Supporting Information

Materials and methods:

Chemicals: Fmoc-amino acids were obtained from GL Biochem (Shanghai). Thiazolidine-2-one was purchased from BePharm Ltd. 30% Hydrogen peroxide (30% \( \text{H}_2\text{O}_2 \)) were purchased from Aladdin Chemistry CO. Ltd. Commercially available reagents were used without further purification, unless noted otherwise. Nanopure water was used for all experiments. All other chemicals were reagent grade or better.

General methods: The synthesized compounds were characterized using \(^1\text{H} \) NMR (Bruker ARX 400). LC-MS and HR-MS spectrometric analyses were performed at the SHIMADZU LCMS-2020 System and Thermo Finnigan LCQ AD System respectively. HPLC was conducted at LUMTECH HPLC (Germany) system using a C\(_{18} \) RP column with MeOH (0.05% of TFA) and water (0.05% of TFA) as the eluents. TEM images were done on a Tecnai G2 F20 system, operating at 200 kV. Rheology test was done on an AR 1500ex (TA instrument) system, 25 mm parallel plates was used during the experiment at the gap of 500 \( \mu \text{m} \).

Synthesis and characterizations:

![Scheme S-1. Synthesis of compounds 1](image)

Synthesis of thiazolidine decorating aspartic acid (D (Thi)): DCC (1.03 g, 5 mmol) and DMAP (61 mg, 0.5 mmol) were added to a solution of Fmoc-Asp (OtBu)-OH (1.028 g, 2.5 mmol) and thiazolidine-2-one (258 mg, 2.5 mmol) in \( \text{CH}_2\text{Cl}_2 \). The reaction was completed 4 hours later at room temperature. The reaction mixture was filtered and the resulted solution was concentrated by vacuum. The purified product (a) was obtained via silica gel chromatography eluting with 20% ethyl acetate in petroleum ether and the
protecting group was cleaved by 95% TFA in CH$_2$Cl$_2$. The final yield of the product (b) was 70%.

**Peptide synthesis:** The peptide derivative was synthesized by solid phase peptide synthesis (SPPS) using 2-chlorotrityl chloride resin, the corresponding N-Fmoc protected amino acids with side chains properly protected by different groups. The first amino acid was loaded on the resin at the C-terminal with the loading efficiency of about 1.2 mmol/g. 20% piperidine in anhydrous N,N'-dimethylformamide (DMF) was used during deprotection of Fmoc group. Then the next Fmoc-protected amino acid was coupled to the free amino group using O-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluroniumhexafluorophosphate (HBTU) as the coupling reagent. The growth of the peptide chain was according to the established Fmoc SPPS protocol. At the final step, 2-naphthaleneacetic acid was used to attach to the peptide. After the last coupling step, excessive reagents were removed by a single DMF wash for 5 minutes (5 mL per gram of resin), followed by five steps of washing using DCM for 2 min (5 mL per gram of resin). The peptide derivative was cleaved using 95% of trifluoroacetic acid with 2.5% of TIS and 2.5% of H$_2$O for 30 minutes. 20 mL per gram of resin of ice-cold diethylether was then added to cleavage reagent. The resulting precipitate was filtrated and washed by ice-cold diethylether. The crude product was purified by HPLC and dried by lyophilizer.

**Compound (a):** $^1$H NMR (400 MHz, DMSO) δ 7.90 (d, J = 7.5 Hz, 2H), 7.71 (d, J = 7.4 Hz, 2H), 7.67 (d, J = 8.0 Hz, 1H), 7.42 (t, J = 7.4 Hz, 2H), 7.33 (t, J = 7.4 Hz, 2H), 4.43 – 4.37 (m, 1H), 4.30 (dd, J = 14.6, 8.6 Hz, 2H), 4.22 (t, J = 6.6 Hz, 1H), 4.11 – 4.01 (m, 2H), 3.38 (d, J = 7.2 Hz, 2H), 3.27 (d, J = 11.9 Hz, 1H), 3.11 (dd, J = 17.5, 7.6 Hz, 1H), 1.37 (s, 9H). ESI-MS: calc. M = 496.17, obsvd. (M+H)$^+$=497.20, (M+Na)$^+$=519.20.
Compound (b): $^1$H NMR (400 MHz, DMSO) $\delta$ 7.89 (d, $J = 7.5$ Hz, 2H), 7.89 (d, $J = 7.5$ Hz, 2H), 7.71 (d, $J = 7.4$ Hz, 2H), 7.63 (d, $J = 8.1$ Hz, 1H), 7.42 (t, $J = 7.4$ Hz, 2H), 7.33 (t, $J = 7.4$ Hz, 2H), 4.45 (dd, $J = 13.1, 7.8$ Hz, 1H), 4.30 (d, $J = 6.8$ Hz, 2H), 4.22 (t, $J = 6.9$ Hz, 1H), 4.13 – 4.01 (m, 2H), 3.41 – 3.36 (m, 2H), 3.28 (dd, $J = 13.1, 7.8$ Hz, 1H), 3.15 (dd, $J = 17.8, 7.9$ Hz, 1H). ESI-MS: calc. $M = 440.10$ obsvd. $(M+H)^+ = 441.15$, $(M+Na)^+ = 463.10$. 

