Journal of Organometallic Chemistry, 434 (1992) 269–285
Elsevier Sequoia S.A., Lausanne
JOM 22551

Stereoselective hydrostannation: synthesis and absolute configuration of (−)-menthyl 2,3-diphenyl-3-(trimethylstannyl) propanoates and derivatives *

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(Received August 5, 1991; in revised form November 26, 1991)

Abstract

Free radical hydrostannation of (−)-menthyl (*E*)-2,3-diphenylpropenoate (**1**) leads to a mixture of four adducts: two threo diastereoisomers (approx. 90%) and two erythro diastereoisomers (approx. 10%). Whereas *threo* diastereoisomers **2** (38%) and **3** (51.2%) could be isolated by column chromatography and fractional recrystallization, *erythro* diastereoisomers **4** and **4'** (6.5% and 4.3%) could not be separated. Bromodestannylation of **2** and **3** yielded two diastereoisomers in each case, **9–10** and **11–12**, respectively, which were isolated and characterized by spectroscopic methods. The reduction of bromo esters **9–12** with lithium aluminium hydride gave (*R*)-(−)- and (*S*)-(+)-2,3-diphenyl propanols **13** and **14** of known absolute configuration. Working back from the stereochemistry of **13** and **14** and taking into account the NMR data, the stereochemistry of their precursors was assigned. Full ^{1}H, ^{13}C, and ^{119}Sn NMR data are given.

Introduction

In previous studies on the addition of organotin hydrides to open-chain and cyclic activated olefins, we reported that these additions take place with a high degree of stereoselectivity [1]. Recently, and making use of Karplus type relationships, the relative configurations and preferred conformations of a series of organotin adducts have been reported [2].

The results obtained from studies carried out with the aim of determining the absolute configurations of the adducts obtained in the addition of trimethyltin hydride to (−)-menthyl (*E*)-2,3-diphenylpropenoate are reported.

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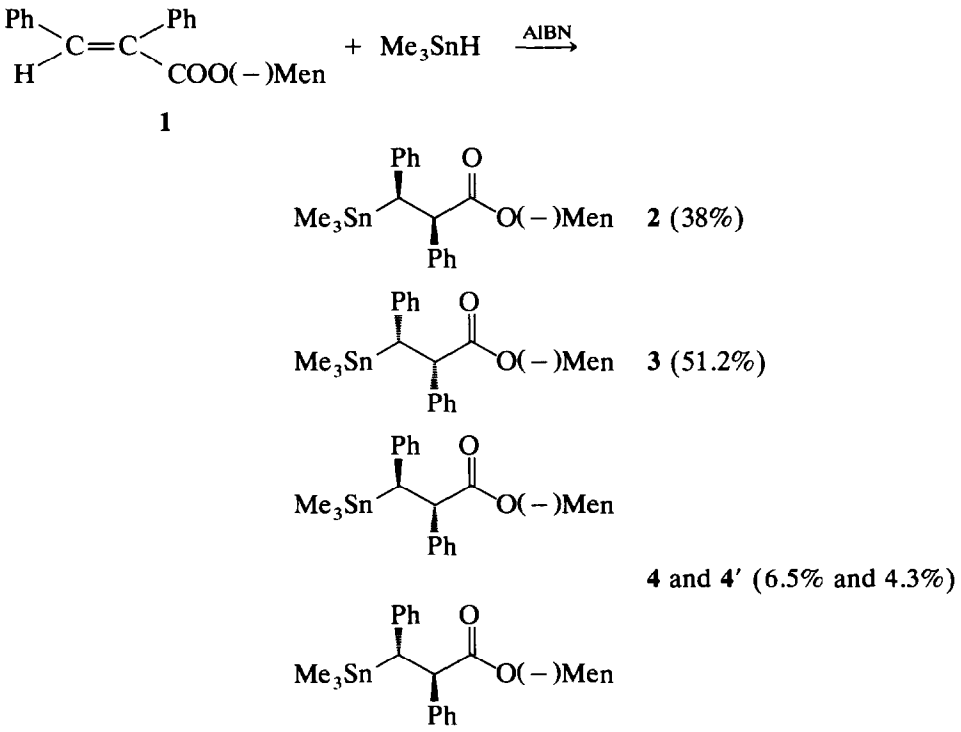
* Dedicated to Professor Wilhelm Paul Neumann on his 65th birthday.

Taking into account the fact that these optically active functionally substituted organotin compounds can be selectively transformed in a series of organic compounds [3,4], these results should be of interest for organic chemists engaged in stereoselective synthesis research.

Results and discussion

The addition under free radical conditions of trimethyltin hydride to (−)-menthyl (*E*)-2,3-diphenylpropenoate (**1**), leads to a mixture of the four diastereoisomers expected according to Scheme 1. The analysis of ^{119}Sn NMR of the crude product shows it to consist of a mixture of four diastereomers, two of them in higher proportion (38% and 51.2%).

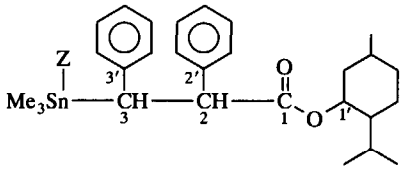
Although separation of diastereomers by column chromatography (silica-gel 60) is not really efficient, this method enabled us to separate the stereoisomers obtained in higher yield (**2** and **3**, Scheme 1) from those obtained in lower yield (**4** and **4'**, Scheme 1). Stereoisomers **2** and **3** were then obtained by fractional recrystallization in ethanol from the mixture obtained in the chromatography (see Experimental section). On the other hand, although the mixture of stereoisomers obtained in lower yield (**4** and **4'**) could not be separated by this method, we were able to obtain mixtures enriched in each diastereoisomer which enabled us to obtain the NMR characteristics of each diastereoisomer. The main spectroscopic



Scheme 1 Diastereomers obtained in the addition of trimethyltin hydride to (−)-menthyl (*E*)-2,3-diphenylpropenoate (**1**)

Table 1

^{13}C and ^{119}Sn NMR characteristics of compounds **2–8** [a]

