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Supporting Information

Reversible Photoelectrochemical Microsensor for Dynamically Monitoring Sulfur Dioxide in Epileptic Brain

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1.1 Chemicals and Reagents

4'-Dimethylaminoacetophenone, 4-(diethylamino) salicylaldehyde, 4-aminoacetophenone, kainic acid (KA), N-methylmaleimide (NMM) and acetyl chloride were purchased from sigma-Aldrich. Adenosine triphosphate (ATP), glucose, lactose, 3-mercaptopropionic acid (MPA), ascorbic acid (AA), dopamine (DA), L-arginine (Arg), L-cysteine (L-Cys), L-glutamine (Glu), L-histudine (His), L-leucine (Leu), glutathione (GSH), L-tryptophan (Try), valine (Val), lysine (Lys), methionine (Met) and homocysteine (Hcy) were purchased from Aladdin Reagent. $Y(NO_3)_3 \cdot 5H_2O$, $Yb(NO_3)_3 \cdot 5H_2O$, $Er(NO_3)_3 \cdot 5H_2O$, NaF, $NaTeO_3$, $NaBH_4$, $Cd(NO_3)_2$, $NaNO_3$, $NaNO_2$, NaClO, Na_2SO_4, Na_2SO_3, Na_2S and other chemicals were purchased from Sinopharm Chemical Reagent Co. ltd. (Shanghai, China). AR grade regents were obtained from commercial sources and were used without further purification. Ultrapure water obtained from a Millipore water purification system (Milli-Q, 18.25 MΩ•cm) was used in all experiments at room temperature. Artificial cerebrospinal fluid (aCSF) was prepared as reported previously[1]. In the selectivity test, different reactive oxygen species (ROS) and reactive nitrogen species (RNS) were produced as follows: hydroxy radical (•OH) was generated through Fenton Chemistry (Fe^{2+}/H_2O_2 = 1: 6). Peroxynitrite ($ONOO^-$) stock solution was prepared by a reported method: HCl (0.6 M, 10 mL) was added to a vigorously stirred solution of $NaNO_2$ (0.6 M, 10 mL) and H_2O_2 (0.7 M, 10 mL) in ultrapure water at 0°C, immediately followed by the rapid addition of NaOH (1.5 M, 20 mL). Other ROS were prepared according to literature methods[2].

1.2 Animal experiments

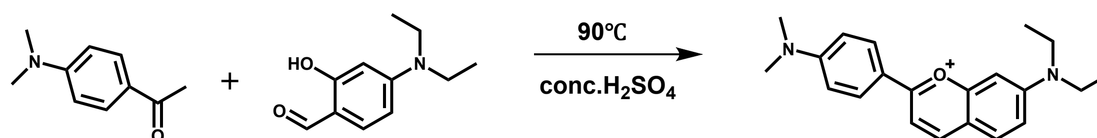
Adult female Kunming mice (25 g) were purchased from Experimental Animal Center of China Three Gorges University (Yichang, China). The mice were housed on a 12:12 h light-dark schedule with food and water freely. All animal experiments were performed according to the

Guidelines for the Care and Use of Laboratory Animals of the Chinese Animal Welfare Committee and approved by the Institutional Animal Care and Use Committee, Wuhan University Center for Animal Experiment, Wuhan, China.

1.3 Apparatus and Measurements

Nuclear magnetic resonance ^{1}H (^{1}H NMR) spectra and nuclear magnetic resonance ^{13}C (^{13}C NMR) spectra were recorded on a Varian INOVA 600 spectrometer, with TMS as an internal standard. High-resolution mass spectra (ESI-HRMS) were obtained from Thermo Fisher Scientific mass spectrometer of Exactive Plus. Scanning electron microscope (SEM) images and energy dispersive spectroscopy (EDS) were measured under the field emission scanning electron microscope (FE-SEM, Zeiss Sigma 500) at an acceleration voltage of 5 kV. The size and morphology were acquired by high resolution transmission electron microscopy (TEM, Tecnai G20, 200KV). Absorption spectra were recorded by UH-4150 spectrophotometer (Hitachi, Japan). Fluorescence spectra excited by a 980 nm laser were measured by F-4600 fluorometer (Hitachi Instrument). Local injections were controlled with a microinjection pump (kd Scientific LEGATO130, USA). Photoelectrochemical experiments were performed on an electrochemical workstation (CHI 660E, Chenhua Co. Ltd, Shanghai, China) with a standard three-electrode system consisting of an Ag/AgCl electrode as the reference electrode and a platinum wire as the counter electrode, and the work electrode was prepared as the following described. Ag/AgCl electrode was self-prepared by dipping the silver wire (0.15 mm) in $FeCl_3$ solution (1 M) for 30 min.