![Fig. S-1. $^1$H NMR of Compound (a)](image1)

![Fig. S-2. ESI-MS of Compound (a)](image2)
Fig. S-3. $^1$H NMR of Compound (b)

Fig. S-4. ESI-MS of Compound (b)

**Compound 1:** $^1$H NMR (400 MHz, DMSO) $\delta$ 9.16 (s, 1H), 8.16 (dd, J = 46.7, 21.6 Hz, 6H), 7.81 (dd, J = 27.9, 23.6 Hz, 5H), 7.46 (dd, J = 22.3, 7.6 Hz, 3H), 7.16 (d, J = 9.7 Hz, 8H), 7.04 (d, J = 8.3 Hz, 2H), 6.64 (d, J = 8.3 Hz, 2H), 4.69 (d, J = 7.5 Hz, 1H), 4.52 – 4.43 (m, 3H), 4.04 (t, J = 6.0 Hz, 2H), 3.81 – 3.51 (m, 8H), 3.11 (d, J = 11.2 Hz, 1H), 2.95 (dd, J = 20.0, 13.9 Hz, 4H), 2.82 – 2.62 (m, 4H). HR-MS: calc. M = 957.34, obsvd. (M+H)$^+$ = 958.75.
Fig. S-5. $^1$H NMR of Compound 1

Fig. S-6. HR-MS of Compound 1
Hydrogel formation:

0.2 mg compound 1 was firstly dissolved in 200 μL 1× PBS with 2 equiv. Na₂CO₃ to adjust the pH value to 7.4. Upon heating, clear solution of compound 1 was obtained and hydrogel would form within 5 minutes after cooling down.

H₂O₂-response sensitivity of hydrogel of compound 1: The H₂O₂-response sensitivity of the hydrogel of compound 1 was evaluated by following the gel–sol transition after the addition of 0–100 mM H₂O₂ present in the gel, the proportion of the volumes of hydrogel and H₂O₂ solutions added was 10:1.
**Fig. S-9.** Photographs of hydrogel of compound 1 after the addition of varying amounts of H$_2$O$_2$ at 37 °C within 24 hours: A, 0 mM; B, 1 mM; C, 2 mM, D, 4 mM; E, 10 mM; F, 20 mM; G, 40 mM; H, 80 mM; I, 100 mM.

**Fig. S-10.** Response times of gel-sol change of compound 1 after the addition of varying amounts of H$_2$O$_2$ at 37 °C within 24 hours

**Determination of conversion percentage:**

20 equiv. H$_2$O$_2$ in 10 μL 1×PBS was added on the top of each 200 μL hydrogel formed by compound 1 and incubated at 37 °C (the final concentration of H$_2$O$_2$ was 40 mM). At predetermined time points, each hydrogel was dissolved in 300 μL CH$_3$OH followed by LC-MS analysis. The areas of peaks in LC-MS spectra were used to determine the conversion percentage.
**Fig. S-11.** Conversion percentage of compound 1 upon addition of 40 mM H$_2$O$_2$

**Rheology:**
The rheology test was done on an AR 1500ex (TA Instrument) system, 25 mm parallel plates was used during the experiment at the gap of 500 μm. The gels were firstly characterized by the mode of dynamic frequency sweep in the region of 0.1–100 rad/s at the strain of 0.5% followed by a dynamic strain sweep at the frequency of 1 rad/s at the region of 0.1%-10%.

**Fig. S-12.** Dynamic frequency sweep of hydrogel at the strain of 0.5% after the addition of 40 mM H$_2$O$_2$ at different time points: 0 hour (A), 2$^{\text{th}}$ hour (C) and 4$^{\text{th}}$ hour (E); strain sweep of hydrogel after the addition of 40 mM H$_2$O$_2$ at different time points: 0 hour (B), 2$^{\text{th}}$ hour (D) and 4$^{\text{th}}$ hour (F).