APPLIED ORGANOMETALLIC CHEMISTRY
Appl. Organometal. Chem. 2005; **19**: 465–472
Published online in Wiley InterScience (www.interscience.wiley.com). DOI:10.1002/aoc.794

Synthesis of chiral organotins suitable for the preparation of asymmetric heterogeneous catalysts†

M. Belén Faraoni[1], Alicia D. Ayala[1], Virginia Vetere[2], Mónica L. Casella[2], Osmar A. Ferretti[2,3,4] and Julio C. Podestá[1,4]*

[1]INIQO Departamento de Química, Universidad Nacional del Sur, Av. Alem 1253, 8000 Bahía Blanca, Argentina
[2]CINDECA, Departamento de Química, Facultad de Ciencias Exactas, UNLP-CONICET, 47 N° 257, 1900 La Plata, Argentina
[3]Facultad de Ingeniería, UNLP, 47 N° 257, 1900 La Plata; Argentina
[4]CONICET, Buenos Aires, Argentina

Received 20 June 2004; Revised 21 July 2004; Accepted 25 August 2004

A key step in the preparation of asymmetric heterogeneous catalysts based on silica-supported rhodium and platinum chemically modified with chiral organotins, is the synthesis of optically pure tin derivatives. We report on the synthetic pathways leading to the synthesis of (−)-menthyltin derivatives without the formation of epimerization by-products. The physical properties (including full ^{1}H, ^{13}C and ^{119}Sn NMR spectra) of the new compounds, containing between one and three (−)-menthyl ligands attached to the tin atom, are reported. The preparation of two catalysts based on silica-supported rhodium and platinum chemically modified with (−)-menthyldiphenylmethyltin, as well as some studies on the catalytic hydrogenation of ethyl pyruvate, are also described. These studies show that the reductions lead to (*R*)- and (*S*)-ethyl lactates as the only products, that the (*S*) enantiomer was the isomer formed preferentially, and that the degree of conversion observed using both catalytic systems was almost quantitative (97–100%). The enantiomeric excesses observed were in the range 7–8%. One important advantage of these catalytic systems is their stability. Recycling of the used catalysts is possible, without any loss in the degree of conversion or enantiomeric excess.

KEYWORDS: heterogeneous catalysts; organotin; chiral ligand; synthesis; hydrogenation

INTRODUCTION

The first systematic studies on the synthesis of chiral organotin compounds with chiral tin atoms were carried out by Gielen and coworkers.[1–5] Owing to the configurational instability of chiral triorganotin halides (the usual intermediates in the synthesis of chiral tetraorganotins), several techniques have been developed for increasing the configurational stability of these compounds.[6–11] Thus, in order to control the metal configuration, Schumann and coworkers attached the (−)-menthyl ligand to the tin atom.[12–14] In 1994, hexa-(−)-menthylditin was obtained, and from this compound various derivatives containing three (−)-menthyl ligands.[15] Those studies confirmed that the attachment of the (−)-menthyl ligand to the tin atom via the reaction between (−)-menthylmagnesium chloride and tin tetrachloride takes place with retention of configuration.

On the other hand, the industrial synthesis of chiral compounds is mostly carried out by processes that perform the asymmetric transformations using homogeneous catalysts. Some serious drawbacks of these expensive catalysts are their difficult separation and recycling. This led to the development of methods that make use of heterogeneous or heterogenized chiral catalysts, which in many cases combine the good activities and selectivities of homogeneous catalysts with the simplicity of recovery and reuse that is possible with heterogeneous catalysts.[16]

In the case of hydrogenation processes, one of the methods used in order to modify the enantioselectivity of a system is the addition of a chiral auxiliary to the solution of metal

*Correspondence to: Julio C. Podestá, Departamento de Química, Universidad Nacional del Sur, Av. Alem 1253, 8000 Bahía Blanca, Argentina.
E-mail: jpodesta@uns.edu.ar
†Dedicated to the memory of Professor Colin Eaborn who made numerous important contributions to the main group chemistry.
Contract/grant sponsor: CONICET, Argentina.
Contract/grant sponsor: Universidad Nacional del Sur.
Contract/grant sponsor: Agencia Nacional de Promoción Científica y Técnica; Contract/grant number: 14-04 378.

catalyst. Two useful heterogeneous asymmetric catalytic systems of this kind have been reported: (i) nickel catalysts modified with tartrate/NaBr,[17] and (ii) Pt(Pd) modified with cinchona alkaloids.[18,19] The main problems of many of these heterogeneous chiral catalysts are the leaching of the active metal or the chiral auxiliary into the solvent and the decrease of enantioselectivity. In order to solve these problems, some research groups are currently engaged in the development of a new type of asymmetric heterogeneous catalyst, prepared by using techniques derived from surface organometallic chemistry on metals. These techniques involve the reaction between a supported and reduced transition-metal catalyst with an organometallic compound.[20,21] In previous papers it was demonstrated that it is possible to react $SnBu_4$ with a monometallic catalyst and to generate an organometallic phase (retaining Bu groups on the surface) with very interesting properties in the selective hydrogenation of carbonyl compounds.[22,23]

Taking into account these previous results, we considered of interest the preparation of catalytic systems via the anchorage of organotin compounds containing chiral ligands onto monometallic catalysts. Here we report on the procedures used to obtain the (−)-menthyltin compounds needed for the preparation of chiral catalytic systems, and on some results obtained in the hydrogenation of ethyl pyruvate using these systems.

EXPERIMENTAL

^1H, ^{13}C and ^{119}Sn NMR spectra were obtained using a Bruker ARX 300 instrument. Mass spectra were obtained using a Hewlett Packard CGL-Ms 6890/5972 instrument. Melting points were determined in a Kofler hot stage and are uncorrected. Specific rotations were measured with a Polar L-μP, IBZ Messtechnik. All the solvents and reagents used were analytical reagent grade. Triphenylmethyltin (**1**),[24] di(−)-menthyldimethyltin (**12**),[25] tri(−)-menthyltin bromide (**16**),[15] (−)-menthylmethyltin dibromide (**6**),[14] tribenzyltin chloride (**8**), and dibenzyltin dichloride (**10**)[26] were prepared following known techniques. Full ^{13}C and ^{119}Sn NMR spectra of the new organotins are summarized in Tables 1 and 2.