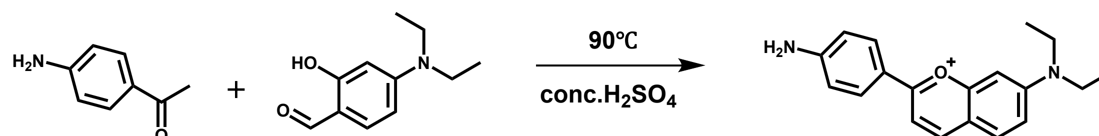
1.4 Synthesis of rSO_2-1



A mixture of 4'-Dimethylaminoacetophenone (0.163g, 1 mmol) and 4-(diethylamino) salicylaldehyde (0.193 g, 1 mmol) was dissolved in conc.H_2SO_4 (3 mL). The resulting reaction mixture was then stirred at 90 °C for 1.5 h. After cooling to the room temperature, 70% perchloric acid (0.5 mL) was added, followed by pouring the solution into ice water (100 mL). The resulting crude product was obtained by filtration and washed with water. The crude product was further purified by column chromatography on silica gel, using a mixture of CH_2Cl_2 and CH_3OH in a ratio of 20:1. This purification process afforded rSO_2-1 as a violet black powder with a yield of 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 8.5 Hz, 1H), 8.06 (d, J = 9.1 Hz, 2H), 7.65 (d, J = 9.2 Hz, 1H), 7.53 (d, J = 8.6 Hz, 1H), 7.02 (dd, J = 9.2, 2.2 Hz,

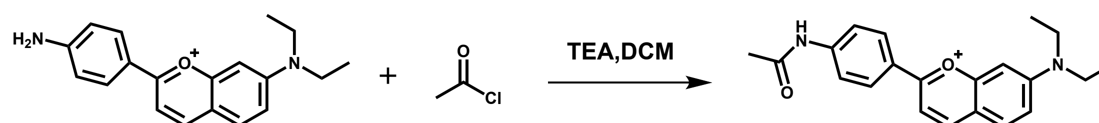
1H), 6.94 (d, J = 1.9 Hz, 1H), 6.78 (d, J = 9.1 Hz, 2H), 3.61 (q, J = 7.1 Hz, 4H), 3.14 (s, 6H), 1.32 (t, J = 7.1 Hz, 6H). HRMS (ESI): calcd. for $C_{21}H_{25}N_2O^+$, $[M^+H]^+$, m/z, 321.1961, found: 321.1953.

1.5 Synthesis of rSO_2-2



4-aminoacetophenone (0.135g, 1 mmol) and 4-(diethylamino) salicylaldehyde (0.193 g, 1 mmol) were dissolved in conc.H_2SO_4 (3 mL). The resulting mixture was stirred at 90 °C for 1.5 h. After the reaction, the solution was cooled to room temperature an 70% perchloric acid (0.5 mL) was added. The mixture was then poured into ice water (100 mL). The crude product was obtained by filtering and washing with water. To purify the crude product, column chromatography on silica gel was performed using a mixture of CH_2Cl_2 and CH_3OH in a ratio of 30:1 as the eluent. This purification process yielded rSO_2-2 as fuchsia powder with a yield of 85%. ^1H NMR (400 MHz, DMSO-d_6) δ 8.53 (d, *J* = 8.6 Hz, 1H), 8.17 (d, *J* = 8.7 Hz, 2H), 7.84 (d, *J* = 9.6 Hz, 1H), 7.82 (d, *J* = 11.1 Hz, 1H), 7.28 (d, *J* = 9.3 Hz, 1H), 7.21 (s, 1H), 6.78 (d, *J* = 8.7 Hz, 2H), 5.32 (s, 2H), 3.63 (q, *J* = 6.8 Hz, 4H), 1.22 (t, *J* = 6.9 Hz, 6H). HRMS (ESI): calcd. for $C_{21}H_{25}N_2O^+$, $[M^+H]^+$, m/z, 293.1648, found: 293.1640.