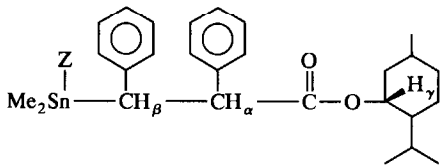


No.	Z	Me–Sn	C(1)	C(2)	C(3)	C(1′)	C(2′)	C(3′)	Other signals	^{119}Sn
2	Me	−8.78	174.13	54.39	37.80	74.69	139.97	143.80	15.51; 20.57; 22.12; 22.8; 25.02; 31.38; 34.20; 40.87;	15.61
		(325.5)	(7.6)	– [b]	(320.4)		(50.2)	(30.5)	47.32; 123.62; 126.59; 126.93; 127.94; 127.97; 128.07	
3	Me	−8.62	174.24	54.52	38.44	74.89	139.97	144.15	16.10; 20.93; 21.94; 23.04; 25.82; 31.25; 34.14, 39.82;	11.43
		(328.0)	(8.9)	(10.2)	(323.0)		(44.5)	(30.3)	46.75; 123.75; 126.53; 126.88; 127.87; 128.06; 128.09	
4 [c]	Me	−10.08	173.24	54.87	39.47	74.23	138.83	144.06	15.62; 20.71; 21.86; 23.09; 25.34; 31.22; 39.48; 40.37;	9.62
		(325.5)	(76.3)	– [b]	(324.2)		(8.9)	(29.2)	47.06; 124.20; 126.33; 127.74; 128.30; 128.44; 128.64	
4′ [d]	Me	−9.97	173.12	55.18	39.91	73.94	138.69	143.94	15.47; 20.68; 21.84; 22.86; 25.31; 31.17; 39.91; 40.33;	8.36
		(325.5)	(76.3)	– [b]	(330.6)		– [b]	(28.0)	46.90; 124.16; 126.28; 126.73; 127.69; 128.24; 128.60	
5	Cl	−1.92, 3.18	180.97	55.72	47.23	78.70	138.38	143.32	15.58; 20.42, 21.95; 22.79; 25.34, 31.38; 33.87; 40.18;	42.57
		(475.6, 424.8)	(34.3)	(19.1)	(445.0)		– [b]	(47.0)	46.79; 125.06; 125.92; 127.23; 127.62; 128.47; 128.75	
6	Cl	−1.96, 3.18	181.08	55.21	47.46	78.67	138.26	143.30	15.80; 20.72; 21.88; 22.92; 26.98; 31.37; 33.85; 39.86;	44.33
		(476.8, 431.0)	(33.0)	(17.8)	(443.7)		– [b]	(47.0)	46.72; 125.16; 125.91; 126.99; 127.60; 128.44; 128.98	
7	Br	−1.21, 4.32	181.06	55.95	47.46	78.80	138.36	143.22	15.60; 20.47; 22.00; 22.81; 25.38; 31.45; 33.92; 40.23;	31.09
		(462.8, 426.0)	(33.0)	(17.8)	(434.8)		– [b]	(45.8)	46.84; 125.22; 126.10; 127.30; 127.70; 128.50; 128.83	
8	Br	−1.28, 4.23	181.11	55.41	47.68	78.72	138.21	143.15	15.82; 20.74; 21 90; 22 95; 26.30, 31.40; 33.87; 39.87;	32.86
		(462.8, 419.6)	(33.0)	(17.8)	(432.4)		– [b]	(45.8)	46.74; 125.28; 126.06; 127.02; 127.65; 128.44; 129.02	

[a] In $CDCl_3$; chemical shifts, δ, in ppm with respect to external TMS or Me_4Sn; tin–carbon coupling constants J in Hz in parentheses. [b] Not observed. [c] From a mixture of (**4**+**4′**) with **4** in excess. [d] From a mixture of (**4**+**4′**) with **4′** in excess.

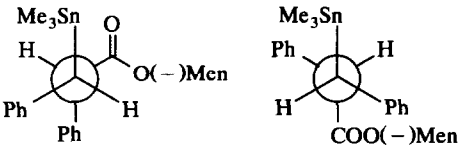
Table 2

^{1}H NMR characteristics of compounds **2–8** [a]



No.	Z	Me–Sn	H_α	H_β	$^3J(H_\alpha, H_\beta)$	H_γ	Other signals
2	Me	0.01	4.23	3.30	12.0	4.59	0.32 (d, 3H, 7.0 Hz); 0.54 (d, 3H, 7.0 Hz); 0.75–1.10 (m, 7H); 1.21 (m, 1H);
		(52.2)	(36.0)	(62.9)		(m)	1.43–1.69 (m, 3H); 2.04 (m, 1H); 6.82–6.91 (m, 2H); 7.16–7.23 (m, 8H)
3	Me	0.00	4.25	3.17	10.0	4.68	0.60–0.71 (m, 2H); 0.78 (d, 3H, 7.0 Hz); 0.81 (d, 3H, 6.6 Hz); 0.90 (d, 3H, 7.0 Hz);
		(52.4)	(43.7)	(63.2)		(m)	1.04 (m, 1H); 1.26–1.52 (m, 2H); 1.61–1.70 (m, 2H); 1.77 (m, 1H);
							1.95 (m, 1H); 6.85–6.92 (m, 4H); 7.07–7.11 (m, 4H); 7.12–7.17 (m, 2H)
4 [b]	Me	−0.35	4.27	3.27	13.4	4.42	0.30 (d, 3H, 6.8 Hz); 0.59 (d, 3H, 6.9 Hz); 0.65–0.94 (m, 6H); 2.02–2.41
			(43.0)	(56.6)		(m)	(m, 3H); 2.66–3.41 (m, 3H); 6.93–7.35 (m, 8H); 7.47–7.50 (m, 2H)
4′ [c]	Me	−0.33	4.25	3.39	13.3	4.44	– [d]
			(42.6)	(56.6)		(m)	
5	Cl	0.21, 0.75	4.37	3.25	0.9	4.84	0 59 (d, 3H, 6.8 Hz); 0.67 (d, 3H, 6.8 Hz); 0.80–1.10 (m, 4H); 1.20 (m, 1H);
		(62.5, 64.3)	(131.3)	(90.1)		(m)	1.30–1.44 (m, 2H); 1.47–1 75 (m, 4H); 2.10 (m, 1H); 7.02–7 16 (m, 4H);
							7.26–7.32 (m, 6H)
6	Cl	0.22, 0.74	4.45	3.26	[e]	4.96	0.85–1.20 (m, 10H); 1.48–1.61 (m, 3H); 1.68–1.82 (m, 3H); 1.97 (m, 1H);
		(62.5, 64.3)	(134.6)	(88.6)		(m)	2.11 (m, 1H); 7.07–7.19 (m, 4H); 7 27–7.38 (m, 6H)
7	Br	0.32, 0.86	4.37	3.32	[e]	4.85	0.60 (d, 3H, 6.0 Hz), 0.68 (d, 3H, 6.0 Hz); 0.90–1.78 (cs, 11H, including
		(61.6, 63.0)	(130.2)	(86.4)		(m)	a doublet at 0.99, 6.5 Hz); 2.12 (m, 1H); 6.90–7.50 (m, 10H)
8	Br	0.31, 0.83	4.43	3.31	[e]	4.95	0.89–1.10 (cs, 12H); 1.44–2.18 (m, 6H); 6.98–7.55 (m, 10H)
		(62.0, [f])	(131.2)	(84.6)		(m)	

[a] In $CDCl_3$; chemical shifts, δ, in ppm with respect to external TMS; coupling constants in Hz; tin–proton coupling constants in parentheses. Multiplicity: d stands for doublet, m for multiplet, and cs for complex signal [b] From a mixture of (**4**+**4′**) with **4** in excess. [c] From a mixture of (**4**+**4′**) with **4′** in excess. [d] Signals of **4** and **4′** superimposed. [e] ^3J(H,H) lower than 0.2 Hz [f] Not observed.



I (*threo*) II (*erythro*)

Fig. 1. Preferred conformations of *threo* and *erythro* compounds **2**–**4** (only one stereoisomer of each is shown).

characteristics of the compounds and some derivatives are summarized in Tables 1 and 2.

The stereochemistry of diastereoisomers **2** and **3** was assigned as follows. In the ^{13}C NMR, the observed ^3J(Sn–C–C=O) coupling constants for compounds **2** and **3** were 7.6 and 8.9 Hz, respectively (Table 1). These values, according to our previous work [2], correspond to a dihedral angle close to 60°C. Similarly, values of ^3J(Sn–C–C–Ph) coupling constants for compounds **2** and **3** were 50.2 and 44.5 Hz, respectively, which correspond to a dihedral angle close to 180°C. ^1H NMR spectra (Table 2) show that the ^3J(H,H) coupling constants of the protons attached to C-2 and C-3 are 12 Hz (compound **2**) and 10.7 Hz (compound **3**), indicating a dihedral angle of approx. 180° between them. The ^3J(Sn–C–C–H) coupling constants for compounds **2** (36.0 Hz) and **3** (43.7 Hz) suggest [2] a dihedral angle of approx. 60°. Taking these values into account, it is possible to attribute a *threo* configuration, *i.e.*, (2*R*,3*R*)- and (2*S*,3*S*)- (Fig. 1, **I**) to both diastereoisomers.

