## SUPPORTING INFORMATION

**General.** $^1$H NMR spectra were recorded on a 300 MHz spectrometer. Chemical shifts for $^1$H NMR spectra are reported (in parts per million) relative to internal tetramethylsilane ($Me_4Si$, $\delta = 0.0$ ppm) with $CDCl_3$ as solvent, to sodium 3-(trimethylsilyl)propionate-2,2,3,3-$d_4$ (TSP, $\delta = 0.0$ ppm) when $D_2O$ was the solvent, and to acetone ($CHD_2COCD_3$, $\delta = 2.04$ ppm) with $d_6$-acetone. $^{13}$C NMR spectra were recorded at 75 MHz. Chemical shifts for $^{13}$C NMR spectra are reported (in parts per million) relative to $CDCl_3$ ($\delta = 77.0$ ppm), relative to $CD_3COCD_3$ ($\delta = 29.8$ ppm), and relative to internal $CH_3OH$ ($\delta = 49.0$ ppm) or internal $CH_3CN$ ($\delta = 1.4$ ppm) in $D_2O$. FAB mass spectra were performed by University of South Carolina (Columbia, SC). Elemental analyses were performed by Atlantic Microlab Inc. (Norcross, GA). Melting points were uncorrected and were determined using a Mel-Temp II melting point apparatus.

Radial chromatography was carried out with a Harrison Associates Chromatotron using 1, 2 or 4 mm layers of silica gel 60 $PF_{254}$ containing gypsum (E. Merck). Silica gel 60 (40 - 63 μm, E. Merck) was used for flash chromatography. Analytical thin-layer chromatography (TLC) utilized precoated plates of silica gel 60 F-254 (0.25 mm, E. Merck or Whatman). TLC plates were visualized by immersion in anisaldehyde stain (by volume: 93% ethanol, 3.5% sulfuric acid, 1% acetic acid and 2.5% anisaldehyde) followed by heating. Dimethylformamide, N-methylformanilide and acetone were dried and stored over activated Linde 4Å molecular sieves under Ar. Tetrahydrofuran and diethyl ether were distilled under nitrogen from sodium benzophenone ketyl. *n*-Hexanes and TMEDA were distilled from sodium under Ar and stored over activated Linde 4Å molecular sieves under Ar. Organic solutions of products were dried over $MgSO_4$.

For $^1$H NMR quantitation of solute concentrations during microbial synthesis of *myo*-inositol and *myo*-2-inosose, solutions were concentrated to dryness under reduced pressure, concentrated to dryness one additional time from $D_2O$, and then redissolved in $D_2O$ containing a known concentration of TSP purchased from Lancaster Synthesis Inc. Concentrations were determined by comparison of integrals corresponding to each compound with the integral corresponding to TSP ($\delta = 0.00$ ppm) in

the $^1$H NMR. Protein concentrations were determined using the Bradford dye-binding procedure[1] by comparison with a standard curve prepared with bovine serum albumin. Protein assay solution was purchased from Bio-Rad. *E. coli* DH5α is available from Gibco BRL.

**Culture Medium.** All culture solutions were prepared in distilled, deionized water. LB medium (1 L) contained Bacto tryptone (10 g), Bacto yeast extract (5 g), and NaCl (10 g). M9 salts (1 L) contained $Na_2HPO_4$ (6 g), $KH_2PO_4$ (3 g), NaCl (0.5 g) and $NH_4Cl$ (1 g). M9 minimal medium (1 L) consisted of 1 L of M9 salts containing D-glucose (10 g), $MgSO_4$ (0.12 g), and thiamine hydrochloride (0.001 g). Ampicillin was added (0.05 g/L) where indicated. Solutions of M9 salts, $MgSO_4$, and glucose were autoclaved individually and then mixed. Ampicillin was sterilized through a 0.22 μm membrane. Solid medium was prepared by addition of 1.5% (w/v) Difco agar to medium.

