SUPPORTING INFORMATION

General. For ^1H NMR quantitation of solute concentrations, 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 the sodium salt of 3-(trimethylsilyl)propionic-*2,2,3,3-d*$_4$ acid (TSP) purchased from Lancaster Synthesis Inc. Concentrations were determined by comparison of integrals corresponding to each compound with the integral corresponding to TSP (δ=0.00 ppm) in the ^1H NMR. All ^1H NMR spectra were recorded on a Varian VXR-300 FT-NMR Spectrometer (300 MHz).

Culture Medium. All medium was prepared in distilled, deionized water. 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), thiamine hydrochloride (0.001 g), L-phenylalanine (0.040 g), L-tyrosine (0.040 g), L-tryptophan (0.040 g), *p*-hydroxybenzoic acid (0.010 g), potassium *p*-aminobenzoate (0.010 g), and 2,3-dihydroxybenzoic acid (0.010 g). Ampicillin was added (0.05 g/L) where indicated. Solutions of M9 salts, $MgSO_4$, and glucose were autoclaved individually and then mixed. Aromatic amino acids, aromatic vitamins, and ampicillin were sterilized through 0.22-μm membranes.

Fermentation medium (1 L) contained K_2HPO_4 (7.5 g), ammonium iron (III) citrate (0.3 g), citric acid monohydrate (2.1 g), L-phenylalanine (0.7 g), L-tyrosine (0.7 g), L-tryptophan (0.35 g), and concentrated H_2SO_4 (1.2 mL). 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 or 23 g), $MgSO_4$ (0.24 g), *p*-hydroxybenzoic acid (0.010 g), potassium *p*-aminobenzoate (0.010 g), 2,3-dihydroxybenzoic acid (0.010 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 aromatic vitamins and trace minerals were sterilized through 0.22-μm membranes.

Fermentations. Fermentations employed a 2.0 L working capacity B. Braun M2 culture vessel. Utilities were supplied by a B. Braun Biostat MD that was controlled by a DCU-1. Data acquisition utilized a Dell Optiplex Gs+ 5166M 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.

Inoculants were started by introduction of a single colony into 5 mL of M9 medium containing ampicillin. The culture was grown at 37 °C with agitation at 250 rpm for 24 h and subsequently transferred to 100 mL of M9 medium containing ampicillin. After growth at 37 °C, 250 rpm for an additional 12 h, the inoculant was ready for transfer into the fermentation vessel. The initial glucose concentration in the fermentation medium was 20 g/L for SP1.1/pKD12.112 runs and 23 g/L for QP1.1/pKD12.112 runs. Three staged methods were used to maintain D.O. levels at 10% air saturation during the course of run. With the airflow at an initial setting of 0.06 L/L/min, D.O. concentration was maintained by increasing the impeller speed from its initial set point of 50 rpm to its preset maximum of 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 a preset maximum of 1.0 L/L/min. At constant impeller speed and constant airflow rate, D.O. levels were finally maintained at 10% air 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 1 h before glucose (65% w/v) feeding started. The PID control parameters were set to 0.0 (off) for the derivative control (τ_D) and 999.9 s (minimum control action) for integral control (τ_I). X_p was set to 950% to achieve a K_c of 0.1 and 125% to achieve a K_c of 0.8.

Samples (10 mL) of fermentation broth were taken at 6 h intervals. 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}. The remaining fermentation broth was centrifuged for 4 min using a Beckman microcentrifuge to obtain cell-free broth. Solute concentrations in the cell-free broth were determined by ^1H NMR.

Purification of Shikimic Acid from Fermentation Broth. The fermentation broth (1100-1200 mL) was centrifuged at 14000*g* for 20 min and the cells were discarded. The resulting supernatant was refluxed for 4 h, cooled to room temperature, and the pH adjusted to 2.5 by addition of concentrated H_2SO_4. After centrifugation at 14000*g* for 20 min, a clear yellow solution was poured away from the cellular debris and adjusted to pH 6.9 by addition of concentrated NH_4OH. The solution was combined with 5 g of Darco KB-B activated carbon, swirled at 50 rpm for 1-2 h, and then filtered through Whatman 5 filter paper. Filtered material was washed with an additional 250 mL of water. The combined filtrates were then treated in the same way with a second batch of activated carbon.

Following treatment of the solution with carbon, the dark color was less intense than prior to treatment, but the solution was not colorless. Addition of glacial acetic acid to a final concentration of 15% afforded a clear, yellow solution which was then eluted through a column of AG1-x8 (acetate form, 5 cm x 20 cm) at 4 °C. Following elution of the column with an additional 400 mL of 15% aqueous acetic acid, the combined eluents were passed through a column of Dowex 50 (H^+ form, 5 cm x 20 cm) at 4 °C which was then washed with 400 mL of 15% aqueous acetic acid. The eluents off the cation exchange column were combined and concentrated to approximately 150 mL by boiling and then to dryness by rotary evaporation, leaving a hard white solid (83% recovery through this step). Recrystallization from a mixture of methanol and ethyl acetate afforded shikimic acid as a fine white powder (61% recovery based on shikimic acid quantified in crude fermentation broth).

Purification of Quinic Acid from Fermentation Broth. The fermentation broth (1100-1200 mL) was centrifuged at 14000*g* for 20 min and the cells were discarded. The resulting supernatant was refluxed for 1 h, cooled to room temperature, and the pH adjusted to 2.5 by

addition of concentrated H_2SO_4. After centrifugation at 14000*g* for 20 min, a clear yellow solution was poured away from the cellular debris and adjusted to pH 6.9 by addition of concentrated NH_4OH. The solution was combined with 10 g of Darco KB-B activated carbon, swirled at 50 rpm for 1-2 h, and then filtered through Whatman 5 filter paper. Filtered material was washed with an additional 300 mL of water.

Following treatment with activated carbon, the solution was slightly gray in color. Addition of glacial acetic acid to a final concentration of 25% afforded a clear, yellow solution which was then eluted through a column of AG1-x8 (acetate form, 5 cm x 20 cm) at 4 °C. Following elution of the column with an additional 400 mL of 25% aqueous acetic acid, the combined eluents were passed through a column of Dowex 50 (H^+ form, 5 cm x 20 cm) at 4 °C which was then washed with 400 mL of 25% aqueous acetic acid. The eluents off the cation exchange column were combined and were concentrated to dryness by rotary evaporation, leaving a hard white solid (80% recovery through this step). Recrystallization from ethanol afforded a fine, white powder (52% recovery based on quinic acid quantified in crude fermentation broth).