Supporting Information

Organic Synthesis of Geranyl Sulfate Analogue:

Chemicals and reagents. All chemical reagents were of analytical grade, obtained from commercial suppliers, and used without further purification unless otherwise noted. With the exception of reactions performed in aqueous media, all reaction vessels were flame–dried before use. Reactions were performed under an N_2 atmosphere, except in the case of reactions performed in aqueous media, and liquid reagents were added via syringe unless otherwise noted. Tetrahydrofuran (THF) was distilled under N_2 from Na/benzophenone immediately before use and CH_2Cl_2 was dried over CaH_2 and distilled under a N_2 atmosphere. Flash chromatography was carried out with Merck 60 230–400 mesh silica gel. Analytical thin layer chromatography (TLC) was performed on glass–backed Uniplate GHLF silica gel plates and visualized by staining with ceric ammonium molybdate. Organic extracts were dried over Na_2SO_4, and solvents were removed with a rotary evaporator at reduced pressure (20 torr) unless otherwise noted. ^1H and ^{13}C NMR spectra were obtained with 400 MHz or 500 MHz Bruker spectrometers. Chemical shifts are reported in ™ ppm referenced to the solvent peak. Coupling constants (*J*) are reported in Hz.

Synthesis of SII. (Scheme S1) Acetic anhydride (1.2 ml, 13.0 mmol) was added to a solution of geraniol (SI) (1.0 g, 6.5 mmols) in pyridine (13.0 ml) at room temperature. The reaction was stirred overnight and was quenched with water (5.0 ml). The aqueous layer was extracted with ether (3 x 50 ml), and the combined organic extracts were washed with water (3 x 50 ml) and brine (1 x 50 ml), and then dried and concentrated. The product was purified by silica gel chromatography (20% Et_2O/hexanes), resulting in a yellow oil (1.3 g, 100%). ^1H NMR ($CDCl_3$, 400 MHz): ™ 1.55 (s, 3H), 1.63 (s, 3H), 1.66 (s, 3H), 2.01 (m, 5H), 2.05 (m, 2H), 4.53 (d, 2H, J = 7.2), 5.02 (t, 1H, J = 6.4), 5.22 (t, 1H, J = 6.8). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 16.3, 17.6, 20.9, 25.5, 26.2, 39.4, 61.2, 118.2, 123.6, 131.7, 142.1, 171.0.

Synthesis of SIII. (Scheme S1) Selenium dioxide (44.4 mg, 0.4 mmol) was dissolved in a mixture of CH_2Cl_2 (6.0 ml) and 70% *tert*–butyl hydrogen peroxide in water (w/v, 0.2 ml, 1.6 mmol) and stirred for 30 min. Compound SII (0.160 g, 0.8 mmols) was dissolved in CH_2Cl_2 (1.2 ml) and was added to the reaction and stirred for 24 h at room temperature. When TLC analysis showed depletion of starting material, $NaBH_4$ (45.4 mg, 1.2 mmol) was added, and the reaction was stirred for 1 h. The reaction was quenched with water (5 ml) and the organic layer was extracted with water (3 x 25 ml) and dried. The desired product (191.8 mg, 12%) was purified from a mixture of at least six compounds by column chromatography (gradient of 20 to 100% Et_2O/hexanes). ^1H NMR ($CDCl_3$, 400 MHz): ™ 1.55 (s, 3H), 1.63 (s, 3H), 1.66 (s, 3H), 2.01 (m, 5H), 2.05 (m, 2H), 4.53 (d, 2H, J = 7.2), 5.02 (t, 1H, J = 6.4), 5.22 (t, 1H, J = 6.8). ^{13}C NMR ($CDCl_3$, 400 MHz): δ 16.3, 17.6, 20.9, 25.5, 26.2, 39.4, 61.2, 118.2, 123.6, 131.7, 142.1, 171.0.

Synthesis of SIV. (Scheme S1) Sulfur trioxide–pyridine complex (215.7 mg, 1.4 mmol) was added to a solution of compound SIII (191.8 mg, 0.9 mmol) in THF (3.6 ml) at 0 °C. The reaction was stirred until TLC analysis showed depletion of starting material. The reaction was quenched with MeOH (2 ml), concentrated on a rotary evaporator, and the product was purified directly by column chromatography (gradient of 20 to 30% MeOH/$CHCl_3$), yielding the

pyridinium salt SIV (233.4 mg, 82% yield) as a white solid. ^{1}H NMR (MeOD, 500 MHz): ™ 2.09 (s, 3H), 2.12 (s, 3H), 2.43 (s, 3H), 2.50 (m, 2H), 2.58 (m, 2H), 4.11 (s, 2H), 4.93 (d, 2H, J = 22.5), 5.74 (t, 1H, J = 7.0), 5.88 (t, 1H, J = 6.5). ^{13}C NMR (MeOD, 500 MHz): δ 14.0, 16.3, 27.2, 40.1, 50.0, 55.4, 59.5, 75.2, 125.3, 130.2, 132.1, 139.0.

Supplementary Figure Legends

Scheme S1: Schematic for the organic synthesis of geranyl sulfate.

Figure S1: Enrichment of S881 after anion exchange separation. A) The negative ion mode FT–ICR mass spectrum of a crude lipid extract from *M. tuberculosis*. The major components of this extract identified in the negative ion mode are phosphatidyl inositol (PI), and phosphatidyl–inositol mannosides (PIMs). A zoom of this spectrum shows that S881 is a minor component of this extract, and is isobaric with another metabolite at m/z = 881.60 (inset). B) The FT–ICR mass spectrum of the purest fraction of S881 after separation. S881 is the characteristic peak in its purest fraction after anion exchange separation, and is completely separated from the contaminating isobar (inset).

Table S1: Generated elemental compositions within 3ppm of S881. The exact mass of S881 was measured at 881.5755 Da via FT–ICR MS with internal calibration. The molecular formula generation algorithm from the DataAnalysis software was used to generate elemental compositions within 3 ppm of the measured mass of S881, with the following restrictions: C≥49, N=even value, O≥4, S=1.

Table S2: Exact mass measurements of S881 dissociation ions. S881 was analyzed via FT–ICR MS^n and the resulting spectrum was calibrated internally to generate the listed dissociation ions.