Fermentation medium (1 L) contained $K_2HPO_4$ (7.5 g), ammonium iron(III) citrate (0.3 g), citric acid monohydrate (2.1 g), and concentrated $H_2SO_4$ (1.2 mL). The fermentation medium was adjusted to pH 7.0 by addition of concentrated $NH_4OH$ before autoclaving. The following supplements were added immediately prior to initiation of the fermentation: D-glucose (20 g), $MgSO_4$ (0.24 g), and trace minerals including $(NH_4)_6(Mo_7O_{24})\cdot 4H_2O$ (0.0037 g), $ZnSO_4\cdot 7H_2O$ (0.0029 g), $H_3BO_3$ (0.0247 g), $CuSO_4\cdot 5H_2O$ (0.0025 g), and $MnCl_2\cdot 4H_2O$ (0.0158 g). D-Glucose and $MgSO_4$ were autoclaved separately while trace minerals were sterilized through 0.22 μm membranes prior to addition to the medium.

**Genetic Manipulations.** Standard procedures were used for the construction, purification, and analysis of plasmid DNA.[2] *E. coli* DH5α served as the host strain for all plasmid constructions. The *INO1* open reading frame was amplified from pJH318[3] using PCR. Inclusion of *Eco*RI recognition sequences facilitated localization of *INO1* into the *Eco*RI site in pJF118EH[4] to afford pAD1.45A. Transcription of *INO1* in pAD1.45A utilized the vector-encoded *tac* promoter ($P_{tac}$) which was regulated by vector-encoded expression of $lacI^q$. Digestion of pD2625 with *Dra*I and *Eco*RV liberated a 1.9 kb *serA* fragment that was subsequently ligated into the *Sma*I site of pAD1.45A to provide pAD1.88A.

*E. coli* JWF1 was prepared by homologous recombination of a non-functional *serA* gene into *E. coli* RB791(W3110 *lacI*$^q$). Localization of the 1.9 kb *serA* fragment obtained from pD2625 into pMAK705[5] provided pLZ1.68A. Linearization of pLZ1.68A at the unique *Bam*HI site internal to *serA* followed by treatment with Klenow fragment and dNTP's and religation afforded pLZ1.71A. Homologous recombination[6] of the resulting non-functional *serA* locus of pLZ1.71A into RB791 afforded JWF1.

***myo*-Inositol 1-phosphate synthase activity.** Partial purification of cellular lysate was required to quantify *myo*-inositol 1-phosphate synthase activity over background cellular phosphatase activity. Cells were collected from 30 mL of fermentation broth by centrifugation at 2000*g* for 6 min at 4 °C. Cells were resuspended in 10 mL of resuspension buffer consisting of Tris·HCl (20 mM), pH 7.4, $NH_4Cl$ (10 mM), 2-mercaptoethanol (β-ME, 10 mM), phenylmethylsulphonyl fluoride (PMSF, 2 mM), and EDTA (1 mM). Resuspended cells were frozen at -80 °C for up to 4 days until purification was carried out.

Thawed cells were lysed by two passages through a French press at 2000 psi. Cellular debris was removed by centrifugation at 30000*g* for 30 min at 4 °C. Clarified cellular lysate containing approximately 200 mg of protein was loaded onto a DEAE cellulose column (5 x 25 cm) at 4 °C. The column was eluted with a step gradient of $NH_4Cl$ in the following buffer (Buffer A): Tris·HCl (20 mM), pH 7.4, β-ME (10 mM), PMSF (1 mM), and EDTA (1 mM). The step gradient consisted of 20 mL of Buffer A with $NH_4Cl$ (10 mM), 45 mL of Buffer A with $NH_4Cl$ (90 mM), and 100 mL of Buffer A with $NH_4Cl$ (150 mM). Fractions (9 mL) were collected throughout the step gradient. Fractions 10-18 were collected and concentrated to less than 5 mL using an Amicon Ultrafiltration Stirred Cell equipped with a PM10 membrane. Concentrated protein (1.5-2.0 mg) was used to measure *myo*-inositol 1-phosphate synthase activity. The *myo*-inositol 1-phosphate synthase activity was measured as previously reported[7] except that the assay solution contained Tris·HCl (20 mM), pH 7.4, $NH_4Cl$ (2 mM), and DTT (0.2 mM).