Alkylation reactions: synthesis of compounds 3, 4, 9, 11 and 17

To a stirred solution of the organotin halide either in dry tetrahydrofuran (THF), diethyl ether or benzene, under a nitrogen atmosphere, was added dropwise a solution of the appropriate Grignard reagent either in dry THF or diethyl ether. The reaction mixture was stirred under reflux for 2–5 h. Then, it was decomposed with a 10% HCl solution, and the organic layer was washed with water and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the resulting product was purified either by recrystallization or column chromatography to yield the corresponding pure derivative.

*(1R,2S,5R)-Menthyldiphenylmethyltin (**3**) and (1S,2S,5R)-neomenthyldiphenylmethyltin (**4**)*

Compounds **3** and **4** were obtained following two routes. (a) Compound **2** (5.3 g, 13.0 mmol) in THF (10.3 ml) reacted with (−)-menthylmagnesium chloride (9.2 ml of a 1.5 M solution in THF, 14.0 mmol), leading to a colorless oil. When purified by column chromatography (silica gel 70–230), this gave a mixture of compounds **3** and **4** in the fraction eluted with hexane (4.3 g, 10.0 mmol, 77%). (b) Compound **5** (2.0 g, 4.5 mmol) in diethyl ether (4.0 ml) reacted with methylmagnesium iodide (3.9 ml of a 1.5 M solution in diethyl ether, 5.8 mmol) to give a colorless oil that was treated as above (1.6 g, 3.7 mmol, 83%). ^1H NMR ($CDCl_3$) δ 0.67 [s, 3H, ^2J(Sn,H) 50.4]; 0.78 [s, 3H, ^2J(Sn,H) 48.5]; 0.88 (d, 6H); 0.97 (d, 3H); 1.00 (d, 3H); 1.03 (d, 3H); 1.06 (d, 3H); 1.09–2.27 (m, 20H); 7.47–7.62 (m, 12H); 7.68–7.87 (m, 8H).

*(1R,2S,5R)-(−)-Menthyldiphenylmethyltin (**3**)*

The reaction of compound **6** (5.0 g, 12.0 mmol) in diethyl ether (20.0 ml) with phenylmagnesium bromide (24.8 ml of a 1.4 M solution in diethyl ether, 34.7 mmol) afforded a colorless oil. When purified by column chromatography (silica gel 70–230), this gave compound **3** (4.5 g, 10.0 mmol, 91%) in the fraction eluted with hexane. $[\alpha]_D^{20} = -21.4°$ (c 1.7, C_6H_6). ^1H NMR ($CDCl_3$) δ 0.38 [s, 3H, ^2J(Sn,H) 50.3]; 0.59 (d, 3H); 0.72 (d, 3H); 0.74 (d, 3H); 0.77–2.08 (m, 10H); 7.14–7.53 (m, 10H). MS *m/z* (relative intensity): 413 (3) $[M - CH_3]^+$; 351 (2) $[M - C_6H_5]^+$; 289 (100) $[M - C_{10}H_{19}]^+$; 274 (2) $[M - C_{10}H_{19} - CH_3]^+$; 197 (13) $[SnC_6H_5]^+$; 120 (9) $[Sn]^+$; 83 (7) $[C_6H_{11}]^+$; 55 (15) $[C_4H_7]^+$; 43 (7) $[C_3H_7]^+$; 41 (9) $[C_3H_5]^+$.

*(−)-Menthyltribenzyltin (**9**)*

The reaction of compound **8** (9.7 g, 23.0 mmol) in THF (20.0 ml) with (−)-menthylmagnesium chloride (18.8 ml of a 1.2 M solution in THF, 23.0 mmol) gave a colorless oil. When purified by column chromatography (silica gel 70–230), this yielded compound **9** (9.8 g, 18.4 mmol, 80%) in the fraction eluted with hexane. $[\alpha]_D^{20} = -42.0°$ (c 1.0, C_6H_6). ^1H NMR ($CDCl_3$) δ 0.74 (d, 3H); 0.76 (d, 3H); 0.78 (d, 3H); 0.84–1.79 (m, 10H); 2.16 [s, 6H, ^2J(Sn,H) 53.2]; 6.59–6.70 (m, 6H); 6.82–6.93 (m, 3H); 6.97–7.10 (m, 6H). MS *m/z* (relative intensity): 441 (42) $[M - C_7H_7]^+$; 259 (4) $[M - 3C_7H_7]^+$; 211 (100) $[C_7H_7Sn]^+$; 120 (18) $[Sn]^+$; 91 (5) $[C_7H_7]^+$; 83 (38) $[C_6H_{11}]^+$; 69 (16) $[C_5H_9]^+$; 67 (4) $[C_5H_7]^+$; 65 (10) $[C_5H_5]^+$; 57 (9) $[C_4H_9]^+$; 55 (23) $[C_4H_7]^+$.

*Di(−)-menthyldibenzyltin (**11**)*

The reaction of compound **10** (8.0 g, 22.0 mmol) in THF (15 ml) with (−)-menthylmagnesium chloride (35.0 ml of a 1.3 M solution in THF, 46.0 mmol) afforded a colorless oil. When purified by column chromatography (silica gel 70–230), this gave compound **11** (7.4 g, 13.0 mmol, 60%) in the fraction eluted with hexane. $[\alpha]_D^{20} = -48.0°$ (c 1.0, C_6H_6). ^1H NMR ($CDCl_3$) δ 0.85 (d, 6H); 0.99 (d, 6H); 1.03 (d, 6H); 1.12–1.96 (m, 20H); 2.46 [s, 4H, ^2J(Sn,H) 52.6];

7.06–7.27 (m, 10H). MS *m/z* (relative intensity): 489 (36) $[M - C_7H_7]^+$; 441 (4) $[M - C_{10}H_{19}]^+$; 398 (6) $[M - 2C_7H_7]^+$; 350 (17) $[M - C_{10}H_{19} - C_7H_7]^+$; 302 (10) $[M - 2C_{10}H_{19}]^+$; 259 (9) $[C_{10}H_{19}Sn]^+$; 211 (100) $[C_7H_7Sn]^+$; 120 (16) $[Sn]^+$; 91 (6) $[C_7H_7]^+$; 83 (24) $[C_6H_{11}]^+$; 69 (13) $[C_5H_9]^+$; 65 (7) $[C_5H_5]^+$; 55 (15) $[C_4H_7]^+$.