1.6 Synthesis of rSO_2-3



rSO_2-2 was dissolved in anhydrous dichloromethane together with a few drops of triethylamine, and then the solution was stirred for ten minutes under nitrogen atmosphere. Acetyl chloride, also dissolved in anhydrous dichloromethane, was added dropwise to the reaction mixture in an ice bath. The mixture was stirred overnight at room temperature. The excess acetyl chloride was quenched by adding a small amount of water, and the crude product was extracted with dichloromethane. The crude product was then purified by column chromatography on silica gel (CH_2Cl_2/CH_3OH, 100:1) to afford rSO_2-3 as fuchsia powder (yield, 95%). ^1H NMR (400 MHz, DMSO-d_6) δ 10.54 (s, 1H), 8.79 (d, J = 8.0 Hz, 1H), 8.36 (d, J = 8.8 Hz, 2H), 8.09 7.93 (m, 2H), 7.88 (d, J = 8.8 Hz, 2H), 7.50 (d, J = 9.3 Hz, 1H), 7.36 (s, 1H), 3.72 (d, J = 6.8 Hz, 4H), 2.13 (s, 3H), 1.26 (t, J = 6.8 Hz, 6H). HRMS (ESI): calcd. for $C_{21}H_{25}N_2O^+$, $[M^+H]^+$, m/z, 335.1751, found: 335.1754.

1.7 Synthesis of CdTe quantum dots

CdTe quantum dots (CdTe QDs) were synthesized according to a previously described method.[3] Briefly, a mixture solution containing 59 mg of $Cd(NO_3)_2$, 100 mg of trisodium citrate, 25 μL of MPA (3-mercaptopropionic acid), and 25 mL of ultrapure water was prepared. The pH of the solution was adjusted to 10.5 using 10 M NaOH under stirring. Sequentially, 11.1 mg of Na_2TeO_3 and 18.9 mg of $NaBH_4$ were added to the solution. The reaction mixture was then refluxed for 180 minutes under an oil bath maintained at 120°C. The resulting CdTe QDs were precipitated and washed with isopropanol. The solvent was subsequently removed by centrifugation at 8000 rpm, and the product was dried and stored in a dark environment.

1.8 Synthesis of PAA-$NaYF_4$:Yb,Er upconversion nanoparticles

$NaYF_4$:Yb,Er upconversion nanoparticles (UCNPs) were obtained by a typical solvothermal method as described previously. In briefly, the mixture including $Y(NO_3)_3·5H_2O$ (4 mmol), $Yb(NO_3)_3·5H_2O$ (0.9 mmol), $Er(NO_3)_3·5H_2O$ (0.1 mmol) were dissolved in 8 mL ultrapure water and 18 mL ethyl alcohol under 60°C. NaF solution (4 mmol in 3 mL ultrapure water) was dropwise added into the foregoing solution under vigorous stirring. After stirring for another 30 min to clarify the solution, the suspension was carefully transferred into a 50 mL Teflon-lined autoclave. The autoclave was heated at 200°C for 10 hours with a programmed temperature rise rate of 15 °C/min. Subsequently, UCNPs were washed with ethanol and ultrapure water for three times. To obtain PAA-functionalized UCNPs, the resulting UCNPs were mixed with poly (acrylic acid) (PAA) dissolved in ultrapure water with a quality ratio of 1:20. The suspension was stirred vigorously at room temperature for 24 h. The resulting PAA-coated UCNPs were then precipitated by centrifugation and washed for three times with EtOH and ultrapure water, and finally redispersed in 10 mL ultrapure water for the further use.

1.9 Preparation of the rSO_2-UCNPs

The UCNPs were mixed various concentrations of an aqueous solution of rSO_2 (containing 1% DMSO) in a total volume of 1 mL. The mixture solution was shaken gently overnight, and then centrifuged to remove the excess rSO_2. The resulting products were washed with ultrapure water for several times until the supernatant appeared clean. Subsequently, the rSO_2-UCNPs were redispersed in ultrapure water for the further use.

1.10 Preparation of acidified multi-wall carbon nanotubes

Acidified multi-wall carbon nanotubes (MWCNTs) were prepared through acid treatment. Commercial MWCNTs with the outer diameter of 10 - 20 nm and the length of 10 - 30 μm were

added into a flask containing concentrated nitric acid and then the mixture was refluxed for 4 h at 140 °C to accomplish the acidification process. After cooling to the room temperature, the products were washed with an ample of deionized water until the pH of the solution reached 7.0. Then the solution was filtered and dried at 60 °C for 6 h. Finally, the acidified MWCNTs were obtained.

