Controlling Regiochemistry in Negishi Carboaluminations.

Fine Tuning the Ligand on Zirconium

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Supporting Information

Standard carboalumination of alkynes using catalytic (*rac*-Brint)$_2$ZrCl$_2$ / catalytic MAO / excess Me$_3$Al. To a flame dried argon purged 25 mL round bottomed (rb) flask was added *rac*-ethylenebis(indenyl)zirconocene dichloride **3** (20.9 mg, 0.050 mmol, 5.0 mol %), followed by the dropwise addition at rt of Me_3Al (2.0 M solution in toluene, 0.75 mL, 1.50 mmol, 1.5 equiv). While stirring at rt, MAO (10% w/w solution in toluene, 33 μL, 0.050 mmol, 5 mol %) was then added. Lastly, the alkyne (1.00 mmol) was introduced and the homogeneous golden orange solution stirred at rt until TLC analysis (5% CH_2Cl_2/pet ether) indicated that the carboalumination was complete.

((*E*)-3-Methylbut-3-enyloxy)triisopropylsilane (Table 2, entry A). Using the standard procedure outlined above, the following amounts of reagents were used: zirconocene **3** (21.0 mg, 0.050 mmol, 5.0 mol %), Me_3Al (2.0 M solution in toluene, 0.75 mL, 1.50 mmol, 1.5 equiv), MAO (10% w/w solution in toluene, 33 μL, 0.050 mmol, 5 mol %), and 1-Triisopropylsiloxy-3-butyne (0.25 mL, 1.0 mmol). The reaction was allowed to proceed for 8 h. The reaction was diluted with pet ether and quenched into 0.10 M aqueous HCl (*caution should be exercised when quenching Me_3Al directly into water!*). The aqueous phase was extracted with pet. ether (2 x 10 mL) and the combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* and the residue purified by silica gel chromatography (5% CH_2Cl_2/pet. ether), isolating 199 mg of the title compound as a colorless oil (82%). R_f = 0.41(5% CH_2Cl_2/pet. ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.76 (s, 1H), 4.71 (s, 1H), 3.79 (t, J = 7.2 Hz, 2H), 2.28 (t, *J* = 7.2 Hz, 2H), 1.76 (s, 3H), 1.15(b m, 21H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.5, 111.6, 62.7, 41.5, 23.2, 18.2, 12.2; HREIMS calcd for $C_{14}H_{30}OSi$ $(M-C_3H_7)^+$ 199.1519; found 199.1518. Regioselectivity: 99.8/0.2 by capillary GC.

***E*–α-Methyl-β-deuteriostyrene (Table 2, entry B).** Using the standard procedure outlined above, the following amounts of reagents were used: zirconocene **3** (21.0 mg, 0.050 mmol, 5.0 mol %), Me_3Al (2.0 M solution in toluene, 0.75 mL, 1.50 mmol, 1.5 equiv), MAO (10% w/w solution in toluene, 33 μL, 0.050 mmol, 5 mol %), and phenylacetylene (0.11 mL, 1.0 mmol). The reaction was allowed to proceed for 7.5 h, and then quenched with D_2O (20 mL) and diluted with petroleum ether (20 mL). The aqueous phase was extracted with petroleum ether (2 x 10 mL) and the combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (5% CH_2Cl_2/petroleum ether) to yield 100.1 mg of the title compound as a colorless oil (84%). R_f = 0.45 (5% CH_2Cl_2/pet. ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.5 (m, 2H), 7.35 (m, 2H), 7.29 (m, 1H), 5.4 (s, 1H), 2.10 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.0, 141.0, 128.4, 127.6, 125.7, 112.0, 21.9; LREI (*m/z*, rel. %) 47(15), 51(28), 58(10), 65(7), 74(6), 78(45), 84(54), 88(6), 92(18), 104(51), 119(100), 120(11). Regioselectivity: 99.3:0.7 (GC).