*Tri(−)-menthylmethyltin (**17**)*

The reaction of compound **16** (1.9 g, 3.0 mmol) in benzene (5 ml) with methylmagnesium iodide (3.8 ml of a 2.4 M solution in diethyl ether, 9.0 mmol) gave a white solid that was recrystallized from ethanol (1.3 g, 2.4 mmol, 80%); m.p.: 70.5–71.5 °C. $[\alpha]_D^{20} = -82.1°$ (c 1.2, C_6H_6). ^{1}H NMR ($CDCl_3$) δ 0.00 [s, 3H, ^2J(Sn,H) 39.4]; 0.77 (d, 9H); 0.87 (d, 9H); 0.95 (d, 9H); 1.01–1.93 (m, 30H). MS *m/z* (relative intensity): 537 (8) $[M - CH_3]^+$; 413 (39) $[M - C_{10}H_{19}]^+$; 274 (15) $[M - 2C_{10}H_{19}]^+$; 259 (6) $[C_{10}H_{19}Sn]^+$; 139 (12) $[C_{10}H_{19}]^+$; 137 (100) $[C_{10}H_{17}]^+$; 135 (9) $[CH_3Sn]^+$; 83 (35) $[C_6H_{11}]^+$; 81 (30) $[C_6H_9]^+$; 69 (16) $[C_5H_9]^+$; 57 (13) $[C_4H_9]^+$; 55 (30) $[C_4H_7]^+$; 43 (11) $[C_3H_7]^+$; 41 (11) $[C_3H_5]^+$.

Synthesis of compounds 5, 7 and 14

To a stirred solution of (−)-menthylmagnesium chloride in dry THF under a nitrogen atmosphere was added dropwise a solution of the organotin derivative and triphenylphosphine in dry THF. The reaction mixture was stirred under reflux for 1–4 h. Then, it was decomposed with a 10% HCl solution, extracted with CH_2Cl_2 and the organic layer washed with water and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure. The residue thus obtained was treated with a mixture of hexane and CH_2Cl_2 and the precipitated triphenylphosphine was filtered off. Removal of the solvent gave a liquid residue that was then purified by column chromatography (silica gel 70–230), the tetraalkyltin derivatives being eluted with hexane.

*(ep)-Menthyldiphenyltin chloride (**5**)*

To the Grignard reagent (3.7 ml of a 1.6 M solution, 5.8 mmol) was added a solution of a mixture of diphenyltin dichloride (2.0 g, 5.8 mmol) and triphenylphosphine (0.2 g, 0.9 mmol) in THF (7.0 ml), which after work-up yielded compound **5** (2.1 g, 4.7 mmol, 81%). ^{1}H NMR ($CDCl_3$) δ 0.81 (d, 3H); 0.95 (d, 3H); 1.0 (d, 3H); 1.29–2.70 (m, 10H); 7.42–7.63 (m, 6H); 7.63–8.09 (m, 4H). MS *m/z* (relative intensity): 405 (2) $[M - C_3H_7]^+$; 356 (1) $[M - C_4H_9 - Cl]^+$; 197 (41) $[SnC_6H_5]^+$; 155 (61) $[SnCl]^+$; 139 (50) $[C_{10}H_{19}]^+$; 120 (22) $[Sn]^+$; 95 (14) $[C_7H_{11}]^+$; 83 (100) $[C_6H_{11}]^+$; 77 (33) $[C_6H_5]^+$; 69 (41) $[C_5H_9]^+$; 67 (17) $[C_5H_7]^+$; 57 (20) $[C_4H_9]^+$; 55 (81) $[C_4H_7]^+$; 51 (19) $[C_4H_3]^+$.

*(−)-Menthyltributyltin (**7**)*

To the Grignard reagent (3.3 ml of a 1.6 M solution, 5.3 mmol) was added a solution of a mixture of tributyltin chloride (1.5 g, 4.6 mmol) and triphenylphosphine (1.3 g, 4.6 mmol) in THF (7.5 ml), which after work-up yielded compound **7** (1.7 g, 4.0 mmol, 87%). $[\alpha]_D^{20} = -30.5°$ (c 1.5, C_6H_6). ^{1}H NMR ($CDCl_3$) δ 0.54–0.93 (m, 24H); 0.94–1.89 (m, 22H). MS *m/z* (relative intensity): 373 (57) $[M - C_4H_9]^+$; 316 (3) $[M - 2C_4H_9]^+$; 291 (53) $[M - C_{10}H_{19}]^+$; 234 (33) $[M - C_{10}H_{19} - C_4H_9]^+$; 177 (100) $[C_4H_9Sn]^+$; 139 (2) $[C_{10}H_{19}]^+$; 97 (5) $[C_7H_{13}]^+$; 95 (8) $[C_7H_{11}]^+$; 83 (29) $[C_6H_{11}]^+$; 81 (14) $[C_6H_9]^+$; 69 (21) $[C_5H_9]^+$; 67 (5) $[C_5H_7]^+$; 57 (16) $[C_4H_9]^+$; 55 (55) $[C_4H_7]^+$; 43 (23) $[C_3H_7]^+$; 41 (35) $[C_3H_5]^+$.

