Supplementary Information

Modular Assembly of Cytotoxic Acetogenin Mimetics by Click Linkage with Nitrogen Functionalities

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List of Contents

1. Experimental details and characterizations of new compounds p. 1 - 11
2. Details of biological experiments p. 12 - 12
3. 1H and 13C NMR spectra for new compounds p. 13 - 23
1. **Experimental details and characterizations of new compounds**

**General:** Optical rotations were measured at room temperature. Infrared spectra (IR) were recorded on a Fourier transform infrared spectrometer (FTIR). $^1$H NMR spectra were recorded at 300 MHz and are reported in ppm ($\delta$) downfield relative to CDCl$_3$ as internal standard, and $^{13}$C NMR spectra were recorded at 75 MHz and assigned in ppm ($\delta$). HRMS spectra were recorded on Agilent 6210 TOF-MS. Elemental analyses were performed on VARIO EL Elemental Apparatus. All melting points were uncorrected.

**Compound 13:** To a stirred solution of 12 (1.36 g, 6.12 mmol) in dry THF (29 mL) was added 1M BH$_3$ THF complex in THF (12.24 mL, 12.24 mmol) at 0 $^\circ$C under N$_2$. After the reaction was stirred for 3 hrs, H$_2$O (5 mL) was cautiously added dropwise followed by 15% NaOH (9 mL) and 30% H$_2$O$_2$ (9 mL). The mixture was stirred for 2.5 hrs at room temperature and then quenched by aq. Na$_2$S$_2$O$_3$ solution (20 mL), and extracted with ethyl ether for three times. The combined organic extracts were washed with brine, dried over Na$_2$SO$_4$, filtered and concentrated. The residue was purified by flash chromatography (PE-EA, 2:1) to give 13 (0.88 g, 60%) as a white wax.

$[\alpha]_D^{25} = +36.5 \ (c = 1.0, \text{CHCl}_3)$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$: 1.29 (10H, brs), 1.39 (3H, d, $J = 6.9$ Hz), 1.52-1.61 (5H, m), 2.24-2.29 (2H, m), 3.62 (2H, t, $J = 6.6$ Hz), 4.98 (1H, dq, $J=1.8, 6.9$ Hz), 6.98 (1H, d, $J = 1.2$ Hz) ppm. $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$: 174.0, 149.0, 134.1, 77.4, 62.8, 32.6, 29.3, 29.3, 29.1, 29.0, 27.3, 25.6, 25.0, 19.1 ppm; IR (KBr): 3309, 2923, 2850, 1743, 1471, 1325, 1081, 1031, 951 cm$^{-1}$; MS (ESI, $m/z$): 263 (M+Na$^+$); HRMS (ESI, $m/z$) calcd. for C$_{14}$H$_{24}$O$_3$ (M+Na$^+$): 263.1618, found: 263.1615.
**Compound 14:** To a solution of 13 (708 mg, 2.95 mmol) in CH₂Cl₂ (50 mL) was added triethylamine (0.534 mL, 3.84 mmol) and methanesulfonyl chloride (0.274 mL, 3.54 mmol) at 0 °C. The mixture was stirred at the same temperature for 3.5 hrs, and gradually warmed to room temperature. The mixture was poured into water (20 mL), and extracted with DCM for three times. The combined organic extracts were dried over anhydrous Na₂SO₄, filtered and concentrated. The residue was purified by column chromatography (PE-EA, 4:1) to afford mesylate 14 (844 mg, 90%) as a white wax.

