Electronic Supplementary Information

Thermal Epimerization of Diastereomeric Grignard Reagents

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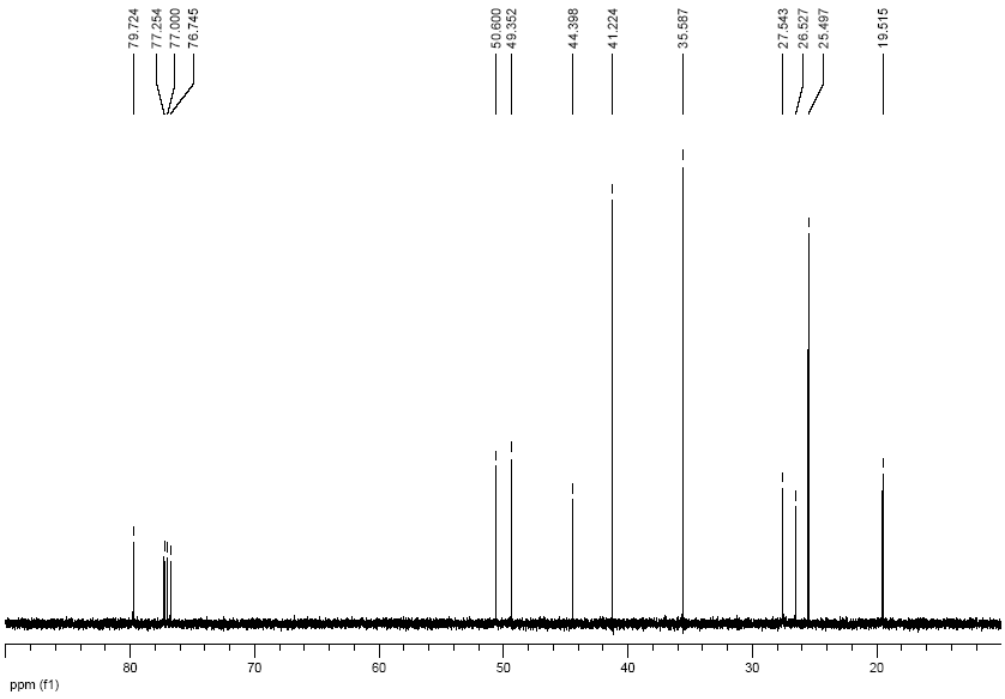
Experimental Section

General. (1R)-(+)-*endo*-α-fenchol, (1S)-(–)-*endo*-borneol and (1S)-(–)-β-pinene were obtained from Aldrich and used as received. ^{119}Sn-, ^{13}C- and ^{1}H-NMR spectra were collected in $CDCl_3$ using a Jeol JNM-LA 400 FT spectrometer and a Jeol Eclipse+ 500 FT spectrometer. Chemical shifts are given in ppm relative to Me_4Si and Me_4Sn. The assignment of the ^{13}C- and ^{1}H-NMR resonances was achieved using standard 2D NMR techniques including ^{1}H-^{1}H COSY, ^{1}H-^{1}H-NOESY, ^{1}H-^{13}C-HSQC and ^{1}H-^{13}C-HMQC. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. Microanalyses were obtained from a Vario EL elemental analyzer.

Synthesis of (1S, 2S, 4S)-*exo*-isobornyl chloride and (1R, 2S, 4S)-*exo*-β-fenchyl chloride. A solution of (1S)-(–)-*endo*-borneol or (1R)-(+)-*endo*-α-fenchol (36.0 g, 233 mmol) and PPh_3 (123 g, 469 mmol) in CCl_4 (660 mL) was heated under reflux for 18 h. Hexane (600 mL) was added and the precipitated Ph_3PO collected by filtration. The filtrate was purified by absorptive filtration using a short silica column and hexane. After removal of the solvent the product was purified by vacuum distillation (bp. 70°C / 12 mbar).

