Enantioselective Ring Opening of Aza and Oxabicyclic Alkenes with Dimethylzinc

Mark Lautens*, Sheldon Hiebert, Jean-Luc Renaud

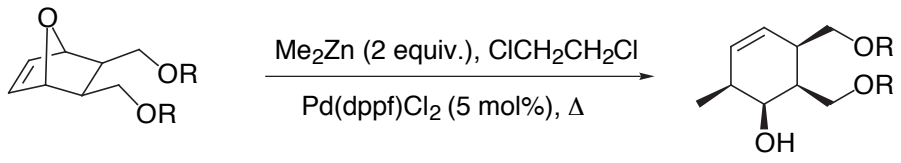
Department of Chemistry, University of Toronto

Toronto, Ontario, M5S 3H6 Canada

Supplementary Material

The following includes general experimental procedures, specific details for representative reactions, and isolation and spectroscopic information for the compounds prepared. All ^{1}H and ^{13}C NMR spectra were recorded using a Varian XL 400 spectrometer. IR spectra were obtained using a Nicolet DX FT-IR spectrometer. High resolution mass spectra were obtained on a VG 70-250S (double focusing) mass spectrometer at 70 eV.

General Procedure for the Alkylative Ring Opening of [2.2.1] and [3.2.1] Oxabicycle Alkenes.

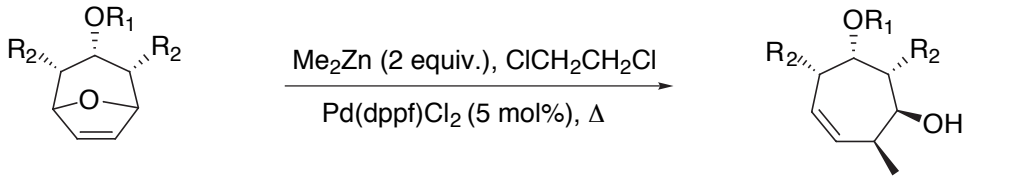


1a-c **2a-c**

R = PMB, TBDPS, Me

To an orange solution of [2.2.1] alkene **1** (1 mmol) and (bis(diphenylphosphino)-ferrocenyl)dichloropalladium (5 mol%) in distilled refluxing dichloroethane (30 mL) was added, under argon a solution of dimethylzinc (2.0M in toluene). The resulting solution

was allowed to reflux until completion by TLC analysis. After cooling to room temperature, the flask was opened to air and a few drops of water were added. This solution was stirred for half an hour, filtered through a short plug of celite and concentrated. The crude mixture was purified by flash chromatography on silica gel to afford cyclohexenol **2**.

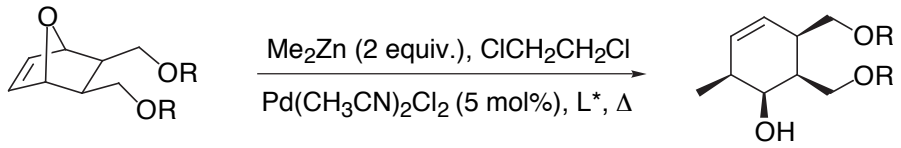


3a-e **4a-e**

R_1 = H, TBDPS, TIPS
R_2 = H, Me

To an orange solution of [3.2.1] alkene **3** (1 mmol), zinc triflate (1 mmol) and (bis(diphenylphosphino)ferrocenyl)dichloropalladium (5 mol%) in distilled refluxing dichloroethane (30 mL) was added, under argon a solution of dimethylzinc (2.0M in toluene). The resulting solution was allowed to reflux until completion by TLC analysis. After cooling to room temperature, the flask was opened to air and a few drops of water were added. This solution was stirred for half an hour, filtered through a short plug of celite and concentrated. The crude mixture was purified by flash chromatography on silica gel to afford cyclohexenol **4**.

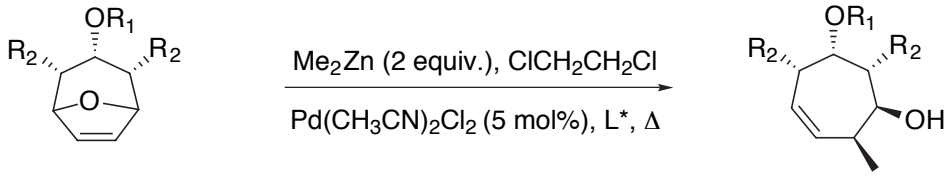
General Procedure for the Enantioselective Alkylative Ring Opening of [2.2.1] and [3.2.1] Oxabicycle Alkenes and Azabenzonorbornadienes.