1.11 Preparation of anti-fouling substrate film

A 3D anti-fouling substrate film was prepared according to the optimal condition described in the previous report. [4] Briefly, 5 mg/mL BSA was dissolved in 1 mL PBS (pH 7.4), and then 1 μL GA (25%, wt%) was added to the solution. The mixed solution was gently shaken and transferred to a refrigerator (4 °C) for a minimum of 24 h to accomplish the crosslinking process. As a result, a 3D porous matrix colloid crosslinked with BSA and GA was obtained for the electrode fouling resistance.

1.12 Preparation of CdTe-MWCNTs nanocomposites

A mixture of 5 mg/mL of MWCNTs and 10 mg/mL of CdTe QDs was prepared in a 1:1 (v/v) ratio. The mixture was subjected to ultrasonication for 20 min to facilitate the self-assembly process. Subsequently, CdTe-MWCNTs nanocomposites were purified by centrifugation and then dispersed in ultrapure water to yield the composite solution.

1.13 Preparation of TiME

Commercialized titanium wire with a diameter of 100 μm was etched with the mixed acid consisting of 3% hydrofluoric acid, 6% nitric acid and 91% ultrapure water for 6 minutes. The etched titanium wire was then sequentially ultrasonicated in acetone, ethanol and water. After dying at 37°C, the titanium wire was cut into 1 cm-long segments. These treated titanium wire segments were connected to the copper wires by using conductive silver glue, forming titanium wire electrodes. Next, the titanium wire electrode was placed in the center of the capillary tube pre-drawn by a capillary puller, along with an optical fiber (0.2 mm in inter diameter). The assembly was left to dry overnight at the room temperature to ensure firm adhesion of the glue. Then, the capillary was filled with optical glue and cured by a UV lamp. Finally, any excessive titanium wire was cut off, leaving a 0.6 mm tip exposed as the working electrode (referred to as TiME) for the further use.

1.14 Modification of RPMS

The TiME was immersed in 2 μL solution of CdTe-MWCNTs nanocomposites for 24 h. Afterward, the modified electrode was immersed in 2 μL solution of rSO_2-UCNPs composites

and dried at room temperature for 6 h to accomplish the modification process. The microelectrode was then immersed in BSA-GA crosslinking solution and dried at 37 ℃ to form a film. The resulting microelectrode, which underwent the final modification process, was referred as to as RPMS and was stored for the further use.

1.15 Preparation of fluorescein isothiocyanate-labeled BSA and protein adsorption test.

To study the protein adsorption efficiency, BSA labeled with a green fluorescent dye named fluorescein isothiocyanate (FITC) was utilized. Firstly, BSA (10 mg/mL) and FITC (0.2 mg/mL) were separately dissolved in 0.1 mol/L carbonate bicarbonate buffer at pH 9.0. Equal volumes of BSA and FITC solutions were mixed and incubated in the dark at 4 ℃ for 4 h to form FITC-BSA. FITC-BSA was then washed several times with ultrapure water until no fluorescence was detected in the solution, which was monitored at 450 nm by fluorescence spectrometer. The purified FITC-BSA was obtained by ultrafiltration (10 kDa, 5000 rpm, 10 min). Finally, the prepared FITC-BSA was concentrated to 40mg/mL and stored at 4 ℃ in the dark for the further use. To test the protein adsorption ability, both the microelectrode with and without BSA-GA anti-fouling film modification were immersed in 1% FITC-BSA solution for 8 h. Afterward, they were gently washed with ultrapure water. Finally, fluorescence images of the microelectrodes were captured using confocal laser scanning microscopy.

1.16 Photoelectrochemical (PEC) and electrochemical (EC) measurements

PEC and EC measurements were both carried out on a CHI 660E electrochemical workstation using a conventional three-electrode configuration. For in vitro PEC tests, the proposed RPMS was employed as the working electrode, while Ag/AgCl electrode served as the reference electrode, and the platinum wire acted as the counter electrode. A 980 nm laser was employed as the excitation light source for UCNPs in the PEC measurements. The electrolyte solution was artificial cerebrospinal fluid (aCSF, 100 mM) containing 200 μM AA if not stated otherwise. The concentration of Na_2SO_3 in the testing system was increased by adding different volume of concentrated Na_2SO_3 solution and decreased by adding different volume of aCSF solution containing 200 μM AA. All the PEC measurements were performed under the bias voltage of 0 V.

During in vivo detection, the mice were induced into anesthesia with 3% isoflurane and maintained in an anesthetized state with 1% isoflurane. Subsequently, the anesthetized mice were positioned on a stereotaxic frame (RWD Life Science 680026, China) following standard stereotaxic procedures. Carefully clip the scalp to expose the skull, and using a bone drill to carefully create a hole based on the stereotactic coordinates. Then, the RPMS was insert into

the corresponding brain region through the hole by a positioning arm. A counter electrode and an Ag/AgCl reference electrode was inserted in a 2 mm plastic cannula, which positioned at around 3 mm away from the working electrode.

