Journal of Organometallic Chemistry 935 (2021) 121680

Contents lists available at ScienceDirect

Journal of Organometallic Chemistry

journal homepage: www.elsevier.com/locate/jorganchem

Synthesis of new mixed (-)-menthylalkyltin dihydrides. stereoselective reduction of chiral and prochiral ketones

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ARTICLE INFO

Article history:
Received 9 November 2020
Revised 1 January 2021
Accepted 2 January 2021
Available online 5 January 2021

Key words:
(-)-menthylalkyltin dihydrides
Use in stereoselective reductions
Reduction of (-)-menthone
Reduction of acetophenone, Reduction of 2-acetylnaphthalene

ABSTRACT

This paper reports de synthesis of a series of (-)-menthylalkyltin dihydrides, (-)-MenRSnH$_2$ (R = Me, n-Bu, i-Pr, t-Bu, Neophyl), starting from (-)-menthyltrimethyltin. The new (-)-menthylalkyltin dihydrides **12**–**16** were used in a study on the stereoselective reduction of chiral (-)-menthone under different reaction conditions. Also the results obtained in the reductions of prochiral acetophenone (**27**) and 2-acetylnaphthalene (**28**), with (-)-menthylmethyl- (**12**) and (-)-menthyl*i*-propyltin (**14**) dihydrides are informed. Some physical properties as well as full ^{1}H-, ^{13}C-, and ^{119}Sn NMR data of the new organotin compounds are informed.

1. Introduction

Among the organometallic compounds of Group 14 elements, the organosilicon and organotin derivatives are the more used because of the wide range of chemical reactions they can undergo. In addition, organotin and organosilicon compounds have lower costs and toxicities compared with those of the corresponding derivatives of germanium and lead respectively. Nowadays, the enantioselective reduction of ketones is one of the more exciting fields in development. Thus, the hydrosilylation of ketones has been achieved with remarkable high enantioselectivities carrying out the reactions with organosilanes (Me_2SiHCl, Ph_2SiH_2, $PhSiH_3$, and others) in the presence of transition metals like Fe [1], and Rh [2] containing chiral organic ligands.

Organotin hydrides have found many uses in organic synthesis not only as reducing reagents [3], but also as intermediates in the generation of carbon-carbon bonds [4], and in the synthesis of macrocycles *via* cyclohydrostannation [5]. Since one of the seminal papers on the reduction of carbonyl compounds with mono-, di-, and triorganotin hydrides was published in 1961 [6], mainly the triorganotin hydrides (R_3SnH) have been used routinely for the selective free radical reduction of alkyl halides and many other functional groups [3,4]. At present triphenyl- and tri-*n*-butyltin hydrides are commercially available. Triorganotin hydrides containing mixed alkyl and (-)-menthyl organic ligands have been reported [7].

On the other hand, there are fewer reports on the uses of diorganotin dihydrides (R_2SnH_2), mostly restricted to the use of Ph_2SnH_2 and n-Bu_2SnH_2 as reagents for the reduction of carbonyl compounds. We have not found reports on the synthesis of diorganotin dihydrides containing mixed alkyl and (-)-menthyl ligands.

In this paper we wish to report the synthesis of mixed diorganotin dihydrides containing a bulky chiral (-)-menthyl substituent and alkyl groups of increasing steric volumes. We also report the results obtained in the reductions of chiral and prochiral ketones with the new (-)-menthylalkyltin dihydrides.

2. Results and discussion

The synthesis of the new organotins was carried out taking into account the reported sequence for the easy of brominolysis of carbon-tin bonds in tetraalkyltins [8]:

$$Ph > Me > Et > Pr > n-Bu > sec-Pr > tert-Bu$$

The new diorganotin dihydrides were obtained according to Scheme 1. The starting organotin compound containing the optically pure (-)-menthyl ligand was the known (-)-menthyltrimethyltin (**1**), obtained by stereospecific alkylation of trimethyltin chloride with (-)-menthylmagnesium chloride. Brominolysis of compound **1** in methanol using 1 equiv of bromine affords the also known (-)-menthyldimethyltin bromide (**2**) [7]. On

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https://doi.org/10.1016/j.jorganchem.2021.121680
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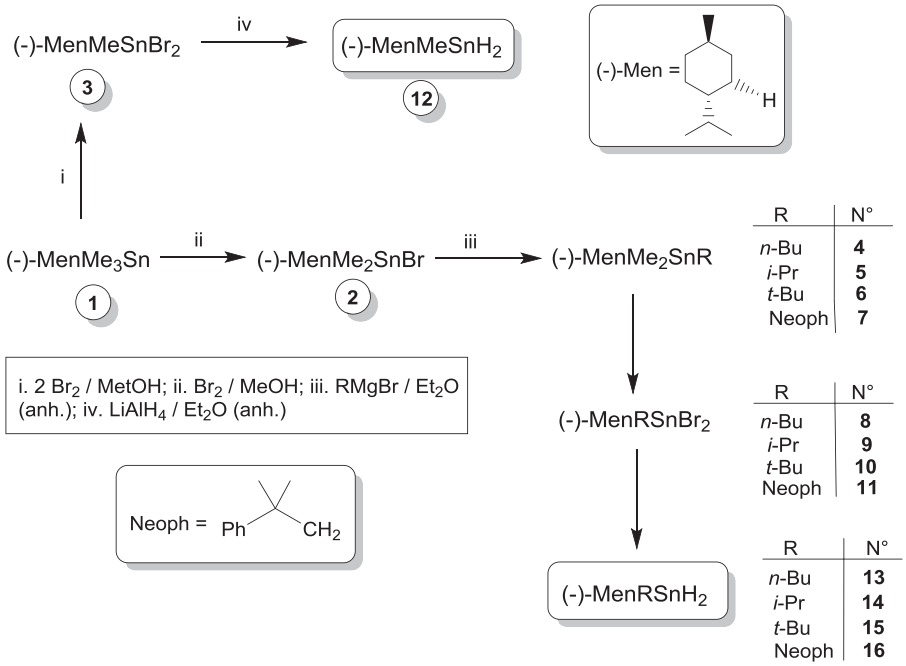


Scheme 1. Synthesis of diorganotin dihydrides **12**–**16**.

the other hand, the brominolysis of **1** with 2.5 equiv of bromine led to the corresponding (-)-menthylmethyltin dibromide (**3**) in 75% yield [9].

Then, the alkylation of (-)-menthyldimethyltin bromide **2** with *n*-butylmagnesium bromide, *i*-propyl magnesium bromide, *t*-butylmagnesium bromide, and neophylmagnesium bromide enabled the synthesis of the corresponding (-)-menthylalkyldimethyltin derivatives **4**–**7** in average yields of 82%. The reaction of tetraorganotin compounds **4, 5**, and **7** with 2.5 equiv of bromine in methanol led to dibromides **8, 9**, and **11** respectively. On the other hand, we were able to obtain *t*–butyl(-)menthyltin dibromide (**10**) in only a 30% yield; it is to note that the reported yield for this reaction is 58% [10].

Dibromides **3**, and **8**–**11** were reduced with $LiAlH_4$ in diethyl ether at room temperature (rt) in the dark, leading to the corresponding (-)-menthylalkyltin dihydrides **12**–**16** in average yields above 90%. In Scheme 1, besides dihydrides **12**–**16**, (-)-menthylalkyldimethyltin compounds **4** and **7**, and also (-)-menthylalkyltin dibromides **8, 9**, and **11** have not been reported previously. ^{119}Sn and ^{13}C NMR spectra of diorganotin diahydrides **12**–**16** are summarized in Table 1. It should be noted that in a previous communication we have reported the synthesis of some of the compounds included in Scheme 1 following less convenient synthetic routes and giving only some NMR selected values [11].