[α]D<sup>25</sup> = +23.1 (c = 1.0, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ: 1.30-1.42 (10H, brs), 1.41 (3H, d, J = 6.9 Hz), 1.50-1.57 (2H, m), 1.70-1.79 (2H, m), 2.24-2.29 (2H, m), 3.0 (3H, s), 4.22 (2H, t, J = 6.6 Hz), 5.0 (1H, dq, J = 1.5, 6.6 Hz), 6.99 (1H, d, J = 1.5 Hz) ppm. ¹³C NMR (75 MHz, CDCl₃) δ: 173.8, 149.1, 134.0, 77.4, 70.2, 37.2, 29.1, 29.0, 28.8, 27.3, 25.3, 25.0, 19.1 ppm; IR (KBr): 2921, 2852, 1744, 1473, 1340, 1326, 1169, 981, 945 cm⁻¹; MS (ESI, m/z): 341 (M+Na⁺); HRMS (ESI, m/z) calcd. for C₁₅H₂₆O₅S (M+H⁺): 319.1574, found: 319.1571

**Compound 15:** To a solution of azide 14 (700 mg, 2.2 mmol) in anhydrous EtOH (60 mL) was added NaN₃ (286 mg, 4.4 mmol). After the addition, the reaction mixture was heated to 90 °C and stirred for 12 hrs. Solvent was removed under the reduced pressure; the residue was extracted with ether (50 mL x 3). The combined organic layers were washed with H₂O and brine, and dried over Na₂SO₄. After filtration and concentration, the residue was purified by column chromatography (PE-EA, 8:1) to afford 15 (501 mg, 86%) as a colorless oil.
\[ \alpha_\text{D}^{25} = +23.7 \ (c = 1.0, \text{CHCl}_3) \]; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\): 1.30 (10H, brs), 1.41 (3H, d, \(J = 6.9 \text{ Hz}\)), 1.50-1.64 (5H, m), 2.23-2.29 (2H, m), 3.25 (2H, t, \(J = 6.6 \text{ Hz}\)), 5.0 (1H, dq, \(J = 1.8, 6.9 \text{ Hz}\)), 6.99 (1H, d, \(J = 1.5 \text{ Hz}\)) ppm. \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\): 173.8, 148.9, 134.1, 77.3, 51.3, 29.2, 29.1, 29.0, 29.0, 28.7, 27.3, 26.6, 25.0, 19.1 ppm; IR (KBr): 2929, 2856, 2096, 1755, 1456, 1319, 1075, 1027, 951 cm\(^{-1}\); MS (ESI, \(m/z\)): 288 (M+Na\(^+\)); HRMS (ESI, \(m/z\)) calcd. for C\(_{14}\)H\(_{23}\)N\(_3\)O\(_2\) (M+Na\(^+\)): 288.1682, found: 288.1680.

**Compound 16:** A solution of 11 (88 mg, 0.212 mmol) in methanol (2.5 mL) was treated with conc. HCl (0.65 mL) overnight at room temperature. Aqueous NaHCO\(_3\) was added to quench the reaction. Solvent was evaporated, and the mixture was extracted with ethyl acetate (30 mL x 3). The combined extracts were washed with brine, dried over Na\(_2\)SO\(_4\), filtered, and concentrated. The residue was purified by flash chromatography (PE-EA, 1.5:1) to afford 16 (61 mg, 88%) as a white wax.

\[ \alpha_\text{D}^{25} = +20.1 \ (c = 1.0, \text{CHCl}_3) \]; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\): 0.88 (3H, t, \(J = 6.6 \text{ Hz}\)), 1.26-1.45 (18H, m), 2.04 (1H, t, \(J = 2.7 \text{ Hz}\)), 2.43-2.46 (2H, m), 2.68 (1H, d, \(J = 2.4 \text{ Hz}\)), 2.97 (1H, d, \(J = 4.2 \text{ Hz}\)), 3.29-3.35 (1H, m), 3.49-3.56 (2H, m), 3.61-3.73 (5H, m), 3.76-3.79 (1H, m), 3.95-3.99 (1H, m) ppm; \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\): 80.3, 75.9, 74.1, 70.5, 70.3, 70.3, 70.1, 68.5, 32.9, 31.8, 29.6, 29.5, 29.5, 29.2, 25.5, 23.2, 22.6, 14.0 ppm; IR (neat): 3419, 3312, 2924, 2855, 2120, 1467, 1355, 1249, 1170, 940, 916 cm\(^{-1}\); MS (ESI, \(m/z\)): 351 (M+Na\(^+\)); HRMS (ESI, \(m/z\)) calcd. for C\(_{19}\)H\(_{36}\)O\(_4\) (M+Na\(^+\)): 351.2506, found: 351.2515.

