Supporting Information

For

Total Synthesis of Eleuthoside A; Application of Rh-Catalyzed Intramolecular Cyclization of Diazonaphthoquinone.

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1. General Methods and Materials.
2. Experimental procedures and spectroscopic date of the starting materials and products.
3. Copies of 1H NMR and 13C NMR for starting materials and products.

**General Methods.** All reactions were carried out under a nitrogen atmosphere. 1H NMR (500.0 MHz) and 13C NMR (100.6 MHz, 125.7 MHz) spectra were recorded on a JEOL JNM-A500 in CDCl3 or CD3OD solutions. [In CDCl3, CHCl3 (for 1H, δ = 7.26) or CDCl3 (for 13C, δ = 77.0) was used as an internal standard. [In CD3OD [TMS (for 1H, δ = 0), CD3OD (for 1H, δ = 4.87, 3.31), or CD3OD (for 13C, δ = 49.1) was used as an internal standard]. IR spectra were recorded on a JEOL JIR-WINSPEC50. High-resolution mass spectra were obtained with a JEOL JMS-SX102A mass spectrometer. The melting points were uncorrected. Optical rotation was measured on a JASCO DIP-1000 digital polarimeter. Column chromatography and
preparative TLC (PTLC) were performed on silica gel (Fuji Silysia Silica gel PSQ-100B or Kanto Chemical Silica Gel 60N).

**Materials.** Anhydrous tetrahydrofuran (THF) was purchased from Wako Co. Ltd. Benzene and Toluene were distilled from P₂O₅ and stored over 4Å molecular sieves. Rh₂(oct)₄ and sodium azide were purchased from Wako Co. Ltd. and were used as received. Triethylamine was distilled from KOH and stored over KOH. Phosphonate 4, diester 6, acid 7 and naphthoate 8 were prepared and confirmed according to the reported procedures. (S. A. Snyder, T. C. Sherwood, A. G. Ross, *Angew. Chem. Int. Ed.*, 2010, 49, 5146).

**Naphthol 9**

![Naphthol 9](image)