On the other hand, ^{13}C NMR spectra (Table 1) show that the ^3J(Sn–C–C=O) coupling constant is 76.3 Hz for both compounds **4** and **4′**, indicating a dihedral angle close to 180°. The small values of ^3J(Sn–C–C–Ph) coupling constants for compounds **4** (8.0 Hz) and **4′** (not observed), suggest a dihedral angle of approx. 60° between the trimethyl stannyl group and the phenyl group attached to C-2.

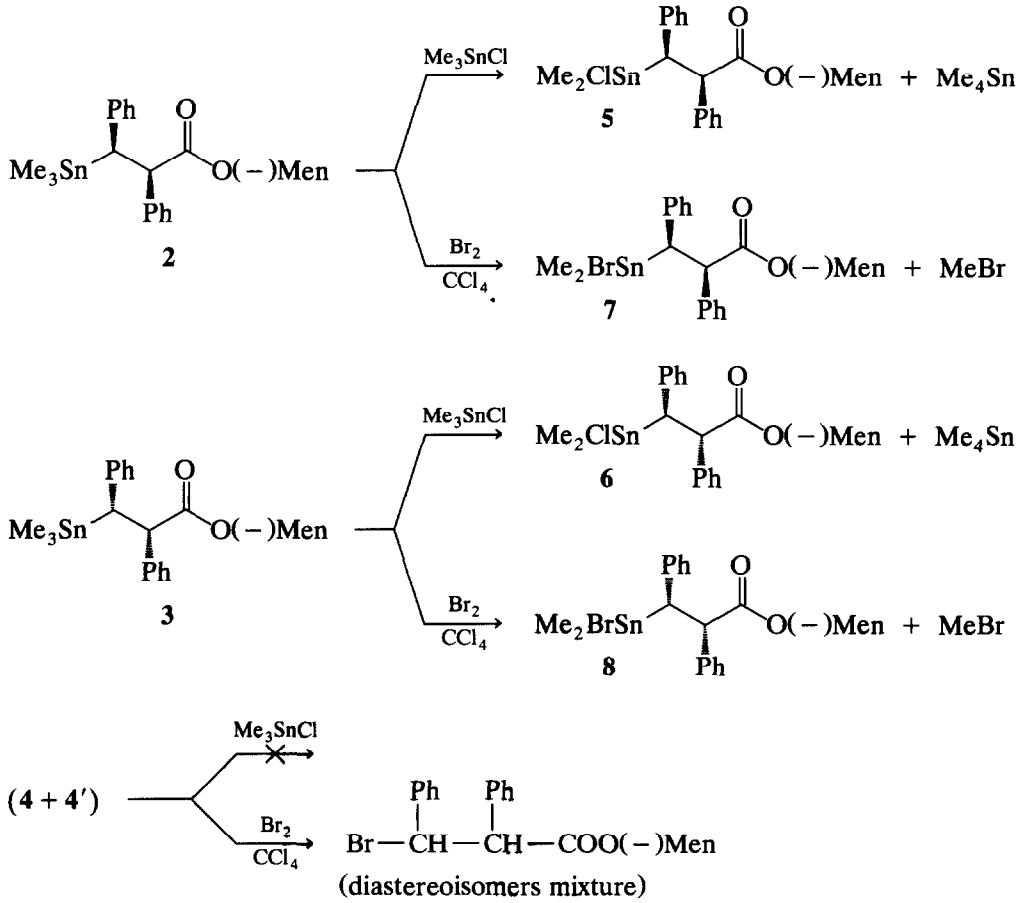
^1H NMR spectra (Table 2) show that the ^3J(H,H) coupling constants for the protons attached to C-2 and C-3 are 13.4 Hz for compound **4**, and 13.3 Hz for compound **4′**, indicating that the dihedral angle between these protons should be close to 180°. The ^3J(Sn–C–C–H) coupling constants for compounds **4** (43.0 Hz) and **4′** (42.6 Hz) suggest a dihedral angle of approx. 60°. These values strongly suggest that compounds **4** and **4′** have the erythro configuration, *i.e.*, (2*S*,3*R*)- and (2*R*,3*S*)- (Fig. 1, **II**).

In order to obtain additional information on their stereochemical features, diastereoisomers **2**, **3** and also the mixtures enriched in both **4** and **4′**, were made to react with Me_3SnCl according to Scheme 2.

These reactions proceeded smoothly to give quantitative yields of exchange products in the case of adducts **2** and **3**. On the other hand, the mixtures of adducts **4** and **4′** did not react with trimethyltin chloride.

The study of the ^{13}C and ^1H NMR spectra of compounds **5** and **6** (Tables 1 and 2), by correlation between coupling constants and dihedral angles as was done for compounds **2** and **3**, lead us to the conclusion that the preferred conformation for these compounds is as shown in Fig. 2.

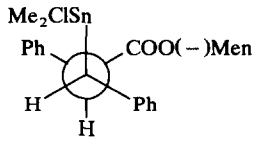
Additional support for conformation **III** (Fig. 2) was obtained from the ^{119}Sn NMR spectra (Table 2), which show high-frequency shifts of approx. 27 ppm for



Scheme 2. Methyl/chlorine exchange reactions with trimethyltin chloride and bromodestannylation of adducts **2**, **3**, and **(4+4′)**.

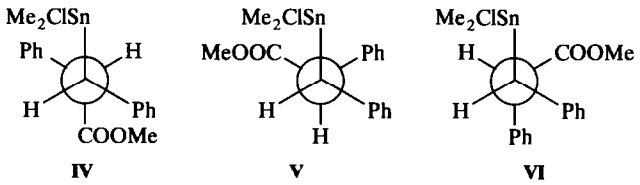
compound **5**, and 33 ppm for compound **6**, with respect to their corresponding starting adducts **2** and **3**, respectively. These shifts indicate the existence of intramolecular coordination between the tin atom and the C=O of the ester group. Coordination renders the two methyl groups on tin non-equivalent, and this is shown by the appearance of two signals in the ^{13}C NMR spectra (Table 1) of **5** and **6**, with ^{1}J(Sn–C) values which differ by up to about 50 Hz. In the proton spectra, the two methyl resonances are also split (Table 2).

In previous studies, we were able to obtain [1c] and characterize [2] the *erythro* derivative of methyl 2,3-diphenyl-3-(chlorodimethylstannyl)propanoate, *i.e.*, the



III

Fig. 2 Preferred conformations for compounds **5** and **6** (one stereoisomer is shown).



IV V VI

Fig. 3 Possible conformations for *erythro* methyl 2,3-diphenyl-3-(chlorodimethylstannyl)propanoates (one enantiomer of each is shown).

methyl ester instead of the (−)-menthyl ester. The NMR characteristics of this compound clearly indicate that the more preferred conformation was close to **IV** (Fig. 3).