The ^{13}C NMR spectra of these compounds (Table 1), showed that all of them were obtained without epimerization at the menthyl carbon directly attached to tin [C(1)] atom. In all cases, the 10 carbon resonances of the menthyl group were clearly distinguishable. The DEPT experiments together with the magnitude of the $^{n}J(^{13}C,^{119}Sn)$ coupling constants $|^{1}J| > |^{3}J| > |^{2}J| > |^{4}J|$ enabled the easy assignment of the signals, and, therefore, to establish the structure of the new compounds. The use of the Karplus-type relationship existing between the value of the ^{3}J(C, Sn) coupling constants and the dihedral angle [12] allowed us to deduce the stereochemistry of the (-)-menthy1 ligands. Thus, the ^{3}J(C,Sn) values in the range 60–73 Hz for carbons C-3 and C-5 of the (-)-menthyl group in all the compounds included in Table 1, indicate dihedral angles of *ca.* 180° between these carbons and the tin moiety attached to C-1, *i.e.*, *anti* positions with respect to the dihydroalkylstannyl group. On the other hand, the values in the range 20–23 Hz found for the ^{3}J(C,Sn) coupling constants of C-8 suggest a dihedral angle of around 60° with respect to the organostannyl substituent.

From the previous discussion it is possible to conclude that in these compounds the organotin moiety occupies an equatorial position in the cyclohexane ring of the (-)-menthyl group. These results are in agreement with those obtained by Schumann et al. [10].

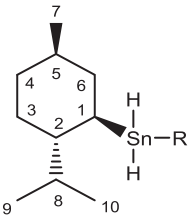
The ^{13}C NMR spectrum of compound **14** shows more than one resonance for carbons C-1 and C-1′. This multiplicity of signals could be connected with the steric crowding rather than with any effect of the chiral menthyl ligand, as shown in previous investigations of our group [13,14].

Dihydrides **12**–**16** are dense and, most of them, colorless oils. We attempted to determine the relative stabilities of the dihydrides. This was done by leaving the (-)-menthylalkyltin dihydrides **12**–**16** in the dark, at rt, and in the open air (Scheme 2), and measuring the times needed for the ν_{Sn-H} band to disappear in the FT-IR spectra. We found that whereas the decomposition at rt of dihydrides **12** and **13** takes 14 h, dihydrides **14**–**16** were still active after five weeks.

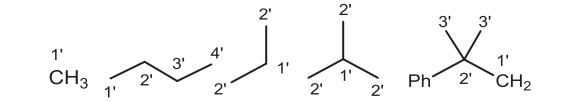
The reduction of ketones with diorganotin dihydrides proceeds according to Scheme 2. An interesting feature of the reduction with diorganotin dihydrides is that the two atoms of hydrogen are transferred to the substrate directly, *i.e.*, these reactions avoid the formation of intermediate alkoxides. Therefore, a hydrolysis step and acidic or basic conditions are not needed. This could be important in the reduction of certain types of sensitive compounds. It should be added that the reduction of the polydialkylstannanes (**P**) obtained in the reduction of the ketones led to the diorganotin dihydrides in average yields of 48%.

In order to test possible uses in asymmetric transformations, we considered it of interest to carry out a study on the reduction of (-)-menthone (**22**) with dihydrides **12**–**16**. The reduction of **22** should lead to a mixture of (-)-menthol (**24**), the thermodynamically more stable diastereomer (three equatorial substituents), and (+)-*neo*menthol (**25**), the less stable diastereomer (two equatorial substituents) (see scheme included in Table 2). Taking into account that the (-)-menthone (**22**) used in our studies consisted of a mix-

Table 1
^{13}C- and ^{119}Sn-NMR [a] characteristics, and optical rotations of (-)-menthylalkyltin dihydrides **12**–**16**.

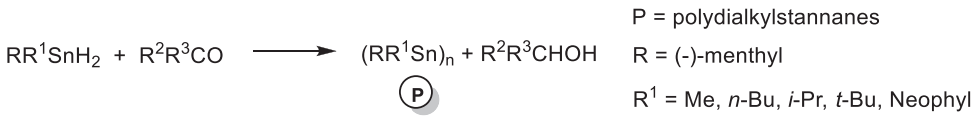


R	N°
Me	**12**
n-Bu	**13**
i-Pr	**14**
t-Bu	**15**
Neof	**16**



	Comp. **12** [c]	Comp. **13** [d]	Comp. **14** [e]	Comp. **15** [f]	Comp. **16** [g]
δ-C-1 (^1J)	31.29 (439.5)	31.89 (416.9)	32.72 (396.4)	33.90 (382.0)	31.69 (422.3)
δ-C-2 (^2J)	47.70 (17.2)	47.89 (17.1))	47.86 (17.2)	47.58 (16.7)	47.57 (17.9)
δ-C-3 ($^3J_{trans}$)	26.83 (66.1)	26.89 (65.2)	26.95 (62.7)	26.92 (60.1)	26.83 (64.8)
δ-C-4 (^4J)	35.79 (NO)	35.85 (7.3)	35.86 (8.0)	35.83 (NO)	35.80 (7.1)
δ-C-5 ($^3J_{trans}$)	35.55 (72.2)	35.68 (71.4)	35.75 (67.5)	35.80 (68.1)	35.58 (72.9)
δ-C-6 (^2J)	42.59 (19.3)	43.13 (18.3)	43.47 (18.8)	43.89 (18.5)	42.81 (17.9)
δ-C-7	22.70	22.72	22.71	22.75	22.70
δ-C-8 ($^3J_{gauche}$)	33.84 (23.2)	34.04 (21.0)	34.23 (21.4)	34.21 (20.8)	33.67 (23.0)
δ-C-9	22.12	22.17	22.17	22.15	22.12
δ-C-10	15.57	15.63	15.68	15.73	15.60
δ-C-1′ (^1J)	−15.51 (328.0)	7.27 (353.6)	13.78 (393.1)	25.78 (NO)	27.52 (353.2)
δ-C-2′ (^2J)	–	31.12 (23.7)	23.79 (14.4))	32.63 (NO)	37.56 (21.0)
δ-C-3′ (^3J)	–	27.35 (58.1)	–	–	32.18 (34.3) 32.49 (36.0)
^{119}Sn	−204	−191	−159	−144	−223
$[\alpha]_D^{20}$(c,[b]benzene)	−32.5° (0.0278)	−32.5° (0.0278)	−31.55° (0.0773)	−23.8° (0.0230)	−29.8° (0.0636)

[a] In C_6D_6; chemical shifts (δ) in ppm with respect to the central peak of C_6D_6 (^{13}C NMR) and Me_4Sn (^{119}Sn-NMR);coupling constants $^nJ(^{119}Sn,^{13}C)$ in Hz (in brackets); NO = not observed.[b] In gr/mL.
[c] Other signals: ^{119}Sn NMR: ^{1}J(Sn,H) 1346 Hz; ^{1}J(Sn,C) 456.2 Hz.
[d] Other signals ^{119}Sn NMR: ^{1}J(Sn,H) 1384 Hz; ^{1}J(Sn,C) 460,3 Hz; ^{13}C NMR: ^{1}J(Sn,C) 13,92 Hz.
[e] Other signals: ^{119}Sn NMR::^{1}J(Sn,H) 1326 Hz; ^{1}J(Sn,C) 463.4 Hz.
[f] Other signals: ^{119}Sn NMR: ^{1}J(Sn,H) 1391 Hz; ^{1}J(Sn,C) 466.0 Hz.
[g] Other signals: ^{119}Sn NMR: ^{1}J(Sn,H) 1384 Hz; ^{1}J(Sn,C) 460,3 Hz; ^{13}C NMR: 125,63; 126,06; 128,52; 150,90.



Scheme 2. Reduction of ketones with diorganotin dihydrides.

ture of **22** (95%) and (+)-*iso*menthone (**23**) (5%), the crude mixture of reduction products should also contain (-)-*neo*isomenthol (**26**) the product of the reduction of (+)-*iso*menthone (**23**). The mixture of **22** (95%) and (+)-*iso*menthone (**23**) (5%) used in the studies will be referred to as **Mix-22–23** from here onwards.