NaH (60% dispersion in mineral oil, 1.96 g, 49.1 mmol) was added dropwise to a cooled solution of triethyl phosphonoacetate 3 (8.5 mL, 44.6 mmol) in THF (80 mL) at 0 °C. The resultant suspension was allowed to stir for 10 min at 0 °C. Then, t-butyl bromoacetate (7.5 mL, 53.5 mmol) was added dropwise, and the solution was allowed to stir overnight with slow warming to room temperature. Upon completion, the reaction contents were quenched with saturated NH₄Cl (75 mL), poured into water (50 mL), and extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with water (75 mL) and brine (75 mL), dried (MgSO₄), and concentrated. The resultant crude, colorless oil was purified by column chromatography (silica gel, CH₂Cl₂/MeOH, 19:1, Rᵢ = 0.48) to give phosphonate 4 (13 g, 90%) as a colorless oil. ¹H NMR (500 MHz, CDCl₃) δ 4.30–4.28 (m, 2 H), 4.18 (q, 2 H, J = 7.5 Hz), 4.09 (q, 4 H, J = 7.0 Hz), 2.98–2.93 (m, 1 H), 1.44 (s, 9 H), 1.33 (t, 6 H, 7.0 Hz), 1.27 (t, 3 H, J = 7.5 Hz). Phosphonate 4 (11.5 g, 34 mmol) in THF (50 mL) was added slowly over 10 min to a solution of NaH (60% dispersion in mineral oil, 2.22 g, 37.4 mmol) in THF (30 mL) at 0 °C. After that, a solution of bromomethoxy aldehyde 5 (6 g, 10 mmol) in THF (40 mL) was added portionwise and the reaction mixture was allowed to reach room temperature slowly. Upon completion (1 h), the reaction contents were quenched with water, and extracted with EtOAc (3 × 30 mL). The combined organic layers were then washed with brine (40 mL), dried (Na₂SO₄), and concentrated to give the desired diester 6 (13.8 g) as a yellow oil used directly in the next step, Rᵢ = 0.44 (hexane/EtOAc, 9:1). ¹H NMR (500 MHz, CDCl₃) δ 7.84 (s, 1 H),
7.48 (d, 1 H, J = 8.8 Hz), 6.94 (d, 1 H, J = 3.0 Hz), 6.78 (dd, 1 H, J = 3.0, 8.8 Hz), 4.27 (q, 2 H, J = 7.2 Hz), 3.79 (s, 3 H), 3.33 (s, 2 H), 1.45 (s, 9 H), 1.34 (t, 3 H, J = 7.2 Hz). Next, this diester 6 (13 g, 32.5 mmol) was dissolved in TFA: H2O, 7:1 (70 mL) and allowed to stir for 1 h at room temperature. Upon completion, the reaction contents were concentrated and azeotroped with toluene (3 × 50 mL) to give the desired monoacid intermediate 7 as a yellow oil (16 g), Rf = 0.55 (hexane/EtOAc, 4:1). 1H NMR (500 MHz, CDCl3) δ 7.89 (s, 1 H), 7.49 (d, 1 H, J = 8.9 Hz), 7.19 (d, 1 H, J = 3.0 Hz), 6.82 (dd, 1 H, J = 3.0, 8.9 Hz), 4.31 (q, 2 H, J = 7.1 Hz), 3.81 (s, 3 H), 3.34 (s, 2 H), 1.29 (t, 3 H, J = 7.1 Hz). This acid 7 was immediately dissolved in Ac2O (150 mL), and NaOAc (6 g, 61.4 mmol) was added at room temperature. The resultant yellow suspension was warmed to 140 °C and stirred at that temperature for 5 h. After completion, the reaction contents were cooled to room temperature, concentrated, and redissolved in EtOAc (75 mL). Then, the organic layer was poured into water (50 mL), and extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with saturated NaHCO3 (50 mL) and brine (50 mL), dried (Na2SO4), and concentrated. The resultant crude solid was purified by column chromatography (silica gel, hexane/EtOAc, 3:2, Rf = 0.11) to give naphthoate 8 (3 g, 30 % yield over 3 steps) as a yellow crystalline solid. 1H NMR (500 MHz, CDCl3) δ 8.88 (d, 1 H, J = 1.6 Hz), 7.76 (d, 1 H, J = 8.4 Hz), 7.73 (d, 1 H, J = 1.6 Hz), 6.82 (d, 1 H, J = 8.4 Hz), 4.45 (q, 2 H, J = 7.1 Hz), 3.93 (s, 3 H), 2.38 (s, 3 H), 1.44 (t, 3 H, J = 7.1 Hz). Finally, naphthoate 8 (0.5 g, 36.5 mmol, 1.0 eq.) was dissolved in EtOH (6 mL) and CH2Cl2 (4 mL) at 25 °C. Pd/C (10%, 0.312 g, 3.65 mmol, 0.1 eq.) was added and the reaction contents were placed under H2 atmosphere. After stirring the resultant suspension for 48 h at 25 °C, the reaction contents were filtered through a pad of celite. Then, NaOEt (0.357 g, 110 mmol, 3.0 eq.) was added portionwise to the filtrate at 0 °C. The resultant solution was warmed to 25 °C and allowed to stir overnight. Upon completion, the contents were cooled to 0 °C, quenched with the addition of 1 M HCl (10 mL), and concentrated. The reaction contents were redissolved in EtOAc (4 mL), poured into water (3 mL), and extracted with EtOAc (3 × 3 mL). The combined organic extracts were washed with water (3 mL) and brine (3 mL), dried (MgSO4), and concentrated to give the desired naphthol 9 (0.34 g, 90 %) as a yellow solid over 2 steps and after purification by column chromatography. Rf = 0.48 (silica gel, hexane/EtOAc, 7:3). 1H NMR (500 MHz, CDCl3) δ 9.34 (s, 1 H, br-\text{OH}), 8.05 (d, 1 H, J = 1.5 Hz), 7.53 (d, 1 H, J = 8.1 Hz), 7.45 (d, 1 H, J = 1.5 Hz), 7.39 (dd, 1 H, J = 7.9, 8.1 Hz), 6.90 (d, 1 H, J = 7.9 Hz), 4.43 (q, 2 H, J = 7.1 Hz), 4.12 (s, 3 H), 1.44 (t, 3 H, J = 7.1 Hz). 13C NMR (125 MHz, CDCl3) δ 163.1, 159.8, 137.7, 133.7, 122.8, 122.1, 120.0, 119.7, 111.7, 62.9, 56.7, 14.1. IR
(ATR): 3304 (OH), 2971,1700 (C=O) cm\(^{-1}\). HRMS (ESI\(^{+}\)) m/z [M]\(^{+}\)calcd for C\(_{14}\)H\(_{14}\)O\(_{4}\); 246.0892 found, 246.0994.

