Supporting Information

Experimental Procedures and Characterization Data

A Practical Synthesis of (–)-Kainic Acid

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General Remarks: All melting points were determined with a Stanford Research Systems OptiMelt melting point apparatus and are uncorrected. Optical rotations were measured on a JASCO P-1020 polarimeter at room temperature, using the sodium D line. Infrared spectra were recorded with a Perkin-Elmer spectrum 100 spectrometer. Nuclear magnetic resonance (^1H NMR (400 MHz), ^{13}C NMR (100 MHz)) spectra were determined on a JEOL JNM-ECA-400 or –ECX-400P spectrometer. Chemical shifts for ^1H NMR are reported in parts per million (δ value) downfield from tetramethylsilane, using tetramethylsilane and/or residual solvents as an internal standard. Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad peak. Chemical shifts for ^{13}C NMR are reported in parts per million relative to the center line of a triplet at 77.0 ppm or ppm from tetramethylsilane as the internal standard. Chemical shifts in D_2O are reported in ppm relative to the singlet at 30.9 ppm for acetone. Measurements of mass spectra were performed with a JEOL JMS-SX-102X mass spectrometer. Data for elemental analyses are within $\pm 0.3\%$ of the theoretical values, and were determined by a Yanaco CHN-corder MT-6. Unless otherwise noted, all the experiments were carried out using anhydrous solvents under an atmosphere of argon. Throughout this study, Merck precoated TLC plates (Silica gel 60 F254, 0.25 mm) were used for thin layer chromatographic (TLC) analysis, and all of the spots were visualized using UV light followed by coloring with phosphomolybdic acid or ninhydrine. Silica gel 60N (40–100 μm ; Kanto Chemical Co., Inc., Tokyo, Japan) was used for the flash column chromatography.

(1*S*,4*S*,6*S*)-1-Methyl-4-(prop-1-en-2-yl)-7-oxabicyclo[4.1.0]heptan-2-one (4)

To a solution of (+)-carvone (**2**) (100 g, 0.666 mol) in methanol (666 mL) was added 4.0 M aqueous sodium hydroxide (57.9 mL) at 0 °C. To this was added 30% hydrogen peroxide (82.7 mL, 0.799 mol) dropwise over a period of 1 h at 0 °C. After stirring for 1 h, the reaction was quenched with aqueous saturated sodium sulfite. The resulting mixture was filtered through a Celite pad, and the organic solvent of the filtrate was removed under reduced pressure. The aqueous mixture was extracted with ethyl acetate three times. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The crude product was purified by distillation (95–96 °C, 2.0 Torr) to give **4** (98.5 g, 89.0%) as a colorless oil. R_f = 0.6 (ethyl acetate/hexane = 1/2). $[\alpha]_D^{24}$ = -79.4 (c 1.33, CHCl_3). IR (ATR, cm^{-1}): 1705, 1439, 1118, 889, 814. ^1H NMR (CDCl_3 , 400 MHz): δ 4.79 (1H, s), 4.72 (1H, s), 3.45 (1H, d, J = 3.0 Hz), 2.68–2.76 (1H, m), 2.59 (1H, ddd, J = 17.6, 4.8, 1.2 Hz), 2.38 (1H, dt, J = 14.7, 3.0 Hz), 2.03 (1H, dd, J = 17.6, 11.5 Hz), 1.90 (1H, dd, J = 14.7, 11.5 Hz), 1.72 (3H, s), 1.42 (3H, s). ^{13}C NMR (CDCl_3 ,

100 MHz): δ 205.3, 146.2, 110.4, 61.2, 58.7, 41.7, 34.9, 28.6, 20.5, 15.2. HRCIMS Calcd for $C_{10}H_{15}O_2$ $[M+H]^+$: 167.1072; Found: 167.1063.

2-((3S)-2-(Iodomethyl)-2-methyl-5-oxotetrahydrofuran-3-yl)acetaldehyde (**6**)

