

## Synthesis and Absolute Configuration of Optically Active *E*-1-Alkoxymethoxybut-2-enyl(tri-*n*-butyl)stannanes: Stereoselective Reactions with Aldehydes

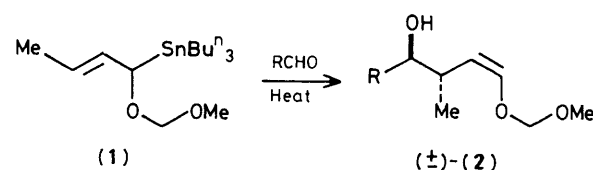
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(1*R*)- and (1*S*)-1-[(−)-menthoxy-methoxy]-*E*-but-2-enyl(tri-*n*-butyl)stannanes (**5**) and (**6**), whose configurations at C(1) were assigned by correlation with (2*R*)- and (2*S*)-pentan-2-ol, react stereoselectively on heating with benzaldehyde to give (3*S*,4*S*)- and (3*R*,4*R*)-4-hydroxy-3-methyl-*cis*-1,2-enol ethers (**11**) and (**13**), respectively.

(±)-*E*-1-Methoxymethoxybut-2-enyl(tri-*n*-butyl)stannane (**1**) reacts stereoselectively with aldehydes on heating to give (±)-*anti*-4-hydroxy-3-methyl-*cis*-1,2-enol ethers (**2**).<sup>†</sup> We report here the preparation and characterization of optically active 1-[(−)-menthoxy-methoxy]-*E*-but-2-enyl(tri-*n*-butyl)stannanes (**5**) and (**6**) together with details of their reactions with aldehydes.

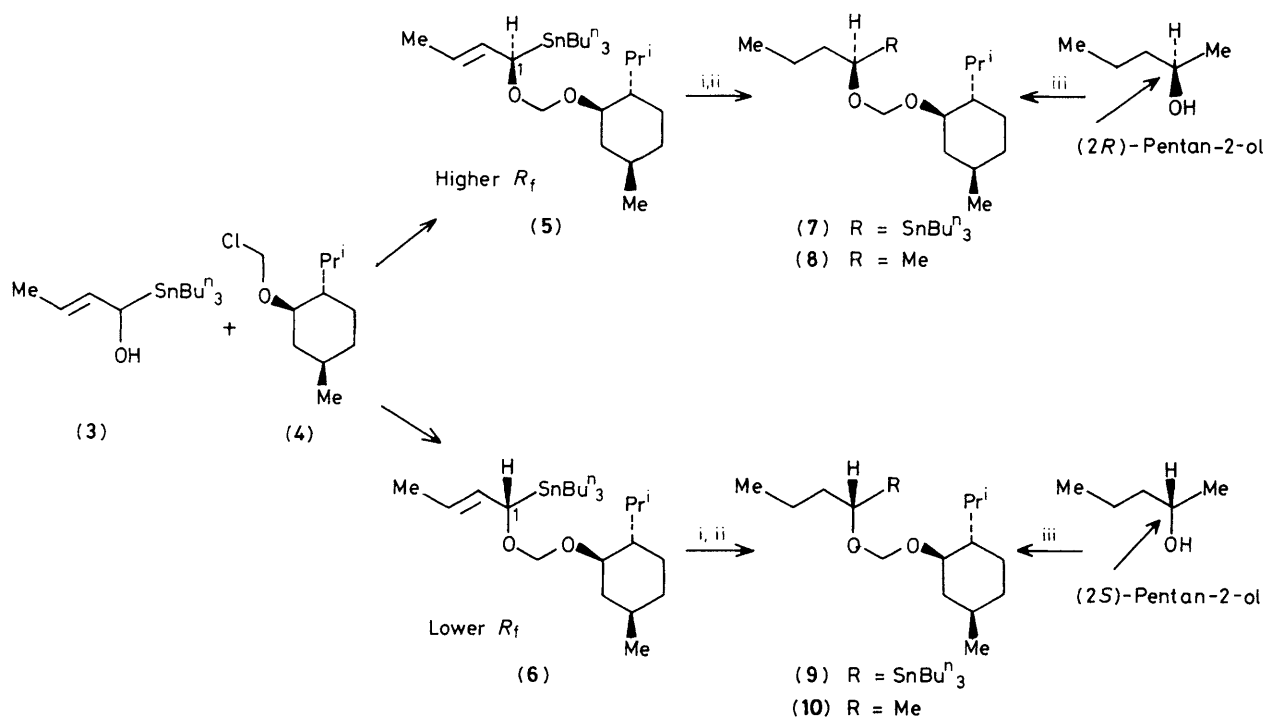
Chloromethyl (−)-menthyl ether (**4**)<sup>3</sup> was prepared by bubbling anhydrous HCl through a solution of (−)-menthol and trioxane in CH<sub>2</sub>Cl<sub>2</sub> in the presence of anhydrous MgSO<sub>4</sub> (b.p. 82–84 °C at 0.8 mm Hg, 54%), and was added to a mixture of racemic stannol (**3**)<sup>1</sup> and di-isopropylethylamine in CH<sub>2</sub>Cl<sub>2</sub> to give, after 2 h at 0 °C and 2 h at 20 °C, a mixture of the diastereoisomeric but-2-enylstannanes (**5**) and (**6**), isol-



