Supporting Information

Sulphhydryl-Based Dendritic Chain Reaction

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**General methods.** All reactions requiring anhydrous conditions were performed under an Argon atmosphere. All reactions were carried out at room temperature unless stated otherwise. Chemicals and solvents were either A.R. grade or purified by standard techniques. Thin layer chromatography (TLC): silica gel plates Merck 60 F$_{254}$; compounds were visualized by irradiation with UV light. Flash chromatography (FC): silica gel Merck 60 (particle size 0.040-0.063 mm), eluent given in parentheses. $^1$H-NMR spectra were measured using Bruker Avance operated at 400MHz as mentioned. $^{13}$C-NMR spectra were measured using Bruker Avance operated at 100 MHz as mentioned. The chemical shifts are expressed in $\delta$ relative to TMS ($\delta = 0$ ppm) and coupling constants $J$ in Hz. The spectra were recorded in CDCl$_3$ as solvent at room temperature unless stated otherwise. All general reagents, including salts and solvents, were purchased from Sigma-Aldrich.

**Abbreviations.** AcOH- Acetic acid, ACN- Acetonitrile, DBTL- Dibutyltin dilaurate, DCM- Dichloromethane, DMF- N,N'-Dimethylformamide, Et$_2$O- Diethyl ether, EtOAc- Ethylacetate, Hex- n-Hexanes, MeOH- Methanol, NMM- N-Methylmorpholine, p-TsOH- p-Toluene sulfonic acid, THF- Tetrahydrofurane, TFA- Trifluoroacetic acid.
Compound 1B
Compound 1A (190 mg, 0.79 mmol), compound 4 (200 mg, 0.86 mmol) and catalytic amount of DBTL were suspended in 4 mL toluene, and heated to 90°C for 20 min. The reaction mixture was monitored by TLC (EtOAc/Hex 50:50). After completion, the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (EtOAc/Hex 45:55) to give compound 1B (220 mg, 63%) as a white powder.

1H NMR (400MHz, CDCl₃): δ = 7.85 (1H, s), 7.41-7.19 (9H, m), 5.88 (1H, t, J = 6.4 Hz), 5.01 (2H, s), 4.41 (2H, d, J = 6.4 Hz), 3.66 (2H, s), 3.22 (2H, s), 1.44 (9H, s). 13C NMR (100MHz, CDCl₃): δ = 170.7, 170.1, 156.6, 138.4, 135.2, 132.7, 129.9, 129.6, 129.5, 128.0, 120.5, 82.7, 67.2, 45.3, 45.1, 33.2, 28.5. MS (ESI+): m/z calc. for C₂₃H₂₈N₂O₅S: 444.5 ; found: 467.2 [M+Na]+.

Compound 1
Compound 1B (50 mg, 0.11 mmol) was dissolved in 1.5 mL mixture of TFA/DCM 1:5, and stirred at RT for 20 min. After completion, the solvents were evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (EtOAc/AcOH 99:1) to give compound 1 (17 mg, 41%) as a white powder.

1H NMR (400MHz, CDCl₃): δ = 7.32-7.11 (10H, m), 5.72 (1H, t, J = 6.4 Hz), 5.04 (2H, s), 4.39 (2H, d, J = 6.4 Hz), 3.68 (2H, s), 3.29 (2H, s). 13C NMR (100MHz, CDCl₃): δ = 175.5, 169.9, 157.0, 139.1, 134.7, 133.3, 133.0, 129.6, 129.4, 128.5, 118.5, 66.9, 45.5, 45.2, 34.0. MS (ESI+): m/z calc. for C₁₉H₂₀N₂O₅S: 388.4 ; found: 411. [M+H]⁺.
Compound 2A

Commercially available 5-amino-2-nitrobenzoic acid (1 g, 5.49 mmol) was dissolved in 17 mL of 1,4-dioxane in a sealed tube, and H$_2$SO$_4$ (2.2 mL) was added slowly. The reaction mixture was cooled to -40°C, and 17 mL of isobutylene were bubbled and the vessel was sealed. The mixture was warmed to room temperature and stirred overnight. After completion, the vessel was cooled to 0°C, opened slowly, and the mixture was diluted with 110 mL of EtOAc and was washed with 2M NaOH (110mL x 3) followed by brine (50 mL x 3). The organic layer was separated, dried over Na$_2$SO$_4$, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (EtOAc/Hex 40:60) to give compound 2A (785 mg, 60%) as a yellow powder.