It has been reported that the reduction of pure (-)-menthone (**22**) with $LiAlH_4$ leads to a mixture of menthol, *neo*menthol and *neo*isomenthol in a ratio = 71 / 27 / 2 respectively [15]. A similar ratio for the mixture of alcohols **24, 25**, and **26** (72 / 27 / 1) was reported more recently [16].This ratio should reflect the asymmetric induction exerted by the two stereocenters already present in (-)-menthone (**22**), and it also suggests that there is some isomerization of **22** to **23** before reduction takes place. We carried out the reduction of **Mix-22–23** with $LiAlH_4$ in ether and found a ratio **24** (68) / **25** (27) / **26** (5) (Table 2, entry 1).

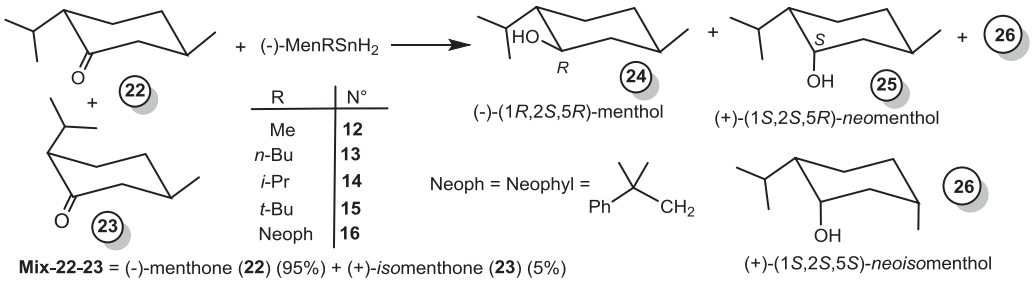
The reduction of (-)-menthone (**22**) with *n*-Bu_2SnH_2 was first reported in 1961 [4]. Unfortunately, the authors only reported the yield of the reaction (81.5%) but not the relationship among the diastereomers in the crude mixture of reaction. We reduced **Mix-22–23** with *n*-Bu_2SnH_2 in ether (Table 2, entry 2) and found a proportion **24** (65%), **25** (31%), and **26** (4%), *i.e.*, similar to that obtained in the reduction with $LiAlH_4$ (Table 2, entry 1).

Taking into account that we wanted to determine the approximate degree of asymmetric induction that can be achieved using the new dihydrides, we calculated the diastereomer ratios (*dr*) between **24** and **25**, *i.e.*, the alcohols resulting from the reduction of **22**. In those cases where the more stable diastereomer **24** (1*R*) was in higher proportion than **25** (1*S*) the diastereomer ratio is represented in the scheme of Table 2 as *dr* **I**. When **25** was in higher proportion than **24** the ratio is represented as *dr* **II**.

The reduction of **Mix-22–23** with (-)-menthylmethyltin dihydride (**12**) was done without solvent and also in solution in several solvents (Table 2, entries 3–8). Thus, the FT-IR spectrum of the reduction of **Mix-22–23** with dihydride **12**, carried out without solvent, after 3 h reaction at rt showed that the ν_{Sn-H} band corresponding to **12** had disappeared (Table 2, entry 3). The total yield of reduction products **24**–**26** was 78.8%. Some unreacted starting ketones **22** and **23** (16.7 and 4.4% respectively) were still present in the crude product. The diastereomeric ratio *dr***I** = 1.69, indicates that the more stable diastereomer **24** was obtained in lower proportion than in the case of the reduction with *n*-Bu_2SnH_2 (Table 2, entry 2). The same mixture after 6 h of reaction at −75 °C (Table 2, entry 4) gave the products of reduction **24**–**26** in quantitative yields. However, in this case the *dr***I** = 1.0 indicates that the diastereomer **24** and **25** were formed in approximately the same proportion.

Then, we studied the effect of using solvents of different polarity on the reaction between **Mix-22–23** and hydride **12**. Using toluene at rt (Table 2, entry 5) the FT-IR spectrum showed that the ν_{Sn-H} band corresponding to **12** disappeared after 14 h of reaction. The yield of reduction products was 73.8%, but unreacted starting ketones **22** and **23** were still present in 23% and 3.2% respectively. The *dr***I** = 1.89 indicates that also in this case the more stable diastereomer **24** predominates.

Table 2
Reduction of (-)-menthone with chiral diorganotin dihydrides **12**–**16**.[a].



Mix-22-23 = (-)-menthone (**22**) (95%) + (+)-*iso*menthone (**23**) (5%)

				Product distribution			Starting comp.[c] (%)	Yield (%)[d]			
N°	Hydride	Solv.[b]	Time (h)	**24** (%)	**25** (%)	**26** (%)		**24**+**25** + **26**	dr **I** [e]	dr **II** [f]	de [g] (%)
1	$LiAlH_4$	Et_2O	0.5	68	27	5	–	100	2.51	–	41
2	Bu_2SnH_2	Et_2O	6	65	31	4	–	100	2.09	–	34
3	**12**	–	3	47.4	27.9	3.5	**22** (16.7) **23** (4.4)	78.8	1.69	–	19.5
4	**12** (−75 °C)	–	6	48.7	48.5	2.8	–	100	1.00	–	0.2
5	**12**	Toluene	14	46.2	24.4	3.2	**22** (23.0) **23** (3.2)	73.8	1.89	–	21.8
6	**12**	Et_2O	14	50.7	22.3	3.3	**22** (20.8) **23** (2.8)	76.3	2.27	–	28.4
7	**12**	THF	14	46.9	20.3	2.7	**22** (27.6) **23** (2.4)	69.9	2.31	–	26.6
8	**12**	MeOH	3	59.5	33.7	4.6	**22** (1.5) **23** (0.7)	97.8	1.76	–	25.8
9	**13**	–	24	28.5	68.5	3.0	–	100	–	2.40	40
10	**13**	Et_2O	14	41.4	54.4	4.2	–	100	–	1.31	13
11	**13**	MeOH	12	36.4	57.4	4.2	**22** (1.9)	98	–	1.57	21
12	**14**	–	12	26.6	68.3	5.1	–	100	–	2.56	41.7
13	**14**	Et_2O	24	32.9	62.1	5.0	–	100	–	1.88	29.2
14	**14**	MeOH	12	32.0	63.7	4.4	–	100	–	1.99	31.7
15	**15**	–	14	38.4	58.0	3,6	–	100	–	1.51	19.6
16	**15**	Et_2O	14	59.2	33.4	7,6	–	92,6	1.77	–	25.8
17	**15**	MeOH	3	66.7	29.8	3,5	–	100	2.23	–	36.9
18	**16**	–	21	36.9	59.0	4,1	–	100	–	1.59	22.1
19	**16**	Et_2O	70	26.2	59.1	4.9	**22** (9.7) **23** (0.1)	90,2	–	2.25	32.9
20	**16**	MeOH	14	21.8	27.5	3.4	**22** (45.6) **23** (1.7)	52,7		1.26	5.7

[a] Yields from GS-MS analysis. Retention times (RT) of **Mix-22–23**, 6.505 min (**22**), 6.791 min (**23**); RT of alcohols, 8208 min (**24**); 7.798 min (**25**); 8.109 min (**26**); the results included in the Table are the average of five reactions; reactions at rt except when otherwise stated.
[b] Dry solvents; Tol = toluene; THF = tetrahydrofuran.
[c] Starting unreacted compounds (%).
[d] Total yields on reduction products (%), **24** + **25** + **26**.
[e] Diastereomeric ratio, dr ***I*** = [**24**] / [**25**].
[f] dr **II** = [**25**] / [**24**].
[g] de = diastereomeric excess = [**24**]% – [**25**]% (N° 3–8 and 16–17) and [**25**]% – [**24**]% (N° 9–15 and 18–20).