1a-c **2a-c**

R = PMB, TBDPS, Me

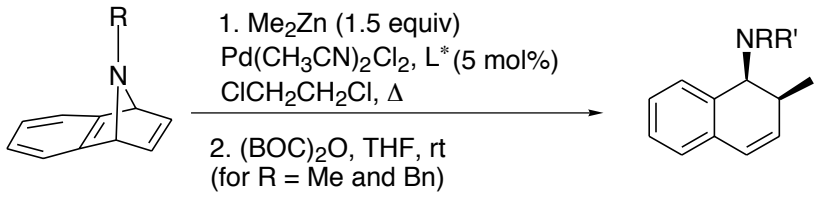
A flame dried round bottom flask was charged, under argon, with bis(acetonitrile)palladium dichloride (5 mol%) and the appropriate ligand (5 mol%). 1 mL of distilled dichloroethane was added and the solution strirred at room temperature for two hours. To this solution was added at room temperature *via* canula a solution of the suitable oxabicycle alkene **1** (1 mmol) in dichloroethane (30 mL). This solution was warmed to reflux and a solution of dimethylzinc (2.0M in toluene) was then added. The resulting solution was warmed until completion by TLC analysis. The flask was opened to air and a few drops of water were added. This solution was stirred for half an hour, filtered through a short plug of celite and concentrated. The crude mixture was purified by flash chromatography on silica gel to afford the alcohol **2**.



3a-e **4a-e**

R_1 = H, TBDPS, TIPS
R_2 = H, Me

A flame dried round bottom flask was charged, under argon, with bis(acetonitrile)palladium dichloride (5 mol%) and the appropriate ligand (5 mol%). 1 mL of distilled dichloroethane was added and the solution strirred at room temperature for two hours. To this solution was added at room temperature *via* canula a solution of the suitable oxabicycle alkene **3** (1 mmol) and zinc triflate (1 mmol) in dichloroethane (30 mL). This solution was warmed to reflux and a solution of dimethylzinc (2.0M in toluene) was then added. The resulting solution was warmed until completion by TLC analysis. The flask was opened to air and a few drops of water were added. This solution was stirred for half an hour, filtered through a short plug of celite and concentrated. The crude mixture was purified by flash chromatography on silica gel to afford the alcohol **4**.

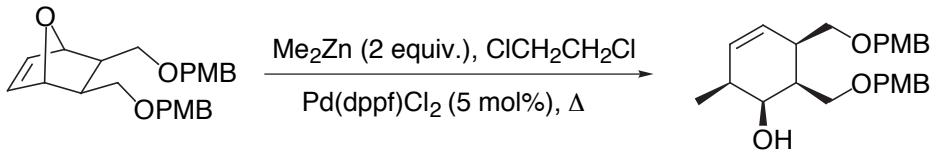


9 **10**

A flame dried round bottom flask was charged, under argon, with bis(acetonitrile)palladium dichloride (5 mol%) and the appropriate ligand (5 mol%). 1 mL of distilled dichloroethane was added and the solution strirred at room temperature for two hours. To this solution was added at room temperature *via* canula a solution of the suitable azabenzonorbornadiene **9** (1 mmol) in dichloroethane (30 mL). This solution was warmed to reflux and a solution of dimethylzinc (2.0M in toluene) was then added. The resulting solution was warmed until completion by TLC analysis. The flask was opened to air and a few drops of water were added. This solution was stirred for half an hour, filtered through a short plug of celite and concentrated. For R = methyl and benzyl the crude was dissolved in THF (2 ml) and $(BOC)_2O$ (2 mmol) added and stirred overnight. Ether was then added

and then washed with sat. $NaHCO_3$ (aq.). This was dried (Na_2SO_4), evaporated, and the crude mixture was purified by flash chromatography on silica gel to afford the amine **10**.

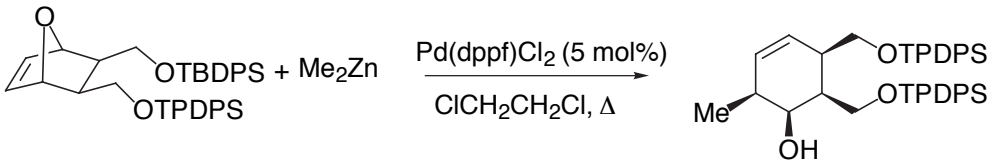
(1S, 2S, 5R, 6R)-5,6-Bis(*p*-methoxybenzyloxymethyl)-2-methyl-cyclohex-3-en-1-ol (2a)