$^{1}$H NMR (400MHz, CDCl$_3$): $\delta = 7.85$ (1H, d, $J = 9.6$ Hz), 6.54 (2H, m), 4.56 (2H, brs), 1.53 (9H, s). $^{13}$C NMR (100MHz, CDCl$_3$): $\delta = 166.8, 152.7, 134.3, 127.7, 114.5, 113.5, 83.9, 28.4$. MS (ESI+): $m/z$ calc. for C$_{11}$H$_{14}$N$_2$O$_4$: 238.2 ; found: [M+Na]$^+$.  

Compound 2B

Toluene was heated to reflux under argon atmosphere and triphosgene (78 mg, 0.26 mmol) in toluene was added. Then, a solution of compound 2A (50 mg, 0.20 mmol) in toluene was slowly added dropwise with a syringe. The reaction mixture was stirred for 30 min at reflux and monitored by $^{1}$H-NMR. After isocyanate derivative was observed, the solvent was removed under reduced pressure. A solution of compound 3B$^3$ (30 mg, 0.16 mmol) in toluene, followed by catalytic amount of DBTL, was added to the isocyanate residue. The reaction mixture was heated to reflux, stirred for 1 h under argon atmosphere and monitored by TLC (EtOAc/Hex 30:70). After completion, the solvent was removed under reduced pressure. The crude
product was purified by column chromatography on silica gel (EtOAc/Hex 25:75) to give compound 2B (44 mg, 62%) as yellow oil.

\(^1\)H NMR (400MHz, CDCl\(_3\)): \(\delta = 7.94\) (1H, d, \(J = 8.8\) Hz), 7.64 (1H, dd, \(J = 8.8, 2.4\) Hz), 7.55 (1H, d, \(J = 2.4\) Hz), 7.18 (1H, s), 5.16 (2H, s), 2.19 (3H, s), 2.05 (6H, s), 1.56 (9H, s). \(^1\)C NMR (100MHz, CDCl\(_3\)): \(\delta = 187.9, 186.6, 165.4, 152.9, 145.9, 143.2, 142.6, 142.1, 141.5, 136.7, 132.4, 126.4, 119.6, 118.7, 84.7, 59.4, 28.5, 13.3, 13.1. MS (ESI+): \(m/z\) calc. for \(C_{22}H_{24}N_2O_8\): 444.1; found: 467.1 [M+Na]^+.

Compound 2

Compound 2B (30 mg, 0.07 mmol) was dissolved in 1.5 mL mixture of TFA/DCM 1:1, and stirred at RT for 20 min. After completion, the solvents were evaporated under reduced pressure to give compound 2 (27 mg, 99%) as a yellow powder.

\(^1\)H NMR (400MHz, CD\(_2\)CN): \(\delta = 8.58\) (1H, s), 7.94 (1H, d, \(J = 9.2\) Hz), 7.76 (1H, d, \(J = 2.4\) Hz), 7.68 (1H, dd, \(J = 9.2, 2.4\) Hz), 5.11 (2H, s), 2.13 (3H, s), 2.00 (6H, s). \(^1\)C NMR (100MHz, CD\(_2\)CN): \(\delta = 187.4, 186.3, 167.0, 165.0, 153.7, 145.6, 144.5, 142.4, 141.8, 141.2, 137.2, 130.8, 126.5, 120.2, 58.9, 12.4, 12.2. MS (ESI+): \(m/z\) calc. for \(C_{18}H_{16}N_2O_8\): 388.1; found: 411.1 [M+Na]^+.

Compound 3C

Toluene was heated to reflux under argon atmosphere and triphosgene (600 mg, 2.0 mmol) in toluene was added. Then, a solution of compound 3A (640 mg, 1.67 mmol)
in toluene was slowly added dropwise with a syringe. The reaction mixture was stirred for 30 min at reflux and monitored by $^1$H-NMR. After isocyanate derivative was observed, the solvent was removed under reduced pressure. A solution of compound 3B$^3$ (300 mg, 1.67 mmol) in toluene, followed by catalytic amount of DBTL, was added to the isocyanate residue. The reaction mixture was heated to reflux, stirred for 1 h under argon atmosphere and monitored by TLC (EtOAc/Hex 20:80). After completion, the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (EtOAc/Hex 10:90) to give compound 3C (914 mg, 93%) as an orange oil.

$^1$H NMR (400MHz, CDCl$_3$): $\delta$ = 8.30 (1H, s), 7.95 (1H, d, $J = 8.4$ Hz), 7.21 (1H, dd, $J = 8.4$, 1.2 Hz), 7.03 (1H, d, $J = 1.2$ Hz), 5.12 (2H, s), 4.69 (2H, s), 4.66 (2H, s), 2.16 (3H, s), 2.04 (6H, s), 0.92 (9H, s), 0.85 (9H, s), 0.07 (6H, s), 0.05 (6H, s). $^{13}$C NMR (100MHz, CDCl$_3$): $\delta$ = 188.3, 186.4, 153.8, 145.2, 141.6, 141.5, 137.8, 137.4, 136.6, 128.7, 127.6, 127.3, 120.4, 66.1, 65.3, 58.3, 26.7, 26.4, 19.1, 18.7, 13.1, -4.5, -4.7. MS (ESI+): $m/z$ calc. for C$_{31}$H$_{49}$NO$_8$Si$_2$: 587.3 ; found: 610.3 [M+Na]$^+$.  