(1S, 2S, 4S)-*exo*-isobornyl chloride[S1]: Yield 23.4 g, 135 mmol, 58%, colourless solid). Anal. Calcd for $C_{10}H_{17}Cl$ (172.70): C, 69.55; H, 9.92. Found: C, 69.47; H, 9.96. **^{1}H-NMR:** δ = 3.96-4.93 (1H, m; H-2), 2.21-1.16 (1H, m; H-3_S), 2.03-1.99 (1H, m; H-3_a), 1.79-1.77 (1H, m; H-4), 1.72-1.69 (2H, m; H-5, H-6), 1.11-1.09 (2H, m; H-5, H-6), 1.09 (3H, br. s; H-8 or H-9), 1.00 (3H, br. s; H-10), 0.85 (3H, s, H-8 or H-9). **^{13}C-NMR:** δ = 68.3 (C-2), 49.7 (C-1 or C-7), 47.4 (C-1 or C-7), 46.0 (C-4), 42.4 (C-3), 36,2 (C-6), 26.9 (C-5), 20.5 (C-8 or C-9), 20.1 (C-8 or C-9), 13.4 (C-10).

(1R, 2S, 4S)-*exo*-β-fenchyl chloride: Yield 12.7 g, 73.5 mmol, 32%, colourless oil. $[\alpha]_D$ = 82.9° (*c* = 1.4 in $CHCl_3$). Anal. Calcd for $C_{10}H_{17}Cl$ (172.70): C, 69.55; H, 9.92. Found: C, 69.32; H, 9.95. **^{1}H–NMR**: δ = 3.49 (1H, d; H-2), 1.84 - 1.88 (1H, m; H-7), 1.76-1.75 (1H, m; H-4), 1.68-1.62 (1H, m; H-5_A), 1.59-1.54 (1H, m; H-6_S), 1.47-1.40 (1H, m; H-5_S), 1.24-1.20 (1H, m; H-6_A), 1.16 (3H, s; H-10), 1.09 (3H, s; H-9), 1.08-1.06 (1H, m; H-7), 1.04 (3H, s; H-8). **^{13}C–NMR**: δ = 79.7 (C-2), 50.6 (C-1), 49.4 (C-4), 44.4 (C-3), 41.2 (C-7), 35.6 (C-6), 27.5 (C-9), 26.5 (C-8), 25.5 (C-5), 19.5 (C-10).



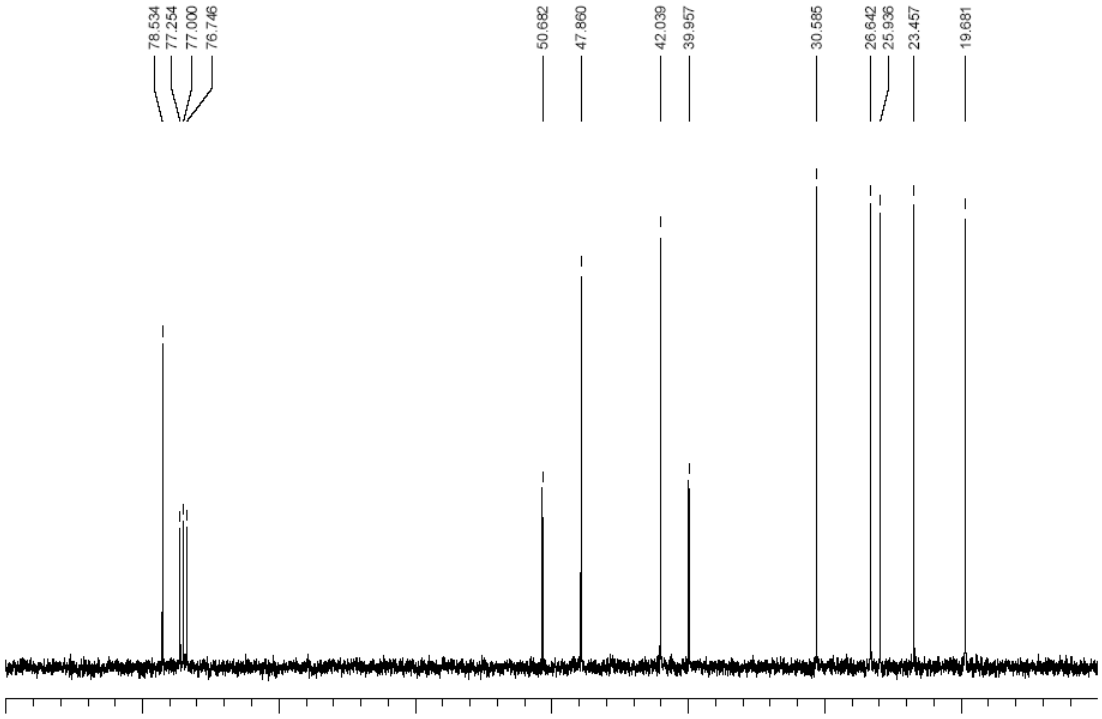
Synthesis of (1S, 2R, 4S)-*endo*-bornyl chloride and (1R, 2R, 4S)-*endo*-α-fenchyl chloride.