*Di(−)-menthyldibutyltin (**14**)*

To the Grignard reagent (8.6 ml of a 1.7 M solution, 14.7 mmol) was added a solution of a mixture of dibutyltin dichloride (1.5 g, 4.9 mmol) and triphenylphosphine (1.3 g, 4.9 mmol) in THF (7 ml), which after work-up yielded compound **14** (0.9 g, 1.9 mmol, 38%). The addition of a solution of *n*-butylmagnesium bromide in diethyl ether (1.4 ml of a 1.9 M solution, 2.8 mmol) to compound **13** (0.6 g, 1.1 mmol) in diethyl ether (5.0 ml) also gave compound **14** (0.5 g, 1.0 mmol, 92%). $[\alpha]_D^{20} = -36.6°$ (*c* 1.4, C_6H_6). ^{1}H NMR ($CDCl_3$) δ 0.66–0.87 (m, 28H); 0.89–1.82 (m, 28H). MS *m/z* (relative intensity): 455 (6) $[M - C_4H_9]^+$; 373 (36) $[M - C_{10}H_{19}]^+$; 316 (5) $[M - C_{10}H_{19} - C_4H_9]^+$; 259 (7) $[C_{10}H_{19}Sn]^+$; 234 (19) $[M - 2C_{10}H_{19}]^+$; 177 (100) $[C_4H_9Sn]^+$; 120 (20) $[Sn]^+$; 97 (9) $[C_7H_{13}]^+$; 83 (53) $[C_6H_{11}]^+$; 81 (27) $[C_6H_9]^+$; 69 (34) $[C_5H_9]^+$; 67 (11) $[C_5H_7]^+$; 57 (21) $[C_4H_9]^+$; 55 (94) $[C_4H_7]^+$.

Halogen/alkyl exchange reactions

*Synthesis of diphenylmethyltin iodide (**2**)*

To a stirred solution of **1** (5.5 g, 15.0 mmol) in chloroform (15 ml), cooled at −20 °C and in the dark, was added iodine (3.8 g, 15.0 mmol). After stirring overnight at room temperature, the solvent and phenyl iodide were removed under reduce pressure and the residue was purified by column chromatography (silica gel 70–230), yielding **2** (5.4 g, 13.0 mmol, 87%) in the fraction eluted with hexane. ^{1}H NMR ($CDCl_3$) δ 1.39 [s, 3H, ^2J(Sn,H) 57.3]; 7.50–7.74 (m, 6H); 7.77–7.88 (m, 4H). ^{13}C NMR ($CDCl_3$) δ (ppm), ^nJ(Sn,C) (Hz) in parentheses: −3.03 (379.7); 128.82 (60.8); 129.99 (13.2); 135.73 (48.6); 137.29. ^{119}Sn NMR ($CDCl_3$) −68.1. MS *m/z* (relative intensity): 401 (25) $[M - CH_3]^+$; 339 (5) $[M - C_6H_5]^+$; 289 (100) $[M - I]^+$; 247 (31) $[SnI]^+$; 197 (60) $[SnC_6H_5]^+$; 120 (44) $[Sn]^+$; 77 (19) $[C_6H_5]^+$; 51 (28) $[C_4H_3]^+$.

*Synthesis of di(−)-menthyltin dibromide (**13**)*

Compound **13** was obtained following two procedures. (a) To a stirred solution of compound **11** (1.5 g, 2.6 mmol) in CCl_4 (15.0 ml), cooled at 0 °C and in the dark, was added dropwise a solution of bromine (0.9 g, 5.7 mmol) in CCl_4 (15 ml). After stirring for 72 h at room temperature, the solvent and the benzyl bromide were removed under reduced pressure and the residue was purified by recrystallization in ethanol, yielding compound **13** (0.8 g, 1.4 mmol, 55%). (b) To a stirred solution of **12** (1.3 g, 3.0 mmol) in methanol (15 ml), cooled at 0 °C and in the dark, was added dropwise a solution of bromine (1.0 g, 6.3 mmol) in methanol (15 ml). After stirring 24 h at room temperature, the solvent and methyl bromide were removed under reduce pressure. After purification

yielded compound **13** (1.2 g, 2.2 mmol, 74%); m.p.: 78–80 °C (ethanol). $[\alpha]_D^{20} = -20.5°$ (*c* 1.0, C_6H_6). ^{1}H NMR ($CDCl_3$) δ 0.87 (d, 6H); 0.93 (d, 6H); 1.02 (d, 6H); 1.09–2.32 (m, 20H). MS *m/z* (relative intensity): 556 (1) $[M]^+$; 417 (3) $[M - C_{10}H_{19}]^+$; 338 (9) $[C_{10}H_{19}SnBr]^+$; 199 (5) $[SnBr]^+$; 139 (100) $[C_{10}H_{19}]^+$; 97 (16) $[C_7H_{13}]^+$; 95 (7) $[C_7H_{11}]^+$; 83 (51) $[C_6H_{11}]^+$; 81 (27) $[C_6H_9]^+$; 69 (16) $[C_5H_9]^+$; 67 (6) $[C_5H_7]^+$; 57 (18) $[C_4H_9]^+$; 55 (29) $[C_4H_7]^+$; 43 (10) $[C_3H_7]^+$; 41 (17) $[C_3H_5]^+$.

*Synthesis of (−)-menthyldibutyltin bromide (**15**)*

As above, and following procedure (b), compound **7** (2.0 g, 4.7 mmol) in methanol (20 ml) was reacted with bromine (0.8 g, 4.7 mmol) in methanol (20 ml). The residue obtained, after solvent and *n*-butyl bromide removal under reduced pressure, was purified by Kügelrohr distillation (200 °C, 1.4 mbar), yielding compound **15** (1.9 g, 4.3 mmol, 92%). $[\alpha]_D^{20} = -33.8°$ (*c* 1.5, C_6H_6). ^{1}H NMR ($CDCl_3$) δ 0.61–0.93 (m, 19H); 1.00–2.00 (m, 18H). MS *m/z* (relative intensity): 395 (15) $[M - C_4H_9]^+$; 313 (15) $[M - C_{10}H_{19}]^+$; 256 (4) $[M - C_{10}H_{19} - C_4H_9]^+$; 199 (21) $[SnBr]^+$; 177 (6) $[C_4H_9Sn]^+$; 139 (36) $[C_{10}H_{19}]^+$; 120 (4) $[Sn]^+$; 97 (15) $[C_7H_{13}]^+$; 83 (100) $[C_6H_{11}]^+$; 81 (11) $[C_6H_9]^+$; 69 (28) $[C_5H_9]^+$; 57 (37) $[C_4H_9]^+$; 55 (45) $[C_4H_7]^+$.