((*E*)-4-Bromo-3-methylbut-3-enyloxy)triisopropylsilane (Table 2, entry C). Using the standard procedure outlined above, the following amounts of reagents were used: zirconocene **3** (21.0 mg, 0.050 mmol, 5.0 mol %), Me_3Al (2.0 M solution in toluene, 0.75 mL, 1.50 mmol, 1.5 equiv), MAO (10% w/w solution in toluene, 33 μL, 0.050 mmol, 5 mol %) and 1-triisopropylsiloxy-3-butyne (0.25 mL, 1.00 mmol). The reaction was allowed to proceed for 8 h, at which point TLC analysis (5% CH_2Cl_2/pet. ether) indicated the carboalumination was complete. The solvent was completely removed *in vacuo* and replaced with dry THF (2.5 mL). In a separate flame dried argon purged 10 mL rb flask was added *N*-bromosuccinimide (214 mg, 1.20 mmol, 1.2 equiv) and THF (2.5 mL). This solution was added dropwise *via* canula to the reaction. After 1 h at rt, the reaction was diluted with pet ether (10 mL). The organic phase was

washed with water and brine (2 x 10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* and the residue purified by silica gel chromatography (5% CH_2Cl_2/pet. ether), isolating a colorless oil, 264 mg (83%). R_f = 0.37 (5% CH_2Cl_2/pet. ether). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96 (s, 1H), 3.77 (t, *J* = 6.4 Hz, 2H), 2.35 (*J* = 6.4 Hz, 2H), 1.83 (s, 3H), 1.11-1.04 (b m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.29, 102.83, 61.78, 41.77, 19.72, 18.18, 12.14; HREIMS calcd for $C_{14}H_{29}BrOSi$ $(M–C_3H_7)^+$ 277.0617; found 277.0623. Regioselectivity: >99:1 (other isomer not detected by GC).

(*E*)-7-Chloro-3-methylhept-2-en-1-ol (Table 2, entry D). Using the standard procedure outlined above, the following amounts of reagents were used: zirconocene **3** (21.0 mg, 0.050 mmol, 5.0 mol %), Me_3Al (2.0 M solution in toluene, 0.75 mL, 1.50 mmol, 1.5 equiv), MAO (10% w/w solution in toluene, 33 μL, 0.050 mmol, 5 mol %) and 6-chloro-1-hexyne (0.121 mL, 1.0 mmol). The reaction was allowed to proceed for 3.5 h. The solvent was completely removed under reduced pressure and replaced with THF (1.0 mL). *n*-BuLi (0.43 mL, 2.33 M solution, 1.0 mmol) was added to the reaction at rt. In a separate flame dried, argon purged 10 mL rb flask paraformaldehyde (90 mg, 3.0 mmol, 3.0 equiv) was dissolved in THF (1.0 mL) and transferred *via* canula to the vinylalane solution. After 1 h, the reaction was diluted with petroleum ether (10 mL) and quenched with 1 M HCl (*ca.* 1 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL), and the combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* and the crude product was purified by silica gel chromatography (3:1 hex/EtOAc) to afford 138 mg of the title compound as a colorless oil (85%). R_f = 0.39 (3:1 hex/EtOAc); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.4 (t, *J* = 6.6 Hz, 1H), 4.18 (m, 2H), 3.55 (t, *J* = 6.8 Hz, 2H), 2.05 (t, *J* = 7.8 Hz, 2H), 1.85 (s, 3H), 1.75 (m, 2H), 1.67

(s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 139.0, 124.0, 59.5, 45.0, 39.0, 34.0, 25.0, 18.0. Regioselectivity: 99.9:0.1 (GC).

(*E*)-Ethyl 3-methylhept-2-enoate (Table 2, entry E). Using the standard procedure outlined above, the following amounts of reagents were used: zirconocene **3** (21.0 mg, 0.050 mmol, 5.0 mol %), Me_3Al (2.0 M solution in toluene, 0.75 mL, 1.50 mmol, 1.5 equiv), MAO (10% w/w solution in toluene, 33 μL, 0.050 mmol, 5 mol %) and hexyne (0.12 mL, 1.0 mmol). The reaction was allowed to proceed for 3 h after which it was cooled to 0 ^{o}C and ethyl chloroformate (0.29 mL, 3.0 mmol, 3.0 equiv) was added dropwise. After 1 h, the reaction was diluted with petroleum ether (10 mL) and quenched with 1 M HCl (*ca.* 1 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL), and the combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* and the crude product was purified by silica gel chromatography (9:1 hex/EtOAc) isolating 151 mg of the title compound as a colorless oil (89%). R_f = 0.31 (9:1 hex/EtOAc); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.65 (m, 1H), 4.13 (q, J = 7.2Hz, 2H), 2.16 (s, 3H), 2.13 (t, J = 8.4 Hz 2H), 1.47 (m, 2H), 1.30 (m, 2H), 1.25 (t, J = 6.7 Hz, 2H), 0.94 (t, J = 7.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 167.2, 160.5, 115.6, 59.6, 40.8, 29.7, 22.4, 18.9, 14.5, 14.1; LREI (*m/z*, rel. %) 43(23), 55(39), 69(27), 82(33), 95(20), 100(39), 113(52), 128(100), 141(26), 170(17). Regioselectivity: >99:1 (other isomer not detected by GC).