***myo*-Inositol.** Fermentations employed a 2.0 L working capacity B. Braun MD2 culture vessel. Utilities were supplied by a B. Braun Biostat MD controlled by a Dell Optiplex $Gs^+$ 5166 personal computer equipped with B. Braun MFCS/Win software. Temperature, pH, and glucose feeding were controlled with PID control loops. Temperature was maintained at 33 °C. pH was maintained at 7.0 by addition of concentrated $NH_4OH$ or 2 N $H_2SO_4$. Dissolved oxygen (D.O.) was measured using a Mettler-Toledo 12 mm sterilizable $O_2$ sensor fitted with an Ingold A-type $O_2$ permeable membrane. D.O. was maintained at 10% air saturation. Antifoam (Sigma 204) was added manually as needed.

Inoculants were started by introduction of a single colony of JWF1/pAD1.88A into 100 mL M9 medium containing ampicillin. The culture was grown at 37 °C with agitation at 250 rpm for 15 h and then transferred to the fermentation vessel. The initial glucose concentration in the fermentation medium was 20 g/L. Three staged methods were used to maintain D.O. levels at 10% air saturation during each fermentor run. With the airflow at an initial setting of 0.06 L/L/min, D. O. concentration was maintained by increasing impeller speed from its initial set point of 50 rpm to its preset maximum of 940 rpm. Approximately 7 h was required for the impeller speed to increase to 940 rpm. With the impeller constant at 940 rpm, the mass flow controller then maintained D.O. levels by increasing the airflow rate from 0.06 L/L/min to its preset maximum of 1.0 L/L/min over approximately 1.5 h. At constant impeller speed and constant airflow rate, D.O. levels were maintained at 10% saturation for the remainder of the fermentation by oxygen sensor-controlled glucose feeding. At the beginning of this stage, D. O. levels fell below 10% air saturation due to residual initial glucose in the medium. This lasted for approximately 50 min before glucose (60% w/v) feeding started. The PID control parameters were set to 0.0 (off) for the derivative control ($\tau_D$) and 999.9 s (minimum control action) for integral control ($\tau_I$). $X_p$ was set to 950% to achieve a $K_c$ of 0.1.

Samples (6 mL) of fermentation broth were taken at 6 h intervals starting at 12 h. isopropyl β-D-thiogalactopyranoside (4.8 mg) was added when both the impeller speed and airflow had reached the maximum settings, and again at 12 h and every 6 h thereafter. Cell densities were determined by dilution of fermentation broth with water (1:100) followed by measurement of absorption at 600 nm

($OD_{600}$). Dry cell weight (g/L) was obtained using a conversion coefficient of 0.43 g/L/$OD_{600}$. Fermentation broth was centrifuged to remove cells. Solute concentrations in cell-free broth were determined by $^1$H NMR. Fermentation broth (30 mL) was removed at designated times for assay of *myo*-inositol 1-phosphate synthase activity. The final concentration at 54 h of *myo*-inositol was 20.9 g/L synthesized in 8.7% yield (mol/mol) from glucose.

The fermentation broth (950-1200 mL) was centrifuged at 18000*g* for 35 min at 4 °C and the cells discarded. The resulting supernatant was acidified to pH 2.0 with concentrated $H_2SO_4$ and then centrifuged at 18000*g* for 20 min to remove precipitated proteins. The clear yellow supernatant was neutralized with concentrated $NH_4OH$. The solution was decolorized with Darco KB-B activated carbon (10 g/L) for 4 h with agitation at 50 rpm and subsequently filtered through Whatman 2 filter paper. The filtered material was washed with an additional 200 mL of water.

The combined filtrates were applied to a column of AG1-x8 (acetate form, 5 cm x 20 cm) at 4 °C and eluted with 1 L $H_2O$. The entire eluent (approximately 2.3 L) was then run through a column of Dowex 50 ($H^+$ form, 5 cm x 20 cm) at 4 °C and eluted with 500 mL $H_2O$. The resulting solution (approximately 2.8 L) was concentrated to 200 mL by boiling and then concentrated to dryness under reduced pressure. The resulting powder was dissolved in a minimal volume of $H_2O$, diluted with 6 volumes of MeOH, and stored at 4 °C to crystallize. Crystals were collected after a few days, washed with MeOH, allowed to air dry overnight, and dried under vacuum to yield white crystals (78 % recovery based on inositol quantified in crude fermentation broth). $^1$H NMR ($D_2O$) δ 4.06 (dd, *J*=3, 3 Hz, 1 H), 3.61 (dd, *J*=10, 9 Hz, 2 H), 3.53 (ddd, *J*=10, 3, 1 Hz, 2 H), 3.28 (ddd, *J*=9, 9, 1 Hz, 1 H). $^{13}$C NMR ($D_2O$) δ 45.3, 43.4, 43.2, 42.1.

