

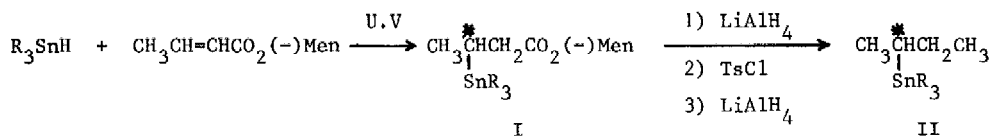
ASYMMETRIC HYDROSTANNATION OF CHIRAL α,β UNSATURATED ESTERS,
 A NEW EXCEPTION TO PRELOG'S GENERALIZATION

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The stereochemical course of the radical hydrostannation of E and Z (-)-menthyl crotonate, under experimental conditions close to the kinetic control, is best taken into account by considering cisoïd conformations for the substrates.

The Prelog type models for asymmetric induction, although not accurate descriptions of real transition states, allow good predictions for a large number of experiments (1), and suffer only a few exceptions (1d,2). We would like to present here a series of reactions between chiral α,β -unsaturated esters and organotin hydrides for which the stereochemical course is the reverse of that predicted by Prelog's generalization. We have performed U.V light initiated hydrostannations, under different experimental conditions on either E or Z(-)-menthyl crotonate and have determined the preferential configurations of the newly created chiral carbon centre :



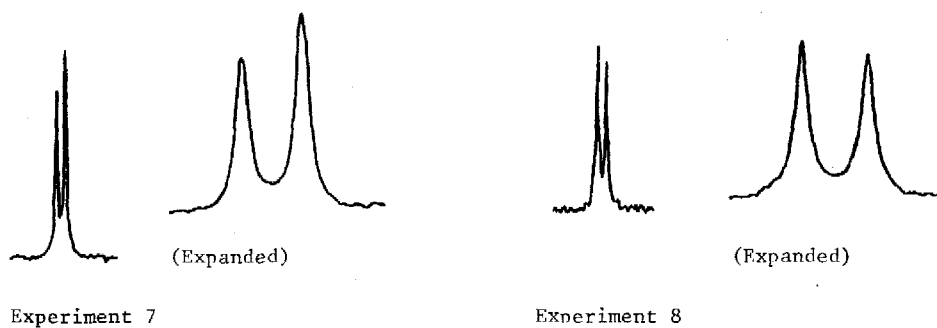
The results are summarized in the following table :

Experiment	R_3SnH	Menthyl crotonate	Stoichiometry $R_3SnH/crotonate$ (no solvent)	Temperature (°C)	Configuration (enantiomeric excess)
<u>1</u> (3)	Me_3SnH	E	1	50	R (21%)
<u>2</u> (3)	nBu_3SnH	E	1	50	R (22%)
<u>3</u> (3)	iBu_3SnH	E	1	50	R (22%)
<u>4</u>	Me_3SnH	Z	1	50	R (18%)
<u>5</u>	Me_3SnH	E	3	-20	R (14%)
<u>6</u>	Me_3SnH	Z	3	-20	(c.a 0%)
<u>7</u>	Me_3SnH	E	3	-50	R (12%)
<u>8</u>	Me_3SnH	Z	10	-50	S (5%)

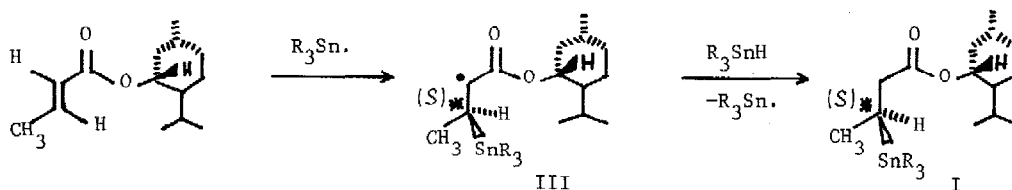
For experiments 1 to 4, the enantiomeric purities were first measured on I by proton NMR of the diastereomers (3) and the predominant configurations were determined polarimetrically on II, the absolute configurations of which are known (4).

Measurements were repeated for experiments 1 and 4 by direct F.T. ^{119}Sn NMR analysis (33.54 MHz) under gated proton decoupling: the diastereomeric adducts I showed two distinct singlets for the tin atoms (10.45 and 10.12 ppm in C_6D_6 with Me_4Sn as external standard) and the integration values were in good agreement with ^1H NMR determinations.

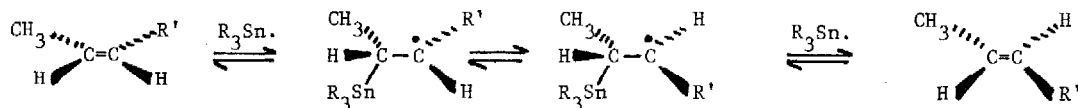
Thus both the enantiomeric excess and the predominant configuration can be easily deduced solely from ^{119}Sn NMR spectra (experiments 5 to 8). As an example, spectra corresponding to experiments 7 and 8 are shown below.