(*E*)-12-Chloro-5-ethyl-8-methyldodec-7-en-6-ol (Table 2, entry F). Using the standard procedure outlined above, the following amounts of reagents were used: zirconocene **3** (21.0 mg, 0.050 mmol, 5.0 mol %), Me_3Al (2.0 M solution in toluene, 0.75 mL, 1.50 mmol, 1.5 equiv), MAO (10% w/w solution in toluene, 33 μL, 0.050 mmol, 5 mol %) and 6-chloro-1-hexyne (0.121 mL, 1.0 mmol). The reaction was allowed to proceed for 3.5 h. The solvent was

completely removed under reduced pressure and replaced with THF (1.0 mL). *n*-BuLi (0.43 mL, 2.33 M solution, 1.0 mmol) was added to the reaction at rt. In a separate flame dried, argon purged 10 mL rb flask 2-ethylhexanal (0.48 mL, 3.0 mmol, 3.0 equiv) was dissolved in THF (1.0 mL) and transferred *via* canula to the vinylalane solution. After 1 h, the reaction was diluted with petroleum ether (10 mL) and quenched with 1 M HCl (*ca.* 1 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL), and the combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* and the crude product was purified by silica gel chromatography (3:1 hex/EtOAc) isolating 236 mg of the title compound as a colorless oil (84%). R_f = 0.31 (3:1 hex/EtOAc)**;** ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.25 (d, *J* = 8.0 Hz, 1H), 4.3 (m, 1H), 3.55 (t, *J* = 6.8 Hz, 2H), 2.05 (t, *J* = 7.7 Hz, 2H), 1.85 (m, 2H), 1.68 (s, 3H), 1.55 (m, 2H), 1.3 (m, 10H), 0.80 (t, 6.5 Hz, 3H), 0.77 (t, 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.3, 127.1, 70.3, 45.9, 45.0, 39.0, 32.1, 29.7, 28.7, 25.0, 23.1, 22.0, 17.4, 15.2, 12.0. Regioselectivity: 99.9:0.1 (GC).

3-((*E*)-2-(Cyclopentylmethyl)prop-1-enyl)cyclohexanone (Table 2, entry G). Using the standard procedure outlined above, the following amounts of reagents were used: zirconocene **3** (21.0 mg, 0.050 mmol, 5.0 mol %), Me_3Al (2.0 M solution in toluene, 0.75 mL, 1.50 mmol, 1.5 equiv), MAO (10% w/w solution in toluene, 33 μL, 0.050 mmol, 5 mol %) and 3-cyclopentyl-1-propyne (0.132 mL, 1.0 mmol). The reaction was allowed to proceed for 2 h. In a separate flame dried argon purged 25 mL rb flask was added Et_2O (4 mL) and CuCN·LiCl (0.10 mL, 1.0 M solution in THF, 0.10 mmol, 10 mol %) and the reaction was cooled to 0 °C. 2-Cyclohexen-1-one (107 μL, 1.1 mmol) was dissolved in Et_2O (1.0 mL) and added to the reaction. The vinylalane solution was then added in a dropwise manner at 0 °C over the course of 1 h. The reaction mixture was then diluted with Et_2O (10 mL) and quenched with 1 M HCl (*ca.* 1 mL).

The aqueous layer was extracted with Et_2O (3 x 10 mL), and the combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* and the crude product was purified by silica gel chromatography (3:1 hex/EtOAc) isolating 185 mg of the title compound as a colorless oil (84%). R_f = 0.35 (3:1 hex/EtOAc); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.0 (d, *J* = 9.0 Hz, 1H), 2.65 (m, 1H), 2.35 (m, 2H), 2.00 (m, 6H), 1.60 (m, 12H), 1.15 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 212.0, 135.5, 129.5, 48.3, 46.2, 42.5, 38.4, 38.0, 32.5, 32.0, 25.5, 25.0, 16.3; HREIMS *m/z* calcd for $C_{15}H_{24}O$ 220.1827; found 220.1818. Regioselectivity: >99:1 (other isomer not detected by GC).