1a 60% **2a**

The reaction was carried out as in the general procedure using substrate **1a** (50 mg, 0.13 mmol), Me_2Zn (2.0 M in toluene, 0.10 mL, 0.20 mmol) and $Pd(dppf)Cl_2$ (5.4 mg, 0.007 mmol). The crude product was purified by flash chromatography on silica gel (40% Et_2O in hexanes) to give the product, **2a**, (32.5 mg, 60%) as an oil. Enantioselective addition using (*S*)-iPr-DIPOF gave the product in 93% yield. The ee was determined to be 90% using HPLC ananlysis on a CHIRACEL OD column, λ = 254nm. Retention times in 5% iPrOH in hexanes were 13.5 min. (major) and 17.4 min. R_f = 0.39 on silica gel (hexanes : ethyl acetate 7 : 3); IR (neat) 3403 (s), 2999 (s), 2860 (s), 1607 (s), 1515 (s), 1460 (m), 1247 (s), 1078 (s), 821 (s), 759 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ 7.25-7.20 (m, 4H), 6.89-6.87 (m, 4H), 5.52 (AB, *J* = 10.4 Hz, 2H), 4.49, 4.23 (AB, *J* = 11.8 Hz, 2H), 4.33 (d, *J* = 10.8 Hz, 2H), 4.06 (d, *J* = 10.4 Hz, 1H), 3.80 (s, 6H), 3.64 (d, *J* = 9.6 Hz, 1H), 3.54 (m, 1H), 3.45 (m, 2H), 3.37 (m, 1H), 2.54 (m, 1H), 2.36 (m, 1H), 2.24 (m, 1H), 1.08 (t, *J* = 6.8 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$)δ 159.5, 159.3, 131.9, 130.5, 130.0, 129.5, 129.2, 127.4, 113.9, 113.8, 73.0, 72.9, 70.5, 67.8, 67.7, 55.3, 41.9, 36.4, 35.9, 17.0; HRMS calcd for $C_{25}H_{32}O_5$ $(M)^+$: 412.2250. Found: 412.2243

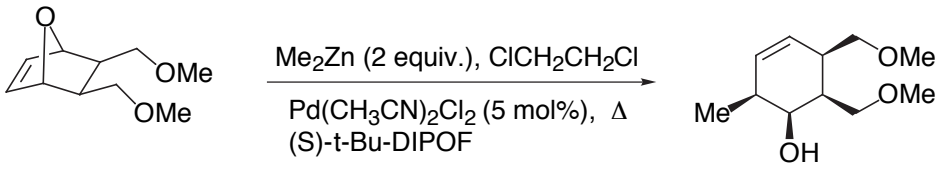
(1S, 2S, 5R, 6R)-5,6-Bis(*tert*-butyldiphenylsilyloxymethyl)-2-methyl-cyclohex-3-en-1-ol (2b)



1b 70% **2b**

The reaction was carried out as in the general procedure using substrate **1b** (50 mg, 0.0793 mmol), Me_2Zn (2.0 M in toluene, 0.08 mL, 0.16 mmol) and $Pd(dppf)Cl_2$ (2.7 mg, 0.004 mmol). The crude product was purified by flash chromatography on silica gel (10% Et_2O in hexanes) to give the product, **2b**, (35 mg, 70%) as a colorless oil. Enantioselective addition using (*S*)-*t*Bu-DIPOF gave the product in 93% yield. The ee was determined to be 98% using HPLC ananlysis on a CHIRACEL OD column, λ = 254nm. Retention times in 0.4% iPrOH in hexanes were 3.7 min. (major) and 4.3 min. R_f = 0.25 on silica gel (hexanes : ether 95 : 5); IR (neat) 3415, 3063, 2951, 2873, 1469, 1430, 1110, 997, 825, 741, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ 7.70-7.60 (m, 8H), 7.45-7.29 (m, 12H), 5.59-5.51 (m, 2H), 4.20 (d, *J* = 10.8 Hz, 1H), 4.03-3.93 (m, 2H), 3.79 (br s, 1H), 3.75 (dd, *J* = 10.8, 1.6 Hz, 1H), 3.50 (dd, *J* = 10.8, 3.2 Hz, 1H), 2.50 (m, 1H), 2.34 (q, *J* = 7.6 Hz, 1H), 2.31-2.29 (m, 1H), 1.16 (d, *J* = 7.2 Hz, 3H), 1.02 (s, 9H), 1.00 (s, 9H) ; ^{13}C NMR (100 MHz, $CDCl_3$)δ 136.2, 135.9, 135.8, 135.7, 134.1, 134.0, 132.7, 132.6, 132.5, 130.1, 130.0, 129.8, 128.0, 127.9, 127.6, 67.1, 64.3, 62.8, 44.7, 37.7, 36.7, 27.1, 26.9, 19.5, 19.4, 17.3 ; HRMS calcd for $C_{37}H_{43}O_3Si_2$ $(M-C_4H_9)^+$: 591.2751. Found: 591.2759.

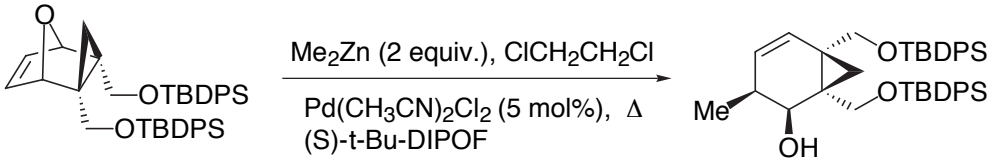
(1S, 2S, 5R, 6R)-5,6-Dimethoxymethyl-2-methyl-cyclohex-3-en-1-ol (2c)