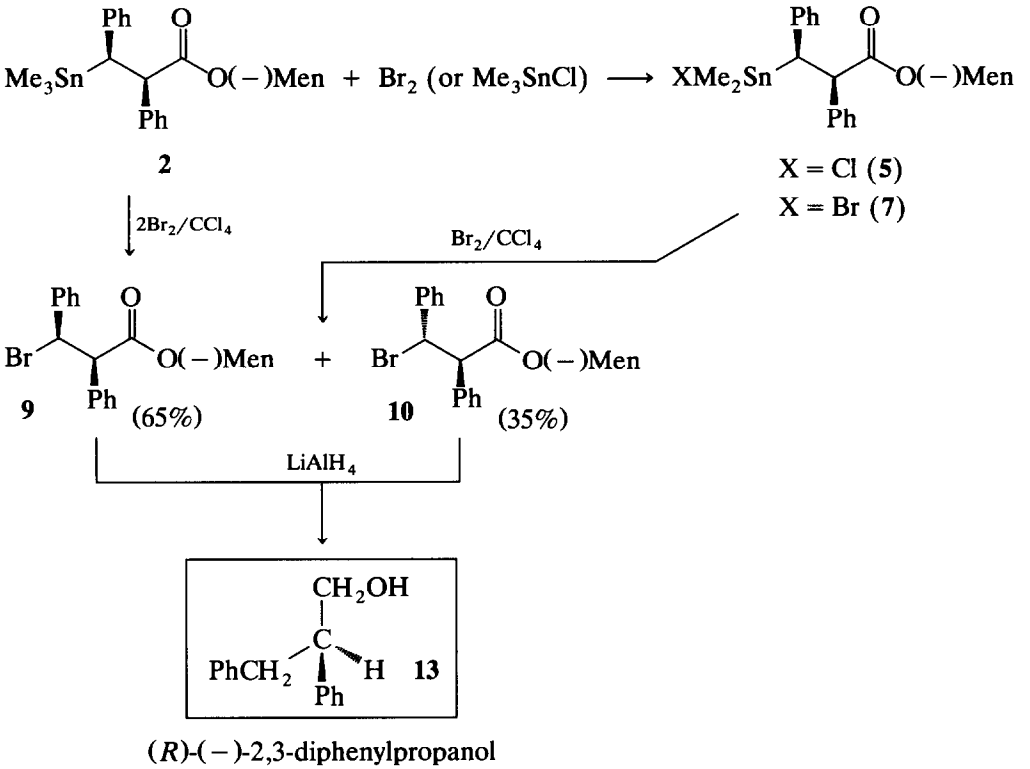
There is no intramolecular coordination in this stereoisomer, due to the fact that in the *erythro* configuration such a coordination would force both phenyl groups to take up a highly unfavourable *gauche* conformation [2] (conformations **V** and **VI**, Fig. 3).

The lack of reaction between the mixtures of diastereoisomers (**4** and **4'**) and trimethyltinchloride (Scheme 2), could be connected by the impossibility of reaching exchange products stabilized by intramolecular coordination.

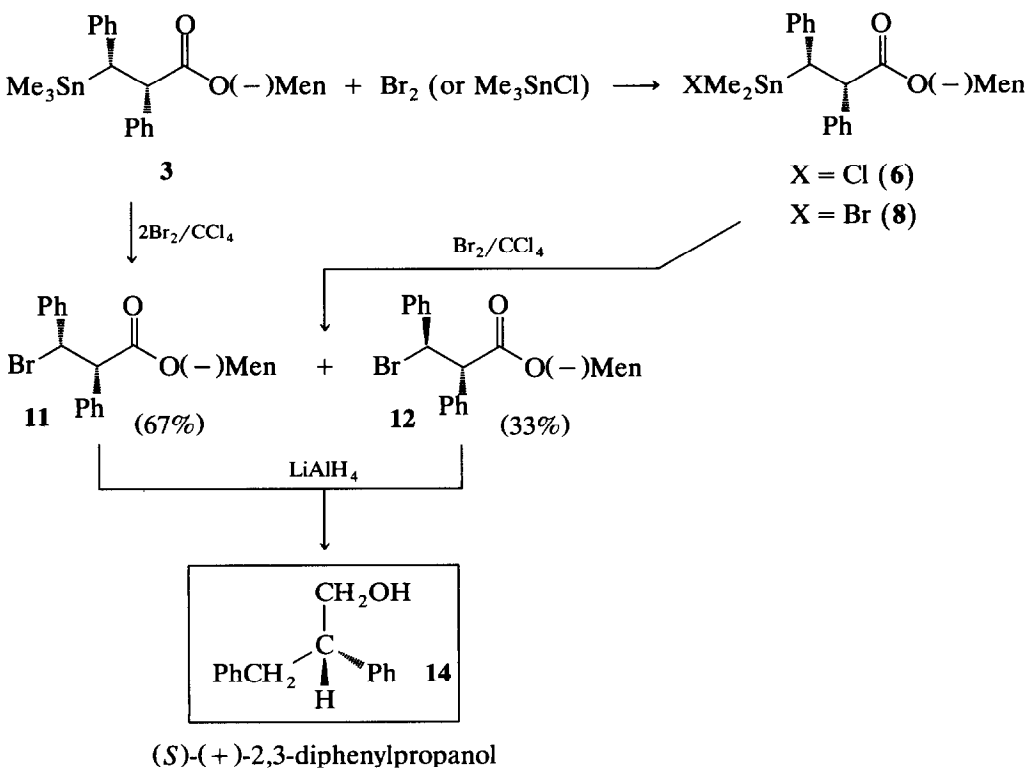
A direct chemical illustration was obtained from the study of the reactions of adducts **2**, **3**, and the mixtures of **4** and **4'**, with bromine in a 1:1 molar ratio, according to Scheme 2. In previous studies [5], we have shown that the formation of bromodealkylation products by this type of adduct when treated with bromine in a 1:1 ratio, is due to the ease of formation of intramolecularly coordinated β-halodialkylstannyl derivatives. The results indicate that whereas adducts **2** and **3** react with bromine to give the intramolecularly coordinated β-bromodimethylstannyl, derivatives **7** and **8**, and the mixtures of **4** + **4'** lead exclusively to a mixture of bromodestannylation products. The NMR characteristics of compounds **7** and **8** are listed in Tables 1 and 2. Additional confirmation of the existence of intramolecular coordination in compounds **5–8** can be obtained from their IR spectra and ^{1}H NMR data. Thus, comparing the IR data for each pair **2**/**5**, **2**/**7**, **3**/**6** and **3**/**7**, it can be seen that the carbonyl stretching frequencies of the chloro- and bromodimethylstannyl esters **5–7** (Table 7), appear at a lower frequency from those of the corresponding starting trimethylstannyl esters **2** and **3**. The ^{1}H NMR ester signals (H-γ) of compounds **5–7** (Table 2) are downfield from the corresponding signals for the trimethylstannyl esters **2** and **3** (compare for example **2**, H-γ 4.59 ppm). These values indicate that in the case of chloro- and bromodimethylstannyl esters **5–8** there is coordination between the carbonyl group of the ester and the Sn atom; this is known to reduce the carbonyl stretching frequency and to have a deshielding effect on the (−)-menthoxy group proton H-γ [1b]. This carbonyl coordination to tin must be intramolecular since the carbonyl stretching frequency remains nearly the same for the pure compound as for a solution.

These results not only confirm our previous report [5], but also support our assumption that adducts **4** and **4'** do not undergo methyl/chlorine exchange with trimethyltin chloride because the products of such exchange cannot be stabilized by intramolecular coordination.

The absolute configuration of adducts **2** and **3** was established by chemical correlation according to Scheme 3.



(*R*)-(−)-2,3-diphenylpropanol

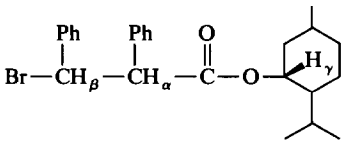


(*S*)-(+)-2,3-diphenylpropanol

Scheme 3. Reaction sequences for obtaining the absolute configuration of adducts **2** and **3**.