(*E*)-2-Phenyl-4-(*p*-fluorophenyl)-2-butene (Table 2, entry H). Using the standard procedure outlined above, the following amounts of reagents were used: zirconocene **3** (21.0 mg, 0.050 mmol, 5.0 mol %), Me_3Al (2.0 M solution in toluene, 0.75 mL, 1.50 mmol, 1.5 equiv), MAO (10% w/w solution in toluene, 33 μL, 0.050 mmol, 5 mol %) and phenylacetylene (0.11 mL, 1.0 mmol). The reaction was allowed to proceed for 7.5 h. The solvent was completely removed under reduced pressure and replaced with THF (1.0 mL). 4-Fluorobenzyl chloride (0.125 mL, 1.05 mmol, 1.05 equiv) was dissolved in THF (0.50 mL) and transferred *via* canula to the reaction. In a separate flask *n*-BuLi (24 μL, 2.5 M solution, 0.06 mmol) was added to a solution of $NiCl_2(PPh_3)_2$ (19.6 mg, 0.030 mmol, 3.0 mol %) in THF (0.50 mL), and the dark red-brown Ni(0) catalyst was immediately transferred to the vinylalane solution at rt. After 3 h, TLC analysis indicated complete disappearance of the vinylalane. The reaction was diluted with EtOAc (10 mL) and quenched with 1 M aqueous HCl (*ca.* 1 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL), and the combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* and the crude product was purified by silica gel chromatography (5% CH_2Cl_2/pet. ether), giving 185 mg of the title

compound as a colorless oil (82%). R_f = 0.26 (5% CH_2Cl_2/pet. ether); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.43 (m, 2H), 7.33 (m, 2H), 7.25 (m, 1H), 7.20 (m, 2H), 7.00 (m, 2H), 5.95 (t, *J* = 8.0 Hz, 1H), 3.55 (d, *J* = 7.0 Hz, 2H), 2.15 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.0, 137.0, 129.9, 129.8, 128.4, 127.1, 126.7, 125.9, 115.5, 115.3, 34.8, 16.3; HREIMS *m/z* calcd for $C_{16}H_{15}F$ 226.1158; found 226.1155. Regioselectivity: 99.3:0.7 (GC).

1-((*E*)-6-Chloro-2-methylhex-1-enyl)-anisole (Table 2, entry I). Using the standard procedure outlined above, the following amounts of reagents were used: zirconocene **5** (21.0 mg, 0.050 mmol, 5.0 mol %), Me_3Al (2.0 M solution in toluene, 0.75 mL, 1.50 mmol, 1.5 equiv), MAO (10% w/w solution in toluene, 33 μL, 0.050 mmol, 5 mol %) and 6-chloro-1-hexyne (0.121 mL, 1.0 mmol). The reaction was allowed to proceed for 3.5 h. The solvent was completely removed under reduced pressure and replaced with THF (1.0 mL). 4-Iodoanisole (257 mg, 1.1 mmol, 1.1 equiv) was dissolved in THF (0.50 mL) and transferred *via* canula to the reaction. In a separate flask *n*-BuLi (24 μL, 2.5 M solution, 0.06 mmol) was added to a solution of $NiCl_2(PPh_3)_2$ (19.6 mg, 0.030 mmol, 3.0 mol %) in THF (0.50 mL), and the active Ni(0) catalyst was immediately transferred to the vinylalane solution at rt. After 3 h, TLC analysis indicated complete disappearance of the vinylalane. The reaction was diluted with EtOAc (10 mL) and quenched with 1 M aqueous HCl (*ca.* 1 mL). The aqueous layer was extracted with EtOAc (3 x 10 mL), and the combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* and the crude product was purified by silica gel chromatography (25% EtOAc/hexanes), to afford 208 mg of the title compound as a colorless oil (87%). R_f = 0.50 (75% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.19 (d, *J* = 7.0 Hz, 2H), 6.88 (d, *J* = 7.0 Hz, 2H), 6.22 (s,1H), 3.82 (s, 3H), 3.60 (t, *J* = 6.5 Hz, 2H), 2.20 (t, *J* = 7.2 Hz, 2H), 1.85 (s, 3H), 1.80 (m, 2H), 1.68 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 130.1, 129.9,

129.8 124.9, 113.6, 55.4, 45.3, 40.0, 32.3, 25.3, 17.7; HREIMS *m/z* calcd for $C_{14}H_{19}ClO$ 238.1124; found 238.1120. Regioselectivity: 99.9:0.1 (GC).