***myo*-2-Inosose.**[8,13] A solution containing sorbitol (1.0 g) and yeast extract (0.05 g) in 10 mL distilled, deionized water was autoclaved for 25 min and cooled to rt. After inoculation with *Gluconobacter oxydans* ATCC 621 the culture was incubated in an orbital shaker at 200 rpm for 24 h at 30 °C. This *G. oxydans* culture was subsequently added to a second sterile solution containing inositol (12.0 g, 66.7 mmol), D-sorbitol (0.4 g), and yeast extract (2.0 g) in 400 mL

distilled, deionized water. After incubation in an orbital shaker at 200 rpm for 48 h at 30 °C, cells were removed by centrifugation. The resulting culture supernatant was concentrated to 75 mL, MeOH (400 mL) added, and the solution maintained at -20 °C for 12 h. Precipitate which formed was filtered, washed with MeOH, and dried to afford *myo*-2-inosose as a white powder (8.17 g, 69%). A second crop of *myo*-2-inosose (3.09 g, 26%) was obtained after maintaining the filtrate at -20 °C for an additional 12 h. mp 188 -192 °C. $^1$H NMR ($D_2O$): δ 4.25 (d, $J$ = 10 Hz, 2 H), 3.66 (dd, $J$ = 9, 9 Hz), 3.26 (m, 2 H). $^{13}$C NMR ($D_2O$): δ 206.0, 94.3, 76.2, 74.5, 74.1, 74.0, 73.3, 73.2.

**1,2,3,4-Tetrahydroxybenzene 1.** A solution of *myo*-2-inosose (11.0 g, 61.2 mmol) in 310 mL of degassed 0.5 M $H_2SO_4$ was refluxed under Ar. After 9 h, the solution was cooled to 4 °C and then adjusted to pH 4 by addition of saturated aqueous $NaHCO_3$. Concentration of the reaction solution to 100 mL was followed by continuous liquid-liquid extraction for 18 h using *t*-butyl methyl ether (500 mL). Upon concentration of the organic layer to 100 mL, a precipitate formed which was filtered, washed with cold hexanes, and dried to afford **1** (4.72 g, 54%) as a tan powder. Addition of hexanes (300 mL) to the filtrate followed by filtering, washing, and drying of the resulting precipitate afforded additional **1** (1.08 g, 12%). mp 162 - 164 °C. $^1$H NMR ($d_6$-acetone): δ 7.24 (s, 4 H), 6.20 (s, 2 H). $^{13}$C NMR ($d_6$-acetone): δ 139.7, 134.7, 106.2. Anal. Calcd for $C_6H_6O_4$: C, 50.71; H, 4.23. Found: C, 50.63; H, 4.32. HRMS (FAB) calcd for $C_6H_6O_4$ ($M+H^+$): 142.0266. Found: 142.0268. **Hydrogenation of 2,3-dibenzyloxy-1,4-benzoquinone 9.** A solution of **9** (0.18 g, 0.56 mmol) in EtOH (7.0 mL) was stirred with 10 % Pd on C (0.050 g) at rt under $H_2$ (1.0 atm) for 3 h. The solution was filtered through Celite ® and concentrated to afford a tan solid (0.079 g, 99%) which was identical by $^1$H and $^{13}$C NMR to **1** obtained from *myo*-2-inosose. **Hydrogenation of 2,3,4-tribenzyloxyphenol 11.** A solution of **11** (5.8 g, 14.1 mmol) in EtOH (100 mL) was stirred with 10% Pd on C (1.0 g) at rt under $H_2$ (1.0 atm) for 2 h. The solution was filtered through Celite® and concentrated. The

residue was purified by flash chromatography (MeOH/$CH_2Cl_2$, 1:9, v/v) affording a product which was was identical by $^1H$ and $^{13}C$ NMR to **1** obtained from *myo*-2-inosose.