**Diazonaphthoquinone 11**

To a solution of 2-chloro-1,3-dimethylimidazolinium chloride\(^4\) (0.88 g, 2.82 mmol, 3.2 eq.) in acetonitrile (10 mL), sodium azide (0.43 g, 3.52 mmol, 3.9 eq.) was added at -20 °C, and the mixture was stirred for 30 min. Then, naphthol 9 (0.40 g, 0.77 mmol, 1 eq.) and triethylamine (0.50 mL, 1.85 mmol, 2.4 eq.) in THF (7 mL) were added to the mixture, which was stirred for 3 h. The reaction was quenched with water, and organic materials were extracted with EtOAc (3 × 5 mL). The combined organic extracts were washed with water and brine, and then dried over anhydrous Na\(_2\)SO\(_4\). The solvent was removed in vacuo to afford crude compound which was purified by crystallization (hexane/EtOAc) to give pure diazonaphthoquinone 11 as an orange crystalline solid (0.37 g, 85%). M.p. 130 °C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.60 (dd, 1 H, \(J = 8.1, 7.7\) Hz), 7.35 (s, 1 H), 7.19 (d, 1 H, \(J = 7.7\) Hz), 7.05 (d, 1 H, \(J = 8.1\) Hz), 4.43 (q, 2 H, \(J = 7.1\) Hz), 1.43 (t, 3H, \(J = 7.1\) Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 177.1, 163.1, 159.6, 137.5, 133.6, 122.8, 122.3, 120.0, 119.7, 111.7, 62.1, 56.2, 14.1 ppm. IR (ATR): 3567, 2111,1706, 1612, 1567, 1452, 1259, 1103 cm\(^{-1}\). HRMS (ESI\(^{+}\)) m/z [M]\(^{+}\)calcd for C\(_{14}\)H\(_{12}\)N\(_2\)O\(_{4}\); 272.0694 found, 272.0684.

**Diol 12**

Side product (see Entries 1,2, Table 1), yellow precipitate, M.p. 139 °C. \(R_F = 0.48\) (silica gel, toluene/acetone, 9:1). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 9.36 (s, 1 H, br-OH), 8.05 (d, 1 H, br-OH, \(J = 1.4\) Hz), 7.52 (d, 1 H, \(J = 8.0\) Hz), 7.45 (d, 1 H, \(J = 1.4\) Hz), 7.37 (dd, 1 H, \(J = 7.5, 8.0\) Hz), 6.89 (d, 1 H, \(J = 7.5\) Hz), 4.42 (q, 2 H, \(J = 7.1\) Hz), 4.07 (s, 3 H), 1.43 (t, 3 H, \(J = 7.1\) Hz).
Benzyl naphthol 13

Side product (see Entry 4, Table 1), orange precipitate, M.p. 179 °C. R_F = 0.72 (silica gel, toluene/acetone, 9:1).\textsuperscript{1}H NMR (500 MHz, CDCl_3) δ 9.73 (s, 1 H, br-OH), 7.83 (s, 1 H), 7.46 (d, 1 H, J = 8.1 Hz), 7.43 (dd, 1 H, J = 7.9, 8.1 Hz), 7.21-7.09 (m, 5 H, Ar-H), 6.85 (dd, 1 H, J = 7.9, 8.1 Hz), 4.49 (s, 2H), 4.29 (q, 2 H, J = 7.1 Hz), 4.04 (s, 3 H), 1.28 (t, 3 H, J = 7.1 Hz).

Ester 15

(-)-(1S)-Camphanoyl chloride 14 (0.33 g, 1.39 mmol) and DMAP (0.023 g, 0.186 mmol) were added to a solution of (±)-eleutherol (2) (0.076 g, 0.31 mmol) in pyridine (1.5 mL) at room temperature and the reaction mixture was stirred for 48 h. The reaction was stopped by adding water and the mixture was extracted with EtOAc (3 × 2 mL). Then, the organic extracts were washed with 2 M HCl (2 × 2 mL), saturated NaHCO_3, and brine and dried over Na_2SO_4 and concentrated. The residue was purified by PTLC (silica gel, toluene/acetone, 4:1, R_F = 0.6). Then, it was further purified by PTLC (silica gel, hexane/toluene/EtOAc, 6:2:2, R_F = 0.3) to finally afford yellow oil as non-separable diastereomers 15 (20 %).\textsuperscript{1}H NMR (500 MHz, CDCl_3) δ 8.34 (s, 1 H), 7.66 (d, 1 H, J = 8.0 Hz), 7.53 (dd, 1 H, J = 7.5, 8.0 Hz), 7.05 (d, 1 H, J = 7.5 Hz), 5.66 (q, 1 H, J = 6.5 Hz), 3.97 (s, 3 H), 2.64-2.58 (m, 1 H), 2.37-2.29 (m, 1 H), 2.08-2.01 (m, 1 H), 1.88-1.82 (m, 1 H), 1.73 (d, 3 H, J = 6.5 Hz), 1.21 (s, 3 H), 1.19 (s, 3 H), 1.18 (s, 3 H).

