2,3-dimethyl-1-(4-nitrophenyl)pent-3-en-1-ol (17b) (160 mg, 69%) as pale yellow oil; $\upsilon_{max.}$ (film) 3460, 1600, 1510, 1340, 1010, 850, 738, and 695 cm^{-1}; δ_H 0.74 (3 H, d, J 7 Hz, 2-CH_3), 1.64 (3 H, dq, J 7, 1 Hz, 5-CH_3), 1.69 (3 H, narrow m, 3-CH_3), 2.56 (1 H, br. s, OH), 2.86 (1 H, m, 2-H), 4.44 (1 H, d, J 9 Hz, 1-H), 5.54 (1 H, br. q, J 7 Hz, 4-H), and 7.51 and 8.14 (each 2 H, br. d, J 9 Hz, aromatic H); m/z (C.I./NH_3) 253 (M^+ + 18, 60%) and 188 (M^+ - 47, 100%).

(3RS, 4SR, 5Z)-2,4,5-trimethylhept-5-en-3-ol (17 c).- A mixture of 2-methylpropanal (100 mg, 1.38 mmol) and the stannane (9) (0.62 g, 1.67 mmol) were heated at 150°C for 18 h. Flash chromatography of the residue using ethyl acetate-light petroleum (1:15) as eluent gave (3RS, 4SR, 5Z)-2,4,5-trimethylhept-

5-en-3-ol (17c) (180 mg, 50%) as a colourless oil; $\upsilon_{max.}$ (film) 3480, 1370, 1230, 970, and 800 cm^{-1}; δ_H 0.91 and 0.92 (each 3 H, overlapping d, J 7 Hz, 2 x CH_3), 1.05 (3 H, d, J 7 Hz, 4-CH_3), 1.52 (1 H, d, J 1 Hz, OH), 1.62-1.66(6 H, m, 2 x CH_3), 1.84 (1 H, m, 2-H), 2.79 (1 H, m, 4-H), 3.30 (1 H, m, 3-H), and 5.46 (1 H, br. q, J 7 Hz, 6-H); m/z (C.I.NH_3) 174 (M^+ + 18, 100%) 157 (M^+ + 1, 80%), and 139 (M^+ - 17, 80%).

(1RS, 2SR, 3SR, 4RS)-2,3-Dimethyl-3,4-epoxy-1-phenylpentan-1-ol (18).- t-Butyl hydroperoxide (0.5 ml of a 1.71 M solution in toluene, 0.85 mmol) was added dropwise to a solution of the 2,3-dimethyl-1-phenylpent-3-en-1-ol (17a) (124 mg, 0.61 mmol) and $VO(acac)_2$ (3 mg) in dichloromethane (2 ml) at 0°C. The mixture was allowed to warm to room temperature, and was stirred for 12 h. Aqueous sodium sulphite (10%, 2 ml) was added, and the stirring continued for 0.5 h. The mixture was extracted with dichloromethane (10 ml), washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. Flash chromatography of the residue with ethyl acetate-light petroleum (1:5) as eluant gave (1RS, 2SR, 3SR, 4RS)-2,3-dimethyl-3,4-epoxy-1-phenylpentan-1-ol (18) (85 mg, 65%) as a colourless oil; $\upsilon_{max.}$ (film) 3480, 3085, 3060, 3015, 1600, 1460, 1377, 1200, 1138, 1097, 1060, 1023, 930, 854, 770, 745, and 704 cm^{-1}; δ_H 0.65 (3 H, d, J 7 Hz, 2-CH_3), 1.33 (3 H, d, J 5 Hz, 5-CH_3), 1.40 (3 H, s, 3-CH_3), 1.69 (1 H, m, 2-H), 2.86 (1 H, q, J 5 Hz, 4-H), 3.52 (1 H, d, J 2 Hz, OH), 4.67 (1 H, dd, J 2, 10 Hz, 1-H), and 7.25-7.35 (5 H, m, aromatic H); m/z (C.I./NH_3) 206 (M^+, 10%) and 187 (M^+ - 19, 100%).