1c 53% **2c**

The reaction was carried out as in the general procedure using substrate **1c** (37 mg, 0.20mmol), Me_2Zn (2.0 M in toluene, 0.15 mL, 0.30 mmol), $Pd(CH_3CN)_2Cl_2$ (2.6 mg, 0.01 mmol) and (*S*)-*t*Bu-DIPOF (6.0 mg, 0.012 mmol). The crude product was purified by flash chromatography on silica gel (40% Et_2O in hexanes) to give the product, **2c**, (20 mg, 53%) as a colorless oil. The ee was determined to be 91% using HPLC ananlysis on a CHIRACEL OD column, λ = 254nm. Retention times in 1% iPrOH in hexanes were 6.9 min. (major) and 7.6 min. R_f = 0.21 on silica gel (hexanes : ethyl acetate 4 : 1); IR (neat) 3415, 2871, 1462, 1130 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ 5.60(td, *J* = 11.0, 3.2 Hz, 1H), 5.48 (d, *J* = 11.0 Hz, 1H), 3.96 (d, *J* = 10.3 Hz, 1H), 3.64 (br d, *J* = 10.3 Hz, 1H), 3.57 (d, *J* = 7.9 Hz, 2H), 3.43 (br s, 1H), 3.38 (s, 6H), 2.55-2.51 9m, 1H), 2.36 (qd, *J* = 7.7, 1.6 Hz, 1H), 2.30-2.20 (m, 1H), 1.09 (d, *J* = 7.3 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$)δ 132.2, 127.2, 73.3, 71.3, 67.4, 59.1, 59.0, 41.8, 36.5, 36.1, 17.0 ; HRMS calcd for $C_{25}H_{32}O_5$ $(M)^+$: 199.133420. Found: 199.132813 ; M (e/z) 199, 183, 167, 151,

(1S, 2S, 3S, 7S)-2,3-Bis(*tert*-butyldiphenylsilyloxymethyl)-7-methyl-tricyclo[4.1.0]hept-4-en-1-ol (2d)

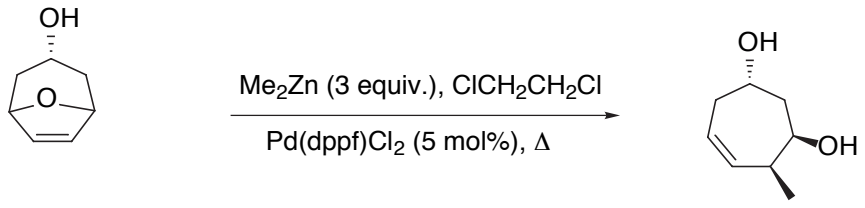


1d 68% **2d**

The reaction was carried out as in the general procedure using substrate **1d** (65 mg, 0.10mmol), Me_2Zn (2.0 M in toluene, 0.075 mL, 0.15 mmol), $Pd(CH_3CN)_2Cl_2$ (1.3 mg,

0.005 mmol) and (*S*)-*t*Bu-DIPOF (3.0 mg, 0.006 mmol). The crude product was purified by flash chromatography on silica gel (40% Et_2O in hexanes) to give the product, **2d**, (44 mg, 68%) as a colorless oil. The ee was determined to be 97% using HPLC ananlysis on a CHIRACEL OD column, λ = 254nm. Retention times in 0.5% iPrOH in hexanes were 8.5 min. and 9.7 min (major). R_f = 0.19 on silica gel (hexanes : ethyl acetate 95 : 5); IR (neat) 3666, 3467, 3065, 3061, 2954, 2864, 1961, 1895, 1828, 1656, 1589, 1470, 1426, 1388, 1363, 1264, 1100 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ 7.62-7.50 (m, 8H), 7.41-7.24 (m, 12H), 5.82 (dd, *J* = 9.7, 1.8 Hz, 1H), 5.45 (dd, *J* = 9.7, 4.4 Hz, 1H), 4.39 (dd, *J* = 4.7, 4.0 Hz, 1H), 3.97 (AB, J_{AB} = 10.8 Hz, 1H), 3.69 (dd, *J* = 11.0, 4.6 Hz, 2H), 3.43 (AB, J_{AB} = 10.8 Hz, 1H), 2.68 (d, *J* = 4.0 Hz, 1H), 2.70-2.60 (m, 1H), 1.06 (d, *J* = 5.5 Hz, 3H), 1.04 (s, 9H), 0.96 (d, *J* = 4.8 Hz, 1H), 0.95 (s, 9H), 0.48 (96 (d, *J* = 5.5 Hz, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$)δ 135.9, 135.8, 135.7, 135.6, 134.9, 133.7, 133.6, 133.2, 133.1, 129.9 (2C), 129.8, 129.7, 129.6, 127.9 (2C), 127.7 (2C), 127.6 (2C), 72.1, 69.4, 67.3, 34.2, 29.2, 27.0 (3C), 26.9 (3C), 26.7, 24.7, 19.3, 16.8 ; HRMS calcd for $C_{42}H_{51}O_2Si_2$ $(M\text{-}OH)^+$: 643.3428 Found: 643.3440

(1S, 3S, 7S)-7-methyl-cyclohept-5-en-1,3-diol (4a)