When the reductions were carried out in ether and THF, the $\nu_{Sn\text{-}H}$ band in the IR spectrum corresponding to **12** disappeared after 14 h reaction (Table 2, entries 6 and 7 respectively). The yields of the reduction products 76.3% (ether) and 69.9% (THF) were similar to those obtained in the reaction in toluene. Also, the observed *dr**I*** = 2.27 and 2.31 indicate that in these cases the more stable alcohol **24** was formed in higher proportion than in the case of the reduction of **Mix-22–23** with *n*-Bu_2SnH_2.

On the other hand, the reaction of **Mix-22–23** with dihydride **12** in methanol (Table 2, entry 8) led to the reduction products after 3 h reaction, remaining a 2.2% of unreacted ketones **22** and **23**. The observed *dr**I*** = 1.76 indicates that alcohol **24** is formed in lower proportion than in the case of the less polar solvents.

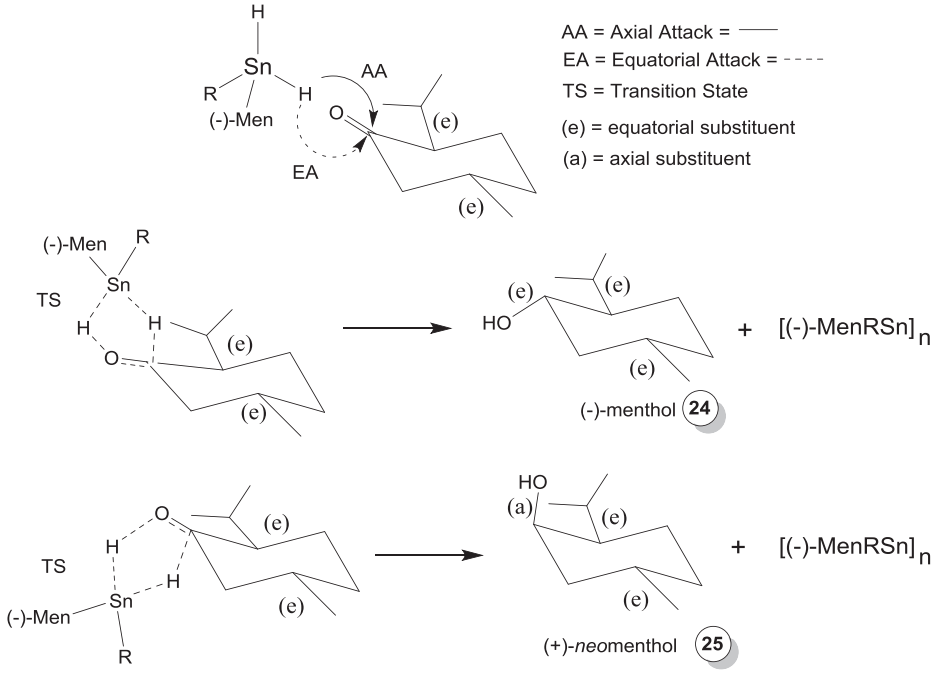
Taking into account the previous results, the study of the reductions with hydrides **13**–**16** was performed under three reaction conditions: without solvent, in ether, and in methanol.

A quick analysis of the results included in Table 2 indicates that, in the case of the reductions of **Mix-22–23** with dihydrides **13**–**16** carried out without solvent (Table 2, entries 9, 12, 15, 18), the yields on reduction products were quantitative. The mixtures obtained contained in all cases the less stable diastereomer **25** (1*S*, see Scheme 3) in higher proportion. It is indeed remarkable the dramatic change that occurred in the diastereomers relationship when dihydrides **13**–**16** were used instead of dihydride **12** for the reduction of (-)-menthone. These results suggest that the increasing steric volume of the alkyl substituent R at the tin atom favors the formation of the less thermodynamically stable product **25**.

In the case of the reductions of **Mix-22–23** using hydrides **13, 14**, and **16**, in ether (Table 2, entries 10, 13, and 19) the mixtures (**24**+**25**+**26**) obtained contained the diastereomer **25** as the main component in quantitative (with dihydrides **13** and **14**) and very high yields (90.2% using dihydride **16**). However, when we carried out the reaction of **Mix-22–23** with dihydride **15** in ether the resulting mixture of reduction products was obtained in high yield (92.6%), containing the thermodynamic diastereomer **24** in higher proportion.

The reactions performed in methanol followed a similar pattern. Thus the reductions of **Mix-22–23** with dihydrides **13, 14**, and **16**, led in all cases to the formation of alcohol **25** as the main component of the mixtures (**24**+**25**+**26**) (Table 2, entries 11, 14 and 16). However, whereas the reactions using dihydrides **13** and **14** took place with very high yields, the reduction of **Mix-22–23** with dihydride **16** afforded just a 52.7% of the mixture (**24**+**25**+**26**) and a high proportion of starting ketones (47.3%). On the other hand, the reduction in methanol with dihydride **15** led to the mixture (**24**+**25**+**26**) in quantitative yield containing, as before with ether, the diastereomer **24** as the main component.

In summary, the results included in Table 2 indicate that whereas the reactions of **Mix-22–23** carried out with dihydrides **13**–**16** in absence of solvent (entries 9, 12, 15, 18) gave quantitatively mixtures of reduction products (**24**+**25**+**26**), under the same



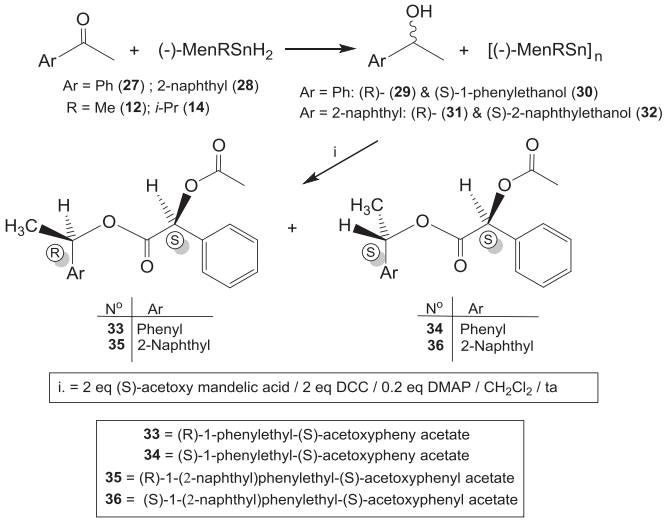
Scheme 3. Stereoselective reduction of ketones with diorganotin dihydrides.

reaction conditions the reduction with (-)-MenMeSnH$_2$ (**12**) (entry 3) led to the mixture (**24**+**25**+**26**) in 78.6% yield plus starting material. These results suggest that the increasing steric volume of the substituent favors the formation of the less thermodynamically stable product **25**.

Our results are in agreement with many studies on the addition of organometallic compounds and hydride-reducing agents to cyclohexanones that show that whereas bulky reagents tend to approach from the equatorial direction, steric approach control (see Scheme 3), smaller nucleophiles usually approach from the axial direction [17,18]. Thus, as shown in Table 2 in the reductions carried out without solvent, only using the (-)-menthylmethyltin dihydride (**12**) (entry 3) could be achieved the preferential axial attack of the hydrogen that leads to the more thermodynamically stable alcohol **24** (Scheme 3). In compound **24**, carbon C-1 has *R* configuration. On the other hand, dihydrides **13**–**16** achieve equatorial hydrogen transfer leading preferentially to alcohol **25** in which the C-1 has the *S* configuration (Scheme 3). It might be possible that the reductions with diorganotin dihydrides could take place *via* a concerted mechanism of the type depicted in Scheme 3.