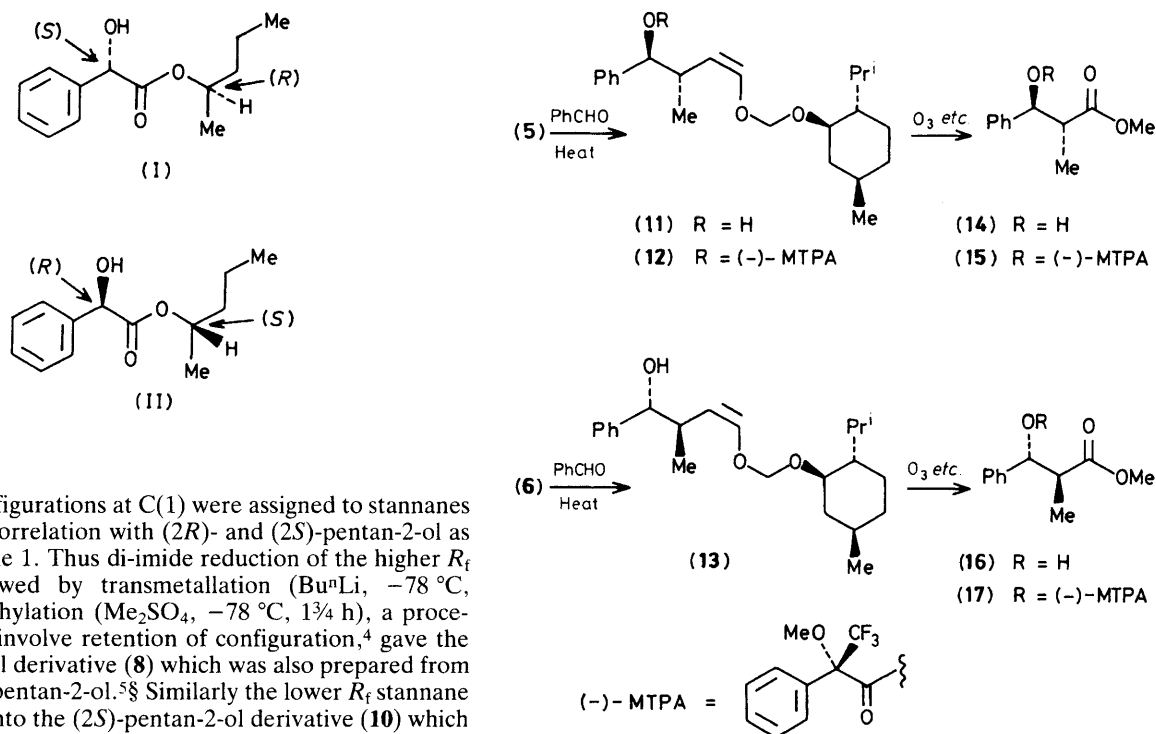
ated as a mixture by flash chromatography (59%). Careful short-column chromatography (eluted with 40/60 petroleum-benzene, 5:1) gave the (1*R*)-diastereoisomer (**5**), [α]<sub>D</sub><sup>20</sup> +12.1° (CHCl<sub>3</sub>), followed by the (1*S*)-diastereoisomer (**6**), [α]<sub>D</sub><sup>20</sup> −91.1° (CHCl<sub>3</sub>), which could be distinguished by t.l.c. and by high field (300 MHz) <sup>1</sup>H n.m.r. spectroscopy.<sup>‡</sup>

<sup>†</sup> For the *syn-anti* nomenclature see the discussion by S. Masamune, ref. 2.