1.17 Cell culture and cytotoxicity test

The cytotoxicity of RPMS was evaluated by calcein-AM/PI double stain kit with HBMEC cells. The cells were seeded on a confocal dish coated with CdTe-MWCNTs/rSO_2-UCNPs/BSA-GA, and cultured in DMEM containing 10% of fetal bovine serum (FBS), and 100 U/mL penicillin-streptomycin at 37 °C under 5% CO_2 atmosphere for 48 h. After that, the cells were washed with PBS, and then calcein-AM (2 μM) and propidium iodide (PI, 4.5 μM) were added to the cell culture and incubated for 15 min. Subsequently, cells were washed again with PBS to remove excess staining solution. for the confocal laser scanning microscopy imaging. Finally, confocal laser scanning microscopy was used to image the cells and assess their viability based on the calcein-AM (live cells, green fluorescence) and propidium iodide (dead cells, red fluorescence) staining.

1.18 Response of rSO_2 in aqueous solution

To obtain UV-Vis and fluorescence spectra under different conditons, the following steps were performed: Different volume of concentrated Na_2SO_3 was added into the aCSF solution containing a fixed amount of rSO_2 or UCNPs-rSO_2. The UV-Vis and fluorescence spectra were recorded after incubated at 37 °C for 1 min. Then. different volume of concentrated NMM was added into the system with a fixed concentration of Na_2SO_3, which was incubated at 37 °C for 2 min. Finally, the UV-Vis and fluorescence spectra of the mixture were measured.

1.19 Local Na_2SO_3 delivery in mice

All animal studies were performed according to the Guidelines for the Care and Use of Laboratory Animals of the Chinese Animal Welfare Committee and approved by the Institutional Animal Care and Use Committee, Wuhan University Center for Animal Experiment, Wuhan, China. The mice were induced into anesthesia with 3% isoflurane and maintained in an anesthetized state with 1% isoflurane. Subsequently, the anesthetized mice were positioned on a stereotaxic frame (RWD Life Science 680026, China) following standard stereotaxic procedures. The exogenous SO_2 source (Na_2SO_3:$NaHSO_3$=3:1, M:M, 500 μM) was injected into the hippocampus at coordinates AP = 2.06 mm, L = 1.875 mm from bregma, and V = 1.583 mm from skull, using microinjector at a perfusion rate of 1 μL/min for 1 min. After injection, the needle was remained in situ for 5 min before being slowly removed. Then, an

RPMS was implanted at the same coordinates and a counter electrode and an Ag/AgCl reference electrode inserted in a 2 mm plastic cannula were positioned at around 3 mm away from the working electrode. To remove the injected Na_2SO_3 and $NaHSO_3$, N-methylmaleimide (NMM, 3 mM) was injected by the same way.

1.20 Model of acute SO_2 poisoning

A mixture of Na_2SO_3 and $NaHSO_3$ with a mole ratio of 3:1 (200 μmol/kg) was intraperitoneally injected into the anesthetized mice to simulate SO_2 intoxication. After 1.5 h, NMM (60 μL, 20 mg/mL) was intravenously injected. Photocurrent signals and AAT activity of hippocampus were recorded by RPMS after the first injection and subsequently recorded every half an hour. AAT activity of hippocampus was measured as described previously according to the instructions of the AAT activity assay kit (Nanjing Jiancheng, Nanjing, China).

1.21 Monitoring SO_2 in the epilepsy model

The kainic acid (KA) induced status epilepticus (SE) mice model was established according to the previously reported method with minor modifications. Specifically, epilepsy models were induced by injecting 50 $mg \cdot kg^{-1}$ KA. The administered mice exhibited repeated tonic-spasm episodes within 10-30 min, and then were fully anesthetized. According to Racine grading standards, mice with facial clonus, rhythmic nodding and myoclonus of forelimbs, but no upright position of hind limbs were classified into Racine III stage, which were selected as the experimental group. Mice in the control group received intraperitoneally injection of the same dose of saline as the SE group. Photocurrent signals were recorded every half an hour from KA injection in different brain regions (CA1: AP = 2.06 mm, L = 1.875 mm from bregma, V = 1.583 mm from skull, M1: AP = 0.62 mm, L = 1.75 mm from bregma, V = 1.05 mm from skull, CPU: AP = 0.62 mm, L = 1.50 mm from bregma, V = 4.00 mm from skull). In SO_2 pretreated group, SO_2 were injected intraperitoneally 30 min before KA injection.