**Compound 17:** To a stirred solution of 16 (86 mg, 0.262 mmol) in CH\(_2\)Cl\(_2\) (5 mL) at 0 \(^\circ\)C
was added pyridine (0.064 mL, 0.786 mmol), acetic anhydride (0.062 mL, 0.655 mmol), and DMAP (cat.). The reaction mixture was then allowed to stir at room temperature for 4 hrs. The mixture was poured into cold water, and extracted with CH$_2$Cl$_2$ (3 × 30 mL). The organic layer was then washed with water and brine. Removal of solvent under reduced pressure followed by column chromatography (PE-EA 6:1) afforded the corresponding acetate 17 (98 mg, 91%) as a colorless oil.

$[\alpha]_{D}^{25} = +11.1$ ($c = 1.0$, CHCl$_3$); $^1$H NMR (300 MHz, CDCl$_3$) δ: 0.88 (3H, t, $J = 6.6$ Hz), 1.25 (16H, brs), 1.56-1.60 (2H, m), 1.99 (1H, s), 2.07 (3H, s), 2.09 (3H, s), 2.51-2.62 (2H, m), 3.49-3.70 (8H, m), 5.00-5.09 (2H, m) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) δ: 170.6, 170.2, 79.2, 72.6, 72.4, 70.8, 70.7, 70.5, 70.3, 70.3, 31.8, 30.7, 29.5, 29.4, 29.4, 29.2, 25.2, 22.6, 21.1, 20.9, 20.6, 14.0 ppm; IR (neat): 3312, 3274, 2925, 2856, 2123, 1740, 1467, 1373, 1240, 1121, 1042, 958 cm$^{-1}$; MS (ESI, $m/z$): 435 (M+Na$^+$); HRMS (ESI, $m/z$) calcd. for C$_{23}$H$_{40}$O$_6$ (M+H$^+$): 413.2898, found: 413.2891

**Compound 18:** A solution of KMnO$_4$ (305 mg, 1.929 mmol) in 20 mL of H$_2$O was cooled in an ice-water bath. In one portion, a solution of alkyne 17 (265 mg, 0.643 mmol), HOAc (3 mL) and TBAB (10 mg, 0.032 mmol) in pentane (15 mL) was added. Without replenishing the ice in the cooling bath, the reaction mixture was stirred for 8 h. After cooling in an ice bath, 2 g of Na$_2$SO$_3$ and 3 mL of 6 N HCl were carefully added to the reaction mixture. After the mixture was stirred for 10 min, the reaction mixture was diluted with 20 mL of H$_2$O and extracted with pentane. The combined organic layers were dried over Na$_2$SO$_4$ and concentrated. The residue was purified by flash chromatography on silica gel (DCM-CH$_3$OH,
40:1) to afford 18 (198 mg, 71%) as a yellowish oil.