To a solution of **4** (98.4 g, 0.592 mol) in tetrahydrofuran (500 mL) and water (100 mL) was added concentrated sulfuric acid (9.47 mL, 0.178 mol). After stirring for 10 h at reflux, the reaction mixture was neutralized with aqueous saturated sodium bicarbonate. After removal of the organic solvent of the mixture under reduced pressure, the aqueous mixture was extracted with ethyl acetate three times. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure to give a crude diol as a yellow oil, which was used to the next reaction without purification. To a solution of the crude diol in 2-propanol (1000 mL) and water (1000 mL) was added sodium periodate (291 g, 1.36 mol) at 0 °C. After stirring for 4 h at 0 °C, the reaction mixture was warmed to room temperature and stirring was continued for 16 h. The mixture was filtered through a Celite pad, and the organic solvent of the filtrate was removed under reduced pressure. The aqueous phase was saturated with sodium chloride, and extracted with ethyl acetate three times. The combined organic layers were extracted with aqueous saturated sodium carbonate. The aqueous extract was saturated with sodium chloride, acidified with concentrated hydrochloric acid until pH 2, and then extracted with ethyl acetate three times. The combined organic extracts were washed with brine, dried over sodium sulfate, filtered, and evaporated under reduced pressure to give a crude acid as a yellow oil. To a solution of the crude acid in dichloromethane (390 mL) and water (390 mL) added sodium bicarbonate (99.5 g, 1.18 mol) at 0 °C. To the mixture was added a solution of iodine (150 g, 0.592 mol) and potassium iodide (295 g, 1.78 mol) in water (592 mL). After stirring for 30 min, the reaction quenched with sodium thiosulfate, extracted with dichloromethane three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure to give **6** (109 g, 65.1%) as a yellow oil. This material was obtained as a 1:0.6 mixture of diastereomers, which were separated by preparative thin layer chromatography for characterization. The diastereomeric ratio was determined by $^1\text{H-NMR}$.

Major isomer: R_f = 0.25 (ethyl acetate/hexane = 1/1). $[\alpha]_D^{26} = +24.5$ (c 0.65, CHCl_3). IR (ATR, cm^{-1}): 1765, 1718, 1382, 1257, 1125, 1043, 955, 911. $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ 9.82 (1H, s), 3.30 (2H, s), 2.89-2.98 (3H, m), 2.75-2.82 (1H, m), 2.45-2.52 (1H, m), 1.64 (3H, s). $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz): δ 198.5, 174.1, 84.1, 43.4, 38.0, 35.4, 27.1, 8.6. HRCIMS Calcd for $\text{C}_8\text{H}_{12}\text{IO}_3$ $[M+H]^+$:

282.9831; Found: 282.9876.

Minor isomer: $R_f = 0.2$ (ethyl acetate/hexane = 1/1). $[\alpha]_D^{26} = +17.5$ (c 0.55, CHCl_3). IR (ATR, cm^{-1}): 1769, 1719, 1383, 1267, 1165, 1037, 926. ^1H NMR (CDCl_3 , 400 MHz): δ 9.80 (1H, s), 3.49 (1H, d, $J = 11.0$ Hz), 3.45 (1H, d, $J = 11.0$ Hz), 3.03-3.11 (1H, m), 2.98 (1H, dd, $J = 17.7, 8.6$ Hz), 2.89 (1H, dd, $J = 18.3, 4.3$ Hz), 2.64 (1H, dd, $J = 18.3, 9.8$ Hz), 2.29 (1H, dd, $J = 17.7, 9.2$ Hz), 1.48 (3H, s). ^{13}C NMR (CDCl_3 , 100 MHz): δ 198.5, 173.4, 84.3, 45.2, 36.8, 35.3, 21.2, 13.7. HRCIMS Calcd for $\text{C}_8\text{H}_{12}\text{IO}_3[\text{M}+\text{H}]^+$: 282.9831; Found: 282.9851.

2-((3S)-2-(Iodomethyl)-2-methyl-5-oxotetrahydrofuran-3-yl)acetic acid (**7**)