(*E*)-1-Bromo-2,3,3-trimethylbut-1-ene (Scheme 3). Using the standard procedure outlined above, the following amounts of reagents were used: zirconocene **3** (21.0 mg, 0.050 mmol, 5.0 mol %), Me_3Al (2.0 M solution in toluene, 0.75 mL, 1.50 mmol, 1.5 equiv), MAO (10% w/w solution in toluene, 33 μL, 0.050 mmol, 5 mol %) and 3,3-dimethyl-1-butyne (0.124 mL, 1.00 mmol). The reaction was allowed to proceed for 12 h, at which point TLC analysis (5% CH_2Cl_2/pet. ether) indicated the carboalumination was complete. The solvent was completely removed *in vacuo* and replaced with dry THF (2.5 mL). In a separate flame dried argon purged 10 mL rb flask was added *N*-bromosuccinimide (214 mg, 1.20 mmol, 1.2 equiv) and THF (2.5 mL). This solution was added dropwise *via* canula to the reaction. After 1 h at rt, the reaction was diluted with pet ether (10 mL). The organic phase was washed with water and brine (2 x 10 mL) and dried over anhydrous $MgSO_4$. The solvent was removed *in vacuo* and the residue purified by silica gel chromatography (5% CH_2Cl_2/pet. ether), isolating a colorless oil, 153.1 mg (86%). R_f = 0.35 (5% CH_2Cl_2/pet. ether). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.02 (s, 1H), 1.82 (s, 3H), 1.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.29, 102.83, 61.78, 41.77, 19.72, 18.18, 12.14; HREIMS *m/z* calcd for $C_7H_{13}Br$ 176.02; found 176.0196. Regioselectivity: >99:1 (other isomer not detected by GC).

Aryl tosylate 13 (Scheme 4). To a flame-dried argon purged 25 mL round-bottom flask was added zirconocene **3** (21.0 mg, 0.05 mmol, 5.0 mol %), and solanesyl alkyne **11**, n = 3 (140.0 mg, 0.57 mmol). Alkyne **11**, n = 9, must be filtered prior to use as a solution in 5% DCM/pet. ether through basic alumina to obtain a colorless viscous oil (which may solidify on standing). CH_2Cl_2 (0.75 mL) was added followed by the addition of Me_3Al (0.75 mL, 2.0 M in toluene, 1.5

mmol, 1.5 equiv) and MAO (33.0 μL, 10% w/v solution in toluene, 0.05 mmol, 5.0 mol %), giving a homogeneous golden-yellow colored solution. The carboalumination was allowed to proceed for 6 h, at which point TLC analysis (5% CH_2Cl_2/pet. ether) indicated the reaction was complete. The solvent was removed *in vacuo* and replaced with dry THF (1.0 mL), and the reaction was cooled to 0 °C in preparation for the coupling. 2,3-Dimethoxy-5-methyl-1-tosyloxybenzyl chloride (**12**, 408 mg, 1.1 mmol, 1.1 equiv) was dissolved in THF (0.75 mL) and transferred *via* cannula to the vinylalane solution. In a separate flask *n*-BuLi (24 μL, 2.5 M solution, 0.06 mmol) was added to a solution of $NiCl_2(PPh_3)_2$ (19.63 mg, 0.030 mmol, 3.0 mol %) in THF (1.0 mL), and the active Ni(0) catalyst was immediately transferred to the vinylalane solution. After 1.5 h, the reaction was diluted with Et_2O and quenched into 0.10 M aqueous HCl. The reaction was extracted with Et_2O (3 x 10 mL) and the combined extracts dried over anhydrous $MgSO_4$. The crude material was purified by column chromatography (25% EtOAc/hexanes) isolating 883 mg (88%). Regioselectivity >99%. Spectral data matched that previously reported.[i]