\([\alpha]_D^{25} = +4.4 \ (c = 1.0, \ \text{CHCl}_3); \ ^1\text{H} \ \text{NMR} \ (300 \ \text{MHz}, \ \text{CDCl}_3) \ \delta: \ 0.88 \ (3\text{H}, \ t, \ J = 6.6 \ \text{Hz}), \ 1.25 \ (16\text{H}, \ \text{brs}), \ 1.55-1.59 \ (2\text{H}, \ m), \ 2.07 \ (3\text{H}, \ s), \ 2.08 \ (3\text{H}, \ s), \ 2.72-2.76 \ (2\text{H}, \ m), \ 3.49-3.71(8\text{H}, \ m), \ 5.01-5.05 \ (1\text{H}, \ m), \ 5.31-5.37 \ (1\text{H}, \ m) \ \text{ppm}; \ ^{13}\text{C} \ \text{NMR} \ (75 \ \text{MHz}, \ \text{CDCl}_3) \ \delta: \ 174.8, \ 171.0, \ 170.3, \ 72.7, \ 72.4, \ 71.3, \ 70.7, \ 70.5, \ 68.9, \ 35.5, \ 31.8, \ 30.7, \ 29.5, \ 29.5, \ 29.4, \ 29.4, \ 29.2, \ 25.2, \ 22.6, \ 21.1, \ 20.9, \ 14.0 \ \text{ppm}; \ \text{IR} \ (\text{film}): \ 3460, \ 2926, \ 2855, \ 1743, \ 1465, \ 1374, \ 1240, \ 1120, \ 1182, \ 1045, \ 958 \ \text{cm}^{-1}; \ \text{MS} \ (\text{ESI}, \ m/z): \ 455 \ (M+Na^+); \ \text{HRMS} \ (\text{ESI}, \ m/z) \ \text{calcd.} \ \text{f} \ \text{or} \ C_{22}H_{40}O_8 (M+Na^+): 455.2615, \ \text{found}: \ 455.2611

**Compound 19:** To a solution of azide 15 (212 g, 0.8 mmol) in anhydrous tetrahydrofuran (15 ml) was added Ph3P (419 mg, 1.6 mmol) at room temperature. The mixture was allowed to stir for 3 hrs. Water (50 µl) was then added to the reaction mixture and stirred for additional 17 hrs. The reaction mixture was poured into 2N aq. HCl and extracted with diethyl ether (3×30 ml). The aqueous layer was then adjusted to basic solution (pH 10) with aq. NaOH and extracted with diethyl ether (5×30 ml). The organic layer was dried over anhydrous Na2SO4 and evaporated to yield 19 (130 mg, 68%) as a pale yellow liquid. Without further purification, this crude product was used for the next step.

**Compound 25:** Under an inert gas, a few drops of neat 23 (2.04 g, 12.75 mmol) was added to predried Mg turnings (0.367 g, 15.3 mmol) in anhydrous diethyl ether (3 mL) to initiate the formation of the organometallic species. The remaining bromide was diluted with diethyl ether (10 mL) and added dropwise to the Mg mixture to maintain gentle reflux. Upon
completion of addition, the Grignard solution was stirred for additional 45 min to give the (cyclopent-3-enylmethyl)magnesium bromide.

To a suspension of CuI (137 mg, 0.722 mmol) in diethyl ether (5 mL) at -40 °C under argon atmosphere was added the freshly prepared Grignard solution (2.6 mL). The mixture was stirred for 10 min, and a solution of compound 10 (100 mg, 0.289 mmol) in diethyl ether (5 mL) was added dropwise to the above solution. The mixture was stirred for 1.5 hrs at the same temperature. The reaction mixture was quenched with saturated aqueous NH₄Cl (6 mL). The separated aqueous layer was re-extracted with diethyl ether and the combined extracts were washed with brine, dried over NaSO₄, filtered, and concentrated in vacuo. Purification of the crude product by column chromatography (PE-EA, 6:1) afforded compound 25 (105 mg, 85%) as a colorless oil.