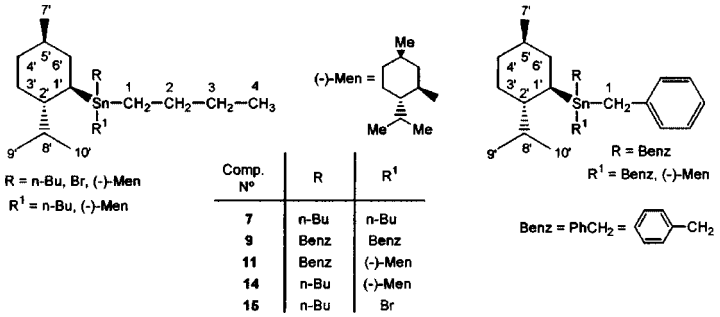
^{13}C and ^{119}Sn NMR spectra

The ^{13}C NMR chemical shifts included in Tables 1 and 2 were assigned through the analysis of the multiplicity of the signals by means of DEPT experiments and taking into account the magnitude of $^nJ(^{13}C, ^{119}Sn)$ coupling constants.

Catalyst preparation

Monometallic catalysts were prepared as described previously, with a metallic concentration of 1 wt% platinum and 1 wt% rhodium in the resulting catalysts.[27] The reduced monometallic catalyst was reacted in a hydrogen atmosphere, with the amounts of the chiral organotin compound used dissolved in *n*-heptane (catalysts based on rhodium, reaction temperature 298 K) or *n*-decane (catalysts based on platinum,

Table 1. ^{13}C and ^{119}Sn NMR characteristics of compounds **7**, **9**, **11**, **14** and **15**[a]

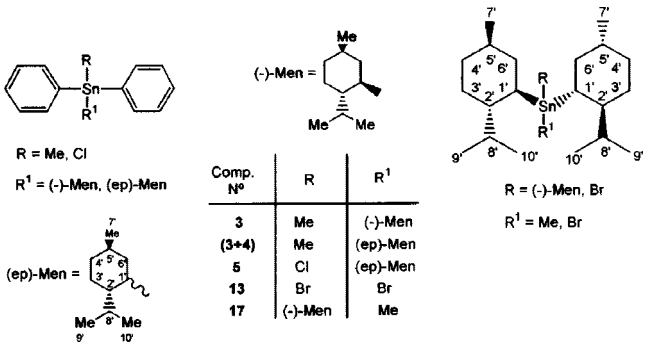


Comp. N°	R	R¹
7	n-Bu	n-Bu
9	Benz	Benz
11	Benz	(-)-Men
14	n-Bu	(-)-Men
15	n-Bu	Br

δC_n ($^nJ(^{13}C, ^{119}Sn)$)	**7**	**9**[b]	**11**[c]	**14**	**15**
C_1 (^1J)	9.05 (295.9)	20.79 (234.5)	19.40 (214.5)	8.45 (278.9)	17.09 (300.4) 18.16 (287.8)
C_2 (^2J)	29.82 (19.2)	–	–	28.49 (18.7)	28.91 (21.6)
C_3 (^3J)	28.04 (54.1)	–	–	26.83 (56.5)	27.31 (62.5)
C_4 (^4J)	14.08	–	–	12.65	13.93
$C_{1'}$ (^1J)	32.57 (409.1)	37.97 (326.4)	35.21 (166.4)	32.37 (335.3)	40.70 (374.5)
$C_{2'}$ (^2J)	47.24 (14.6)	49.32 (10.4)	46.00 (15.0)	45.86 (13.9)	46.91 (12.8)
$C_{3'}$ ($^3J_{trans}$)	27.11 (56.0)	30.33 (14.6)	26.68 (58.2)	25.90 (53.5)	26.96 (74.4)
$C_{4'}$	36.04	35.48	35.29	34.68	35.51
$C_{5'}$ ($^3J_{trans}$)	35.76 (58.2)	33.93 (16.8)	35.74 (112.6)	34.43 (55.6)	35.6 (73.6)
$C_{6'}$ (^2J)	41.79 (16.9)	39.88 (13.1)	41.11 (18.9)	40.75 (16.9)	40.27 (21.6)
$C_{7'}$	23.02	22.26	22.84	21.67	22.75
$C_{8'}$ ($^3J_{gauche}$)	34.0 (17.6)	32.87 (15.0)	33.91 (17.1)	32.76 (16.2)	35.11 (27.1)
$C_{9'}$	22.49	21.84	21.87	21.13	22.29
$C_{10'}$	16.17	15.78	16.00	15.07	16.06
^{119}Sn	−23.8	−58.0	−37.0	−36.7	135.5

[a] In $CDCl_3$; chemical shifts δ (ppm) with respect to tetramethylsilane (TMS) (^{13}C spectra) and Me_4Sn (^{119}Sn spectra); ^nJ(Sn, C) (Hz) in parentheses.
[b] 123.28 (13.7); 127.53 (21.5); 128.22 (11.4); 142.11 (34.8).
[c] 123.10; 128.11; 127.69; 143.00 (31.5).