To a solution of **6** (109 g, 0.385 mol) in *tert*-butyl alcohol (385 mL) and tetrahydrofuran (193 mL) was added 2-methyl-2-butene (419 mL, 3.08 mol) at 0 °C. To the mixture was added a solution of sodium chlorite (69.6 g, 0.770 mol) and sodium dihydrogenphosphate dihydrate (300 g, 1.93 mol) in water (635 mL) dropwise a period of 1 h at 0 °C. After stirring for 1 h, the mixture was warmed to room temperature, and extracted with ethyl acetate three times. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue was diluted with ethyl acetate and extracted with aqueous saturated sodium bicarbonate solution. The aqueous phase was acidified with concentrated hydrochloric acid until pH 2, and then extracted with ethyl acetate three times. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure to give **7** (99.7 g, 86.7%, 1:0.6 diastereomeric mixture) as a pale yellow solid. IR (ATR, cm^{-1}): 2971, 1764, 1700, 1410, 1221, 1152, 960, 912. ^1H NMR (CDCl_3 , 400 MHz): δ 3.50 (0.6H, d, $J = 11.0$ Hz), 3.44 (0.6H, d, $J = 11.0$ Hz), 3.33 (1H, d, $J = 11.0$ Hz), 3.30 (1H, d, $J = 11.0$ Hz), 2.87-3.04 (2+1.2H, m), 2.78 (1H, dd, $J = 16.5, 4.9$ Hz), 2.73 (0.6H, dd, $J = 16.5, 4.9$ Hz), 2.38-2.66 (2+1.2 H, m), 1.65 (3H, s), 1.50 (1.8H, s). ^{13}C NMR (CDCl_3 , 100 MHz): δ 176.1, 176.1, 174.1, 173.5, 84.4, 84.2, 40.3, 38.8, 35.4, 35.3, 35.1, 33.5, 27.1, 21.0, 13.6, 8.3. HRCIMS Calcd for $\text{C}_8\text{H}_{12}\text{IO}_4$ $[\text{M}+\text{H}]^+$: 298.9780; Found: 298.9811.

Methyl (((3*R*)-2-(iodomethyl)-2-methyl-5-oxotetrahydrofuran-3-yl)methyl)carbamate (8**)**

To a suspension of **7** (99.7 g, 0.334 mmol) in toluene (1100 mL) was added triethylamine (60.5 mL, 0.434 mol) and diphenylphosphoryl azide (89.9 mL, 0.401 mmol). After stirring for 2 h at room temperature, the mixture was heated at 110 °C for 30 min. After cooling to 75 °C, to the mixture was added methanol (301 mL, 6.68 mol). After stirring for 7 h at 75 °C, the reaction was diluted with water, and extracted with ethyl acetate three times. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (ethyl acetate/hexane = 3/1 to 1/1) to give **8** (85.5 g, 78.3%, 1:0.6 diastereomeric mixture) as a yellow oil. R_f = 0.2 (ethyl acetate/hexane = 1/1). IR (ATR, cm^{-1}): 2950, 1766, 1698, 1529, 1248, 955. ^1H NMR (CDCl_3 , 400 MHz): δ 4.84 (1H, br s), 4.77 (0.6H, br s), 3.69 (3+1.8H, s), 3.56-3.60 (1H, m), 3.49 (0.6H, d, J = 11.0 Hz), 3.25-3.41 (3+1.8 H, m), 2.62-2.85 (3+1.2 H, m), 2.47-2.49 (0.6H, m), 1.64 (3H, s), 1.52 (1.8H, s). ^{13}C NMR (CDCl_3 , 100 MHz): δ 173.9, 173.4, 157.1, 157.0, 84.1, 84.0, 52.5, 44.5, 43.1, 41.3, 40.2, 33.8, 33.7, 27.7, 20.7, 14.2, 8.2. HRCIMS Calcd for $\text{C}_9\text{H}_{15}\text{INO}_4[\text{M}+\text{H}]^+$: 328.0046; Found: 328.0058.

***tert*-Butyl 2-(((3*S*,4*R*)-5-(iodomethyl)-4-(((methoxycarbonyl)amino)methyl)-5-methyl-2-oxotetrahydrofuran-3-yl)acetate (**9**)**

To a solution of lithium hexamethyldisilazide (ca. 1.6 mol/mL in tetrahydrofuran, 406 mL, 0.650 mol) in tetrahydrofuran (550 mL) was added a solution of **8** (85.5 g, 0.260 mol) in tetrahydrofuran (350 mL) dropwise over a period of 45 min at $-78\text{ }^\circ\text{C}$. After stirring for 15 min, to the mixture was added *tert*-butyl bromoacetate (76.8 mL, 0.520 mol). After stirring for 1 h, the mixture was quenched with a solution of acetic acid (44.9 mL, 0.780 mol) in tetrahydrofuran (100 mL), warmed to room temperature, diluted with water, and extracted with ethyl acetate three times. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and

evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (ethyl acetate/hexane = 4/1 to 1/1) to give **9** (93.6 g, 81.6%) as a yellow oil. This material was obtained as a 1:0.6 mixture of two diastereomers due to the stereogenic center at the γ -position of the lactone. The diastereomeric ratio was determined by $^1\text{H-NMR}$, and the diastereomers were separated by preparative thin layer chromatography for characterization.

