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Supporting Information

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New Insights into the Classic Chiral Grignard Reagent [1R,2S,5R]-Menthyl Magnesium Chloride

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Experimental

General

MenCl and NeomCl were both prepared from (–)-[1*R*,2*S*,5*R*]-menthol according to literature procedures,[S1,S2] the measured optical rotations being comparable to the reported values. A literature procedure was used to prepare (–)-$MenPh_2SnI$,[S3] while Ph_2SnCl_2 and Ph_2PCl were purchased from Aldrich. The ^{1}H, ^{13}C and ^{119}Sn NMR spectra were measured using a Jeol Eclipse Plus 400 spectrometer (at 399.78 (^{1}H), 100.54 (^{13}C) and 149.05 MHz (^{119}Sn)) and were referenced against $SiMe_4$ (^{1}H, ^{13}C) and $SnMe_4$ (^{119}Sn). Optical rotations were measured on a Jasco DIP-1000 digital polarimeter. Microanalysis was carried out by CMAS, Belmont, Australia.

Synthesis of (–)-bis[(1*R*,2*S*,5*R*)-menthyl]diphenyltin (1).

A hot solution of Ph_2SnCl_2 (17.1 g, 50 mmol) in toluene (120 mL) was added drop-wise over 20 minutes to a refluxing solution of MenMgCl prepared from MenCl (43.7 g, 250 mmol) and Mg (6.7 g, 275 mol) in THF (120 mL). The reaction mixture was refluxed for a further 2 hours. After cooling and diluting with hexane (200 mL),

the reaction mixture was quenched with 20% NH_4Cl solution (150 mL). The organic phase was separated, dried over Na_2SO_4, concentrated *in vacuo* and all volatiles removed at 100°C and 10 Pa. Purification by silica gel column chromatography using hexane, followed by crystallization from ethanol gave **1** as a colorless crystalline solid (8.8 g, 32% yield). mp. 75-76°C. $[\alpha]_D^{25}$ –50.2° (c 1.0, $CHCl_3$). $^{119}Sn\{^1H\}$ NMR ($CDCl_3$): δ –89.3.

Synthesis of (–)-[1*S*,2*S*,5*R*]-neomenthyl-[1*R*,2*S*,5*R*]-menthyldiphenyltin (2).

A solution of Ph_2SnCl_2 (17.1 g, 50 mmol) in THF (25 mL) was added drop-wise to a solution of MenMgCl prepared from MenCl (21.8 g, 125 mmol) and Mg (3.3 g, 137 mol) in THF (60 mL), the temperature being maintained below 5°C with ice/water cooling. The resulting mixture was stirred at room temperature for 2 days. After diluting with hexane (200 mL), the reaction mixture was quenched with 20% NH_4Cl solution (150 mL). The organic phase was separated, dried over Na_2SO_4, concentrated *in vacuo* and all volatiles removed at 100°C and 10 Pa. Purification by silica gel column chromatography using hexane, followed by crystallization from ethanol gave **2** as a colorless crystalline solid (5.7 g, 21% yield). mp. 58-59°C. $[\alpha]_D^{21}$ –13.9° (c 1.0, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.65 - 7.47 (m, 4H), 7.37-7.26 (m, 6H), 2.72 (s, 1H, $^3J(^1H\text{-}^{117/119}Sn)$ 53), 2.18 (d, 2H), 1.75 - 0.60 (d, 32H), 0.51 (d, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 143.18 [$^1J(^{13}C\text{-}^{117/119}Sn)$ 354/371, Ph_i]; 142.62 [$^1J(^{13}C\text{-}^{117/119}Sn)$ 359/376, Ph_i], 137.87 (Ph_o), 137.59 (Ph_o), 128.04 (Ph_p), 127.93 (Ph_m), 127.84 (Ph_m), 50.42 [$^2J(^{13}C\text{-}^{117/119}Sn)$ 11, CH], 46.03 [$^2J(^{13}C\text{-}^{117/119}Sn)$ 16, CH], 41.43 [$^2J(^{13}C\text{-}^{117/119}Sn)$ 19, CH_2], 40.71 [$^2J(^{13}C\text{-}^{117/119}Sn)$ 10, CH_2], 36.49 [$^1J(^{13}C\text{-}^{117/119}Sn)$ 353/369, CH], 35.94 (CH_2), 35.64 (CH), 35.38 (CH_2), 34.64 [$^1J(^{13}C\text{-}^{117/119}Sn)$ 361/378, CH], 33.25 (CH), 33.23 (CH), 33.14 (CH), 29.07 (CH_2), 27.15 [$^3J(^{13}C\text{-}^{117/119}Sn)$ 64, CH_2], 22.81 (CH_3), 22.74 (CH_3), 22.74

(CH_3), 21.86 (CH_3), 20.97 (CH_3), 16.88 (CH_3). ^{119}Sn {^{1}H} NMR ($CDCl_3$): δ –84.0. Anal. Calcd. for $C_{32}H_{48}Sn$ (551.43): C 69.70, H 8.77; Found: C 70.05, H 8.65 %.