[α]D²⁵ = +2.8 (c = 0.99, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ: 0.88 (3H, t, J = 6.6 Hz), 1.25 (16H, brs), 1.38-1.60 (6H, m), 1.93-1.99 (2H, m), 2.216-2.24 (1H, m), 2.43-2.51 (2H, m), 3.27-3.33 (1H, m), 3.39 (3H, s), 3.50-3.76 (9H, m), 4.66 (1H, d, J = 6.9 Hz), 4.78 (1H, d, J = 6.9 Hz), 5.65 (2H, s) ppm; ¹³C NMR (75 MHz, CDCl₃) δ: 129.8, 129.8, 95.9, 76.1, 75.7, 74.0, 70.6, 70.5, 55.7, 38.8, 38.8, 37.6, 31.2, 31.9, 31.8, 31.7, 29.6, 29.5, 29.5, 29.2, 25.4, 22.6, 14.0 ppm; IR (film): 3479, 3052, 2924, 2854, 1615, 1466, 1356, 1214, 1142, 1106, 1040, 919 cm⁻¹; MS (ESI, m/z): 451 (M+Na⁺); HRMS (ESI, m/z) calcd. for C₂₅H₄₈O₅(M+Na⁺): 451.3394, found: 451.3399.

**Compound 26:** MOMCl (0.149 mL, 1.96 mmol) was added to a mixture of 25 (210 mg, 0.49 mmol) and diisopropyl ethylamine (0.405 mL, 2.45 mmol) in dry CH₂Cl₂ (15 mL) at 0 °C.
The reaction was stirred at room temperature for 8 hrs, and then quenched with saturated aqueous NH₄Cl. The mixture was extracted with CH₂Cl₂. The extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (PE-EA, 8:1) to afford 26 (205 mg, 88%) as a colorless oil.

\[\alpha\]D²⁵ = -10.7 (c = 1.01, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ: 0.87 (3H, t, J = 6.7 Hz), 1.25-1.56 (22H, m), 1.92-2.00 (2H, m), 2.18-2.23 (1H, m), 2.43-2.51 (2H, m), 3.38 (6H, s), 3.49-3.71 (10H, m), 4.65 (1H, d, J = 6.9 Hz), 4.76 (1H, d, J = 6.9 Hz) ppm; ¹³C NMR (75 MHz, CDCl₃) δ: 129.7, 129.7, 95.9, 76.2, 76.1, 74.0, 73.9, 70.7, 55.3, 55.3, 38.8, 38.7, 37.6, 32.0, 31.9, 31.8, 30.6, 29.6, 29.5 (2C), 29.2, 25.3, 22.5, 14.0 ppm; IR (film): 3052, 2925, 2854, 1615, 1466, 1356, 1214, 1146, 1105, 1042, 919 cm⁻¹; MS (ESI, m/z): 495 (M+Na⁺); HRMS (ESI, m/z) calcd. for C₂₇H₅₂O₆ (M+Na⁺): 495.3656, found: 495.3659

AA005 analogue 1: To a round bottom flask was added alkyne 16 (30 mg, 0.091 mmol), azide 15 (26.5 mg, 0.1 mmol), CuSO₄·5H₂O (2.29 mg, 0.0091 mmol), sodium ascorbate (3.62 mg, 0.0182 mmol), water (2 mL) and THF (2 mL). The mixture was stirred for 12 hrs at room temperature, and then extracted with CH₂Cl₂. The extracts were dried with Na₂SO₄ and concentrated in vacuo. Flash chromatography of the residue on silica gel (DCM-CH₃OH, 30:1) yielded 1 (34 mg, 68%) as a white wax.

\[\alpha\]D²⁵ = +15.8 (c = 1.0, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ: 0.87 (3H, t, J = 6.6 Hz), 1.25-1.42 (33H, m), 1.50-1.56 (2H, m), 1.86-1.91 (2H, m), 2.26 (2H, t, J = 7.8 Hz), 2.85-2.93 (2H, m), 3.31 (1H, t, J = 9.6 Hz), 3.43-3.71 (7H, m), 3.78-3.80 (1H, m), 4.09-4.12 (1H, m),
4.31 (2H, t, $J = 7.2$ Hz), 4.99 (1H, qd, $J = 1.5$, 6.9 Hz), 7.0 (1H, d, $J = 1.2$ Hz), 7.42 (1H, s) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) δ: 148.9, 144.3, 134.1, 121.9, 77.4, 75.8, 74.7, 70.5, 70.4, 70.1, 69.5, 50.2, 32.9, 31.8, 30.2, 29.6, 29.5, 29.5, 29.3, 29.1, 29.0, 29.0, 28.8, 27.3, 26.4, 25.5, 25.1, 22.6, 19.1, 14.1 ppm; IR (neat): 3465, 2920, 2849, 1734, 1467, 1324, 1116, 1095, 1085 cm$^{-1}$; MS (ESI, m/z): 594 (M+H$^+$); HRMS (ESI, m/z) calcd. for C$_{33}$H$_{59}$N$_3$O$_6$ (M+H$^+$): 594.4477, found: 594.4462.