A solution of (1S)-(–)-β-pinene (60.4 ml, 52.5g, 380 mmol) in pentane (50 mL) was perched with dry HCl gas for 6 h at 0°C. The solvent was removed in vacuum and the residual oil cooled to -40°C. The crystalline solid containing the crude *endo*-bornyl chloride was collected by suction and re-dissolved in pentane (20 mL). The solution was washed with sat. $NaHCO_3$ solution (2 × 10 mL) and sat. NaCl solution (20 mL) and dried over Na_2SO_4. After removal of the solvent the *endo*-bornyl chloride was twice recrystallized from methanol. The filtrate containing the remaining *endo*-bornyl chloride and approx. 20% α-fenchyl chloride was subject to preparative HPLC (Gemini 110-5c18, 21.2 × 250 mm, MeOH/H_2O (90:10)) and afforded a small amount of pure α-fenchyl chloride, which has a slighter longer retention time than *endo*-bornyl chloride.

(1S, 2R, 4S)-*endo*-bornyl chloride[S2]: Yield 8.31 g, 48.1 mmol, 13% (not optimized), colourless solid. Anal. Calcd for $C_{10}H_{17}Cl$ (172.70): C, 69.55; H, 9.92. Found: C, 69.51; H, 9.74. **^{1}H-NMR:** δ = 4.18-4.14 (1H, m; H-2), 2.48-1.41 (1H, m; H-3_S), 2.09-2.04 (1H, m; H-6), 1.78-1.70 (1H, m; H-5), 1.68-1.66 (1H, m; H-4), 1.36-1.32 (2H, m; H-3_A, H-6_A), 1.31-1.24 (1H, m; H-5), 0.92 (3H, br. s; H-8 or H-9), 0.87 (3H, s; H-8 or H-9, H-10). **^{13}C-NMR:** δ = 67.9 (C-2), 50.8 (C-1 or C-7), 47.8 (C-1 or C-7), 44.9 (C-4), 40.1 (C-3), 28.1 (C-6), 28.0 (C-5), 20.5 (C-8 or C-9), 19.5 (C-8 or C-9), 13.3 (C-10).

(1R, 2R, 4S)-*endo*-α-fenchyl chloride: Yield 1.20 g, 6.94 mmol, 1.8%, colourless oil. $[\alpha]_D$ = 3.8° (*c* = 1.6 in $CHCl_3$). Anal. Calcd for $C_{10}H_{17}Cl$ (172.70): C, 69.55; H, 9.92. Found: C, 69.62; H, 9.86. **^{1}H-NMR:** δ = 3.61 (1H, d; H-2), 1.77-1.76 (1H, m; H-4), 1.75-1.72 (1H, m; H-6), 1.70-1.64 (1H, m; H-5_A), 1.56-1.52 (1H, m; H-7), 1.45-1.38 (1H, m; H-5_S), 1.30 (1H, dd; H-7), 1.10 (3H, s; H-10), 1.09-1.04 (1H, m; H-6), 1.03 (3H, s; H-9_S), 0.96 (3H, s; H-8_A).

^{13}C-NMR: δ = 78.5 (C-2), 50.6 (C-1), 47.8 (C-4), 42.0 (C-7), 39.9 (C-3), 30.5 (C-9), 26.6 (C-6), 25.9 (C-5), 23.4 (C-8), 19.6 (C-10).