**1,2,3-Tribenzyloxybenzene 8.**[9] Benzyl bromide (57 mL, 0.481 mol) and then $K_2CO_3$ (100 g, 0.725 mol) were added to a solution of pyrogallol (20 g, 0.159 mol) in 200 mL dry, degassed acetone under Ar. This reaction mixture was subsequently stirred for 30 min at rt and then for 24 h at reflux under Ar. A solution of NaOH (1.6 g) in MeOH (32 mL) was then added and the reaction refluxed for an additional 30 min. After cooling to rt, solids were filtered and washed with acetone. The filtrate was concentrated and the residue recrystallized from MeOH to afford **8** (52 g, 83%) as an off-white solid. mp 67 - 68 °C. $^1H$ NMR ($CDCl_3$): δ 7.44-7.19 (m, 15 H), 6.85 (dd, $J$ = 9, 9 Hz, 1 H), 6.57 (d, $J$ = 8.2 Hz, 2 H), 5.05 (s, 2 H), 5.02 (s, 4 H). $^{13}C$ NMR ($CDCl_3$): δ 152.9, 138.4, 137.8, 137.0, 128.4, 128.3, 128.0, 127.8, 127.6 (2), 127.3, 127.2, 123.5, 107.7, 75.0, 70.9.

**2,3-Dibenzyloxy-1,4-benzoquinone 9.** To a solution of 1,2,3-tribenzyloxybenzene **8** (2.0 g, 5.0 mmol) in HOAc (30 mL), $K_3Fe(CN)_6$ (0.82 g, 2.5 mmol) and 30% $H_2O_2$ (1.3 g, 11.5 mmol) were added and the resulting solution stirred at rt for 18 h. The solution was diluted with 50 mL $CH_2Cl_2$ and the organic layer subsequently washed with $H_2O$, saturated aqueous $NaHCO_3$ and brine. Drying and concentration resulted in a red oil. Purification by radial chromatography (2 mm thickness, EtOAc/hexane, 1:19, v/v) afforded **9** as a red oil. $^1H$ NMR ($CDCl_3$): δ 7.36-7.32 (m, 10 H), 6.58 (s, 2 H), 5.20 (s, 4 H). $^{13}C$ NMR ($CDCl_3$): δ 184.1, 145.2, 136.1, 134.6 128.5, 128.4, 128.1, 75.1. Anal. Calcd for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03. Found: C, 75.04; H, 5.06. HRMS (FAB) calcd for $C_{20}H_{16}O_4$ ($M + H^+$): 320.1049. Found: 320.1059.

**2,3,4-Tribenzyloxybenzaldehyde 10.**[10] $POCl_3$ (155 mL, 1.66 mol) was slowly added to *N*-methylformanilide (175 mL, 1.4 mol) at rt under Ar which resulted in formation of a

yellow solid. After 2 h, the solid was treated with a solution of 1,2,3-tribenzyloxybenzene **8** (20 g, 51 mmol) in anhydrous DMF (40 mL) and heated to 60 °C. After 3 h, the resulting crimson solution was cooled to rt and then poured into ice water (3 L) with vigorous stirring for 12 h. The resulting brown precipitate was filtered, washed with hexanes (3 x 100 mL) and finally recrystallized from MeOH to afford **10** (19.8 g, 93%) as a white powder. mp 73 - 74 °C. $^1$H NMR ($CDCl_3$): δ 10.11 (s, 1 H), 7.57 (d, $J$ = 9 Hz, 1 H), 7.44-7.28 (m, 15 H), 6.83 (d, $J$ = 9 Hz, 1 H), 5.21(s, 2 H), 5.16 (s, 2 H), 5.08 (s, 2 H); $^{13}$C NMR ($CDCl_3$): δ 188.8, 158.5, 155.9, 141.1, 136.9, 136.2, 135.8, 128.6, 128.5 (2), 128.3 (2), 128.2, 127.5, 124.0, 109.1, 76.8, 75.5, 70.9. Anal. Calcd for $C_{28}H_{24}O_4$: C, 79.22; H, 5.70. Found: C, 79.17; H, 5.80. HRMS (FAB) calcd for $C_{28}H_{24}O_4$ (M + H$^+$): 424.1675. Found: 424.1669.