Quenching during preparation of (–)-[1*S*,2*S*,5*R*]-neomenthyl-[1*R*,2*S*,5*R*]-menthyldiphenyltin (2).

The reaction was identical to that above for the preparation of **2**, except the reaction was quenched 5 minutes after the complete addition of MenMgCl by the careful addition of 20% NH_4Cl solution (150 mL). After diluting with hexane (200 mL) the organic phase was separated, dried over Na_2SO_4, concentrated *in vacuo* and all volatiles removed at 100°C and 10 Pa. The crude reaction product was analyzed by ^{119}Sn NMR.

Reaction of Grignard prepared from NeomCl with chlorodiphenylphosphine.

A solution of Ph_2PCl (6.62 g, 30.0 mmol) in THF (20 mL) was added drop-wise to a solution of Grignard prepared from NeomCl (7.86 g, 45.0 mmol) and Mg (1.22 g, 50.0 mol) in THF (50 mL), the temperature being maintained at 0°C with ice/water cooling. The resulting mixture was stirred at room temperature overnight. After diluting with hexane (75 mL), the reaction mixture was quenched with 20% NH_4Cl solution (50 mL). The organic phase was separated and stirred for 1 hour with an aqueous solution of H_2O_2 (30%, 50 mL), rinsed with water (100 mL), dried over Na_2SO_4, concentrated *in vacuo* and all volatiles removed at 60°C and 10 Pa. The crude reaction product was analyzed by ^{13}C NMR, which by comparison with literature values[S4] indicated that the main product was almost exclusively $MenPh_2PO$.

Synthesis of (–)-(1*R*,2*S*,5*R*)-menthyldiphenyltin chloride (6).

A solution of (–)-$MenPh_2SnI$ (55.10 g, 102.2 mmol) in 250 mL of Et_2O was stirred vigorously with a solution of saturated aqueous NH_4Cl (200 mL) for 1 hour. The aqueous layer was removed and replaced with a fresh solution of saturated aqueous NH_4Cl (200 mL). This procedure was repeated 4 times to ensure complete conversion to (–)-$MenPh_2SnCl$. The resulting organic layer was dried over Na_2SO_4, filtered and the solvent removed *in vacuo* to give a yellow oil which was crystallized from hexane at -20°C, giving (–)-$MenPh_2SnCl$ as a white powder (39.5 g, 86% yield). mp 56-57°C. $[\alpha]_D^{20}$ –15.5° (c 0.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.35-7.75 (m, 10H), 2.20-2.40 (m, 2H), 1.60-1.90 (m, 4H), 1.30-1.50 (m, 2H), 0.93-1.20 (m, 2H), 0.91 (d, 3H), 0.90 (d, 3H), 0.76 (d, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$): δ 139.64 [^{1}J(^{13}C-$^{117/119}$Sn) 480, Ph_i] (broad), 135.69 [^{2}J(^{13}C-$^{117/119}$Sn) 46, Ph_o], 129.67 [^{4}J(^{13}C-$^{117/119}$Sn) 12, Ph_p], 128.74 [^{3}J(^{13}C-$^{117/119}$Sn) 55, Ph_m], 46.08 [J(^{13}C-$^{117/119}$Sn) 17, CH], 41.76 [^{1}J(^{13}C-$^{117/119}$Sn) 443/463, CH], 39.80 [J(^{13}C-$^{117/119}$Sn) 28, CH_2], 35.35 [J(^{13}C-$^{117/119}$Sn) 25, CH], 35.11 [J(^{13}C-$^{117/119}$Sn) 85, CH], 34.79 [J(^{13}C-$^{117/119}$Sn) 9, CH_2], 26.54 [J(^{13}C-$^{117/119}$Sn) 89, CH_2], 22.27 (CH_3), 21.66 (CH_3), 15.64 (CH_3); ^{119}Sn{^{1}H} NMR ($CDCl_3$): δ 0.5. Analysis calcd. for $C_{22}H_{29}ClSn$ (447.64): C 59.03, H 6.53; found: C 58.87, H 6.73 %.