Synthesis of the bornyl and fenchyl Grignard reagent for the diagnostic reaction with triphenyltin chloride. A solution of the appropriate terpene chloride (862 mg, 5.0 mmol) in THF (8 mL) was slowly added to a suspension of activated Mg turnings (122 mg, 10.0 mmol) in THF (2 mL). After the addition was completed, the mixture was heated under reflux for 12 h. Prior to use, the clear solution was separated from the excess of Mg using a syringe. The yield determined by titration was about 80%.[8]

Synthesis of the *epimerized* bornyl and fenchyl Grignard reagent. A solution of the bornyl or fenchyl Grignard reagent was slowly distilled while toluene (12 mL) was constantly added to replace the THF. The temperature was slowly raised to 111°C and kept there for 12 h. The yield determined by titration was between 65 and 75%.[8]

Reaction of the (*epimerized*) bornyl and fenchyl Grignard reagent with triphenytin chloride. The appropriate Grignard reagent was slowly added to a solution of Ph_3SnCl (1.93 g, 5.00 mmol) in THF (20 mL). The mixture stirred for 4 h at room temperature before it was hydrolyzed by addition of water (15 mL). Diethylether (15 mL) was added and the organic layer separated. After removal of the solvent, the residue was diluted with $CDCl_3$ (400 μL) and an ^{119}Sn NMR spectrum was collected (see ref 6). Then the $CDCl_3$ solution of the crude product was diluted with diethyl ether (20 mL) and stirred with a sat. KF solution (20 mL). After 1 h, the mixture was filtered to remove a small amount of precipitated Ph_3SnF (formed from Ph_3SnCl and Ph_3SnOH). The layers were separated, the organic layer washed with water (2×10 mL) and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the crude product was obtained as oil, which was purified by column chromatography (silica, hexane / ethyl acetate 20:1) to remove organic by-products. After removal of the solvents, the diastereomeric mixtures of stannanes were analyzed by ^1H and ^{13}C NMR spectroscopy. The *endo*-to-*exo* ratio was not influenced by column chromatography and determined by integration of the ^{119}Sn NMR spectra.

(1S, 2R, 4S)-*endo*-bornyltriphenyltin (**3a**): **^{1}H–NMR:** δ = 7.74-7.64 (5H, m; Ph); 7.48-7.40 (10H, m; Ph); 2.52-2.48 (1H, m; H-2); 2.40-2.34 (1H, m; H-3); 1.80-1.78 (1H, m; H-4); 1.77-1.71 (1H, m; H-5); 1.74 (1H, m; $H\text{-}6_S$); 1.70-1.67 (1H, m; H-3), 1.62-1.54 (1H, m; $H\text{-}6_A$); 1.10-1.05 (1H, m; H-5); 1.04 (3H, s; H-9); 0.96 (6H, s; H-10/H-8). **^{13}C–NMR:** δ = 140.1 ($^1J(^{13}C\text{-}^{119}Sn)$ 456 Hz; *i*-Ph), 137.4 ($^2J(^{13}C\text{-}^{119/117}Sn)$ 34 Hz; *o*-Ph), 128.6 ($^4J(^{13}C\text{-}^{119/117}Sn)$ 10 Hz; *p*-Ph), 128.4 ($^3J(^{13}C\text{-}^{119/117}Sn)$ 18 Hz; *m*-Ph), 49.1 ($^2J(^{13}C\text{-}^{119/117}Sn)$ 13 Hz; C-1), 48.1 ($^3J(^{13}C\text{-}^{119/117}Sn)$ 59 Hz; C-7), 45.4 ($^3J(^{13}C\text{-}^{119/117}Sn)$ 21 Hz; C-4), 38.7 ($^1J(^{13}C\text{-}^{119}Sn)$ 456 Hz; C-2), 38.5 ($^3J(^{13}C\text{-}^{119/117}Sn)$ 40 Hz; C-6), 33.2 ($^2J(^{13}C\text{-}^{119/117}Sn)$ 7 Hz; C-3), 28.1 (C-5), 19.6 (C-8), 18.9 (C-9), 16.4 (C-10). **^{119}Sn–NMR:** δ –101.4 ($^1J(^{119}Sn\text{-}^{13}C)$ 456 Hz).