**2,3,4-Tribenzyloxyphenol 11.**[10] A solution of 30% $H_2O_2$ (6 mL, 57.8 mmol) and 85% formic acid (32 mL, 600 mmol) was added dropwise to a solution of 2,3,4-tribenzyloxybenzaldehyde **10** (9.8 g, 23.1 mmol) in $CH_2Cl_2$ (50 mL) over 30 min at 0 °C. After 1 h of stirring at 0 °C, the reaction was stirred at rt for 24 h. The reaction was subsequently cooled to 4 °C and diluted with 10% (w/v) aqueous $Na_2SO_3$ (50 mL). The aqueous phase was washed with $CH_2Cl_2$ (3 x 40 mL). Drying and concentration afforded a brown oil which was dissolved in a methanolic solution of NaOMe (30 mL, 0.1 N) and refluxed. After 10 min, the solution was cooled to 4 °C and acidified with 6 N HCl. MeOH was removed *in vacuo*. The mixture was diluted with $H_2O$ (15 mL) followed by extraction of the aqueous phase with benzene (3 x 40 mL). Drying and concentration afforded **11** (9.0 g, 95%) as a brown oil. $^1$H NMR ($CDCl_3$): δ 7.45 - 7.31 (m, 15 H), 6.65 (d, $J$ = 9 Hz, 1 H), 6.58 (d, $J$ = 9 Hz, 1 H), 5.28 (s, 1 H), 5.12 (s, 2 H), 5.11 (s, 2 H), 5.04 (s, 2 H). $^{13}$C NMR ($CDCl_3$): δ 146.0, 144.0, 142.0, 139.6, 137.3, 137.1, 136.8, 128.4, 128.3 (2), 128.2, 127.9, 127.7, 127.4, 110.4, 109.0, 75.6, 75.3, 71.7. Anal. Calcd for $C_{27}H_{24}O_4$: C, 78.62; H, 5.87. Found: C, 78.71; H, 5.86. HRMS (FAB) calcd for $C_{27}H_{24}O_4$ (M + H$^+$): 412.1675. Found: 412.1673.

**1,2,3,4-Tetramethoxybenzene 12.**[11] A solution of 1,2,3,4-tetrahydroxybenzene **1** (8.4 g, 59 mmol) and dimethyl sulfate (37.5 mL, 0.396 mol) in EtOH (21 mL) was added dropwise to an 8.5 M aqueous solution of NaOH (42 mL) over 20 min at rt. After 2 h, the reaction was diluted with $H_2O$ (300) mL and cooled to -20 °C for 12 h. The resulting preciptitate was filtered, washed with $H_2O$, and then recrystallized from hexanes to afford **12** (8.12 g, 69%) as colorless needles. mp 84 - 85 °C. $^1$H NMR ($CDCl_3$): δ 6.58 (s, 2 H), 3.90 (s, 6 H) 3.82 (s, 6 H). $^{13}$C NMR ($CDCl_3$): δ 147.7, 143.3, 106.3, 61.1, 56.3. Anal. Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.44; H, 7.07.

**2,3,4,5-Tetramethoxytoluene 13.**[11] To a solution of 1,2,3,4-tetramethoxybenzene **12** (4.0 g, 20.2 mmol) and TMEDA (6 mL, 38.0 mmol) in hexanes (44 mL) and THF (80 mL) at 0 °C under Ar, *n*-BuLi in hexane (1.6 M, 25.6 mmol) was added dropwise over a 10 min period and the reaction stirred for 30 min at 0 °C under Ar. Subsequent to dropwise addition of $CH_3I$ (20 mL, 160 mmol) over an 8 min period, the reaction was stirred for 3 h at 0 °C under Ar and then quenched by addition of aqueous $NH_4Cl$ and ether (20 mL). The organic layer was sequentially washed with concentrated $NH_4OH$, water, and brine. Drying and concentration of the organic layer was followed by purification of the residue by flash chromatography (hexanes, hexanes/EtOAc, 19:1, v/v) to afford **13** as a clear oil (3.6 g, 83%). $^1$H NMR ($CDCl_3$): δ 6.45 (s, 1 H), 3.93 (s, 3 H), 3.87 (s, 3 H), 3.82 (s, 3 H), 3.79 (s, 3 H), 2.23 (s, 3 H). $^{13}$C NMR ($CDCl_3$): δ 149.0, 146.9, 145.3, 140.7, 125.7, 108.2, 61.0, 60.9, 60.5, 55.9, 15.7.