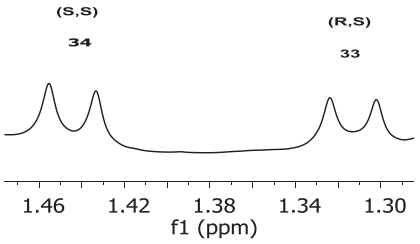
With the aim of determining the degree of asymmetric induction that can be achieved with hydrides **12** and **14**, we also studied the reduction of prochiral acetophenone (**27**) and 2-acetylnaphthalene (**28**) with both hydrides (Scheme 4). In order to analyze the composition of the resulting mixtures of alcohols, the crude products were converted into the corresponding mandelates. It has been previously reported that the ^{1}H NMR spectrum of the mixtures of diastereomeric mandelates derived from (*R*)-(+)-O-acetylmandelic acid displayed two doublets around 1.50 ppm, and that whereas the doublet at higher field (1.41 ppm) belonged to the (*R,S*) diastereomer, the doublet at lower field (1.54 ppm) corresponded to the (*R,R*) diastereomer [19,20].

In our case, *i.e.*, the esters derived from (*S*)-(-)-O-acetylmandelic acid, the ^{1}H NMR of the mixture (**33** + **34**), Fig. 1-i also showed two doublets. We ascribed by analogy, the doublet at lower field (1.46 ppm) to the configuration (*S,S*) of ester **34**, and the doublet at 1.33 ppm to configuration (*S,R*) of compound **33**. Similarly, in the case of the mixture of 1-(*β*-naphthyl)ethylacetoxyphenyl

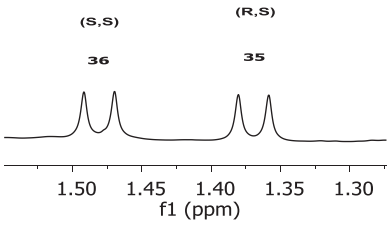


Scheme 4. Reduction of prochiral ketones with chiral dihydrides **12** and **14**.

acetates, Fig. 1-i, the doublet at lower field (1.48 ppm) was attributed to diastereomer **36** with configuration (*S,S*), and the doublet at higher field (1.37 ppm) to diastereomer **35** with configuration (*S,R*). The GC–MS study showed that the mixture (**33** + **34**) gave a chromatogram with two peaks with retention times (rt) of 20.4 and 20.6 min, and the mixture (**35** + **36**) gave also two peaks with rt = 24.8 and 25.1 min. From these results we could correlate the retentions times with the chemical shifts of the doublets observed in the ^{1}H NMR spectra. Thus, in the case of the esters derived from the reduction of acetophenone (**27**) the peaks with rt = 20.4 and 20.6 min could be correlated with the doublet at 1.46 ppm, *i.e.*, corresponding to the diastereomer (*S,S*), and the doublet at 1.33 ppm corresponding to diastereomer (*S,R*) respectively. Similarly, in the case of 2-acetylnaphthalene (**28**) the peaks with rt = 24.8 and 25.1 min could be correlated with the doublets at 1.48 ppm corresponding to configuration (*S,S*), and 1.37 ppm to configuration (*S,R*) respectively (Fig. 1-iii).



(i) Doublets corresponding to phenyl-1-ethyl racemic mandelates **33** + **34** (Table 5, entry 1).

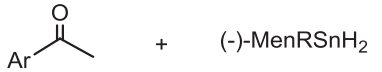


(ii) Doublets corresponding to the mixture of 2-naphthyl-1-ethyl mandelates **35** + **36** (Table 5, entry 10).

iii) Chromatogram of the mixture of 2-naphthyl-1-ethyl mandelates **35** + **36** (Table 5, entry 10).

Fig. 1. Mixtures of racemic mandelates: expansion of the 1.30–1.55 ppm region (^{1}H NMR), i) **33**–**34**. ii) **35**–**36**. iii) Chromatogram of the mixture **35** + **36**.

Table 3
Reduction of acetophenone (**21**) and 2-acetylnaphthalene (**22**) with dihydrides **12** and **14**.



Ar = Ph (**27**); 2-Naphthyl (**28**) R = Me (**12**); *i*-Pr (**14**)

N°	Ar	Hydride	(S,S) (%)	(R,S) (%)	ee (%)
1	pH	$LiAlH_4$	50	50	0
2	pH[a]	**12**	51	49	2
3	pH[b]	**14**	53	47	6
4	Nph	$LiAlH_4$	50	50	0
5	Nph[c]	**12**	53	47	6
6	Nph[d]	**14**	57	43	14

Nph = 2-Naphtyl. Retention times (rt):.
[a] rt = 20.4 min.
[b] rt = 20.6 min.
[c] rt = 24.8 min.
[d] rt = 25.1 min.

In summary, the crude mixture of racemic alcohols (**29** + **30**) and (**31** + **32**) was made to react with (*S*)-(-)-O-acetylmandelic acid. Then, the stereochemistry of the resulting mixtures of diastereomeric mandelates (**33** + **34**) and (**35** + **36**) was assessed by ^{1}H NMR analysis [19,20], and quantified by gc-mass spectra. The mixtures of products resulting from the reduction of ketones **27** and **28** with $LiAlH_4$ were studied following the previous protocol, and then used as reference in the studies of the reductions with diorganotin dihydrides **12** and **14**. The results obtained in the reduction of ketones **27** and **28** are summarized in Table 3.

As shown in Table 3, the reductions proceeded with some degree of stereoselectivity. The reductions of **27** and **28** with (-)-$MenMeSnH_2$ (**12**), led in both cases to mixtures in which some predominance of the (*S*)-enantiomer was observed. This is clearly seen in entries 2 (ee = 2) and 5 (ee = 6). When ketones **27** and **28** were reduced with (-)-Men *i*-$PrSnH_2$ (**14**), it was detected again that the (*S*)-enantiomer was formed in higher proportion, Table 3 entry 3 (ee = 6), and entry 6 (ee = 14).

These results demonstrate that the (-)-menthyl group attached to the tin atom do exert asymmetric induction, and that the steric bulk of the (-)-menthylalkyl dihydrides also affects the stereoselectivity of these reductions. It is to note, that also the bulk of the substituents of the ketones has effect on the stereoselectivity of the reductions. Thus, the reduction of ketone **28** with hydrides **12** and **14** led in both cases to higher ee of the (*S*) enantiomer than those obtained in the reduction of acetophenone (**27**).

In conclusion, we have obtained five new mixed (-)-menthylalkyltin dihydrides, (-)-$MenRSnH_2$ (*R* = Me, *i*-Pr, *n*-Bu, *t*-Bu, Neophyl), carried out the synthesis of five of their new precursors, and determined their structures by multinuclear NMR (^{119}Sn, ^{1}H, and ^{13}C) and other physical methods. The new chiral diorganotin dihydrides show potential as stereoselective reducing reagents as shown by the study of the reduction of a mixture of (-)-menthone (95%) and (-)-*iso*menthone (5%), and of the achiral acetophenone and 2-acetylnaphthalene. Also, whereas the reduction of (-)-menthone with $LiAlH_4$, *n*-Bu_2SnH_2, and (-)-$MenMeSnH_2$ (**12**) leads to the more stable (-)-menthol (**24**) (1*R*) in higher proportion, the use of hydrides **13**–**16** enables to obtain the less stable (+)-neomenthol **25** (1*S*) in higher proportion.