<sup>‡</sup> New compounds were fully characterised spectroscopically and by combustion analysis whenever possible.



**Scheme 1.** Reagents: i,  $\text{TsNHNH}_2$ ,  $\text{NaOAc}$ ,  $\text{EtOH}$ ; ii,  $\text{Bu}^n\text{Li}$ , tetrahydrofuran,  $-78^\circ\text{C}$ , 5 min, then  $\text{Me}_2\text{SO}_4$ ,  $-78^\circ\text{C}$ ,  $1\frac{3}{4}$  h; iii, (4),  $\text{Pr}_2\text{NEt}$ ,  $0^\circ\text{C}$ , 2 h, then  $20^\circ\text{C}$ , 2 h.

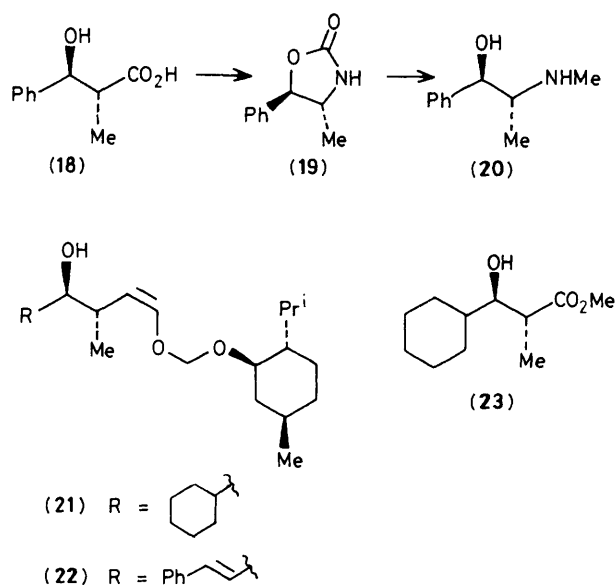


**Scheme 2**

Absolute configurations at C(1) were assigned to stannanes (5) and (6) by correlation with (2R)- and (2S)-pentan-2-ol as shown in Scheme 1. Thus di-imide reduction of the higher  $R_f$  stannane, followed by transmetalation ( $\text{Bu}^n\text{Li}$ ,  $-78^\circ\text{C}$ , 5 min) and methylation ( $\text{Me}_2\text{SO}_4$ ,  $-78^\circ\text{C}$ ,  $1\frac{3}{4}$  h), a procedure known to involve retention of configuration,<sup>4</sup> gave the (2R)-pentan-2-ol derivative (8) which was also prepared from authentic (2R)-pentan-2-ol.<sup>5</sup> Similarly the lower  $R_f$  stannane was converted into the (2S)-pentan-2-ol derivative (10) which was also prepared from (2S)-pentan-2-ol. The pentan-2-ol

§ (±)-Pentan-2-ol was resolved following the procedure of J. K. Whitesell (ref. 6). Using (S)-mandelic acid, the ester (I) of (2R)-pentan-2-ol crystallized out which gave (2R)-pentan-2-ol,  $[\alpha]_D^{20} -13.5^\circ$  ( $\text{CHCl}_3$ ) (lit.<sup>5</sup>  $-16.1^\circ$ ), on hydrolysis. Ester (II) was obtained from (R)-mandelic acid.

derivatives (8) and (10) were clearly distinguished by high field (300 MHz)  $^1\text{H}$  n.m.r. spectroscopy, and enabled configurational assignments to be made as shown.