Table 3

^{1}H NMR characteristics of compounds **9–12** [a]



No.	H_α	H_β	$^3J(H_\alpha, H_\beta)$	H_γ	Other signals
9	4.33 (d)	5.48 (d)	11.7	4.73 (m)	0.61–0.87 (m, 10H); 0.99 (m, 1H); 1.30–1 49 (m, 2H); 1.53–1.69 (m, 3H); 1.76 (m, 1H); 2.00 (m, 1H); 6.99–7.16 (m, 10H)
10	4.35 (d)	5.46 (d)	11.7	4.38 (m)	0.29 (d, 3H, ^3J = 6.8); 0.57–0.94 (m, 8H); 1.08–1 34 (m, 4H); 1.43 (m, 1H); 1.49–1.60 (m, 2H); 7 28–7 41 (m, 8H); 7.51–7.54 (m, 2H)
11	4.42 (d)	5.59 (d)	11 6	4.74 (m)	0.48 (d, 3H, ^3J = 6.9); 0.68 (d, 3H, ^3J = 6.9); 0.85–1.14 (m, 5H); 1.35–1.53 (m, 4H), 1.65 (m, 2H); 2.11 (m, 1H); 7.07–7.24 (m, 10H)
12	4.45 (d)	5.54 (d)	11.6	4.44 (m)	0.36 (d, 3H, ^3J = 6 9), 0.62–0.90 (m, 8H); 1.08–1.40 (m, 6H); 1.56 (m, 1H); 7.30–7.44 (m, 6H); 7.54–7.57 (m, 4H)

[a] In $CDCl_3$; δ values in ppm *versus* TMS; ^nJ values in Hz. Multiplicity: d stands for doublet and m for multiplet.

The reaction of adduct **2** with bromine in a 1 : 2 molar ratio of adduct/bromine in carbon tetrachloride leads to a mixture of diastereoisomers **9** (65%) and **10** (35%). Under the same reaction conditions, adduct **3** yields a mixture of diastereoisomers **11** (67%) and **12** (33%). The ^{1}H and ^{13}C NMR data of β-bromoesters **9–12** are summarized in Tables 3 and 4.

The configuration of (−)-menthyl-3-bromo-2,2-diphenyl-propanoates **9–12** were assigned as follows. The coupling constants for protons H-α and H-β in these stereoisomers lie between 11.6 and 11.7 Hz (Table 7). This indicates that the preferred conformation for diastereoisomers **9–12** are those where H-α and H-β are antiperiplanar (Fig. 4).

In conformations **IX** and **X** (*erythro*), the (−)-menthoxy group is affected by the phenyl group, while in conformations **VII** and **VIII** (*threo*), this type of influence does not exist. As a result the ^{1}H NMR signals corresponding to protons H-γ (of the (−)-menthoxy group) in **IX** and **X** should appear at higher fields.

In Table 3, we can see that proton H-γ in isomers **9** (4.74 ppm) and **11** (4.73 ppm) appears at lower fields than in isomers **10** (4.44 ppm) and **12** (4.38 ppm).

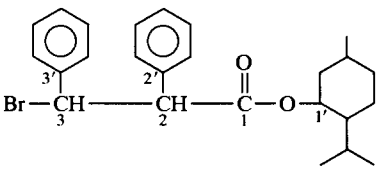
Taking into account these values we can assign *threo* configurations **VII** and **VIII** to stereoisomers **9** and **11**, and *erythro* configurations **IX** and **X** to stereoisomers **10** and **12**.

This is confirmed by the ^{1}H NMR data reported in the literature for the methyl [5] and ethyl [6] esters. The same results were obtained in the bromodestannylation reactions of the β-halodimethylstannyl derivatives **5–8** according to Scheme 3.

These results confirm our previous observations [5] that the reactions of esters of this type with bromine in carbon tetrachloride proceed with a high degree of retention of configuration at the carbon involved in the electrophilic substitution.

Table 4

^{13}C NMR characteristics of compounds **9–12** [a]



No.	C(1)	C(2)	C(3)	C(1′)	C(2′)	C(3′)	Other signals
9	171.07	47.23	61.20	75.55	135.49	138.84	15.97, 20.47; 21.99; 23.42; 25.83; 31.44; 34.29; 40.79; 53.64; 127.68; 128.00; 128.18; 128.27; 128.33
10	169.84	46.84	60.16	75.02	136.91	140.32	15.70; 20.54; 21.78; 23.11; 25.51; 31.12; 34.02; 40.08; 54.89; 127.58; 128.04; 128.47; 128.53; 128.60
11	171.04	47.05	61.20	75.31	135.34	138.84	16.06; 20.83; 21.94; 23.17; 25.96; 31.35; 34.24; 40.22; 53.71; 127.68; 128.00; 128.20; 128.29; 128.36
12	169.88	46.80	60.69	74.87	136.83	140.26	15.67; 20.76; 21.84; 22.94; 25.53; 31.22; 34.07; 40.02; 55 06; 127.87; 128.12; 128.37; 128.57, 128.61

[a] In $CDCl_3$; δ values in ppm *versus* TMS.

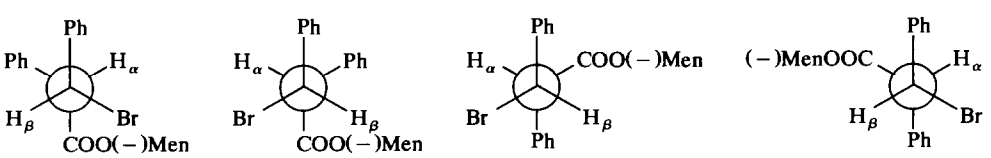
The reduction with an excess of lithium aluminium hydride of esters **9–12** (Scheme 3), leads in the case of esters **9** and **10** to (*R*)-(−)-2,3-diphenylpropan-1-ol (**13**), and to (*S*)-(+)-2,3-diphenylpropan-1-ol (**14**) [6] in the case of esters **11** and **12**.

Working back from the stereochemistry of the propanols obtained (**13** and **14**), it is possible to make the stereochemical assignments for their precursors. Thus the absolute configurations of the bromoesters are (2*R*,3*R*) for compound **9**, (2*S*,3*R*) for compound **10**, (2*S*,3*S*) for compound **11**, and (2*R*,3*S*) for compound **12**. Therefore, the starting adducts, **2** and **3**, are (−)-menthyl (2*R*,3*R*)- and (2*S*,3*S*)-2,3-diphenyl-3-(trimethylstannyl)propanoate, respectively.

The removal of the chiral auxiliary group in adducts **2** and **3** by reduction with lithium aluminium hydride (Scheme 4), leads to the corresponding enantiomers **15** and **16**, respectively.

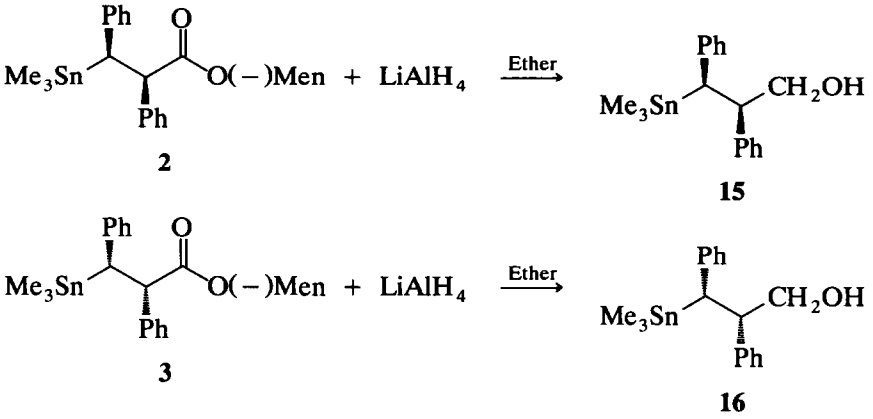
^{13}C, ^{1}H and ^{119}Sn NMR data for compounds **15** and **16** are summarized in Tables 5 and 6.