Methyl (2RS, 3SR)-3-Hydroxy-2-methyl-3-phenylpropanoate (19).- Ozone was bubbled through a stirred solution of 2-methyl-1-phenylpent-3-en-1-ol (16a) (390 mg, 2.2 mmol) in anhydrous methanol (20 ml) at -78°C for 1.5 h. Excess ozone was discharged by bubbling oxygen through the solution for 10 min., then dimethyl sulphide (0.43 g, 7 mmol) was added, and the solution allowed to warm to room temperature and stirred overnight. The mixture was concentrated under reduced pressure to leave a yellow oil which was taken up in ethanol (10 ml). A solution of silver nitrate (0.62 g, 3.5 mmol) in water (20 ml) was added followed by the dropwise addition of aqueous sodium hydroxide (0.62 g, 15 mmol NaOH in 10 ml H_2O). After stirring for 3 h, the mixture was filtered, and the precipitate washed with water. The combined filtrate was extracted with ether, acidified to pH 1 with 3 M aqueousHCl, and re-extracted with ether. These extracts were combined, dried ($MgSO_4$), and concentrated under reduced pressure to leave a red oil (250 mg), identified as (2RS, 3SR)-3-hydroxy-2-methyl-3-phenylpropanoic acid. This crude acid was dissolved in ether (20 ml), and an excess of ethereal diazomethane added. After 5 min at 0°C, the excess of diazomethane was quenched by the addition of glacial acetic acid (5 ml). Saturated aqueous $NaHCO_3$ (20 ml) was added, and the mixture extracted with ether, dried ($MgSO_4$), and concentrated under reduced pressure to leave an oil. Flash chromatography of this residue using ethyl acetate-light petroleum (1:3) as eluant gave methyl (2RS, 3SR)-3-hydroxy-2-methyl-3-phenylpropanoate (19) (206 mg, 53% overall) as a white solid, m.p. 47-50°C (lit.[14] 50.5-51.5°C) identical with an authentic sample.[9]

Lewis Acid Catalysed Reactions between Benzaldehyde and Stannanes (7) and (8).- Boron trifluoride diethyletherate (0.25 g, 2 mmol) was added to a stirred solution of benzaldehyde (0.11 g, 1 mmol) in dichloromethane (5 ml) at -78°C. After 5 min. a solution of the stannane (8) (0.42 g, 1 mmol) in dichloromethane (2 ml) was added, and the mixture stirred for 4 h. at -78°C before being quenched by the addition of water (10 ml). The organic layer was washed with water, dried ($MgSO_4$), and concentrated under reduced pressure. Flash chromatography of the residue using ether-light petroleum (1:3) as eluant gave a colourless oil (0.11 g, 62%) which by ^1H n.m.r. was found to contain the four stereoisomers of 2-methyl-1-phenylpent-3-en-1-ol (16a), (20)-(22), ratio (16a) : (20) : (21) : (22) = 6 : 6: 15: 73, respectively; $\upsilon_{max.}$ (mixture, $CHCl_3$) 3600, 3080, 3060, 3015, 1600, 1450, 1015, 970 and 700 cm^{-1}; δ_H [major isomer (22)] 0.95 (3 H, d, J 7.5 Hz, 2-CH_3), 1.65 (3 H, dd, J 2, 5.5 Hz, 5-CH_3), 1.96 (1 H, d, J 4 Hz, OH), 2.52 (1 H, m, 2-H), 4.6 (1 H, t, J 4 Hz, 1-H), 5.37 and 5.5 (each 1 H, m, vinylic H), and 7.2-7.4 (5 H, m, aromatic H); m/z (mixture) (E.I.) 159 (M^+ - 17, 100%).

Following the above procedure, benzaldehyde (140 mg, 1.33 mmol), titanium tetrachloride (0.38 g, 2 mmol), and stannane (7) (0.7 g, 2 mmol), gave a mixture of the four stereoisomers of 2-methyl-1-phenylpent-3-en-1-ol (165 mg, 71%), ratio (^1H n.m.r.) (16a) : (20) : (21) : (22) = 15 : 56 : 14 : 15; δ_H [major component (20)] 0.83 (3 H, d, J 7 Hz, 2-CH_3), 1.73 (3 H, dd, J 1, 7 Hz, 5-CH_3), 2.25 (1 H, d, J 2 Hz, OH), 2.4 (1 H, m, 2-H), 4.26 (1 H, dd, J 2, 7 Hz, 1-H), 5.4 and 5.69 (each 1 H, m, vinylic H), and 7.2-7.45 (5 H, m, aromatic H).

(1RS, 2SR, 3E)-2,3-Dimethyl-1-phenylpent-3-en-1-ol (23).- Boron trifluoride diethyl etherate (0.25 g, 2 mmol) was added to a stirred solution of benzaldehyde (0.12 g, 1.05 mmol) in dichloromethane (10 ml) at -78°C. After 5 min., the stannane (9) (0.55 g, 1.5 mmol) in dichloromethane (2 ml) was added, and the