CoQ_4 (Scheme 5). Using the standard procedure outlined above, the following amounts of reagents were used: zirconocene **3** (12.0 mg, 0.03 mmol, 5.0 mol %), Me_3Al (2.0 M solution in toluene, 429 μL, 0.86 mmol, 1.5 equiv), MAO (10% w/w solution in toluene, 19 μL, 0.03 mmol, 5 mol %) and farnesyl-derived alkyne **11**, n = 3 (140.0 mg, 0.58 mmol). The reaction was allowed to proceed for 8 h, at which point TLC analysis (5% CH_2Cl_2 /pet. ether) indicated the reaction was complete. The solvent was completely removed *in vacuo* and replaced with dry THF (1.0 mL), and the reaction was cooled to -20 °C in preparation for the coupling. Chloromethylated quinone **14** (145.1 mg, 0.629 mmol, 1.1 equiv) was dissolved in THF (0.75

mL) and transferred *via* cannula to the vinylalane solution. In a separate flask *n*-BuLi (13.7 μL, 2.5 M solution, 0.03 mmol) was added to a solution of $NiCl_2(PPh_3)_2$ (11.2 mg, 0.02 mmol, 3.0 mol %) in THF (0.50 mL), and the active Ni(0) catalyst was immediately transferred to the vinylalane solution. After 2 h at -20 °C the reaction was diluted with Et_2O and quenched into 0.10 M aqueous HCl. The mixture was extracted with Et_2O (3 x 10 mL) and the combined extracts dried over anhydrous $MgSO_4$. Filtration and evaporation led to crude material that was purified by column chromatography (10% EtOAc/pet. ether) to afford 211 mg CoQ_4 (81.1 %). Spectral data matched that previously reported.[i] R_f = 0.33 (10% EtOAc/pet. ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.06 (m, 4H), 4.90 (t, *J* = 7.2 Hz, 1H), 3.97 (s, 3H), 3.95 (s, 3H), 3.15 (d, *J* = 7.2 Hz, 2H), 1.98 (m, 19H), 1.71 (s, 3H), 1.65 (s, 3H), 1.56 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.7, 183.9, 144.2, 141.7, 138.8, 137.6, 135.2, 135.0, 134.9, 131.2, 124.4, 124.2, 124.1, 123.8, 118.8, 61.1, 39.7, 26.8, 26.6, 26.5, 25.7, 25.3, 17.7, 16.3, 16.0, 15.9, 11.9. Regioselectivity: 98.8/1.2.

CoQ_{10} (Scheme 5). Using the standard procedure outlined above, the following amounts of reagents were used: zirconocene **3** (6.9 mg, 0.016 mmol, 5.0 mol %), Me_3Al (2.0 M solution in toluene, 0.25 mL, 0.491 mmol, 1.5 equiv), MAO (10% w/w solution in toluene, 11 μL, 0.03 mmol, 5 mol %) and solanesol-derived alkyne **11**, n = 9 (214.0 mg, 0.33 mmol). Alkyne **11**, n = 9, must be filtered prior to use as a solution in 5% DCM/pet. ether through basic alumina to obtain a colorless viscous oil. The reaction was allowed to proceed for 22 h, at which point TLC analysis (5% CH_2Cl_2 /pet. ether) indicated the reaction was complete. The solvent was completely removed *in vacuo* and replaced with dry THF (1.0 mL), and the reaction was cooled to -20 °C in preparation for the coupling. Chloromethylated quinone **14** (83 mg, 0.36 mmol, 1.1 equiv) was dissolved in THF (1.0 mL) and transferred *via* cannula to the vinylalane solution. In

a separate flask *n*-BuLi (13.7 μL, 2.5 M solution, 0.03 mmol) was added to a solution of $NiCl_2(PPh_3)_2$ (6.4 mg, 0.010 mmol, 3.0 mol %) in THF (0.50 mL), and the active Ni(0) catalyst was immediately transferred to the vinylalane solution. After 2 h at -20 °C the reaction was diluted with Et_2O and quenched into 0.10 M aqueous HCl. The mixture was extracted with Et_2O (3 x 10 mL) and the combined extracts dried over anhydrous $MgSO_4$. Filtration and evaporation led to crude material that was purified by column chromatography (10% EtOAc/pet. ether) to afford 248.9 mg CoQ_{10} (88%). Regioselectivity: 99.1/0.9 (NMR), 98.5/1.5 (HPLC). Spectral data matched that previously reported.[i]

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i. Lipshutz, B.H.; Mollard, P.; Pfeiffer, S.; Chrisman, W.; *J. Am. Chem. Soc*. **2002**, *124*, 14282