**AA005 analogue 2:** To a solution of acid 18 (62 mg, 0.144 mmol) and amine 19 (41 mg, 0.171 mmol) in DMF (2 mL) was added Et$_3$N (60 µL, 0.43 mmol), EDCI (32.6 mg, 0.171 mmol) and HOBT (27.9 mg, 0.171 mmol) at room temperature. The reaction mixture was stirred for 24 hrs, and quenched with H$_2$O. The mixture was extracted with ether. The organic layer was washed with brine, dried over Na$_2$SO$_4$ and concentrated under reduced pressure.

A solution of the crude product in methanol (5 mL) was treated with NH$_2$NH$_2$.H$_2$O (1 mL). The mixture was stirred overnight at room temperature. Solvent was evaporated, and the mixture was extracted with DCM (30 mL x 3). The combined extracts were washed with brine, dried over Na$_2$SO$_4$, filtered, and concentrated. Flash chromatography of the residue on silica gel (DCM-CH$_3$OH, 25:1) yielded 2 (40 mg, 48% over two steps) as a white wax.

$[\alpha]_D^{25} = -7.4$ (c = 1.0, CHCl$_3$); $^1$H NMR (300 MHz, CDCl$_3$) δ: 0.87 (3H, t, $J = 6.6$ Hz), 1.27 (28H, brs), 1.40 (3H, d, $J = 6.6$ Hz), 1.47-1.53 (2H, m), 2.26 (2H, t, $J = 7.6$ Hz), 2.37-2.39 (2H, m), 3.22 (2H, q, $J = 6.6$ Hz), 3.28-3.34 (1H, m), 3.47-3.70 (7H, m), 3.77-3.80 (1H, m), 4.12-4.16 (1H, m), 4.99 (1H, qd, $J = 1.5$, 6.6 Hz), 6.40 (1H, brs), 6.99 (1H, d, $J = 1.5$Hz) ppm;

$^{13}$C NMR (75 MHz, CDCl$_3$) δ: 173.8, 171.5, 148.9, 134.2, 77.4, 75.7, 74.3, 70.5, 70.3, 70.2,
AA005 analogue 3: To a solution of cycloalkene 26 (89 mg, 0.189 mmol) in THF (3 mL) and water (1.2 mL) at 20 °C was added K₂OsO₈·2H₂O (7 mg, 0.0189 mmol), sodium periodate (200 mg, 0.943 mmol). After 8 hrs, the reaction was diluted with saturated sodium thiosulfate (10 mL), and then extracted with ethyl acetate. The organic layer was dried with sodium sulfate and concentrated. The crude product was used for the next step without further purification.

To a stirred solution of the crude dialdehyde (95 mg, 0.1885 mmol) and amine 19 (54 mg, 0.2262 mmol) in CH₂Cl₂ (2.5 mL) were added NaBH(OAc)₃ (35.5 mg, 0.5655 mmol) and AcOH (65 µL, 1.131 mmol). After being stirred at room temperature for 3.5 hrs, the reaction mixture was diluted with EtOAc. The mixture was washed with saturated aqueous NaHCO₃ and brine. The organic layer was dried over anhydrous Na₂SO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (DCM-CH₃OH, 30:1).