Compound 3D

Compound 3C (910 mg, 1.55 mmol) was dissolved in 10 mL MeOH, and catalytic amount of $p$-TsOH was added. The reaction mixture was stirred for 20 min in RT, and monitored by TLC (EtOAc/Hex 75:25). After completion, the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (EtOAc/Hex 70:30) to give compound 3D (474 mg, 85%) as an orange powder.

$^1$H NMR (400MHz, CDCl$_3$ + CD$_3$OD): $\delta$ = 8.09 (1H, s), 7.74 (1H, s), 7.16 (1H, d, $J = 8.0$ Hz), 7.08 (1H, s), 5.04 (2H, s), 4.52 (2H, s), 4.48 (2H, s), 2.11 (3H, s), 1.98 (6H, s). $^{13}$C NMR (100MHz, CDCl$_3$ + CD$_3$OD): $\delta$ = 188.2, 186.7, 154.5, 145.5, 141.8, 141.5, 139.4, 139.2, 137.4, 136.9, 128.2, 121.7, 64.8, 63.9, 58.6, 13.0. MS (ESI+): $m/z$ calc. for C$_{19}$H$_{21}$NO$_6$: 359.1 ; found: 382.1 [M+Na]$^+$.  

Compound 3E

Compound 3D (100 mg, 0.27 mmol), Compound 4 (193 mg, 0.83 mmol) and catalytic amount of DBTL were suspended in 4 mL toluene, and heated to 90°C for 20 min. The reaction mixture was monitored by TLC (EtOAc/Hex 50:50). After completion, the solvent was evaporated under reduced pressure. The crude product was purified
by column chromatography on silica gel (EtOAc/Hex 40:60) to give compound 3E (150 mg, 73%) as an orange oil.

\(^1\)H NMR (400MHz, CDCl\(_3\)): \(\delta = 8.24\) (1H, s), 7.78 (1H, d, \(J = 6.8\) Hz), 7.25 (2H, m), 5.95 (1H, t, \(J = 6.4\) Hz), 5.79 (1H, t, \(J = 6.4\) Hz), 5.09 (2H, s), 5.00 (2H, s), 4.99 (2H, s), 4.40 (2H, d, \(J = 6.4\) Hz), 4.35 (2H, d, \(J = 6.4\) Hz), 3.21 (2H, s), 3.17 (2H, s), 2.14 (3H, s), 2.00 (6H, s), 1.43 (9H, s), 1.40 (9H, s).

\(^{13}\)C NMR (100MHz, CDCl\(_3\)): \(\delta = 188.2, 186.5, 170.9, 157.0, 156.6, 154.5, 145.5, 141.7, 141.4, 137.5, 132.7, 132.0, 130.5, 126.8, 123.3, 82.8, 69.9, 64.5, 58.7, 45.4, 35.3, 28.6, 13.1. MS (ESI+): \(m/z\) calc. for C\(_{35}\)H\(_{47}\)N\(_3\)O\(_{12}\)S\(_2\): 765.3; found: 788.3 [M+Na]+.

**Compound 3**

Compound 3E (30 mg, 0.04 mmol) was dissolved in 1.5 mL mixture of TFA/DCM 1:5, and stirred at RT for 20 min. After completion, the solvents were evaporated under reduced pressure. The crude product was purified by preparative RP-HPLC (10-90% ACN in water, 20 min) to give compound 3 (11 mg, 40%) as a yellowish powder.

\(^1\)H NMR (400MHz, CD\(_3\)CN): \(\delta = 8.13\) (1H, s), 7.65 (1H, s), 7.34 (2H, m), 6.32 (2H, m), 5.08 (2H, s), 5.05 (4H, s), 4.36 (2H, d, \(J = 6.4\) Hz), 4.32 (2H, d, \(J = 6.4\) Hz), 3.35 (2H, s), 3.33 (2H, s), 2.13 (3H, s), 2.09 (6H, s).

\(^{13}\)C NMR (100MHz, CD\(_3\)CN): \(\delta = 188.0, 186.3, 174.9, 156.9, 156.5, 153.8, 146.1, 141.4, 136.0, 135.1, 133.3, 130.5, 127.8, 122.2, 70.8, 64.6, 59.0, 45.2, 36.8, 13.0. MS (ESI-): \(m/z\) calc. for C\(_{27}\)H\(_{31}\)N\(_3\)O\(_{12}\)S\(_2\): 653.1; found: 652.1 [M-H]-.