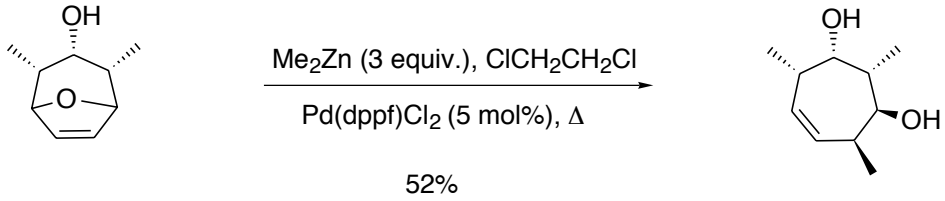


63%

The reaction was carried out as in the general procedure using substrate **3a** (50 mg, 0.40 mmol), Me_2Zn (2.0 M in toluene, 0.60 mL, 1.20 mmol) and $Pd(dppf)Cl_2$ (16 mg, 0.02 mmol). The crude product was purified by flash chromatography on silica gel (60%

EtOAc in hexanes) to give the product, **4a**, (36 mg, 63%) as a white solid. Enantioselective addition using (*S*)-*i*-Pr-DIPOF gave the product in 84% yield. The ee, after protection of the diol with benzoyl chloride, was determined to be 90% using HPLC ananlysis on a CHIRACEL OD column, λ = 254nm. Retention times in 1.5% iPrOH in hexanes were 7.8 min. (minor) and 8.3 min (major). R_f = 0.32 on silica gel (pure EtOAc); mp = 88-90 ℃ ; IR (solution in CH_2Cl_2) 3683, 3620, 3147, 2972, 2901, 1813, 1780, 1645, 1479, 1465, 1377, 1170, 1096, 934, 769 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ 5.84 (m, 1H), 5.39 (ddd, *J* = 10.8, 4.4, 2.2 Hz, 1H), 3.84-3.77 (m, 2H), 2.63-2.56 (m, 1H), 2.44-2.34 (m, 3H), 1.73 (ddd,, *J* = 13.5, 10.8, 2.4 Hz, 1H), 1.44 (d, 1H, OH), 1.39 (s, 1H, br, OH), 1.15 (d, *J* = 7.2 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$)δ 135.4, 127.7, 72.0, 64.0, 47.3, 38.2, 37.7, 19.1 ; HRMS calcd for $C_8H_{14}O_2$ $(M)^+$: 142.099380. Found: 142.098968. M (e/z) : 142, 124, 109, 95, 81, 73, 69, 55.

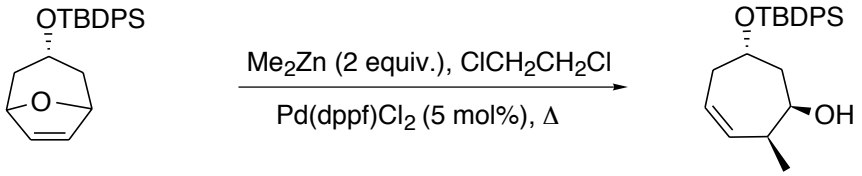
(1S, 2S, 3S, 4S, 7S)-2,4,7-trimethyl-cyclohept-5-en-1,3-diol (4b)



The reaction was carried out as in the general procedure using substrate **3b** (50 mg, 0.324 mmol), Me_2Zn (2.0 M in toluene, 0.49 mL, 0.97 mmol) and $Pd(dppf)Cl_2$ (13.0 mg, 0.016 mmol). The crude product was purified by flash chromatography on silica gel (40% EtOAc in hexanes) to give the product, **4b**, (27 mg, 52%) as an oil. Enantioselective addition using (*S*)-*i*-Pr-DIPOF gave the product in % yield. The ee, after monoprotection of the alcohol with TBDPSCl, was determined to be 95% using HPLC ananlysis on a CHIRACEL OD column, λ = 254nm. Retention times in 0.5% iPrOH in hexanes were 4.3

min. (minor) and 4.8 min (major). R_f = 0.26 on silica gel (hexanes : ethyl acetate 6 : 4); IR 3426, 3010, 2929, 1457, 1377, 1204, 1152, 1108, 919, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$)δ 5.57 (ddd, *J* = 11.4, 6.6, 2.9 Hz, 1H), 5.13 (dd, *J* = 11.4, 2.6 Hz, 1H), 3.48 (dd, *J* = 7.7, 2.9 Hz, 1H), 3.43 (d, *J* = 1.1 Hz, 1H), 2.60 (m, 2H), 2.11 (br s, 2H), 1.87 (m, 1H), 1.05 (d, *J* = 8.1 Hz, 3H), 1.03 (d, *J* = 7.3 Hz, 3H), 1.00 (d, *J* = 7.3 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$)δ 133.0, 132.5, 78.1, 73.6, 42.8, 37.9, 37.7, 20.4, 17.1, 13.9 ; HRMS calcd for $C_{10}H_{18}O_2$ $(M)^+$: 170.1307. Found: 170.1306 ; M (EI) : 170, 152, 137, 135, 134.