The analysis of the ^{1}H and ^{13}C NMR characteristics of enantiomers **15** and **16** (Tables 5 and 6), by correlation between coupling constants and dihedral angles as previously, indicates that these enantiomers have *threo* configuration.



VII (9) **VIII (11)** **IX (10)** **X (12)**

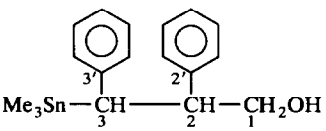
Fig. 4. Preferred conformations of stereoisomers **9–12**



Scheme 4. Removal of the chiral auxiliary group of adducts **2** and **3**.

Table 5

^{13}C NMR characteristics of compounds **15–17** [a]

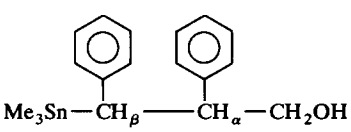


No.	Me–Sn	C(1)	C(2)	C(3)	C(2′)	C(3′)	Other signals
15	−8.89	68.09	51.14	37.78	142.46	144.36	123.47(14.0); 126.24; 127.04(28.9);
	(323.0)	(14.0)	(7.6)	(321.7)	(55.9)	(31.8)	127.93(10.2); 128.14
16	−8.88	68.04	51.16	37.84	142.54	144.39	123.45(14.0); 126.18; 127.05(24.0);
	(323.0)	(14.0)	– [b]	(321.7)	(54.6)	(31.8)	127.91; 128.10
17 [c]	−0.36	67.30	50.65	38.80	142.5	144.43	124.19; 126.52; 127 33; 128.43;
	(321.6)	(61.0)	(11.4)	(338.2)	(11.4)	(30.3)	128.57; 128.86

[a] ^{13}C NMR in $CDCl_3$ (internal lock); δ values in ppm, ^nJ values in (Hz). [b] Not observed. [c] Mixture of enantiomers obtained through reduction of the mixture of (**4**+**4′**) according to Scheme 6.

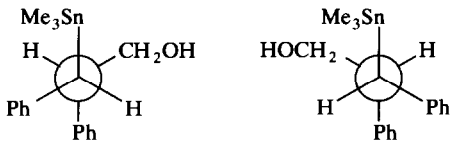
Table 6

^1H and ^{119}Sn NMR characteristics of compounds **15–17** [a]



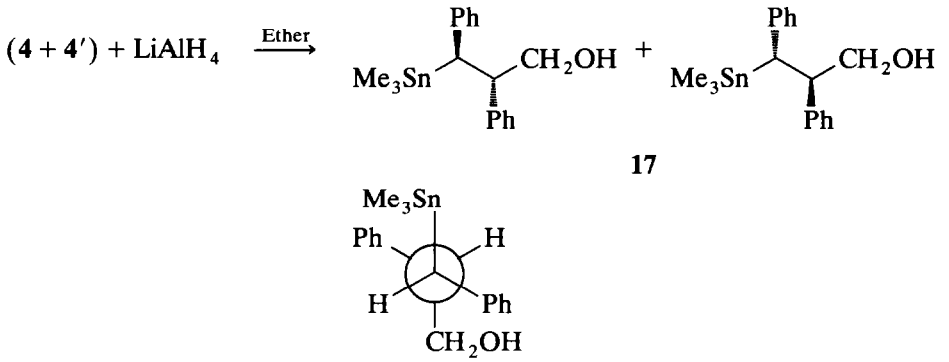
No.	Me–Sn	CH_α	CH_β	$^3J(H_\alpha, H_\beta)$	Other signals	^{119}Sn
15	0.04	3.52	2.91	12.1	3.81 (m, 3H); 6.83–7 15 (m, 10H)	6.67
	(52.2)	(m)	(58.8)			
16	0.04	3.54	2.91	12.1	3 82 (m, 3H); 6.85–7.15 (m, 10H)	6.98
	(52.2)	(m)	(58.6)			
17 [b]	−0.36	3.54	2.84	12.2	3.69 (m, 3H); 7.03–7.39 (m, 10H)	7.94
	(51.3)	(m)	– [c]			

[a] ^1H NMR spectra in $CDCl_3$; δ values in ppm *versus* TMS; J in Hz; tin–carbon coupling constants in parentheses; ^{119}Sn NMR in $CDCl_3$; δ values in ppm *versus* Me_4Sn. [b] From a diastereoisomers' mixture. [c] $^2J(Sn,H)$ could not be calculated due to signals overlapping.



15 16

Fig. 5 Preferred conformations for *threo* enantiomers **15** and **16**.



Scheme 5. Reduction of the mixture of diastereoisomers (**4**+**4'**) and preferred conformation of the mixture of *erythro* enantiomers **17** (one enantiomer is shown)

Taking into account these data, the preferred conformation for the enantiomeric propanols **15** and **16** should be as shown in Fig. 5.

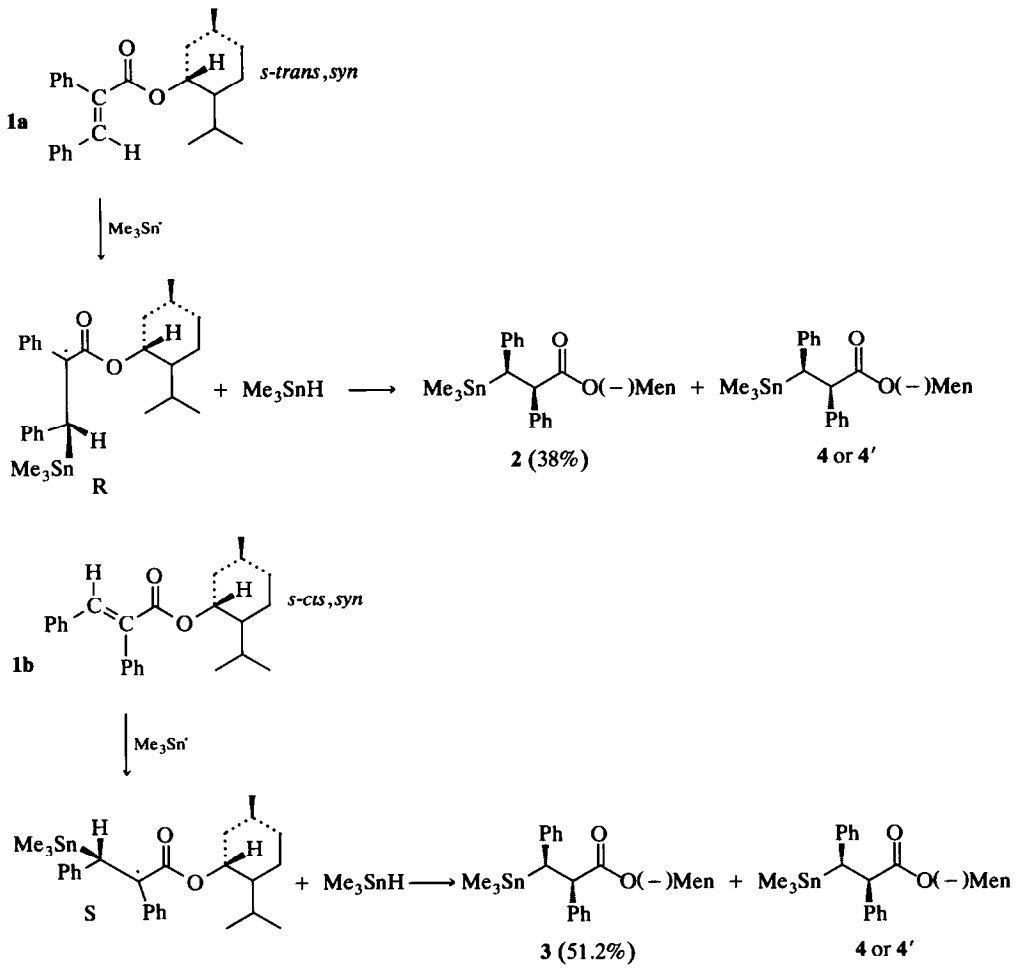
The only NMR parameter in which enantiomers **15** and **16** differ is the ^{119}Sn chemical shift: 6.67 ppm for compound **15** and 6.98 ppm for enantiomer **16** (Table 6).