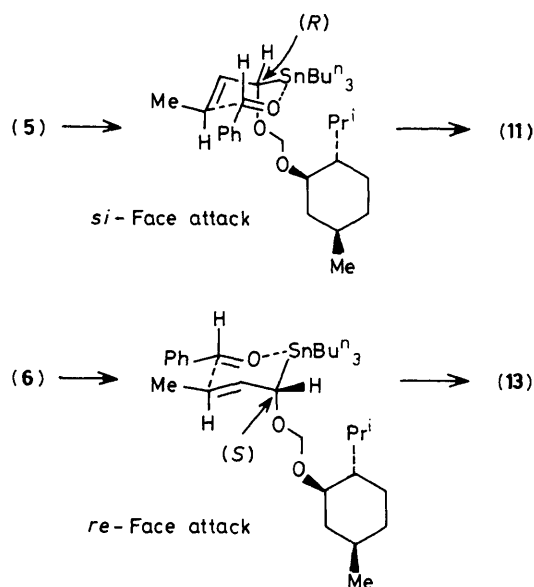


The menthoxymethoxystannanes (5) and (6) were then heated separately with an excess of benzaldehyde (130 °C, 15 h) under an argon atmosphere. The (1*R*)-isomer (5) gave the (3*S*,4*S*)-4-hydroxy-3-methyl-*cis*-1,2-enol ether (11), whereas the (1*S*)-isomer (6) gave the (3*R*,4*R*)-enol ether (13), both isolated in 70–80% yields after flash chromatography. The diastereoisomers (11) and (13) could be distinguished by <sup>1</sup>H n.m.r. spectroscopy, and examination of the crude reaction mixtures showed that no appreciable crossover had occurred, only the (3*S*,4*S*)-isomer (11) being obtained from stannane (5), and only the (3*R*,4*R*)-isomer (13) being obtained from stannane (6); see Scheme 2.

Ozonolysis followed by a dimethyl sulphide work up, oxidation (Ag<sub>2</sub>O), and esterification (CH<sub>2</sub>N<sub>2</sub>) of the enol ethers (11) and (13), gave the enantiomeric hydroxy-esters (14) and (16), respectively (40% overall). The enantiomeric excess of each of these esters exceeded 90% as measured by optical rotation,<sup>7</sup> and by conversion into their (–)-α-methoxy-α-(trifluoromethyl)phenylacetate [(–)-MTPA] derivatives (15) and (17).<sup>8</sup> Prior conversion of the enol ether (11) into its (–)-MTPA ester (12) followed by ozonolysis, oxidation, and esterification gave ester (15) with an enantiomeric excess of >98% so showing that the small amount of racemization observed earlier had occurred during the ozonolysis or subsequent steps perhaps *via* reversible aldol equilibration.

Absolute configurations were assigned to the hydroxy-esters by correlation with pseudoephedrine. Thus the (–)-hydroxy-acid, readily available by cinchonidine resolution<sup>7</sup> of the (±)-acid,<sup>9</sup> was found to have the absolute configuration shown in formula (18) since Schmidt rearrangement [(PhO)<sub>2</sub>P(O)N<sub>3</sub>] and reduction (LiAlH<sub>4</sub>) gave (–)-pseudoephedrine (20) whose absolute configuration is known.<sup>10</sup> Esterification of the (–)-acid (18) with diazomethane gave the (–)-ester (14).

The selective transformations of benzaldehyde into *anti*-4-hydroxy-3-methyl-*cis*-1,2-enol ethers (11) and (13) using the optically active α-alkoxybut-2-enylstannanes (5) and (6), are consistent with the cyclic transition states shown in Scheme 3. The marked preference for the α-alkoxy group to adopt an axial position in each of these transition states<sup>11</sup> ensures that the (1*R*)- and (1*S*)-diastereoisomers (5) and (6) react selectively with the *si*- and *re*-faces of the benzaldehyde carbonyl group as shown.



Scheme 3

Similar discrimination was observed with other aldehydes. Thus the (1*R*)-stannane (5) was heated with an excess of cyclohexanecarboxaldehyde and cinnamaldehyde to give adducts (21) (80%) and (22) (68%). The stereochemistry of these products was assigned by analogy with the benzaldehyde series, and was confirmed for the cyclohexanecarboxaldehyde adduct (21) by ozonolysis, oxidation, and esterification, which gave the (–)-hydroxy ester (23), [ $\alpha$ ]<sub>D</sub><sup>20</sup> –8.1° (CHCl<sub>3</sub>), the absolute configuration of which has been assigned by Meyers.<sup>12</sup>

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