3. Experimental

3.1. General methods

All the solvents and reagents used were analytical reagent grade. Reactions were monitored by thin-layer chromatography on silica gel plates (60F-254) visualized under UV light using 5% phosphomolybdic acid in ethanol. Column chromatography was per-

formed over silica gel 60 (70–230 mesh) doped with 10% of potassium fluoride. ^{1}H-, ^{13}C-, and ^{119}Sn NMR spectra were recorded in $CDCl_3$, except those of the dihydrides which were run in benzene-d_6, on a Bruker Avance 300 Multinuclear instrument (300.1 MHz for ^{1}H, 75.5 MHz for ^{13}C and 111.9 MHz for ^{119}Sn) at 23 °C and calibrated by using signals from solvents referenced to Me_4Si (^{1}H, ^{13}C NMR) and with respect to Me_4Sn in the case of ^{119}Sn NMR spectra. Chemical shifts (δ) are reported in ppm and coupling constants (J) are in Hz. IR spectra were recorded on a Nicolet Nexus FT spectrophotometer instrument. Mass spectra (EI, 70 eV) were obtained using a HP-5890 CG/EM instrument equipped with a selective mass detector and a column INNOWAX, and the quantitative analysis of the mixtures of products obtained in the reductions was carried out with an Agilent CG-78,903 instrument equipped with a selective mass detector MS-5977A MSD and a column HP-5MS (30 m x 0.25 mm x 0.25 m). Specific rotations were measured with a Polar L-μP, IBZ Messtechnik instrument. Elemental analyses (C, H) were performed in Exeter Analytical instruments, model CE-440 at Universidad Nacional del Sur and at UMYMFOR (Universidad de Buenos Aires. Compounds **1**–**3, 5, 6**, and **10** were obtained following known procedures [7,9,10]. The (*S*)-(-)-mandelic acid and (-)-menthone were commercially available.

3.2. Synthesis of the new (-)-menthyldimethyl alkyltin compounds ***4*** *and* ***7***

All the reactions were carried out following the same procedure. One experiment is described in detail in order to illustrate the methods used.

3.2.1. Synthesis of (-)-menthyl-n-butyldimethyltin (*4*)

To a stirred solution of (-)-menthyldimethyltin bromide (**2**) **(**4.00 g, 10.9 mmol) in dry diethyl ether (30 mL) under nitrogen, and at 0 °C, was added dropwise a solution of *n*-butylmagnesium bromide (1.6 M, 10 mL, 16 mmol) in dry diethyl ether. The reaction mixture was further stirred for 12 h at rt. The progress of the reaction was monitored by TLC and GC–MS. The reaction was quenched by slow addition of water (6.6 mL) at 0 °C. The resulting mixture was left under stirring at rt for 1 h. The organic layer was separated, dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica gel 60). The (-)-Menthyl-*n*-butyldimethyltin (**4**) was eluted with hexane (3.20 g, 9.27 mmol, 85%) as a colorless liquid. $[\alpha]^{20}_{D}$ = −26.6° (c. 4.71, benzene). ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.01 (s, 6H, $^{2}J_{Sn,H}$ 47.3 Hz,); 0.74 (d, 3H, $^{3}J_{H,H}$ = 6.8 Hz); 0.77–1.15[*m*, 13H, *superimposed peaks from which clearly emerge three doublets*: 0.85 ($^{3}J_{H,H}$ = 6.6 Hz), 0.91 ($^{3}J_{H,H}$ = 7.2 Hz); 0.93 ($^{3}J_{H,H}$ = 6.8 Hz), 0.96 ($^{3}J_{H,H}$ = 6.8 Hz)]; 1.16–1.78 (m, 11H); 1.81–1.92 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = −11.49 (283.6); −11.56 (283.6); 10.13 (328.2); 13.91; 15.76; 22.25; 22.79; 26.74 (60.2); 27.46 (55.1); 29.36 (20.7); 31.98 (390.3); 33.54 (19.7); 35.44 (64.3); 35.79 (6.6); 41.13 (17.3); 46.81 (15.0). ^{119}Sn NMR ($CDCl_3$): δ = 7.7 ppm. . MS (EI, 70 eV): *m/z* (%) = 346 (1%, $[M]^+$); 331 (4%, $[M\text{-}CH_3]^+$); 289 (44%, $[M\text{-}(C_4H_{11})]^+$); 207 (43%, $[M\text{-}C_{10}H_{19}]^+$); 151(100%, $[Me_2SnH]^+$); 139 (6%, $[C_{10}H_{19}]^+$).Anal. Calc. for $C_{16}H_{34}Sn$: C, 55.68; H, 9.93. Found: C, 55.58; H, 9.89%.

3.2.2. Synthesis of (-)-menthylneophyldimethyltin (*7*)

Following the same procedure, the reaction between (-)-menthyldimethyltin bromide (**2**) **(**5.00 g, 13.6 mmol) and neophylmagnesium chloride (0.17 mL, 0.29 mmol, 2.00 M sol. in diethyl ether), gave compound **7** (2.40 g, 5.70 mmol, 41.9%) as a colorless oil. $[\alpha]^{20}_{D}$ −25.6° (c. 2.23, benzene). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.00 [s, 6H, ($^{2}J_{SnH}$ 46.7 Hz,)]; 0.91 [d, 3H ($^{3}J_{HH}$ 6.6 Hz)]; 0.98–1.27 (m, 9H, from which emerge two doublets at 1.03 ($^{3}J_{HH}$ 6.6 Hz) and 1.12 ($^{3}J_{HH}$ 6.6 Hz)]; 1.30–2.04 (m, 15H, from which emerge a singlet at 1.60 ppm); 7.30–7.41 (m, 1H). 7.43–7.52 (m, 2H); 7.53–7.62 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = −9.35 (286.3); −9.32 (286.3); 15.78; 22.24; 22.80; 26.71 (58.9); 30.10 (322.3); 32.16 (391.9); 33.12 (30.3); 33.20; 33.32 (32.2); 35.37; 35.71 (6.1); 38.33 (19.9); 40.88 (17.4); 46.60 (15.1); 128.20; 125.38; 125.57; 151.66 (21.5). ^{119}Sn NMR ($CDCl_3$): δ = −20.6 ppm. MS (EI, 70 eV): *m/z* (%) = 407 (3%, $[M\text{-}CH_3]^{+\cdot}$); 283 (100%, $[M\text{-}(C_{10}H_{19})]^+$); 139 (2%, $[C_{10}H_{19}]^+$). Anal. Calc. for $C_{22}H_{38}Sn$: C, 62.72; H, 9.09. Found: C, 62.68; H, 9.02%

3.3. Synthesis of (-)-menthylalkyltin dibromides ***8, 9****, and* ***11***

All the reactions were carried out following the same procedure. One experiment is described in detail in order to illustrate the methods used. The dibromides could not be purified neither by fractional distillation nor by column chromatography. So, these compounds were used without further purification. It is to mention that dibromide **3** has already been reported [9].

3.3.1. Synthesis of (-)-menthyl-n-butyltin dibromide (*8*)

To a solution of **4** (2.19 g, 6.35 mmol) in methanol (10 mL) under a nitrogen atmosphere and in the dark, was added dropwise and with vigorous stirring a solution of bromine (2.54 g, 15.9 mmol) in methanol (10 mL) at 0 °C. The reaction mixture was stirred for 12 h at room temperature. Then, the solvent was removed under reduced pressure leading to (-)-menthylnbutyltin dibromide (**8**) (3.02 g, 6.36 mmol, 99%) as an orange liquid. $[\alpha]^{20}_{D}$ −24.5 (c. 3.65, benzene). ^{1}H NMR ($CDCl_3$): δ = 0.85 (d, 3H, $^{3}J_{H,H}$ = 6.8 Hz); 0.89–1.18 (m, 11H, from the multiplet emerge three doublets at 0.92 ($^{3}J_{H,H}$ = 5.8 Hz), 0.95 ($^{3}J_{H,H}$ = 7.2 Hz), and ($^{3}J_{H,H}$ = 6.6 Hz); 1.20–1.56 (m, 5H); 1.59–2.00 (m, 7H); 2.08–2.24 (m, 1H).; 2.26–2.46 (m, 1H). ^{13}C NMR ($CDCl_3$): δ (in ppm) ($^{n}J_{Sn,C}$, in Hz) = 7.27 (353.6); 15.63; 22.17; 22.72; 26.89 (65.2); 27.35 (58.1); 31.12 (23.7); 31.89 (416.9); 34.04 (21.0); 35.85 (7.3); 35.68 (71.4); 43.13 (18.3); 47.89 (17.1). ^{119}Sn NMR ($CDCl_3$): δ = 96.23 ppm.