Major isomer: $R_f = 0.5$ (ethyl acetate/hexane = 1/1). $[\alpha]_D^{26} = -29.7$ (c 0.65, CHCl_3). IR (ATR, cm^{-1}): 2980, 1769, 1709, 1525, 1367, 1250, 1149. $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ 5.29 (1H, s), 3.69 (3H, s), 3.41-3.50 (4H, m), 3.10-3.16 (1H, m), 2.93 (1H, dd, $J = 17.7, 2.4$ Hz), 2.45-2.54 (2H, m), 1.65 (3H, s), 1.47 (9H, s). $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz): δ 175.2, 171.3, 157.1, 82.6, 82.1, 52.4, 51.0, 40.5, 39.1, 35.8, 28.0, 27.9, 9.1. HRCIMS Calcd for $\text{C}_{15}\text{H}_{25}\text{IO}_6$: 442.0727; Found: 442.0743.

Minor isomer: $R_f = 0.45$ (ethyl acetate/hexane = 1/1). $[\alpha]_D^{25} = +34.1$ (c 0.50, CHCl_3). IR (ATR, cm^{-1}): 2978, 1772, 1727, 1700, 1538, 1295, 1250, 1156, 1016. $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ 5.22 (1H, s), 3.69 (3H, s), 3.57 (1H, d, $J = 11.0$ Hz), 3.45 (1H, d, $J = 11.0$ Hz), 3.37-3.42 (2H, m), 2.90-2.99 (2H, m), 2.48-2.58 (2H, m), 1.51 (3H, s), 1.48 (9H, s). $^{13}\text{C NMR}$ (CDCl_3 , 100 MHz): δ 174.7, 171.4, 157.0, 82.5, 82.1, 52.4, 49.4, 40.9, 40.3, 35.6, 28.0, 20.8, 14.4. HRCIMS Calcd for $\text{C}_{15}\text{H}_{25}\text{IO}_6[\text{M}+\text{H}]^+$: 442.0727; Found: 442.0720.

(3*S*,4*S*)-Methyl

3-(2-(*tert*-butoxy)-2-oxoethyl)-2-oxo-4-(prop-1-en-2-yl)pyrrolidine-1-carboxylate (**11**)

To a solution of **9** (93.6 g, 0.212 mol) in ethanol (630 mL) was added zinc (69.3 g, 1.06 mol) and acetic acid (61.0 mL, 1.06 mol) at 0 °C. After stirring for 3 h, the reaction mixture was filtered through a Celite pad, and evaporated under reduced pressure. The mixture was diluted with water, and extracted with ethyl acetate three times. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure to give a crude acid as a yellow oil. To a solution of the crude acid in dichloromethane (1000 mL) was added diethylphosphoryl cyanide (48.3 g, 0.318 mol) and triethylamine (136 mL, 0.848 mol) at room temperature. After stirring for 15 h, the mixture was quenched with aqueous saturated sodium bicarbonate, and extracted with dichloromethane three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (ethyl acetate/hexane = 6/1) to give **11** (37.6 g, 59.6%) as a white solid. $R_f = 0.6$ (ethyl acetate/hexane = 1/1). mp 94-95 °C (hexane). $[\alpha]_D^{25} = +17.2$ (c 0.50, CHCl_3). IR (ATR, cm^{-1}): 1749, 1442, 1361, 1317, 1244, 1149, 894. $^1\text{H NMR}$

(CDCl₃, 400 MHz): δ 4.88 (1H, t, J = 1.5 Hz), 4.78 (1H, s), 3.88 (3H, s), 3.79-3.84 (2H, m), 3.19-3.20 (2H, m), 2.77 (1H, dd, J = 17.7, 3.7 Hz), 2.23 (1H, dd, J = 17.7, 9.8 Hz), 1.61 (3H, s), 1.44 (9H, s). ¹³C NMR (CDCl₃, 100 MHz): δ 173.9, 171.0, 152.1, 142.2, 115.5, 81.0, 53.7, 48.9, 43.2, 41.0, 31.8, 28.0, 19.9. HRCIMS Calcd for C₁₅H₂₄NO₅ [M+H]⁺: 298.1654; Found: 298.1688. Anal. Calcd for C₁₅H₂₃NO₅: C, 60.59; H, 7.80; N, 4.71, Found: C, 60.42; H, 7.65; N, 4.50.