mixture stirred at -78°C for 4 h before being quenched by the addition of water (10 ml). The organic phase was separated, washed with water, dried ($MgSO_4$), and concentrated under reduced pressure. Flash chromatography of the residue using ether-light petroleum (1:4) as eluant gave a colourless oil (155 mg, 73%) shown by ^1H n.m.r. to contain (1RS, 2SR, 3E)-2,3-dimethyl-1-phenylpent-3-en-1-ol (23) together with minor isomers. Prep. g.l.c. gave (1RS, 2SR, 3E)-2,3-dimethyl-1-phenylpent-3-en-1-ol (23); $\upsilon_{max.}$ (film) 3400, 3080, 3060, 3015, 1600, 1450, 1010, 760, and 700 cm^{-1}; δ_H 0.97 (3 H, d, J 7 Hz, 2-CH_3), 1.57 (3 H, d, J 5 Hz, 5-CH_3), 1.63 (3 H, br. s, 3-CH_3), 1.88 (1 H, br. s, OH), 2.45 (1 H, m, 2-H), 4.73 (1 H, d, J 5 Hz, 1-H), 5.30 (1 H, br. q, J 5 Hz, 4-H), and 7.20-7.37 (5 H, m, aromatic H); m/z (E.I.) 190 (M^+, 4%) and 173 (M^+ - 17, 100%).

(1RS, 2RS, 3SR, 4SR)-2,3-Dimethyl-3,4-epoxy-1-phenylpentan-1-ol (25).- Following the procedure outlined above, the 2,3-dimethyl-1-phenylpent-3-en-1-ol (23) (150 mg, 0.74 mmol) was epoxidized using t-butyl hydroperoxide-$VO(acac)_2$. Flash chromatography using ether-light petroleum (1:3) as eluant gave (1RS, 2RS, 3SR, 4SR)-2,3-dimethyl-3,4-epoxy-1-phenylpentan-1-ol (25) (130 mg, 80%) as a white solid, m.p. 104-106°C (from ether-hexane) (Found: C, 76.0; H, 9.0. $C_{13}H_{18}O_2$ requires C, 75.7; H, 8.8%); $\upsilon_{max.}$ ($CHCl_3$) 3600, 3450, 3080, 3060, 1600, 1386, 1378, 1090, 1018, 977, 860, and 703 cm^{-1}; δ_H (benzene-d_6) 0.73 (3 H, d, J 5 Hz, 5-CH_3), 1.02 (3 H, s, 3-CH_3), 1.19 (3 H, d, J 7 Hz, 2-CH_3), 1.55 (1 H, m, 2-H), 1.89 (1 H, br. s, OH), 2.26 (1 H, q, J 5 Hz, 4-H), 4.29 (1 H, br. d, J 7 Hz, 1-H), and 7.0-7.16 (5 H, m, aromatic H); m/z (C.I./NH_3) 207 (M^+ + 1, 15%) and 187 (M^+ - 19, 100%).

(3RS,4SR)-4-Hydroxy-3-methyl-4-phenylbutan-2-one (27).- Ozone was bubbled through a stirred solution of the (1RS, 2RS)-pentenol (17a) (100 mg, 0.53 mmol) in anhydrous methanol (20 ml) at -78°C for 10 min. The excess of ozone was discharged by bubbling oxygen through the solution for 5 min., then dimethyl sulphide (0.2 g, 3 mmol) was added, and the solution allowed to warm to room temperature over 2 h.

The mixture was concentrated under reduced pressure to leave a residue which was flash chromatographed using ether-light petroleum (1:4) as eluant to give (3RS, 4SR)-4-hydroxy-3-methyl-4-phenylbutan-2-one (27) (65 mg, 60%) as a colourless oil; $\upsilon_{max.}$ (film) 3400, 1700, and 700 cm^{-1}; δ_H 0.90 (3 H, d, J 7 Hz, 3-CH_3), 2.21 (3 H, s, 1-CH_3), 2.89 (1 H, dq, J 8.5, 7 Hz, 3-H), 3.05 (1 H, br. s, OH), 4.71 (1 H, d, J 8.5 Hz, 4-H), and 7.22-7.37 (5 H, m, aromatic H); m/z (C.I./NH_3) 178 (M^+, 5%) and 105 (M^+ - 73, 100%).

(3RS, 4RS)-4-Hydroxy-3-methyl-4-phenylbutan-2-one (26).- Following the procedure outlined above, the (1RS, 2SR)-pentanol (23) (125 mg, 0.66 mmol) was ozonolysed to provide (3RS, 4RS)-4-hydroxy-3-methyl-4-phenylbutan-2-one (26) (68 mg, 50%) as a colourless oil; $\upsilon_{max.}$ (film) 3450, 1700, 760, 735, and 700 cm^{-1}; δ_H 1.09 (3 H, d, J 7 Hz, 3-CH_3), 2.14 (3 H, s, 1-CH_3), 2.84 (1 H, dq, J 4, 7 Hz, 3-H), 3.11 (1 H, br. s, OH), 5.09 (1 H, m, 4-H), and 7.24-7.37 (5 H, m, aromatic H); m/z (E.I.) 178 (M^+, 5%), 160 (M^+ - 18, 20%) and 107 (M^+ - 71, 45%).

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