Table 2. ^{13}C NMR characteristics of compounds **3**, (**3** + **4**), **5**, **13** and **17**[a]



δC_n ($^nJ(^{13}C, ^{119}Sn)$)	**3**[b]	(**3** + **4**)[c]	**5**[d]	**13**	**17**
C_1 (^1J)	140.86 (426.2)	140.83 (426.7)	139.20 (482.4)	–	–
	140.91 (427.0)	140.88 (427.0)	140.11 (484.6)		
		142.03 (429.6)	141.31 (475.4)		
		142.23 (426.2)	141.60 (472.0)		
$C_{1'}$ (^1J)	34.23 (411.1)	32.64 (415.2)	41.86 (428.0)	52.22 (355.19)	34.46 (329.8)
		33.73 (418.0)	45.41 (418.0)		
$C_{2'}$ (^2J)	46.38 (16.9)	46.39 (16.5)	46.13 (16.8)	46.04 (18.6)	46.56 (15.3)
		49.57 (10.6)	48.90 (9.3)		
$C_{3'}$ ($^3J_{trans}$)	26.57 (68.4)	26.58 (68.3)	26.55 (88.7)	26.58 (98.3)	26.92 (53.4)
		30.05 (73.4)	30.33 (79.3)		
$C_{4'}$	35.24	35.27	34.78	34.48	35.58
		35.58	35.10		
$C_{5'}$ ($^3J_{trans}$)	35.27 (67.6)	35.23 (70.3)	35.16 (71.2)	35.19 (89.9)	35.31 (57.6)
		36.14 (73.1)	35.40 (75.8)		
$C_{6'}$ (^2J)	41.14 (18.9)	40.03 (15.2)	38.72 (16.5)	39.86 (37.3)	41.64 (16.1)
		41.14 (18.9)	39.81 (27.8)		
$C_{7'}$	22.37	22.26	22.13	22.14	22.69
		22.38	22.21		
$C_{8'}$ ($^3J_{gauche}$)	33.74 (21.0)	33.88 (18.9)	33.56 (19.6)	36.12 (35.6)	33.39 (15.3)
		34.23 (19.9)	34.91 (24.6)		
$C_{9'}$	21.74	21.70	21.63	21.78	22.10
		21.75	21.73		
$C_{10'}$	15.57	15.58	15.61	15.94	16.57
		20.96	20.87		
Sn–CH_3 (^1J)	−10.81 (308.7)	−10.81 (308.7)	–	–	−9.51 (232.3)
		−7.75 (320.0)			
^{119}Sn	−74.6	−74.7	6.5	87.0	−46.0
		−76.5	−0.2		

[a] In $CDCl_3$; chemical shifts δ (ppm) with respect to TMS (^{13}C spectra) and Me_4Sn (^{119}Sn spectra); ^nJ(Sn, C) (Hz) in parentheses.
[b] 128.03 (43.5); 128.14 (28.4); 136.58 (32.1).
[c] 128.04 (43.8); 128.15 (28.2); 136.31; 136.37 (36.5); 136.58 (33.0).
[d] 128.73 (54.8), 129.02; 129.43; 129.48 (18.3); 129.67; 130.35; 135.39; 135.48; 135.63; 135.82; 135.99.

reaction temperature 393 K). Once the reaction had finished, as determined by measuring the consumption of the (−)-$MenPh_2SnMe$ by gas chromatography, the catalyst was washed with *n*-heptane portions in an organ atmosphere. The variation in the concentration of the organotin compound during the preparation of organometallic catalysts was analyzed using a Varian 3400 CX gas chromatograph (column 10% OV-101, flame (FID)) and a CG/EM Shimadzu QP 5050A (capillary column SPB-%TM Supelco). The atomic ratio Sn/M = 0.8 (M = Rh, Pt) was determined based on the tin content in the catalysts, spectrophotometrically measured at 530 nm, after complexing the tin with phenylfluorone.

Catalytic reactions

A typical procedure is as follows. Hydrogenation reactions were carried out in a stirred autoclave reactor. The catalyst

(0.25 g) was placed in the reactor, and then a definite volume of the substrate (2.65 mmol ethyl pyruvate) and 60 ml of 2-propanol (solvent) were introduced into the reactor under a hydrogen atmosphere. The reaction was carried out at 353 K (for platinum-based catalyst) and 313 K (for rhodium-based catalyst) at a hydrogen pressure of 1.0 MPa, with continuous stirring at a rate of 800 rpm. Reactions were followed by analyzing a sufficient number of microsamples by gas chromatography, using the Varian 3400 CX, having a 30 m J&W DB-Wax capillary column and an FID detector. The enantiomeric excess (*ee*) was determined chromatographically on a CP-Chirasil DEX CB column (25 m, 0.25 mm i.d.), and calculated as ee (%) = $100 \times (S - R)/(S + R)$.

In order to verify whether the catalysts under study could be reused, a series of experiments was carried out. The procedure consisted of submitting the catalyst to a hydrogenation test (under the conditions previously mentioned). After finishing the reaction, the remaining liquid was separated, the catalyst was repeatedly washed with 2-propanol, and then another hydrogenation test was performed.

RESULTS AND DISCUSSION

In order to obtain organotin compounds containing one (−)-menthyl ligand, we carried out the studies summarized in Fig. 1. Taking into account the convenience of a synthesis of (1*R*,2*S*,5*R*)-(−)-menthyldiphenylmethyltin (**3**) starting from commercially available reagents, we first attempted two sequences of synthesis starting from triphenyltin chloride and diphenyltin dichloride, as shown in Fig. 1. The alkylation of triphenyltin chloride with methylmagnesium iodide (Fig. 1, sequence **A**) leads to triphenylmethyltin (**1**).[24] The reaction of 1 with an equimolar solution of iodine in chloroform gives diphenylmethyltin iodide (**2**; 87%), which upon treatment with (−)-menthylmagnesium chloride leads to a mixture of (1*R*,2*S*,5*R*)-menthyldiphenylmethyltin (**3**) and (1*S*,2*S*,5*R*)-neomenthyldiphenylmethyltin (**4**) in 77% yield due to the epimerization of the chiral ligand. The ratio of epimers **3**/**4** = 2 : 1. Taking into account that it had been reported that the alkylation of diphenyltin dichloride with 2.1 equivalents of (−)-menthylmagnesium chloride led to the corresponding di(−)-menthyldiphenyltin without epimerization,[28] in order to obtain (−)-menthyldiphenyltin chloride (**5**) we carried out the same reaction but using a 1 : 1 ratio of organotin to alkylating reagent (Fig. 1, sequence **B**). Unfortunately, this route also leads to a mixture of organotin compounds with epimeric menthyl ligands, even when performing the reactions in the presence of triphenylphosphine (see below). The epimers ratio in the mixture **5** was 2 : 1.