(3*S*,4*S*)-Methyl

3-(2-(*tert*-butoxy)-2-oxoethyl)-2-methoxy-4-(prop-1-en-2-yl)pyrrolidine-1-carboxylate (**12**)

To a solution of **11** (37.6 g, 0.126 mol) in tetrahydrofuran (630 mL) was added lithium tri-*tert*-butoxyaluminum hydride (41.7 g, 0.164 mol) at 0 °C. After stirring for 1 h, the mixture was quenched with aqueous saturated ammonium chloride, filtered through a Celite pad, and evaporated under reduced pressure. The mixture was diluted with aqueous saturated potassium sodium tartarate, and extracted with ethyl acetate three times. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure to give a residual aminal as a yellow oil. To a solution of the aminal in methanol (420 mL) was added pyridinium *p*-toluenesulfonate (1.58 g, 6.30 mmol) at 0 °C. After stirring for 15 h, the reaction mixture was quenched with aqueous saturated sodium bicarbonate, and extracted with ethyl acetate three times. The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (ethyl acetate/hexane = 10/1) to give **12** (31.0 g, 78.5%) as a colorless oil. This material was obtained as a mixture of rotamers. R_f = 0.6 (ethyl acetate/hexane = 1/1.5). $[\alpha]_D^{25}$ = -38.9 (c 1.15, CHCl₃). IR (ATR, cm⁻¹): 1709, 1445, 1367, 1147, 1077. ¹H NMR (DMSO-*d*₆, 400 MHz, 100 °C): δ 4.93 (1H, d, J = 1.2 Hz), 4.90 (1H, s), 4.71 (1H, s), 3.65 (3H, s), 3.30 (3H, s), 3.27-3.43 (2H, m), 3.05-3.12 (1H, m), 2.53-2.55 (1H, m), 2.02 (1H, dd, J = 16.3, 4.8 Hz), 1.83 (1H, dd, J = 16.3, 10.3 Hz), 1.71 (3H, s), 1.42 (9H, s). ¹³C NMR (DMSO-*d*₆, 100 MHz, 100 °C): δ 170.4, 140.7, 111.5, 92.4, 79.7, 54.7, 51.6, 45.8, 43.4, 41.8, 31.3, 27.3, 27.1, 21.8. HRFABMS Calcd for C₂₀H₃₉N₂O₇ [M+diethanolamine+H]⁺: 419.2757; Found: 419.2716.

(2*S*,3*S*,4*S*)-methyl 3-(2-(*tert*-butoxy)-2-oxoethyl)-2-cyano-4-(prop-1-en-2-yl)pyrrolidine-1-carboxylate (13a) and (2*R*,3*S*,4*S*)-methyl 3-(2-(*tert*-butoxy)-2-oxoethyl)-2-cyano-4-(prop-1-en-2-yl)pyrrolidine-1-carboxylate (13b)

To a solution of **12** (134 mg, 0.428 mmol) and trimethylsilyl cyanide (0.268 mL, 2.14 mmol) in dichloromethane (4.0 mL) was added boron trifluoride diethyl etherate (18.3 mL, 0.148 mol) at $-60\text{ }^{\circ}\text{C}$. After stirring for 1 h, the mixture was quenched with aqueous saturated sodium bicarbonate, and extracted with dichloromethane three times. The combined organic extracts were dried over anhydrous sodium sulfate, filtered, and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (ethyl acetate/hexane = 4/1) to give **13a** (96.6 mg, 73.4%) as a white solid and **13b** (34.5 mg, 26.1%) as a colorless oil.

13a (This material was obtained as a mixture of rotamers): Rf = 0.6 (ethyl acetate/hexane = 1/1.5). mp $130\text{--}132\text{ }^{\circ}\text{C}$ (hexane-ethyl acetate). $[\alpha]_{\text{D}}^{23} = -63.4$ (*c* 0.53, CHCl_3). IR (ATR, cm^{-1}): 2242, 1715, 1452, 1375, 1160. ^1H NMR (CDCl_3 , 400 MHz): δ 5.00 (1H, s), 4.73 (0.5 H, s), 4.70 (0.5H, s), 4.52 (0.5H, s), 4.50 (0.5H, s), 3.80 (1.5H, s), 3.78 (1.5H, s), 3.60–3.70 (1H, m), 3.37–3.48 (1H, m), 3.13–3.23 (1H, m), 2.96–3.02 (1H, m), 2.17–2.25 (1H, m), 1.97–2.05 (1H, m), 1.78 (3H, s), 1.46 (9H, s). ^{13}C NMR (CDCl_3 , 100 MHz): δ 170.6, 170.3, 154.9, 154.4, 139.9, 139.6, 118.3, 118.1, 113.7, 113.5, 81.8, 53.3, 53.2, 52.3, 51.8, 46.9, 46.7, 46.5, 45.7, 42.9, 41.9, 32.6, 32.5, 28.1, 28.0, 22.7, 22.6. HRCIMS Calcd for $\text{C}_{16}\text{H}_{25}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$: 309.1814; Found: 309.1791. Anal. Calcd for $\text{C}_{16}\text{H}_{24}\text{N}_2\text{O}_4$: C, 62.26; H, 7.85; N, 9.01, Found: C, 62.32; H, 7.84; N, 9.08.