(1R, 2R, 7R)-(3-*tert*-butyldiphenylsilyloxy)-7-methyl-cyclohept-5-en-1,3-diol (4c)

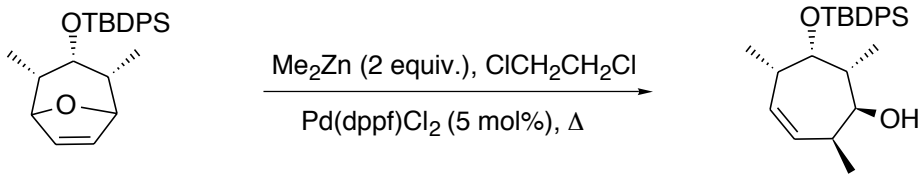


63%

The reaction was carried out as in the general procedure using substrate **3c** (50 mg, 0.137 mmol), Me_2Zn (2.0 M in toluene, 0.14 mL, 0.28 mmol) and $Pd(dppf)Cl_2$ (5.5 mg, 0.007 mmol). The crude product was purified by flash chromatography on silica gel (15% Et_2O in hexanes) to give the product, **4c**, (33 mg, 63%) as an oil. Enantioselective addition using (*S*)-*t*-Bu-POX and zinc triflate gave the product in 60% yield. The ee was determined to be 90% using HPLC ananlysis on a CHIRACEL OD column, λ = 254nm. Retention times in 0.5% iPrOH in hexanes were 9.4 min. (major) and 15.6 min (minor). R_f = 0.27 on silica gel (hexanes : ethyl ether 8 : 2) ; IR (neat) cm^{-1} 3443, 2954, 2923, 2867, 1649, 1451, 1109, 1067; ^1H NMR (400 MHz, $CDCl_3$)δ 7.68-7.65 (m, 4H), 7.44-7.34 (m, 6H),

5.62-5.56 (m, 1H), 5.30-5.25 (m, 1H), 3.86-3.81 (m, 1H), 3.73 (br s, 1H), 2.58-2.48 (m, 1H), 2.40 –2.22 (m, 3H), 1.86 (td, J = 10.4, 2.8 Hz, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$)δ 135.8, 135.1, 134.4, 134.2, 129.6, 129.5, 127.9, 127.5, 72.4, 65.8, 47.6, 38.2, 38.0, 26.9, 19.1, 18.9 ; HRMS calcd for $C_{20}H_{23}O_2Si$ $(M\text{-}C_4H_9)^+$: 323.1467. Found: 323.1482.

(1R, 2S, 3R, 4R, 7R)-(*tert*-butyldiphenylsilyloxyl)-2,4,7-trimethyl-cyclohept-5-enol (4d)

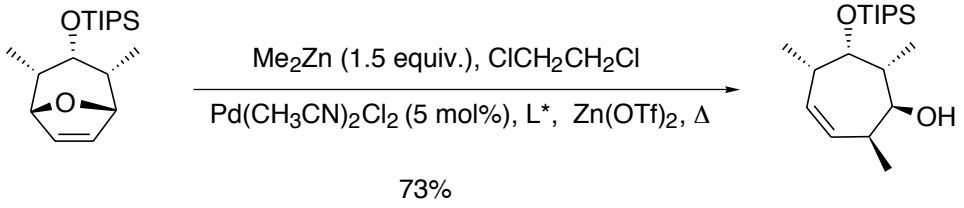


52%

The reaction was carried out as in the general procedure using substrate **3d** (50 mg, 0.127 mmol), Me_2Zn (2.0 M in toluene, 0.13 mL, 0.26 mmol) and $Pd(dppf)Cl_2$ (10.6 mg, 0.013 mmol). The crude product was purified by flash chromatography on silica gel (10% Et_2O in hexanes) to give the product, **4d**, (27 mg, 52%) as an oil. Enantioselective addition using (*S*)-*t*-Bu-DIPOF and zinc triflate gave the product in 70% yield. The ee was determined to be 90% using HPLC ananlysis on a CHIRACEL OD column, λ = 254nm. Retention times in 0.5% iPrOH in hexanes were 8.1 min. (major) and 8.9 min (minor). R_f = 0.30 on silica gel (hexanes : ethyl ether 9 : 1) ; IR (neat) 3056, 2972, 2880, 1726, 1669, 1588, 1550, 1458, 1289, 906 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)δ 7.68-7.65 (m, 4H), 7.46-7.32 (m, 6H), 5.42 (A of ABX, J = 6.4 Hz, 1H), 5.33 (B of ABX, J = 5.2 Hz, 1H), 3.93 (t, J = 3.2 Hz, 1H), 3.65 (d, J = 5.6 Hz, 1H), 2.72 (quint, J = 6.8 Hz, 1H), 2.40 (quint, J = 6.8 Hz, 1H), 2.06-1.99 (m, 1H), 1.57 (br s, OH), 1.15 (d, J = 7.6 Hz, 3H),

1.07 (s, 9H), 1.02 (d, J = 7.2 Hz, 3H), 1.00 (d, J = 7.2 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$)δ 136.1 (4C), 134.5, 133.9, 133.5, 131.5, 129.6, 129.5, 127.5 (2C), 127.3 (2C), 76.3, 73.8, 44.8, 41.3, 36.8, 27.3 (3C), 19.7, 17.1, 16.5, 15.2 ; HRMS calcd for $C_{22}H_{27}O_2Si$ $(M\text{-}C_4H_9)^+$: 351.1780 Found: 351.1762.