Results and Discussion

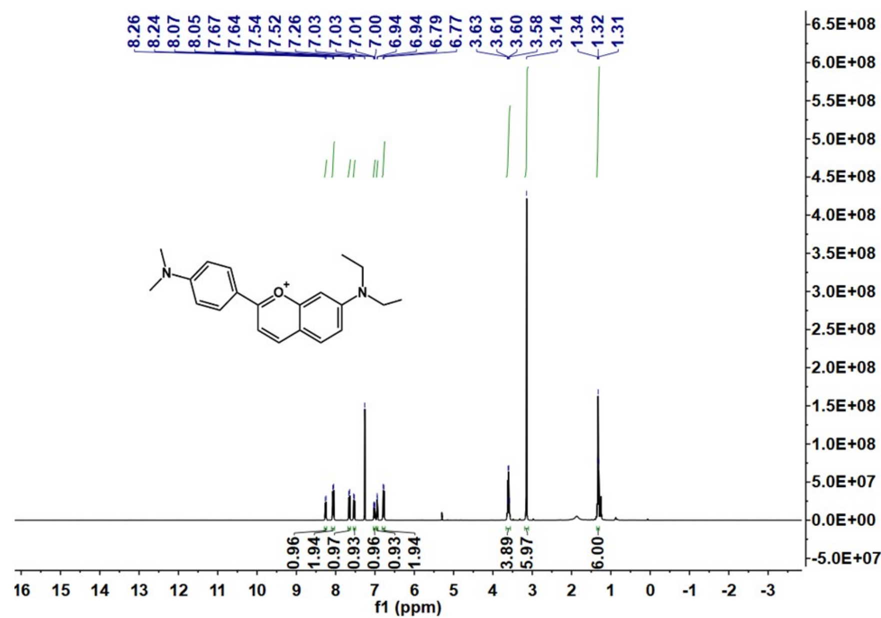


Figure S1. ^{1}HNMR spectrum of compound rSO_2-1 (400 MHz, $CDCl_3$).

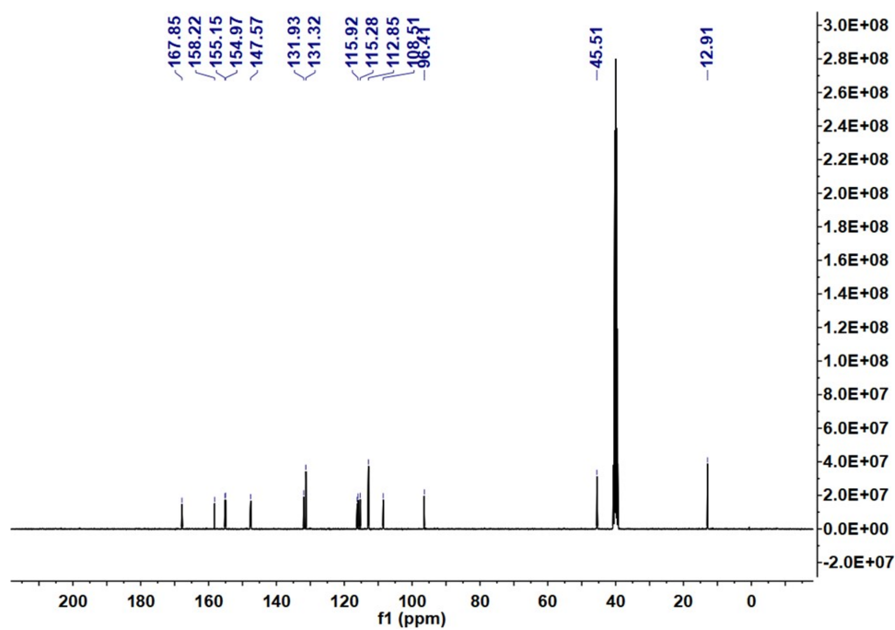
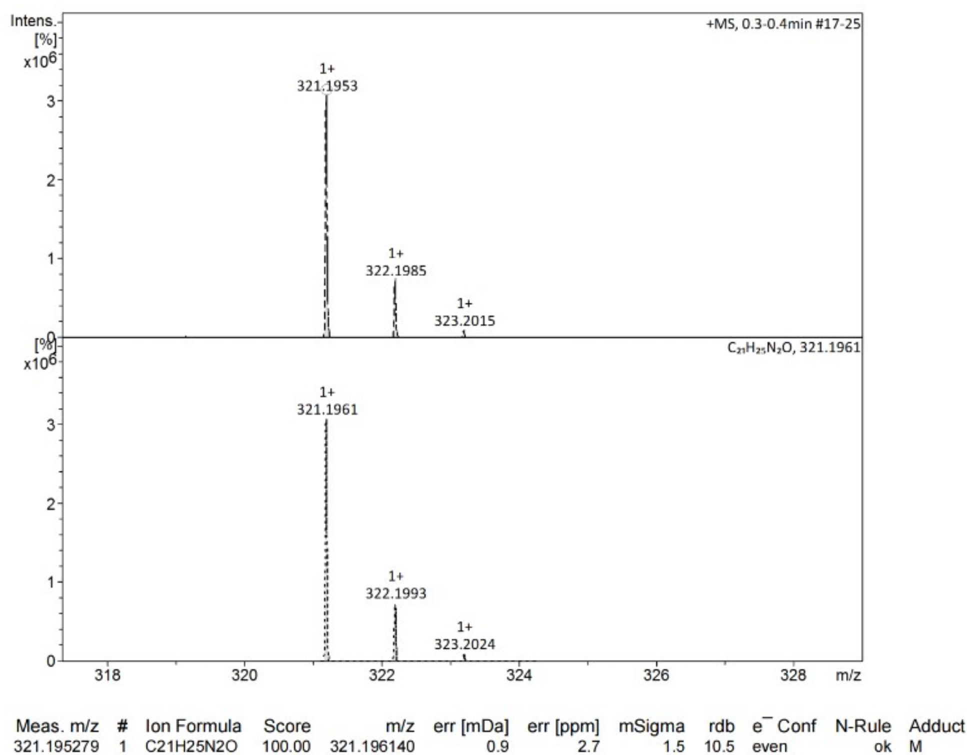