We finally obtained (1*R*,2*S*,5*R*)(−)-menthyldiphenylmethyltin (**3**) in 91% yield and without epimerization, through the reaction between (−)-menthylmethyltin dibromide (**6**)[14] and phenylmagnesium bromide (Fig. 1, sequence **C**).

We were able to prepare (−)-menthyltributyltin (**7**; 87%) free from its epimer by adding (−)-menthylmagnesium chloride to an equimolar mixture of triphenylphosphine and tributyltin chloride (Fig. 1, sequence **D**) in THF. It should be mentioned that this reaction in the absence of triphenylphosphine leads to a 3 : 1 mixture of **7** and its epimer.[29]

Taking into account that di- and tri-benzyltin compounds are easily obtained from the reaction between benzyl chloride and tin metal,[26] we considered it convenient to carry out a study on the synthesis of the corresponding benzyl(−)-menthyltin derivatives. Thus, we determined that the alkylation of tribenzyltin chloride (**8**) with (−)-menthylmagnesium chloride led to (−)-menthyltribenzyltin (**9**) in 80% yield (Fig. 1, sequence **E**) without epimerization. Similarly, the reaction between dibenzyltin dichloride (**10**)

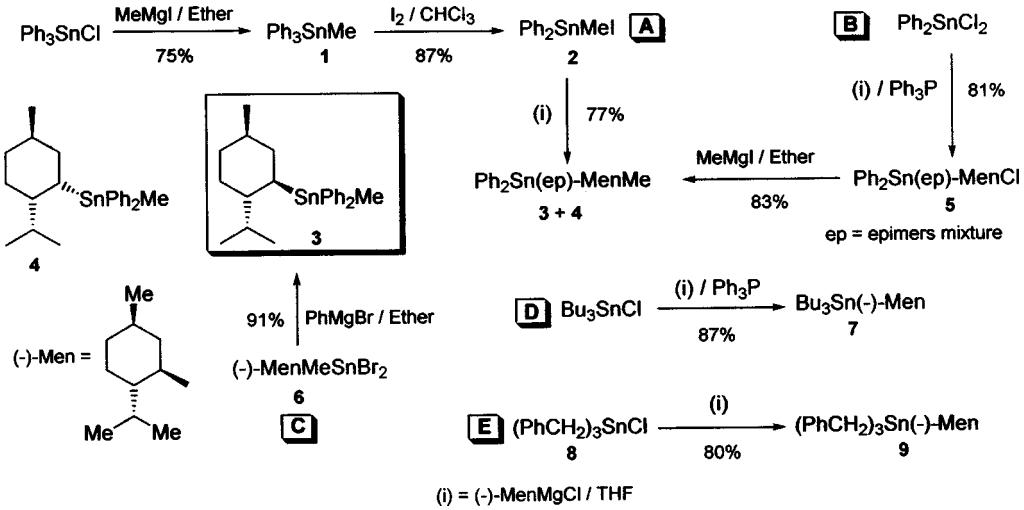


Figure 1. Synthesis of monomenthyltin derivatives.

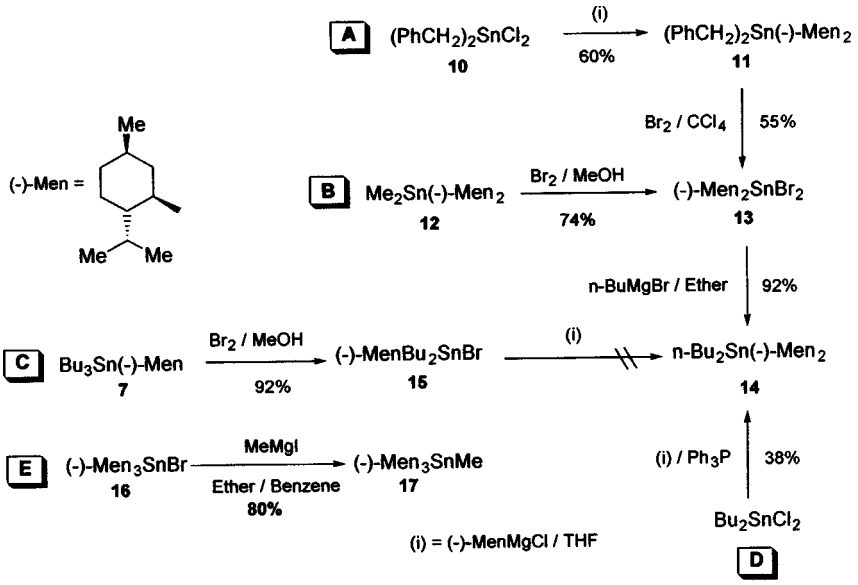


Figure 2. Synthesis of di- and tri-menthyltin derivatives.

and (−)-menthylmagnesium chloride gave the corresponding di(−)-menthyldibenzyltin (**11**) in 60% yield (Fig. 2, sequence **A**), also without epimerization. The addition of bromine in CCl_4 to **11** (ratio Br_2/**11** = 2.2), yielded di(−)-menthyltin dibromide (**13**; 55%). Compound **13** was also obtained in 74% yield by bromination of di(−)-menthyldimethyltin (**12**)[25] (Fig. 2, sequence **B**).

We were unable to obtain di(−)-menthyldibutyltin (**14**) starting from (−)-menthyltributyltin (**7**; Fig. 2, sequence **C**); although the reaction of **7** with bromine leads to the corresponding (−)-menthyldibutyltin bromide (**15**, 92%), all attempts made to alkylate **15** with (−)-menthylmagnesium chloride were unsuccessful. Di(−)-menthyldibutyltin (**14**) was obtained in 92% yield from the reaction between di(−)-menthyltin dibromide (**13**) and *n*-butylmagnesium bromide. Compound **14** was also obtained by addition of (−)-menthylmagnesium chloride to dibutyltin dichloride in the presence of triphenylphosphine (Fig. 2, sequence **D**). However, the yield was low (38%) due to the formation of hexabutylditin and tetrabutyltin.