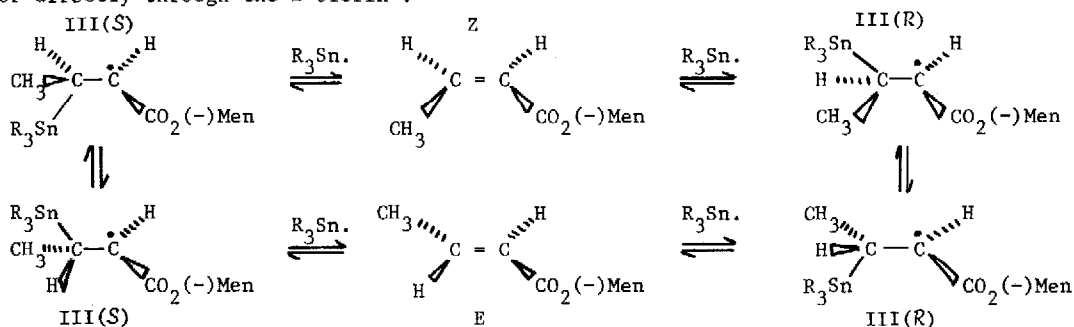
The first three results that we have obtained (3) have revealed an anti-Prelog behaviour. The mechanism by which olefins undergo radical hydrostannation is now well established (5) and Prelog's generalization, which postulates a transoid conformation for the starting ester, would have predicted an excess of the *S* configuration for experiments 1 to 3:



In an other experiment under the same conditions (4), *Z*-menthyl crotonate and trimethyltin hydride have also led to a predominant *R* configuration and the unreacted ester showed almost complete isomerization to the *E* configuration. In fact, *Z*-*E* isomerization along hydrostannation is a known process directly related to the reversibility of the addition of the organotin radical (6):

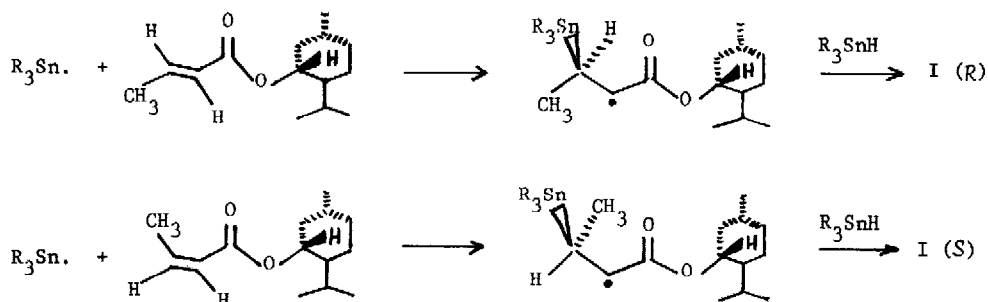


It has been observed that an α,β unsaturated ester of the E configuration, such as methyl fumarate, undergoes a faster hydrostannation than its Z isomer, the latter reaction being accompanied by isomerization from Z to E (7). These data suggest that, under our experimental conditions and independently of the initial configuration of menthyl crotonate, the substrates might have reacted as the E isomer. It was important to slow down the isomerization process, and at the same time to counteract a possible thermodynamic control due to a rapid interconversion between the two diastereomeric radicals III (S) and III (R) through the Z olefin (8), or directly through the E olefin :

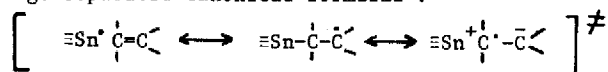


Thus, we have decided to work under experimental conditions favouring a much faster hydrogen transfer from the tin hydride, as compared to the reversal of the addition of the tin radical. This was done by lowering the temperature and increasing the concentration of the organotin hydride (9). Experiments 5 and 6 at -20°C and mainly 7 and 8 at -50°C show clearly that under condition closer to the kinetic control, E and Z crotonates tend to give chiral carbons of opposite configurations : from both isomers, the reverse of what could have been predicted from Prelog's models is observed (10).

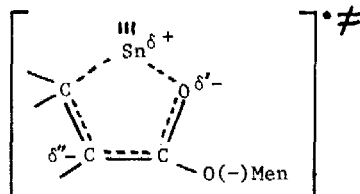
We suggest that these stereochemical results could be ascribed to the fact that the esters actually react in the cisoid conformations :



This proposal is mainly based on the polar effects occurring during radical hydrostannation (11). Trialkylstannyl radicals behave as nucleophilic radicals and the transition states may be described by charge separated canonical formulae :



The negative charges can be delocalized and the cisoïd conformation would allow stabilization of the transition state by electrostatic interaction :



In conclusion, the radical additions of trimethyltin hydride at low temperature on Z and E menthyl crotonates follow a stereochemical course which is the reverse of that predicted on the basis of Prelog's generalization. We suggest that cisoïd, instead of transoïd, conformations for the substrates would lead to more favorable energetic situations. The intervention of cisoïd conformation is not unprecedented : for instance, Munch-Petersen et al., for the case of the addition of Grignard reagents on chiral α,β unsaturated esters, have proposed a mechanism involving nucleophilic assistance of the carbonyl group on the magnesium atom (12). More recently, Welvart et al. emphasized the major influence of the metal on the conformation of the ester group (1e).

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- 9 - J.P. QUINTARD and M. PEREYRE, C.R.Acad.Sc., Paris, Ser.C., 284, 937, (1977).
- 10 - Two additional experiments have been performed with tributyltin hydride in excess and Z or E menthyl crotonate under high pressure (1000 MPa). The results were close to those obtained in exp. 5 and 6 : Z crotonate led to racemic II and E crotonate to an excess (10%) of R configuration. These results suggest that high pressure could set up conditions close to kinetic control.
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