In order to confirm the *threo* nature of enantiomers **15** and **16**, a mixture of (−)-menthyl esters (**4** + **4'**) was reduced with lithium aluminium hydride, according to Scheme 5.

The ^{1}H NMR spectrum of the mixture of enantiomer **17** (Table 5), shows that the ^{3}J(H–C–C–H) coupling constant has a value of 12.2 Hz, indicating that the dihedral angle between these protons is about 180°. The ^{13}C NMR spectrum of **17** (Table 6) shows that the ^{3}J(Sn–C–C–C=O) coupling constant has a value of 61.0 Hz which is compatible with a dihedral angle of approx. 180°. The ^{3}J(Sn–C–C–Ph) coupling constant is 11.4 Hz, indicating an angle of about 60°. These data are compatible with the erythro configuration shown in Scheme 7, thus confirming by contrast the *threo* stereochemistry of enantiomers **15** and **16**. The mixture of enantiomers **17** gives only one ^{119}Sn NMR resonance.

The stereochemical course of the hydrostannation of **1** can be explained well using the principles described by Houk [7,8]. Thus, the trimethylstannyl radical will add to the C-3 of alkene **1** at an angle close to 109°. This attack will take place on the preferred *syn* conformations of the (−)-menthyl (*E*)-2,3-diphenylpropenoate (**1**): *s-trans,syn* (Scheme 6, **1a**) and *s-cis,syn* (Scheme 6, **1b**). Then the hydride will be transferred from another molecule of organotin hydride preferably to the least hindered face of the carbon radical (Scheme 6).

The high diastereoselectivity observed (ratio of *threo/erythro* stereoisomers 8:3) is almost the same as that observed for the addition of trimethyltin hydride to



Scheme 6. Stereochemistry of hydrostannation of the *s-trans,syn* and *s-cis,syn* conformations of (−)-menthyl (*E*)-2,3-diphenylpropenoate (**1a** and **1b**) with trimethyltin hydride.

the methyl ester [1c]. This suggests that in these additions, the ester group might mask one face of the unsaturation, and this masking is independent of the size of the ester group whether or not it is chiral. As for the rather low asymmetric induction observed, as shown by the ratios between stereoisomers **3**/**2** (1.35) and **4**/**4'** (1.5), this might be due to differences in the population of the isomers in the transition state. Thus, Houk [8] has found that for methyl acrylates the *s-cis,syn* conformers are more stable than the *s-trans,syn* conformers, and this might also be true for the *s-cis* and *s-trans,syn* (−)-menthyl 2,3-diphenylpropenoates as suggested by our results.

Experimental

^{1}H, ^{13}C and ^{119}Sn NMR spectra were determined with a Bruker AM300 instrument at Dortmund University (Germany). Infrared spectra were recorded

with a Perkin–Elmer 599B spectrophotometer. The melting points were determined on a Kofler hot stage and are uncorrected. Microanalyses were performed at Dortmund University. All the solvents and reagents used were analytical reagent grade. Trimethyltin hydride was obtained by reduction of trimethyltin chloride with lithium aluminium hydride [9].

Synthesis of (−)-menthyl (E)-2,3-diphenylpropenoate (1)

We followed the method described by Gastaminza [10] for bulky esters. In a round-bottom flask, provided with a reflux condenser with a nitrogen seal, were placed 14.35 g (0.0918 mol) of (−)-menthol, 1.59 g (0.0656 at.g.) of Mg turnings, and 50 ml of toluene. To this mixture, a solution of 2,3-diphenylpropenoyl chloride, prepared from 14.7 g (0.0656 mol) of the acid and 23.4 g (0.197 mol) of thionyl chloride [11] in toluene (26 ml) was added dropwise. The reaction mixture was left overnight with vigorous stirring and then under reflux for 2 h. After cooling, the Mg was decanted and the solvent was removed under reduced pressure. The residue was dissolved in ether and washed with water, then with an aqueous sodium hydrogen carbonate solution, and again with water. After drying over sodium sulphate, the solvent was distilled off under reduced pressure. Recrystallization of the residue in ethanol/water, yielded 19.2 g of **1** (0.053 mol, 80.7%), m.p. 78–79°C (Lit. [12] 81–82°C).

Reaction of (−)-menthyl (E)-2,3-diphenylpropenoate (1) with trimethyltin hydride: synthesis of (−)-menthyl 2,3-diphenyl-3-(trimethylstannyl)propanoates (2, 3, 4 and 4′)

Compound **1** (10 g, 0.0276 mol) was treated for 4 h with trimethyltin hydride (6.823 g, 0.0414 mol) under nitrogen at 65°C and with azobisisobutyronitrile (AIBN) as a catalyst (this optimal time of reaction and the use of an adequate excess of organotin hydride were indicated in earlier experiments involving monitoring of the reaction by taking samples at intervals and observing the disappearance of the Sn–H absorption by IR, and by checking at the end of the reaction that the ^{1}H NMR spectrum of the reaction mixture no longer showed the presence of unchanged olefin). Under these conditions the ^{1}H NMR spectrum showed a quantitative yield (based on starting olefin) of a mixture of diastereoisomeric adducts **2** (38%), **3** (51.2%), **4** (6.5%) and **4′** (4.3%). The relative amount of each diastereoisomer in the mixture was 38% (**2**), 51.2% (**3**), 6.5% (**4**), and 4.3% (**4′**), as shown by the integration of the ^{119}Sn NMR spectrum.

Column chromatography on silica gel 60 of the crude mixture, yielded 11.8 g of a mixture of compounds **2** and **3**, eluted with pentane, pentane/carbon tetrachloride (3 : 1 and 1 : 1) and carbon tetrachloride, and 1.48 g of a mixture of compounds **4** and **4′** in the fraction eluted with carbon tetrachloride/benzene (3 : 1 and 1 : 1).

Fractional recrystallization (ethanol) of the mixture eluted with the less polar solvents, yielded succesively 4.0 g (0.0076 mol) of **2**, m.p. 140–141°C; then 2.75 g (0.0052 mol) of a mixture of **2** (25%) and **3** (75%), and finally diastereomer **3**, 5.03 g (0.0095 mol), m.p. 105–107°C. The mixture of isomers **4** and **4′** obtained from the chromatography could not be separated by fractional recrystallization. However, mixtures obtained from the recrystallizations enriched in both **4** and **4′**, were used for structural analysis and for the study of chemical properties.