A solution of the above product in methanol (3 mL) was treated with conc. HCl (0.6 mL) at room temperature overnight. Aq. NaHCO₃ was added to quench the reaction. Solvent was evaporated, and the mixture was extracted with ethyl acetate (30 mL x 3). The combined extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated. Flash chromatography on silica gel (DCM-CH₃OH, 15:1) yielded 3 (31 mg, 26% over three steps).
as a white wax.

$[\alpha]_D^{25} = +5.8 \ (c = 1.0, \text{CHCl}_3)$; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$: 0.87 (3H, t, $J = 6.6$ Hz), 1.25-1.42 (40H, m), 1.49-1.53 (2H, m), 1.67-1.70 (2H, m), 1.91 (2H, t, $J = 10.8$ Hz), 2.23-2.34 (4H, m), 2.95 (2H, d, $J = 11.1$), 3.31 (2H, t, $J = 9.3$ Hz), 3.51-3.80 (6H, m), 4.99 (1H, qd, $J = 1.8, 6.9$ Hz), 6.98 (1H, d, $J = 1.5$ Hz) ppm; $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$: 173.8, 148.8, 134.2, 77.3, 75.8, 75.7, 70.4, 70.4, 70.3, 70.2, 59.1, 53.9, 35.7, 32.9, 32.2, 32.1, 32.0, 31.8, 30.1, 29.6, 29.5, 29.5, 29.4, 29.3, 29.3, 29.1, 29.1, 27.6, 27.3, 26.8, 25.5, 25.1, 22.6, 19.1, 14.0 ppm; IR (neat): 3512, 2922, 2850, 1743, 1468, 1378, 1324, 1117, 1102, 1088, 1028, 965 cm$^{-1}$; MS (ESI, $m/z$): 624 (M+H$^+$); HRMS (ESI, $m/z$) calcd. for C$_{37}$H$_{69}$NO$_6$ (M+Na$^+$): 624.5198, found: 624.5195.
2. Details of biological experiments

**Reagents:** AA005 and AA005 analogues 1-3 (from School of Chemistry and Chemical Engineering, Nanjing University) were dissolved in 75% ethanol as a 6.6 µM stock solution and kept at -80 °C.

**Cell culture and treatment:**

Six leukemic cell lines were used for the current studies. NB4, a APL cell line was kindly provided by Dr. M. Lanotte’s in France; U937, an acute myelomonocytic leukemic cell line, and a chronic myeloid leukemic cell line K562 were obtained from Cell Bank of Shanghai Institutes of Biological Sciences (Shanghai, China); Kasumi-1, a t(8;21)-positive M2b-type AML cell line was provided by Dr. Kamada in Japan; as well as HL-60, a human promyelocytic cell line and Jurkat, an acute T cell leukemic cell line were provided by Shanghai Institute of Hematology (Shanghai, China).

Six adherent cell lines including five breast cancer cell lines MCF-7, MDA-MB-435S, BT-549, BT-474, SK-Br-3 provided by Chinese Academy of Sciences (Shanghai, China), and a colorectal adenocarcinomic cell line SW620 were used.

All cell lines were cultured in RPMI-1640 medium (Hyclone, Logan, UT) supplemented with 10% heat-inactivated fetal calf serum (FCS, HyClone, Logan, UT).

For experiments, cells were seeded into ninety-six-well plates at the initial density of 1×10^4 cells per well for leukemic cell lines and 2 ×10^3 cells per well for adherent cell lines, followed by incubation with the indicated concentrations of the above compounds and maintained in a 5% CO₂–95% air humidified atmosphere at 37°C. For quantitative analysis of cell growth inhibition ratio, 10 µL of Cell Counting Kit-8 (CCK-8, Dojindo, Kumamoto, Japan) solution was added to each well at 37 °C for 4h, absorbance at 450 nm was monitored with a microplate reader (Spectra Max Plus 384; Molecular Devices). The values obtained were normalized to those of control cells incubated with vehicle only.
3. NMR Spectra of new compounds