**Compound 4A**

Commercially available ethyl-2-mercaptoacetate (0.91 mL, 8.32 mmol) was dissolved in 7 mL DMF and cooled to 0°C under argon atmosphere. K\(_2\)CO\(_3\) (1.4 g, 9.98 mmol) was then added, followed by dropwise addition of commercially available t-butyl
bromo acetate (1.23 mL, 8.32 mmol). The reaction mixture stirred at RT for 2 h. After completion, the reaction mixture diluted with Et₂O, and was washed with saturated aqueous solution of NH₄Cl, followed by brine. The organic layer dried over MgSO₄, and evaporated under reduced pressure to give compound 4A (1.89 g, 97%) as colorless oil.

\[ \text{1H NMR (400MHz, CDCl}_3\text{): } \delta = 4.12 \text{ (2H, quart, } J = 7.2 \text{ Hz), 3.31 (2H, s), 3.23 (2H, s), 1.41 (9H, s), 1.22 (3H, t, } J = 7.2 \text{ Hz). } \]

\[ \text{13C NMR (100MHz, CDCl}_3\text{): } \delta = 170.3, 169.4, 82.3, 61.9, 35.3, 33.9, 28.5, 14.6. \]

**Compound 4B**

Compound 4A (1.78 g, 7.6 mmol) was dissolved in 32 mL THF and cooled to 0°C. A solution of LiOH (202 mg, 8.4 mmol) in 8 mL water was then added slowly, and the reaction mixture stirred at RT for 2 h and monitored by TLC (EtOAc/Hex 15:85). After completion, water was added and the basic mixture was washed with EtOAc. The aqueous mixture was then cooled to 0°C, acidified slowly with 1M HCl (pH = 2) and the product extracted with EtOAc. The organic layer dried over MgSO₄, and evaporated under reduced pressure to give compound 4B (1.28 g, 82%) as colorless oil.

\[ \text{1H NMR (400MHz, CDCl}_3\text{): } \delta = 3.42 \text{ (2H, s), 3.29 (2H, s), 1.44 (9H, s). } \]

\[ \text{13C NMR (100MHz, CDCl}_3\text{): } \delta = 176.5, 169.9, 83.1, 35.6, 34.1, 28.7. \] MS (ESI-): m/z calc. for C₈H₁₄O₄S: 206.2 ; found: 205.1 [M-H]⁻.

**Compound 4**

Compound 4B (400 mg, 1.94 mmol) was dissolved in 4 mL dry THF and cooled to (-15)°C. NMM (0.27 mL, 2.42 mmol) was added dropwise, followed by dropwise addition of isobutyl chloroformate, and the reaction mixture stirred at that temperature for 15 min. NaN₃ (253 mg, 3.88 mmol) in 2 mL water was added, and the reaction mixture was allowed to stir for 30 min at RT. After completion, the reaction mixture diluted with EtOAc and was washed with saturated aqueous solution of NH₄Cl. The organic layer dried over MgSO₄, and evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel (EtOAc/Hex 10:90) to give compound 4 (300 mg, 67%) as colorless oil.
$^1$H NMR (400MHz, CDCl$_3$): $\delta = 3.32$ (2H, s), 3.24 (2H, s), 1.43 (9H, s). $^{13}$C NMR (100MHz, CDCl$_3$): $\delta = 177.2, 169.2, 82.7, 36.1, 35.3, 28.5$. MS (ESI+): $m/z$ calc. for C$_8$H$_{13}$O$_3$S: 231.2; found: 232.1 [M+H]$^+$.  

**General assay conditions**

All stock solutions were prepared in ACN [10 mM]. In a typical assay, compound 3 [1000 $\mu$M] and compound 2 [500 $\mu$M], were incubated in TRIS buffer [pH = 7.2] with EDTA [10 mM]. Various amounts of ethyl-2-mercaptoacetate were added, and the release of 5-amino-2-nitrobenzoic acid was monitored using spectrophotometer at 405 nm.

**Representative Example**

To 80 $\mu$L of TRIS buffer [pH = 7.2] with EDTA [10 mM] were added 5 $\mu$L of Compound 2 [500 $\mu$M] and 10 $\mu$L of Compound 3 [1000 $\mu$M]. Finally, 5 $\mu$L of ethyl-2-mercaptoacetate, from a 1mM stock solution in ACN, was added [50 $\mu$M, 0.10 Eq.], and the release of 5-amino-2-nitrobenzoic acid was monitored using spectrophotometer at 405 nm.

Total assay volume: 100 $\mu$L.

Total water v/v%: 80%.

Total ACN v/v%: 20%.

**References**