Table 7

Some physical properties, IR data, and elemental analyses of the new compounds obtained

No	IR [a] ν(C=O)	Melting point (°C) [b]	$[\alpha]_D$ [c]	Elemental analyses: found (calc.) (%)	
				C	H
2	1716	140–141	−62.7 (*c*, 0.71)	63.45 (63.77)	7.59 (7.65)
3	1718	105–107	−5.91 (*c*, 0.83)	63.70 (63.77)	7.72 (7.65)
5	1704	120–121	−95.34 (*c*, 0.41)	59.23 (59.20)	6.90 (6.81)
6	1653	126–128	+34.87 (*c*, 0.59)	59.19 (59.20)	6.83 (6.81)
7	1687	105–106	−83.33 (*c*, 0.25)	54.83 (54.75)	6.25 (6.30)
8	1639	93–94	−20.57 (*c*, 0.29)	54.85 (54.75)	6.38 (6.30)
9	1718	103–104	−41.92 (*c*, 0.63)	67.58 (67.71)	7.12 (7.05)
10	1698	152–153	−107.54 (*c*, 0.69)	67.79 (67.71)	6.98 (7.05)
11	1718	– [f]	−27.51 (*c*, 0.39)	67.83 (67 71)	7.14 (7.05)
12	1698	197–198 [d]	+52.83 (*c*, 0.75)	67.70 (67.71)	7.08 (7.05)
15	3380 [e]	73–74	+41.22 (*c*, 0.74)	57.80 (57.63)	6.36 (6.45)
16	3380 [e]	73–74	−39 74 (*c*, 0.15)	57.69 (57.63)	6.29 (6.45)

[a] IR spectra as KBr pressed disc; ν in cm^{-1}. [b] Recrystallized from ethanol except when otherwise stated. [c] In benzene, at 25°C, except when otherwise stated. [d] From CCl_4. [e] OH stretching vibration. [f] Liquid, refractive index 1.5328 at 20°C.

^1H, ^{13}C and ^{119}Sn NMR data of diastereoisomers **2**, **3**, **4** and **4'** are included in Tables 1 and 2; other physical characteristics as well as elemental analyses (C,H) are given in Table 7.

Chloro / alkyl exchange reactions: exchange between (−)menthyl (2R,3R)-2,3-diphenyl-3-(trimethylstannyl)propanoate (2) and trimethyltin chloride; synthesis of (−)menthyl (2R,3R)-2,3-diphenyl-3-(chlorodimethylstannyl)propanoate (5)

Adduct **2** (1.60 g, 0.00303 mol) was added to trimethyltin chloride (0.73 g, 0.00367 mol) under nitrogen. In order to obtain a homogenous mixture (both compounds are solid), the mixture was heated to 50°C with stirring, and then left at room temperature for 40 h. The ^1H NMR spectrum showed a complete reaction. The excess of trimethyltin chloride as well as the tetramethyltin formed were distilled off under reduced pressure. The solid residue was recrystallized from ethanol; m.p. 120–121°C (1.53 g, 0.00279 mol, 92%).

Under the same conditions, adduct **3** reacted with trimethyltin chloride to give (−)menthyl (2*S*,3*S*)-2,3-diphenyl-3-(chlorodimethylstannyl)propanoate (**6**) with 91% yield; m.p. 126–128°C (ethanol).

Bromodestannylation reactions: reaction of (−)menthyl (2R,3R)-2,3-diphenyl-3-(trimethylstannyl)propanoate (2) with bromine; synthesis of (−)menthyl (2R,3R)- and (2R,3S)-2,3-diphenyl-3-bromopropanoates (9 and 10)

To a solution of **2** (3.20 g, 0.00607 mol) in carbon tetrachloride (15 ml) was added dropwise, a solution of bromine in carbon tetrachloride (15.5 ml of a 0.8 *M* solution, 0.0124 mol), with stirring, in the dark. After 4 h, the ^1H NMR spectrum showed a quantitative yield of a mixture of (−)menthyl (2*R*,3*R*)- (**9**) and (2*R*,3*S*)-2,3-diphenyl-3-bromopropanoates (**10**) in a ratio of **9**/**10** of 1.86. The solvent was distilled off under reduced pressure. Fractional recrystallization of the solid

residue, from ethanol, gave 1.26 g (0.0028 mol) of **9** (m.p. 103°C) and 0.71 g (0.0016 mol) of **10** (m.p. 152–153°C).

The same compounds in the same ratio were obtained from the reaction between (−)menthyl (2*R*,2*R*)-2,3-diphenyl-3-(chlorodimethylstannyl)propanoate (**5**) and (−)menthyl (2*R*,3*R*)-2,3-diphenyl-3-(bromodimethylstannyl)propanoate (**7**) with bromine in a ratio of organotin compound/bromine of 1:1.

Under the same experimental conditions, **3**, in a ratio of organotin/bromine of 1:2, and **6** or **8** in a ratio of organotin/bromine of 1:1, gave a quantitative yield of a mixture of **11** (67%) and **12** (33%). Whereas **12** was obtained through fractional recrystallization from carbon tetrachloride (m.p. 197–198°C), **11** could not be recrystallized, yielding an oily product n_D 1.5328 (69% of pure compound). The spectroscopic characteristics of compounds **9–12**, as well as elemental analyses and other physical characteristics are given in Tables 3, 4 and 7.

*Reduction of the β-bromoesters: reaction of (−)menthyl (2*R*,3*R*)-2,3-diphenyl-3-bromopropanoate (**9**) with lithium aluminum hydride; synthesis of* R(−)*-2,3-diphenylpropan-1-ol (**13**).*

To a suspension of 0.164 g (0.0043 mol) of lithium aluminium hydride in anhydrous ether (5 ml) was added slowly, a suspension of **9** (0.64 g, 0.00144 mol) in 30 ml of ether, and the mixture was heated under reflux for 6 h. Then, the mixture was decomposed with a solution of hydrochloric acid (20%, 0.6 ml), the organic layer was dried with magnesium sulphate and the solvent distilled off under reduced pressure. Elimination of the (−)-menthol with the aid of a cool finger, gave 0.73 g (80% yield) of alcohol **13**, $[\alpha]_D^{20}$ −82.6° in ether (*c*, 1.45).

Under the same experimental conditions, the bromoester **10** gave the same alcohol (78% yield, $[\alpha]_D^{20}$ −84.86° in ether (*c*, 2.3).

The reduction of bromoesters **11** and **12** gave alcohol **14** in yields of approx. 80%, $[\alpha]_D^{20}$ +81.5° in ether (*c*, 1.45); Lit. [6] +107.6° in the same solvent (*c*, 4.18).

Reduction of adducts 2, 3, 4 and 4'

The same procedure was used in all the reactions between β-trimethylstannylpropanoates and lithium aluminium hydride. One experiment is described in detail to illustrate the method.

*Reaction of (−)menthyl (2*R*,3*R*)-2,3-diphenyl-3-(trimethylstannyl)propanoate (**2**) with lithium aluminium hydride; synthesis of (2*R*,3*R*)-2,3-diphenyl-3-(trimethylstannyl)propan-1-ol (**15**).* To a suspension of lithium aluminium hydride (0.305 g, 0.00803 mol) in 20 ml of anhydrous ether was added with stirring a solution of **2** (4.24 g, 0.00803 mol) in 28 ml of ether. The mixture was heated under reflux for 5 h under a nitrogen atmosphere. After cooling, the mixture was decomposed by the addition of a saturated solution of ammonium chloride. The organic layer was dried with calcium oxide and the solvent was distilled off under reduced pressure. The (−)-menthol generated in the reaction was eliminated with the aid of a cool finger (under reduced pressure). Recrystallization of the solid residue from petroleum ether (30–60), gave 2.26 g (0.006 mol, 75%) of **15**, m.p. 73–74°C, $[\alpha]^{20}$ +41.22° in benzene (*c*, 0.74). The spectroscopic characteristics of compounds **15** and **16**, as well as elemental analyses and the other physical properties are given in Tables 5, 6, and 7.

Acknowledgments

This work was carried out with the financial support of CONICET (Argentina). A fellowship from the Alexander von Humboldt Foundation (Germany) to J.C.P. is gratefully acknowledged.

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