Figure S2. ^{13}CNMR spectrum of compound rSO_2-1 (400 MHz, DMSO-d_6).



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule	Adduct
321.195279	1	C21H25N2O	100.00	321.196140	0.9	2.7	1.5	10.5	even	ok	M

Figure S3. ESI-HRMS spectrum of compound rSO_2-1.

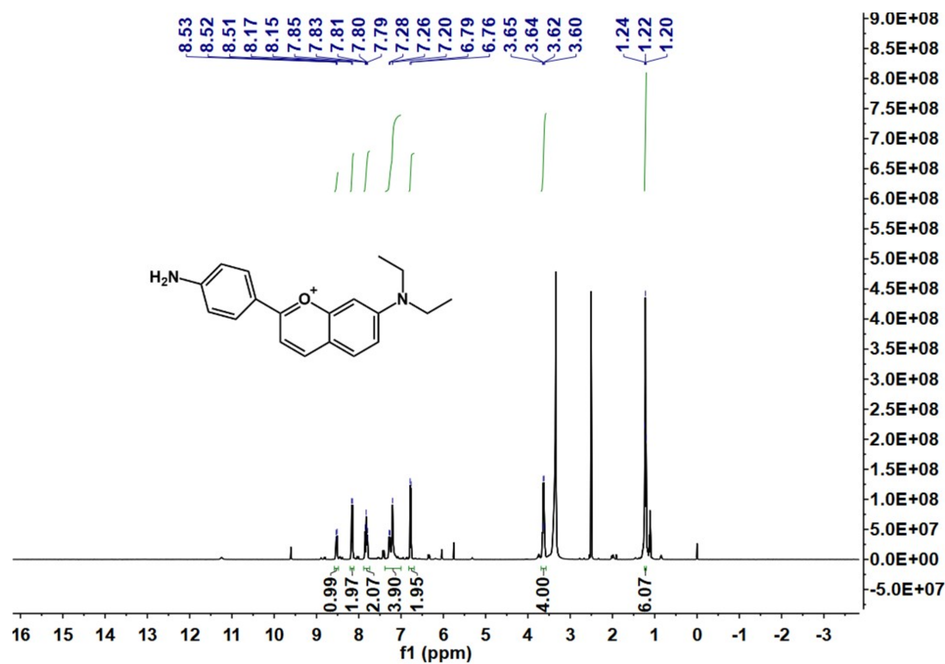


Figure S4. ^{1}HNMR spectrum of compound rSO_2-2 (400 MHz, DMSO-d_6).