**Protected coenzyme $Q_3$ 14.**[12] *n*-BuLi (1.6 M, 0.9 mL) was added dropwise over a 15 min period to a solution of 1,2,3,4-tetramethoxytoluene **13** (0.212 g, 1 mmol) and TMEDA (0.3 mL, 1.9 mmol) in hexane (2.2 mL) at 0 °C under Ar. This yellow precipitate-containing reaction mixture was then stirred at 0 °C under Ar for 30 min, diluted with THF (4 mL) and ether (11 mL), followed by addition of CuCN (0.125 g, 1.4 mmol). After stirring for 30 min at 0 °C under Ar, the temperature was reduced to -78 °C, and a solution of farnesyl bromide (0.285 g, 1 mmol) in

hexane (2 mL) was dropwise added over a 30 min period. Further reaction for 3 h at -78 °C and subsequent slow warming to rt was followed by addition of saturated aqueous $NH_4Cl$ ( 10 mL) and ether (20 mL). Washing the organic phase with concentrated $NH_4OH$, water, and brine was followed by drying and concentration. Purification of the residue by radial chromatography (2 mm thickness, hexane/EtOAc, 9:1, v/v) afforded **14** as a clear oil (0.236 g, 57%). $^1H$ NMR ($CDCl_3$): δ 5.12-5.01 (m, 3 H), 3.90 (s, 6 H), 3.78 (s, 6 H), 3.32 (d, $J$ = 7 Hz, 2 H), 2.14 (s, 3 H), 2.08-1.91 (m, 8 H), 1.77 (s, 3 H), 1.66 (s, 3 H), 1.58 (s, 6 H). $^{13}C$ NMR ($CDCl_3$): δ 147.8, 147.6, 144.9, 144.6, 135.0, 134.9, 131.2, 129.2, 125.4, 124.3, 124.1, 122.8, 61.1, 60.6, 39.7, 26.7, 26.5, 25.7, 25.6, 17.6, 16.2, 15.9, 11.7.

**Coenzyme $Q_3$ 4.**[12] A suspension maintained at 0 °C resulting from addition of pyridine-2,6-dicarboxylate (0.125 g, 0.75 mmol) to a solution of protected coenzyme $Q_3$ **14** in $CH_3CN$ (1.4 mL) and water (0.6 mL) at 0 °C was reacted with a 0 °C solution of $(NH_4)_2Ce(NO_3)_6$ (0.411 g, 0.75 mmol) in $CH_3CN$ (0.4 mL) and water (0.4 mL) added dropwise over a 10 min period. After 40 min at 0 °C, the reaction was warmed to rt and stirred for 20 min. Water (10 mL) was added to the reaction mixture and the resulting solution extracted with $CH_2Cl_2$ (3x 100 mL). The combined organic phases were dried, concentrated, and purified by radial chromatography (1 mm thickness, hexane/EtOAc, 19:1, v/v) to afford **4** (0.053 g, 46%) as an orange oil. $^1H$ NMR ($CDCl_3$): δ 5.07 (dd, $J$ = 7, 7 Hz, 1 H), 5.05 (dd, $J$ = 7, 7 Hz, 1 H), 4.94 (dd, $J$ = 7, 7 Hz, 1 H), 3.99 (s, 3 H), 3.98 (s, 3 H), 3.18 (d, $J$ = 6.8 Hz, 2 H), 2.08-1.91 (m, 8 H), 2.01 (s, 3 H), 1.74 (s, 3 H), 1.67 (s, 3 H), 1.59 (s, 3 H), 1.58 (s, 3 H); $^{13}C$ NMR ($CDCl_3$): δ 184.7, 183.9, 144.3, 144.2, 141.6, 138.8, 137.6, 135.2, 131.3, 124.3, 123.8, 118.8, 61.1, 39.7, 26.7, 26.4, 25.7, 25.3, 17.6, 16.3, 16.0, 11.9; HRMS (FAB) calcd for $C_{24}H_{34}O_4$ ($M+H^+$): 386.2457. Found: 386.2461

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