(1S, 2S, 4S)-*exo*-isobornyltriphenyltin (**3b**): **^{1}H–NMR:** δ = 7.74-7.70 (5H, m; Ph); 7.47-7.45 (10H, m; Ph); 2.43-2.35 (2H, m; H-2,H-3); 1.97-1.83 (4H, m; H-3,H-4,H-5,H-6); 1.66-1.56 (1H, m; H-6); 1.51-1.41 (1H, m; H-5); 0.96 (3H, s; H-8/H-9); 0.94 (3H, s; H-8/H-9); 1.11 (3H, s, H-10). **^{13}C–NMR:** δ = 140.7 (*i*-Ph), 137.3 (^{2}J(^{13}C-$^{119/117}$Sn) 32 Hz; *o*-Ph), 128.4 ^{4}J(^{13}C-$^{119/117}$Sn) 10 Hz; *p*-Ph), 128.2 (*m*-Ph), 49.1 (C-1), 17.6 (C-7), 46.9 (^{3}J(^{13}C-$^{119/117}$Sn) 21 Hz; C-4), 41.5 (^{3}J(^{13}C-$^{119/117}$Sn) 66 Hz; C-6), 39.3 (C-2), 35.0 (C-3), 27.8 (C-5), 21.3 (C-8 or C-9), 19.5 (C-8 or C-9), 18.7 (C-10). **^{119}Sn–NMR:** δ –108.1 (^{1}J(^{119}Sn-^{13}C) 456 Hz).

Representative microanalysis of a mixture of **3a** and **3b**: Anal. Calcd for $C_{28}H_{32}Sn$ (487.27): C, 69.02; H, 6.62; Found: C, 69.06; H, 6.42.

(1R, 2R, 4S)-*endo*-α-fenchyltriphenyltin (**4a**): **^{1}H–NMR**: δ = 7.75-7.64 (6H, m; Ph), 7.42-7.35 (9H, m; Ph), 2.23 (1H, d; H-2), 1.82-1.80 (1H, m; H-4), 1.77-1.74 (1H, m; H-5), 1.72-1.70 (1H, m; H-7), 1.53-1.51 (2H, m; H-6, H-5), 1.35-1.29 (2H, m; H-6, H-7), 1.18 (3H, s; H-8 or H-9), 1.15 (3H, br. s; H-8 or H-9), 1.14 (3H, br. s; H-10). **^{13}C–NMR**: δ = 141.6 (^{1}J((^{13}C-^{119}Sn) 453 Hz; *i*-Ph), 137.2 (*o*-Ph), 128.3 (*m*-Ph), 128.2 (*m*-Ph), 58.2 (^{1}J(^{13}C-^{119}Sn) 435 Hz; C-2), 50.7 (^{2}J(^{13}C-$^{119/117}$Sn) 11 Hz; C-1), 49.4 (^{3}J(^{13}C-$^{119/117}$Sn) 26 Hz; C-4), 47.1 (^{3}J(^{13}C-$^{119/117}$Sn) 57 Hz; C-7), 41.8 (C-3), 35.5 (^{3}J(^{13}C-$^{119/117}$Sn) 32 Hz; C-6), 32.8 (^{3}J(^{13}C-$^{119/117}$Sn) 18 Hz; C-8 or C-9), 29.9 (^{3}J(^{13}C-$^{119/117}$Sn) 46 Hz; C-8 or C-9), 26.5 (C-5), 23.4 (C-10). **^{119}Sn–NMR**: δ = –123.5 (^{1}J(^{119}Sn-^{13}C) 453 Hz).

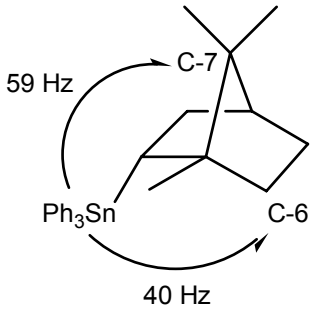
(1R, 2S, 4S)-*exo*-β-fenchyltriphenyltin (**4b**): **^{1}H–NMR**: δ = 7.71-7.67 (6H, m; Ph), 7.42-7.35 (9H, m; Ph), 2.08 (1H, d; H-2), 1.90-1.85 (2H, m; H-5, H-7), 1.82-1.80 (1H, m; H-4), 1.57-1.54 (2H, m; H-5, H-6), 1.49-1.44 (1H, m; H-6), 1.25 (3H, br s; H-10), 1.22 (3H, s; H-9), 1.20-1.17 (1H, m; H-7), 1.15 (3H, s; H-8). **^{13}C–NMR**: δ = 141.9 (^{1}J(^{13}C-^{119}Sn) 449 Hz; *i*-Ph), 137.1 (*o*-Ph), 128.3 (^{3}J(^{13}C-$^{119/117}$Sn) 46 Hz; *m*-Ph), 128.2 (*m*-Ph), 56.5 (^{1}J(^{13}C-^{119}Sn) 420 Hz; C-2), 50.2 (^{3}J(^{13}C-$^{119/117}$Sn) 167 Hz; C-4), 49.8 (^{2}J(^{13}C-$^{119/117}$Sn) 9 Hz; C-1), 45.5 (C-7), 43.9