13b (This material was obtained as a mixture of rotamers): Rf = 0.5 (ethyl acetate/hexane = 1/1.5). $[\alpha]_{\text{D}}^{23} = +45.7$ (*c* 0.65, CHCl_3). IR (NaCl, cm^{-1}): 2243, 1715, 1433, 1373, 1155. ^1H NMR (CDCl_3 , 400 MHz): δ 5.03 (1H, s), 4.88 (1H, brs), 4.81 (0.5H, s), 4.79 (0.5H, s), 3.81 (1.5H, s), 3.78 (1.5H, s), 3.51–3.67 (2H, m), 3.05–3.13 (1H, m), 2.87–2.94 (1H, m), 2.53–2.56 (2H, m), 1.81 (3H, s), 1.46 (9H, s). ^{13}C NMR (CDCl_3 , 100 MHz): δ 170.7, 170.5, 154.9, 154.5, 141.6, 116.6, 116.2, 115.4, 115.3, 81.6, 53.3, 53.2, 51.5, 50.9, 50.3, 49.8, 46.8, 45.8, 40.2, 39.1, 33.5, 33.4, 28.0, 22.7. HRCIMS Calcd for $\text{C}_{16}\text{H}_{25}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$: 309.1814; Found: 309.1820.

(–)-Kainic acid (1)

To a solution of **12** (31.0 g, 98.9 mmol) and trimethylsilyl cyanide (37.1 mL, 0.297 mol) in dichloromethane (495 mL) was added boron trifluoride diethyl etherate (18.3 mL, 0.148 mol) at –60 °C. After stirring for 1 h, the mixture was quenched with aqueous saturated sodium bicarbonate, and extracted with dichloromethane three times. The combined organic extracts were dried anhydrous over sodium sulfate, filtered, and evaporated under reduced pressure to give a crude nitrile. To a suspension of the crude nitrile in water (198 mL) was added sodium hydroxide (79.1 g, 1.98 mol). After stirring for 18 h at reflux, the alcohols generated in situ (methanol and *tert*-butanol) were removed under atmospheric pressure. After stirring for 24 h at reflux, the mixture was diluted with water, neutralized with Amberlite-CG-50 (H⁺ form), filtered, and evaporated under reduced pressure. The residue was diluted with water, filtered through a Celite pad, and evaporated under reduced pressure. The crude product was purified by ion exchange column chromatography (DOWEX 1X8 200-400 mesh, OH[–] form, water to 5% aqueous acetic acid), and recrystallization from water to give (–)-kainic acid (**1**) (14.6 g, 69.2%) as colorless needle crystals. R_f = 0.2 (*n*-butanol/acetic acid/water = 4/1/1). mp 245 °C (water), [α]_D²⁷ = –14.6 (*c* 0.63, H₂O). IR (ATR, cm^{–1}) : 3545, 2973, 2541, 1689, 1614, 1382, 1314, 1275, 1242, 888. ¹H NMR (D₂O, 400 MHz): δ 5.05 (1H, s), 4.77 (1H, s), 4.11 (1H, d, *J* = 3.6 Hz), 3.64 (1H, dd, *J* = 11.5, 6.7 Hz), 3.44 (1H, t, *J* = 11.5 Hz), 2.99–3.13 (2H, m), 2.49 (1H, dd, *J* = 17.0, 6.7 Hz), 2.39 (1H, dd, *J* = 17.0, 8.5 Hz), 1.76 (3H, s). ¹³C NMR (D₂O, 100 MHz): δ 176.6, 173.8, 140.5, 114.1, 66.2, 47.0, 46.3, 41.3, 33.8, 22.7. HRCIMS Calcd for C₁₀H₁₆NO₄ [M+H]⁺: 214.1079; Found: 214.1080. Anal. Calcd for C₁₀H₁₅NO₄: C, 56.33; H, 7.09; N, 6.57, Found: C, 56.45; H, 7.04; N, 6.47.