2,3,4,6-Tetra-O-acetyl-D-glucopyranosyl bromide (18) was prepared and its NMR spectral data were in agreement with those reported previously (R. S. Mancini, C. A. McClary, S. Anthonipillai, M. S. Taylor, J. Org. Chem., 2015, 80, 8501).

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The peracetate of eleuthoside A 20

Quinoline (2.5 mL) and Ag₂O (0.02 g, 0.026 mol, 1.08 eq.) were added to (0.025 g, 0.024 mol, 2 eq.) of 2,3,4,6–tetra-O-acetyl-α-D-glucopyranosyl bromide (18) and (0.010 g, 0.024 mol, 1 eq.) of eleutherol (2). Then, the mixture was stirred overnight at room temperature. Upon completion (TLC), 5 mL of CHCl₃ was added and the mixture was filtered. The filtrate was vigorously shaken with 5% H₂SO₄ and the CHCl₃ layer was then washed with water, dried over anhydrous calcium chloride and evaporated under vacuum. The crude product was purified twice by PTLC (toluene/acetone, 4:1; then hexane/EtOAc, 7:3) affording traces of α-glycoside 1% and our desired β-glycoside as pale yellow amorphous solid (0.0147 g, 64%) as diastereoisomeric mixture (1:1). M.p. 107 °C. Rf = 0.28 (Hexane/EtOAc, 7:3).¹H NMR (500 MHz, CDCl₃) δ 8.24, 8.21 (2 s, 1 H each, H-1), 7.63, 7.60 (2d, 1 H each, J = 8.0 Hz, H-2), 7.51 (2dd, 2 H, J = 6.0, 8.0 Hz, H-3), 7.04 (2d, 2 H J = 6.0 Hz, H-4), 5.85 (2 q, 1 H each, J = 6.6 Hz, H-6), 5.44 (2 dd, 2 H, J = 7.8, 9.9 Hz, H-2’), 5.33 (d, 1 H, J = 9.9 Hz, H-4’), 5.31 (d, 2 H, J = 7.8 Hz, H-1’), 5.20 (2 dd, 2 H, J = 9.3, 9.9 Hz, H-3’), 4.27 (2 dd, 1 H each, J = 4.8, 12.4 Hz, H-6b’), 4.12-4.10 (m, 1 H, H-4’), 4.04-4.02 (2s, 3 H each, OCH₃), 3.86 (2dd, 1 H each, J = 2.4, 12.4 Hz, H-6a’), 3.58-3.53 (m, 2 H, H-5’), 2.18, 2.09, 2.07, 2.05, 2.02, 2.01, 1.92, 1.81 (8s, 3 H each, OCOCH₃×8), 1.78 (2d, 3 H each, J = 6.6 Hz, 7-CH₃).¹³C NMR (125 MHz, CDCl₃) δ 170.3, 170.2, 169.8, 169.6, 169.4, 169.3, 169.2, 169.2, 156.1, 155.5, 145.6, 144.8, 139.6, 137.8, 137.7, 136.0, 127.3, 127.0, 124.9, 123.7, 123.7, 123.0, 122.6, 122.3, 108.6, 108.2, 101.4, 100.6, 78.8, 77.6, 72.9, 72.5, 71.9, 71.9, 71.5, 68.6, 68.2, 61.3, 61.2, 60.4, 55.6, 55.4, 21.0, 20.8, 20.7, 20.6, 20.6, 20.5, 20.4, 20.3, 20.2, 19.0, 14.2. IR (ATR): 1748, 1587, 1362, 1035 cm⁻¹. HRMS (FAB⁺) m/z [M+H]+ calcd for C₂₈H₃₁O₁₃; 575.1765 found, 575.1764.