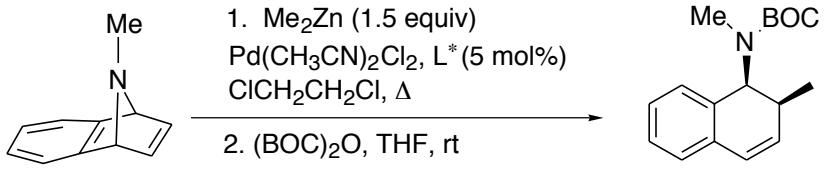
(1R, 2S, 3R, 4R, 7R)-3-tri*iso*propylsilyloxy2,4,7-trimethyl-cyclohept-5-enol (4e)



The reaction was carried out as in the general procedure using substrate **3e** (50 mg, 0.161 mmol), Me_2Zn (2.0 M in toluene, 0.12 mL, 0.24 mmol) and $Pd(dppf)Cl_2$ (6.5 mg, 0.008 mmol). The crude product was purified by flash chromatography on silica gel (10% Et_2O in hexanes) to give the product, **4e**, (27 mg, 51%) as an oil. Enantioselective addition using (*S*)-*t*-Bu-DIPOF or (*S*)-*i*-Pr-DIPOF gave the product in 73% yield. The ee was determined, after esterification with benzoyl chloride, to be 93% using HPLC ananlysis on a CHIRACEL OD column, λ = 254nm. Retention times in 0.3% iPrOH in hexanes (flow 0.5 ml/min.) were 17.5 min. (minor) and 20.9 min (major). R_f = 0.33 on silica gel (hexanes : ethyl ether 8 : 2) ; IR (neat) 3403, 2945, 2865, 1653, 1461, 1382, 1212, 1089, 887, 854 cm^{-1} ; ^{1}H NMR (400 MHz, $CDCl_3$)δ 5.65 (ddd, J = 11.5, 7.5, 1.6 Hz, 1H), 5.34 (dd, J = 11.5, 5.3 Hz, 1H), 4.19 (dd, J = 5.0 , 3.6 Hz, 1H), 3.65 (td, J = 7.0, 2.0 Hz, 1H), 2.73 (m, 1H), 2.51 (quint. d, J = 7.3, 3.5 Hz, 1H), 2.26 (quint., J = 7.0 Hz, 1H), 1.60 (dd, J = 7.0 , 6.8 Hz, 1H), 1.17 (d, J = 7.5 Hz, 3H), 1.14 (d, J = 7.3 Hz,

6H), 1.07 (br s, 18 H) ; ^{13}C NMR (100 MHz, $CDCl_3$)δ 133.1, 132.0, 77.2, 71.2, 45.6, 42.6, 36.6, 18.4, 17.6, 16.1, 14.4, 12.8 ; HRMS calcd for $C_{26}H_{36}O_2Si$ $(M)^+$: 326.263281. Found: 326.264109 ; M(e/z) : 309, 283, 265, 135, 123, 103, 95, 75, 61.

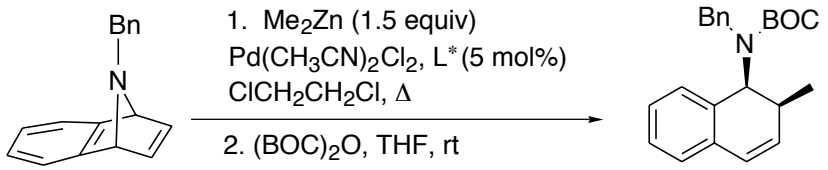
(1S, 2S)-N-BOC-1-methylamino-2-methyldihydronaphthalene (10a)