3.3.2. Synthesis of (-)-menthyl i-propyltin dibromide (*9*)

Following the same procedure, the reaction of (-)-menthyl-*i*-propyldimethyltin (**5**) (1.55 g, 3.68 mmol) with Br_2 (2.64 g (16.5 mmol) in methanol led to (-)-menthyl-*i*-propyl tin dibromide (**9**) (3.05 g, 6.62 mmol, 99%) as an orange liquid. $[\alpha]^{20}_{D}$ −25.7 (c. 2.03, benzene). ^{1}H NMR ($CDCl_3$): δ = 0.79 (d, 3H, $^{3}J_{H,H}$ = 6.9 Hz); 0.86 (d, 3H, $^{3}J_{H,H}$ = 6.1 Hz); 0.95 (d, 3H, $^{3}J_{H,H}$ = 6.6 Hz); 1.00–1.46 (m, superimposed peaks, 10H): two doublets arising at 1.37 ($J_{H,H}$ 2.5 Hz) and 1.40 ($J_{H,H}$ 2.5 Hz); 2.00–2.40 (m, 3H). ^{13}C NMR ($CDCl_3$): δ = 15.83; 20.46 (15.1); 20.48 (20.1); 21.95; 22.38 (7.2); 26.61 (100.2); 33.71 (371.9); 34.71 (12.6); 35.43 (92.2); 36.29 (34.2); 39.88 (37.3); 46.05 (16.4); 50.42 (361.2). ^{119}Sn NMR ($CDCl_3$): δ = 101.5 ppm.

3.3.3. Synthesis of (-)-menthylneophyltin dibromide (*11*)

The reaction of (-)-menthylneophyldimethyltin (**7**) (2.19 g, 6.61 mmol) with Br_2 (1.47 g, 9.20 mmol) in methanol led to (-)-menthylneophyltin dibromide (**11**) (2.03 g, 3.68 mmol, 6.62 mmol, 99%)) as an orange oil. $[\alpha]^{20}_{D}$ −22.5 (c. 1.61, benzene). ^{1}H NMR ($CDCl_3$): δ = 0.58–0.95 (m, superimposed peaks, 12H), three doublets emerging at 0.65 ($J_{H,H}$ 6.8 Hz), 0.75 ($J_{H,H}$ 6.6 Hz), and 0.83 ($J_{H,H}$ 6.6 Hz); 1.00–2.00 (m, superimposed peaks, 13H), two singlets emerging at 1.49 and 1.50 ppm; 2.25–2.65 (m, 2H); 7.12–7.23 (m, 1H); 7.25–7.34 (m, 2H); 7.35–7.44 (m, 2H). ^{13}C NMR ($CDCl_3$): δ = 15.91; 21.74; 22.33 (9.5); 26.63 (111.9): 32.25 (51.2); 32.51 (55.9); 34.47 (13.0); 34.73 (32.0); 35.11; 38.98 (16.7); 39.21 (31.4); 45.75 (23.3); 50.12 (322.9); 50.52 (429.8); 129.22; 125.16; 126.88; 149.81 (35.1). ^{119}Sn NMR ($CDCl_3$): δ = 49.9 ppm.

3.4. Synthesis of (-)-menthylalkyltin dihydrides **12**–**16**

All the reactions were carried out following the same procedure. One experiment is described in detail in order to illustrate the methods used. All the manipulations involving the preparation of the dihydrides were carried out under an argon atmosphere.

3.4.1. Synthesis of (-)-menthylmethyltin dihydride (**12**)

To a solution of $LiAlH_4$ (0.160 g, 4.16 mmol) in dry Et_2O (4 mL) at 0 °C, was added dropwise a solution of **3** (1.50 g, 3.57 mmol) in dry Et_2O (4 mL). Then, the solution was further stirred at rt for 5 h. After cooling, the mixture was decomposed by the addition of a saturated solution of ammonium chloride (15 mL). The organic layer was dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure. The (-)-Menthylmethyltin dihydride (**12**) (0.805 g, 82%) was obtained as a clear liquid. $[\alpha]^{20}_D$ –32.5° (c, 2.78, benzene). FT-IR (film): $\nu_{Sn\text{-}H}$ = 1832 cm^{-1}. ^1H NMR (C_6D_6): δ = 0.14 (t, 3H, $^3J_{HH}$ 2.7 Hz; $^2J_{SnH}$ 55.1 Hz); 0.73 (d, 3H, $^3J_{HH}$ 6.9 Hz); 0.78–1.00 [m, 7H; from the multiplet emerge two doublets at 0.84 ($^3J_{HH}$ = 6.1 Hz) and 0.89 ($^3J_{HH}$ 6.8 Hz)]; 1.00–1.48 (m, 4H); 1.50–1.75 (m,2H); 1.76–1.95 (m, 1H); 4.79 (br, 2H, $^1J_{SnH}$ =1677.3 Hz).). MS (EI, 70 eV): *m/z* (%) = 276(2%, $[M\text{-}2]^+$); 261(5%, $[M\text{-}(CH_3)]^+$); 231(35%,$[C_8H_{16}Sn]^+$), (22%, $[C_{10}H_{19}]^+$); 134 (60%, $[CH_2Sn]^+$), 119 (23%, $[Sn]^+$), 83(100%, $[C_6H_{11}]^+$). Anal. Calc. for $C_{11}H_{24}Sn$: C, 48.04; H, 8.79. Found: C, 48.46; H, 8.92%.

3.4.2. Synthesis of (-)-menthyl-n-butyltin dihydride (**13**)

Following the previous procedure, the reduction of **8** (1.73 g, 3.64 mmol) with $LiAlH_4$ (0.166 g, 4.37 mmol) in ether, led to (-)-menthyl-*n*-butyltin dihydride (**13**) (0.923 g, 2.91 mmol, 76%) as a colorless liquid. $[\alpha]^{20}_D$ –29.5° (c. 4.71, benzene). FT-IR (film): $\nu_{Sn\text{-}H}$ = 1818 cm^{-1}. ^1H NMR (C_6D_6): δ = 0.76 (d, 3H, $^3J_{HH}$ = 6.9 Hz); 0.79–1.06 [m, 13H, three doublets emerge at 0.85 (d, $^3J_{HH}$ = 6.4 Hz), 0.90 (d, $^3J_{HH}$ = 7.2 Hz), and 0.91 (d, $^3J_{HH}$ = 6.7 Hz)]; 1.08–1.41 (m, 5H); 1.44–1.80 (m, 6H); 1.84–2.00 (m, 1H); 4.92 (br, 2H, $^1J_{SnH}$ 1628.6 Hz). MS (EI, 70 eV): *m/z* (%) = 346 (1%, $[M]^+$); 331 (4%, $[M\text{-}CH_3]^+$); 289 (44%, $[M\text{-}(C_4H_{11})]^+$); 207 (43%, $[M\text{-}C_{10}H_{19}]^+$); 151(100%, $[Me_2SnH]^+$); 139 (6%, $[C_{10}H_{19}]^+$). Anal. Calc. for $C_{14}H_{30}Sn$: C, 53.03; H, 9.53. Found: C, 53.33; H, 9.60%.