The synthesis of organo tri(−)-menthyltin derivatives can be achieved in very good yields by alkylation of tri(−)-menthyltin bromide (**16**)[15] when the organic group is small, e.g. as in the preparation of tri(−)-menthylmethyltin (**17**; 80%) shown in Fig. 2 (sequence **E**). All attempts made to obtain tetra(−)-menthyltin by alkylation of **16** with (−)-menthyltin chloride were unsuccessful due, probably, to steric hindrance.

These studies show that in order to obtain organotin compounds with chiral ligands like the (−)-menthyl group free from epimerization by-products, it is necessary to take into account principally the structural characteristics of the other ligands attached to the tin atom. Thus, when the starting organotins already contain phenyl ligands (Fig. 1, sequences **A** and **B**), the introduction of a (−)-menthyl group via the Grignard reaction leads to mixtures of organotins containing the (−)-menthyl group and its epimer, even in the presence of triphenylphosphine. If the organic ligands already attached to the tin are *n*-butyl groups, then the addition of triphenylphosphine makes it possible to obtain the desired butyl(−)-menthyltin derivatives without epimerization (Figs 1 and 2, sequences **D**), but in some cases in low yield (Fig. 2, sequence **D**). On the contrary, it seems that methyl and benzyl ligands do not hinder the introduction of the (−)-menthyl groups, and the corresponding products are obtained free of epimerization derivatives.

These results also show that once the (−)-menthyl group is already attached to the tin, it is possible to carry out reactions like halogenations and alkylations without epimerization of the (−)-menthyl ligands.

These organotins with chiral ligands are being used at present to modify supported nickel, rhodium and platinum heterogeneous asymmetric catalysts and to study their enantioselectivity in hydrogenation reactions. In order to illustrate these studies, in this paper we report the results obtained in the hydrogenation of ethyl pyruvate using catalytic systems of platinum and rhodium modified with (−)-menthyldiphenylmethyltin (**3**).

The preparation of the organometallic catalysts was performed following the same procedure used to generate systems modified by tetrabutyltin.[30] The stoichiometry of the reaction is conveniently represented by the following general equation:

$$M/SiO_2 + ySnR_4 + xy/2H_2 \xrightarrow[M = Pt, Rh]{} M[SnR_{4-x}]_y/SiO_2 + xyRH$$

The hydrogenations of ethyl pyruvate (Fig. 3) in the presence of the chiral systems based on platinum (PtSnOM*) and rhodium (RhSnOM*) lead in both cases to (*R*)-ethyl

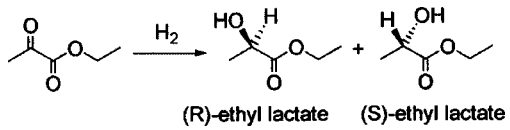


Figure 3. Hydrogenation of pyruvic acid.

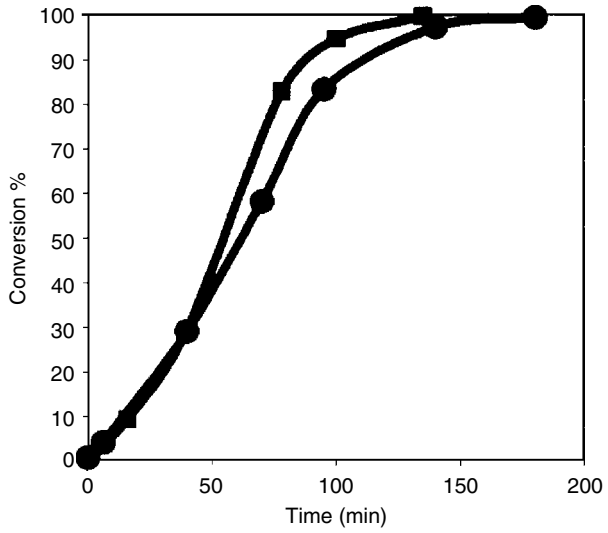


Figure 4. Enantioselective hydrogenation of ethyl pyruvate on PtSnOM* catalyst. Conversion as a function of time for two subsequent runs (for the experimental conditions see the text): (o) first run; (□) second run.

lactate and (*S*)-ethyl lactate as the only products. In all the catalytic tests performed it was found that, unlike the observations made in the hydrogenations of ethyl pyruvate using platinum/cinchonidine systems as catalysts, the (*S*) enantiomer of ethyl lactate was the isomer formed preferentially.

The degree of conversion observed using both catalytic systems was almost quantitative (97–100%). On the other hand, the enantiomeric excesses obtained were actually low: around 7% in the case of the PtSnOM* system, i.e. Pt(−)-$MenPh_2Sn$, and 8% in the case of the RhSnOM* system. It is worth mentioning that in the enantioselective hydrogenation of acetophenone (a nonactivated ketone) using Pt/SiO_2 modified with (−)-Men_3SnSn(−)-Men_3 an ee value of around 20% was obtained, which is higher than previously reported values obtained using conventional asymmetric heterogeneous catalysts for the reduction of this substrate, and this could only be explained by the presence of (−)-menthyl groups on the catalytic surface.[30]

One important advantage of these catalytic systems is their stability. Thus, as shown for the PtSnOM* system (Fig. 4), reusing the catalyst is possible without any loss in the degree of conversion or in the ee value obtained.

These results encourage us to follow our studies, extending the use of organotin ligands to generate heterogeneous chiral catalytic systems, capable of producing the enantioselective hydrogenation of other substrates, e.g. ketones, enamines, etc.

Acknowledgements

This work has been sponsored by the Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET, Argentina), the Universidad Nacional del Sur (Bahía Blanca, Argentina), and the Agencia Nacional de Promoción Científica y Técnica (PICT No. 14-04378, Argentina).

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