Synthesis of (–)-bis[(1*R*,2*S*,5*R*)-menthyldiphenyltin] oxide (7).

A solution of **6** (2.00 g, 4.47 mmol) in 20 mL of Et_2O was stirred vigorously with an aqueous solution of NaOH (0.71 g, 17.9 mmol, 20 mL) for 1 hour. The organic layer was separated, dried over Na_2SO_4, filtered and the solvent removed *in vacuo* to give (–)-$(MenPh_2Sn)_2O$ as a clear oil (1.80 g, 96% yield). $[\alpha]_D^{20}$ –10.7° (c 0.2, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 0.93 (d, 6H), 1.05 (m, 12H), 1.00-1.30 (m, 4H), 1.40-1.60 (m, 4H), 1.70-2.00 (m, 6H), 2.00-2.20 (m, 4H), 2.30-2.50 (m, 2H), 7.40-7.90 (m, 20H);

$^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 143.46 [$^{1}J(^{13}C\text{-}^{117/119}Sn)$ 474/496, Ph_i], 142.67 [$^{1}J(^{13}C\text{-}^{117/119}Sn)$ 478/500, Ph_i], 136.28 [$^{2}J(^{13}C\text{-}^{117/119}Sn)$ 39, Ph_o], 136.20 [$^{2}J(^{13}C\text{-}^{117/119}Sn)$ 42, Ph_o], 128.66 [$^{4}J(^{13}C\text{-}^{117/119}Sn)$ 11, Ph_p], 128.08 [$^{3}J(^{13}C\text{-}^{117/119}Sn)$ 50, Ph_m], 128.03 [$^{3}J(^{13}C\text{-}^{117/119}Sn)$ 52, Ph_m], 45.98 [$J(^{13}C\text{-}^{117/119}Sn)$ 15, CH], 39.84 [$J(^{13}C\text{-}^{117/119}Sn)$ 26, CH_2], 39.47 [$^{1}J(^{13}C\text{-}^{117/119}Sn)$ 487/509, CH], 35.07 (CH_2), 35.02 [$J(^{13}C\text{-}^{117/119}Sn)$ 80, CH], 34.12 [$J(^{13}C\text{-}^{117/119}Sn)$ 23, CH], 26.65 [$J(^{13}C\text{-}^{117/119}Sn)$ 85, CH_2], 22.39 (CH_3), 21.75 (CH_3), 15.79 (CH_3); $^{119}Sn\{^{1}H\}$ NMR ($CDCl_3$): δ –55.6 [$^{2}J(^{119}Sn\text{-}O\text{-}^{117}Sn)$ 506]. Analysis calcd. for $C_{44}H_{58}OSn_2$ (840.35): C 62.89, H 6.96; found: C 62.68, H 6.39 %.

Crystallography

Single crystals of **2** suitable for X-ray crystallography were obtained from a solution of ethanol at 4°C. Crystal data and structure solution at T = 293(2) K: $C_{32}H_{48}Sn$, M_r = 551.40, monoclinic, *P* 2(1), crystal dimensions: 0.20 × 0.25 × 0.30 mm^3, a = 19.529(12), b = 10.694(7), c = 20.471(13) Å, β = 117.904(9) º, V = 3778(4) $Å^3$, Z = 4, ρ_{calcd} = 0.969 Mg m^{-3}, $F(000)$ = 1160, μ = 0.689 mm^{-1}. Intensity data were collected on Bruker SMART Apex CCD diffractometer fitted with Mo-Kα radiation (graphite crystal monochromator, λ = 0.71073 Å) to a maximum of θ_{max} = 25.00° via ω scans (completeness 98.1% to θ_{max}). Data were reduced and corrected for absorption using the programs SAINT and SADABS.[S5] The structure was solved by direct methods and difference Fourier synthesis using SHELX-97 implemented in the program WinGX 2002.[S6] Full-matrix least-squares refinement on F^2, using all data, was carried out with anisotropic displacement parameters applied to all non-hydrogen atoms. Hydrogen atoms were included in geometrically calculated positions using a

riding model and were refined isotropically. The weighting scheme employed was of the type $w = [\sigma^2(F_0^2) + (0.0412\ P)^2]^{-1}$ where $P = (F_0^2 + 2\ F_c^2) / 3$. $R_1 = 0.059$ for 7153 [$I>2\sigma(I)$] reflections and $wR_2 = 0.133$ for 12285 independent reflections; GooF = 1.008. Flack parameter = –0.07(3), The maximum and minimum residual electron densities were 0.884 / –0.996 e $Å^{-3}$. The figures were created using DIAMOND.[S7]

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