9a **10a**

The reaction was carried out as in the general procedure using substrate **9a** (50 mg, 0.32 mmol), Me_2Zn (2.0 M in toluene, 0.24 mL, 0.48 mmol), $Pd(CH_3CN)_2Cl_2$ (4.1 mg, 0.016 mmol), *t*-Bu-POX (6.2 mg, 0.016 mmol), and $(BOC)_2O$ (140 mg, 0.64 mmol). The crude product was purified by flash chromatography on silica gel (25% EtOAc in hexanes) to give the product, **10b**, (23 mg, 26%) as an oil. The ee was determined to be >99% using HPLC ananlysis on a CHIRACEL OD column, λ = 254nm. Retention times in 0.5% iPrOH in hexanes were 3.8 min (major). and 4.4 min. R_f = 0.19 on silica gel (hexanes : ethyl acetate 5 : 1); IR (neat) cm^{-1} 3450, 3015, 2971, 2923, 1681, 1649, 1144, 754; ^{1}H NMR (400 MHz, $CDCl_3$)δ 7.34-7.07 (m, 4H), 6.41 (m, 1H), 5.76 (m, 1H), 5.53, 5.31 (d, *J* = 8.4 Hz, 1H), 2.81 (m, 1H), 2.45, 2.43 (s, 3H), 1.55, 1.46 (s, 9H), 1.16, 1.15 (d, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.4, 134.2, 133.3, 133.2, 129.8, 129.4, 128.1, 127.9, 127.6, 127.5, 126.2, 127.1, 126.0, 126.0, 79.9, 79.2, 53.3, 52.0, 32.6, 32.5, 30.1, 29.4, 28.6, 28.4, 15.2, 15.0. HRMS calcd for $C_{17}H_{23}NO_2$ $(M)^+$: 273.1729. Found: 273.1725

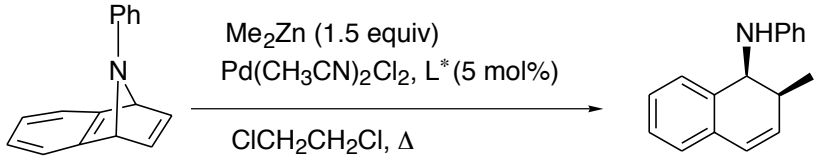
(1S, 2S)-N-BOC-1-benzylamino-2-methyldihydronaphthalene (10b)



9b **10b**

The reaction was carried out as in the general procedure using substrate **9b** (50 mg, 0.21 mmol), Me_2Zn (2.0 M in toluene, 0.16 mL, 0.32 mmol), $Pd(CH_3CN)_2Cl_2$ (2.8 mg, 0.011 mmol), *t*-Bu-POX (4.3 mg, 0.011 mmol), and $(BOC)_2O$ (92 mg, 0.42 mmol). The crude product was purified by flash chromatography on silica gel (15% EtOAc in hexanes) to give the product, **10b**, (2 mg, 3%) as an oil. The ee was determined to be 98% using HPLC ananlysis on a CHIRACEL OD column, λ = 254nm. Retention times in 0.5% iPrOH in hexanes were 5.9 min (major). and 6.8 min. R_f = 0.2 on silica gel (hexanes : ethyl acetate 5 : 1); IR (neat) cm^{-1} 3427, 2977, 2916, 1685, 1394, 1163, 1116, 754; ^1H NMR (400 MHz, $CDCl_3$)δ 7.47-7.96 (m, 9H), 6.71 (m, 1H), 6.40 (dd, *J* = 9.2, 2.8 Hz, 1H), 5.77, 5.66 (d, *J* = 8.8 Hz, 1H), 4.15 (AB, *J* = 16.0 Hz, 2H), 2.91 (m, 1H), 1.54, 1.28 (s, 9H), 1.22 (d, *J* = 8.0 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$)δ; HRMS calcd for $(M)^+$: . Found:

(1S, 2S)-1-phenylamino-2-methyldihydronaphthalene (10c)



9c **10c**

The reaction was carried out as in the general procedure using substrate **9c** (50 mg, 0.23 mmol), Me_2Zn (2.0 M in toluene, 0.17 mL, 0.34 mmol), $Pd(CH_3CN)_2Cl_2$ (2.9 mg, 0.011 mmol), and *t*-Bu-POX (4.4 mg, 0.011 mmol). The crude product was purified by

flash chromatography on silica gel (5% EtOAc in hexanes) to give the product, **10a**, (49 mg, 92%) as an oil. The ee was determined to be 98% using HPLC ananlysis on a CHIRACEL OD column, λ = 254nm. Retention times in 0.5% iPrOH in hexanes were 9.2 min. and 11.9 min (major). R_f = 0.6 on silica gel (hexanes : ethyl acetate 5 : 1); IR (neat) cm^{-1} 3412, 3015, 2962, 1600, 1503, 1310, 1280, 750; ^1H NMR (400 MHz, $CDCl_3$)δ 7.35 (d, *J* = 7.2 Hz, 1H), 7.22-7.11 (m, 4H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.72-6.80 (m, 3H), 6.48 (d, *J* = 9.6 Hz, 1H), 5.98 (dd, *J* = 9.6, 5.2 Hz, 1H), 4.77 (dd, *J* = 10.0, 14.0 Hz, 1H), 3.97 (d, *J* = 10.0 Hz, 1H), 2.76 (q, *J* = 6.4 Hz, 1H), 1.00 (d, *J* = 7.4 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$)δ 136.2, 133.5, 133.1, 129.4, 127.5, 127.4, 126.9, 126.2, 125.8, 117.4, 113.6, 109.8, 54.8, 32.7, 12.9; HRMS calcd for $C_{17}H_{17}N(M)^+$: 235.1361. Found: 235.1359.