3.4.3. Synthesis of (-)-menthyl-i-propyltin dihydride (**14**)

Following the previous procedure, the reaction of dibromide **9** (0.600 g, 1.30 mmol) with $LiAlH_4$ (0.059 g, 1.56 mmol) in ether gave (-)-menthyl-i-propyltin dihydride (**14**) (0.307 g, 1.01 mmol, 78%) as a clear liquid. $[\alpha]^{20}_D$ –31.5° (c. 7.73, benzene). FT-IR (film): $\nu_{Sn\text{-}H}$ = 1825 cm^{-1}. ^1H NMR (C_6D_6): δ = 0.51 (d, 3H, $^3J_{HH}$ = 6.5 Hz); 0.55–0.85 [m, 11H, two doublets emerge two doublets at 0.61 ($^3J_{HH}$ = 6.0 Hz), and 0.68 ($^3J_{HH}$ = 7.1 Hz)]; 0.86–1.60 [m, 13H one doublet emerge at 1.10 ($^3J_{HH}$ = 7.1 Hz)]; 1.61–1.81 (m, 1H); 4.78 [s, 1H, $^1J_{SnH}$ = 1585.3 Hz)]; 4.83 [s, 1H, $^1J_{SnH}$ = 1582.3 Hz)]. MS (EI, 70 eV): *m/z* (%) = 302(1%, $[M\text{-}2]^{+\cdot}$); 261 (17%, $[M\text{-}(C_3H_7)]^+$); 165 (15%, $[C_{10}H_{19}]^+$); 137(100%, $[C_{10}H_{17}]^+$); 119(48%, $[Sn]^+$). Anal. Calc. for: C, 51.52; H, 9.31. Found: C, 51.82; H, 9.27%.

3.4.4. Synthesis of (-)-menthyl-t-butyltin dihydride (**15**)

Following the previous procedure, the reaction between *t*–butyl(-)-menthyltin dibromide (**10**) (0.507 g, 1.07 mmol) and $LiAlH_4$ (0.049 g, 1.28 mmol) in ether gave *t*–butyl(-)-menthyltin dihydride (**15**) (0.400 g, 1.26 mmol, 70%) as a colorless liquid. $[\alpha]^{20}_D$ –23.8° (c. 2.30, benzene). FT-IR (film): $\nu_{Sn\text{-}H}$ = 181,815 cm^{-1}. ^1H NMR (C_6D_6): δ = 0.77 (d, 3H, $^3J_{HH}$ 6.4 Hz); 0.82–1.05 (m, 8H, two doublets emerging at 0.85 ($^3J_{H,H}$ 6.4 Hz) and 0.92 ($^3J_{H,H}$ 6.7 Hz); 1.07–1.50 (m, 11H, one singlet emerge at 1.29 ($^3J_{SnH}$ 69.3 Hz); 1.55–1.90 (m, 4H); 1.96–2.10 (m, 2H); 5.27 (d, 2H, $^1J_{SnH}$ 1550.3 Hz, $^2J_{HH}$ 4.6 Hz, $^3J_{SnH}$ 37.4 Hz). MS (EI, 70 eV): *m/z* (%) = 316(1%, $[M\text{-}2]^{+\cdot}$); 261(17%, $[M\text{-}(C_4H_9)]^+$); 177 $[t\text{-}BuSnH]^+$, 139 (15%, $[C_{10}H_{17}]^+$); 119 (64%, $[Sn]^+$), 83(100%, $[C_6H_{11}]^+$). Anal. Calc. for $C_{14}H_{30}Sn$: C, 53.03; H, 9.53. Found: C, 53.28; H, 9.58%.

3.4.5. Synthesis of (-)-menthylneophyltin dihydride (**16**)

Following the previous procedure, the reduction of dibromide **11** (1.30 g, 2.36 mmol) with $LiAlH_4$ (0.107 g, 2.83 mmol) led to (-)-menthyl *neo*phyltin dihydride (**16**) (0.722 g, 1.83 mmol, 78%) as a colorless liquid. $[\alpha]^{20}_D$ –29.8° (c. 6.36, benzene). FT-IR (film): $\nu_{Sn\text{-}H}$ = 1826 cm^{-1}. ^1H NMR (C_6D_6): δ = 0.77 (d, 3H, $^3J_{HH}$ 6.4 Hz); 0.81–1.00 (m, 7H, two doublets emerging at 0.90 ($^3J_{H,H}$ 6.1 Hz) and 0.94 ($^3J_{H,H}$ 6.7 Hz); 1.04–1.38 (m, 4H); 1.45 (s, 6H); 1.50–1.58 (m, 5H); 1.59–1.86 (m, 2H); 4.81 (s, 2H, $^1J_{SnH}$ 1653.9 Hz); 7.05–7.15 (m, 1H); 7.19–7.30 (m, 2H); 7.32–7.41 (m, 2H). MS (EI, 70 eV): *m/z* (%) = 392 (1%, $[M\text{-}2]^{+\cdot}$); 255 (100%i-propyltin dibromide, $[M\text{-}(C_{10}H_{19})]^+$); 197 (73%, $[C_6H_6Sn]^+$); 119 (61%, $[Sn]^+$); 139 (6%, $[C_{10}H_{19}]^+$); 91 (96%, $[(C_7H_7)]^+$); 55(%, $[(C_4H_7)]^+$). Anal. Calc. for $C_{20}H_{34}Sn$: C, 61.09; H, 8.72. Found: C, 61.25; H, 8.82%.

3.5. Reduction of (-)-menthone with (-)-menthylalkyltin dihydrides **12**–**16**

3.5.1. General method

A mixture of (-)-menthone (0.187 g, 1.21 mmol) and dihydride (1.82 mmol, 1.5 equiv) in an argon atmosphere, was stirred at rt until the IR spectrum showed that de band corresponding to $\nu_{C=O}$ had disappeared. The reaction mixture was diluted with ethanol (10 ml) for 2hs. The solid was filtered and the solution concentrated by removal of the solvent under reduced pressure. The crude product mixture was analyzed by GC–MS.

3.6. Reduction of acetophenone (**27**) and 2-acetylnaphthalene (**28**) using (-)-menthylalkyltin dihydrides **12** and **14**, and lialh$_4$. synthesis of alcohols (**29**+**30**) and (**31**+**32**)

All the reactions were carried out following the same procedure. One experiment is described in detail in order to illustrate the methods used.

3.6.1. General method

A mixture of acetophenone (0.050 g, 0.42 mmol) and dihydride (0.62 mmol, 1.5 equiv) was stirred at rt until the $\nu_{C=O}$ band in the IR spectrum disappeared (aprox. 3 h), The reaction mixture was then diluted with ethanol (10 ml) for 2hs. The solid was filtered and the solution concentrated by removal of the solvent under reduced pressure. The crude product mixture was transferred to a Kugelrohr system, and the distillation under reduced pressure (150 °C/30 mmHg) gave 1-phenylethanol (0.045 g, 0.37 mmol, 72%) as a colorless liquid.

Similarly, the reduction of 2-acetylnaphthalene (0.050 g, 0.29 mmol) with (-)-menthylalkyltin dihydrides (1.5 equiv), after column chromatography using silica gel 60, led to 1-(naphthalen-2-yl)ethan-1-ol (0.038 g, 0.22 mmol, 75%) as a white solid, mp 74–78 °C (Lit. Beilstein, 72–75 °C).

3.7. Synthesis of the mixtures of mandelates (**33** + **34**) and (**35**+**36**)

To a solution of 1-phenylethan-1-ol (0.024 g, 0.2 mmol) in dichloromethane (2 mL), was added 1-dicyclohexylcarbodiimide (DCC) (0.083 g, 0.4 mmol), (*S*)-(-)-O-acetyl mandelic acid (0.077 g, 0.4 mmol), and 4-dimethylaminopyridin (DMAP) (0.048 g, 0.04 mmol). After 15 min of stirring at room temperature, the stirring bar was removed and add an additional 2 ml of dichloromethane were added. The solution was washed with HCl 10% (1 mL), then a with saturated solution of NaCl (brine, 1 mL), a

5% NaOH (1,5 mL), and with brine (1.5 mL). The dichloromethane was dried on anhydrous sodium sulfate, and then filtered and concentrated at reduced pressure.

The same procedure was used to prepare the mixture of the mandelates corresponding to 1-(naphthalen-2-yl)ethan-1-ol.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

This work was supported by grants from CONICET, Buenos Aires, Argentina, PIP project N° 112–201501–00574), and Universidad Nacional del Sur (Bahía Blanca, Argentina, PGI 24/Q069). A fellowship from CIC-PBA to VFT is gratefully acknowledged.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2021.121680.

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