(^2J(^{13}C-$^{119/117}$Sn) 23 Hz; C-3), 40.6 (^3J(^{13}C-$^{119/117}$Sn) 61 Hz; C-6), 33.5 (^3J(^{13}C-$^{119/117}$Sn) 68 Hz; C-9), 28.2 (^3J(^{13}C-$^{119/117}$Sn) 17 Hz; C-8), 25.4 (C-5), 25.3 (^3J(^{13}C-$^{119/117}$Sn) 27 Hz; C-10).

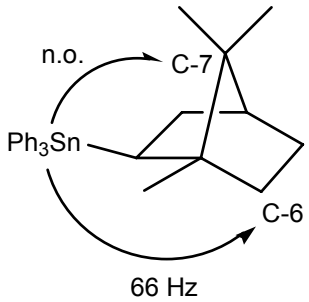
^{119}Sn–NMR: δ = –126.4 (^1J(^{119}Sn-^{13}C) 449 Hz).

Representative microanalysis of a mixture of **4a** and **4b**: Anal. Calcd for $C_{28}H_{32}Sn$ (487.27): C, 69.02; H, 6.62; Found: C, 68.95; H, 6.30.

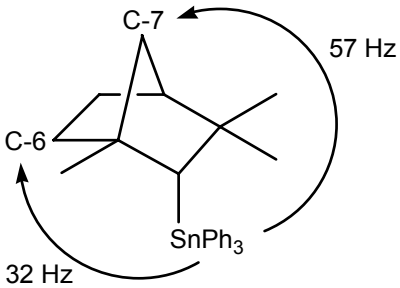
Assignment of the *endo* and *exo*-configuration was achieved by comparison of indicative ^3J(^{119}Sn-CC-^{13}C) couplings with those of *endo*-and *exo*-norbornyltrimethyltin based on the Karplus relation.[7]



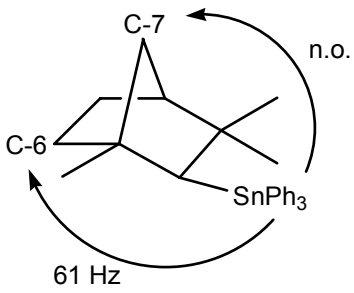
(1S, 2R, 4S)-*endo*-bornyltriphenyltin (**3a**)



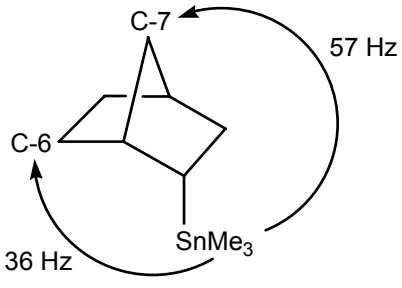
(1S, 2S, 4S)-*exo*-isobornyltriphenyltin (**3b**)



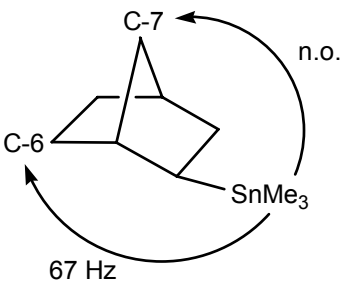
(1R, 2R, 4S)-*endo*- α fenchyltriphenyltin **(4a**)



(1R, 2S, 4S)-*exo*-β-fenchyltriphenyltin (**4b**)



rac-*endo*-norbornyltrimethyltin



rac-*exo*-norbornyltrimethyltin

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