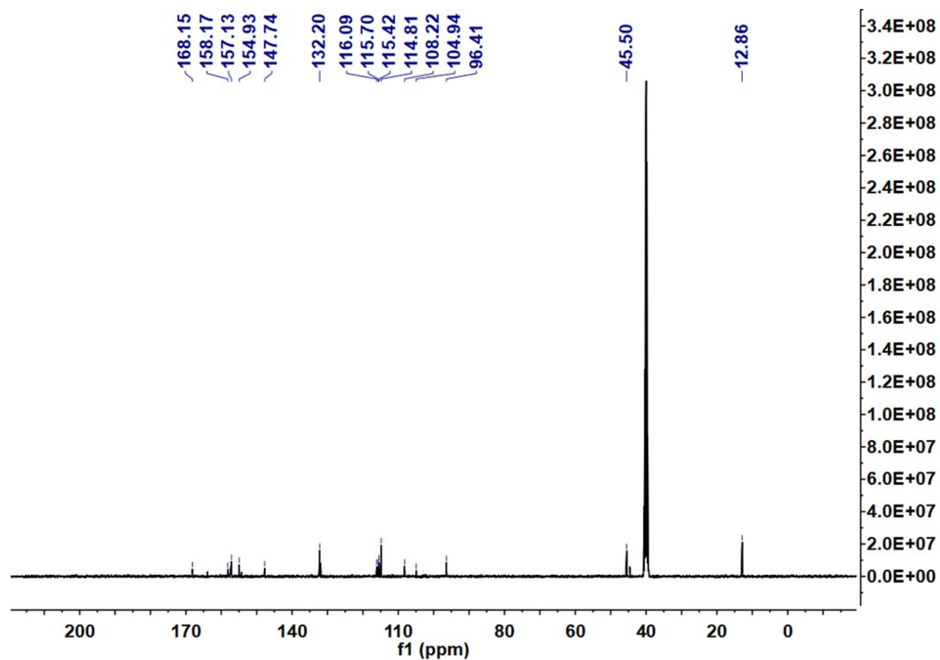


Figure S5. ^{13}CNMR spectrum of compound rSO_2-2 (400 MHz, DMSO-d_6).

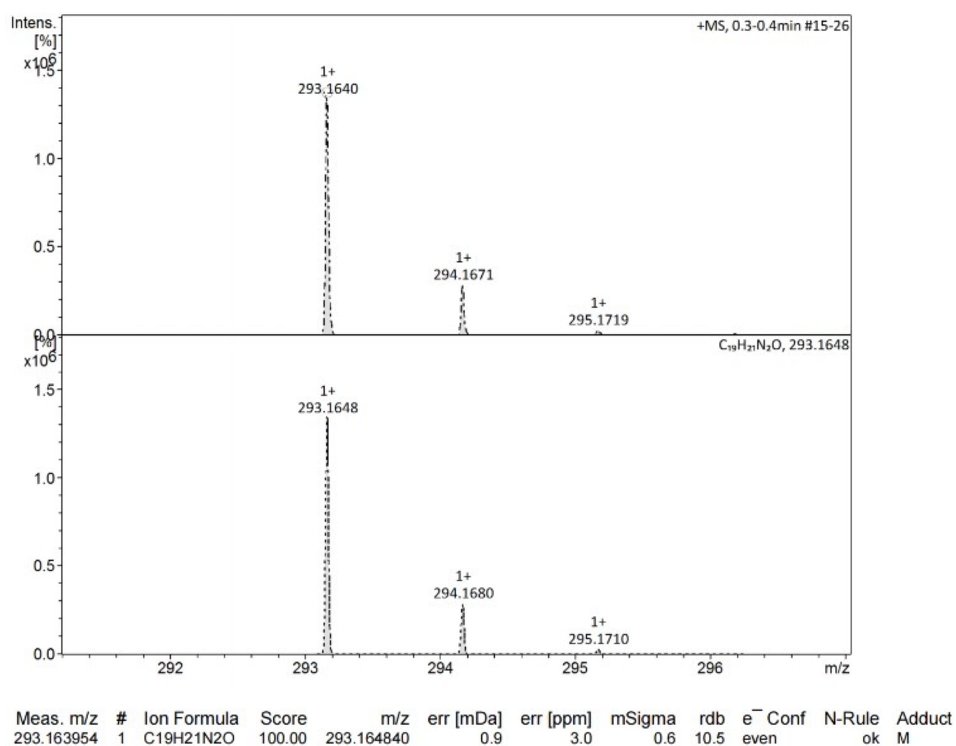


Figure S6. ESI-HRMS spectrum of compound rSO_2-2.

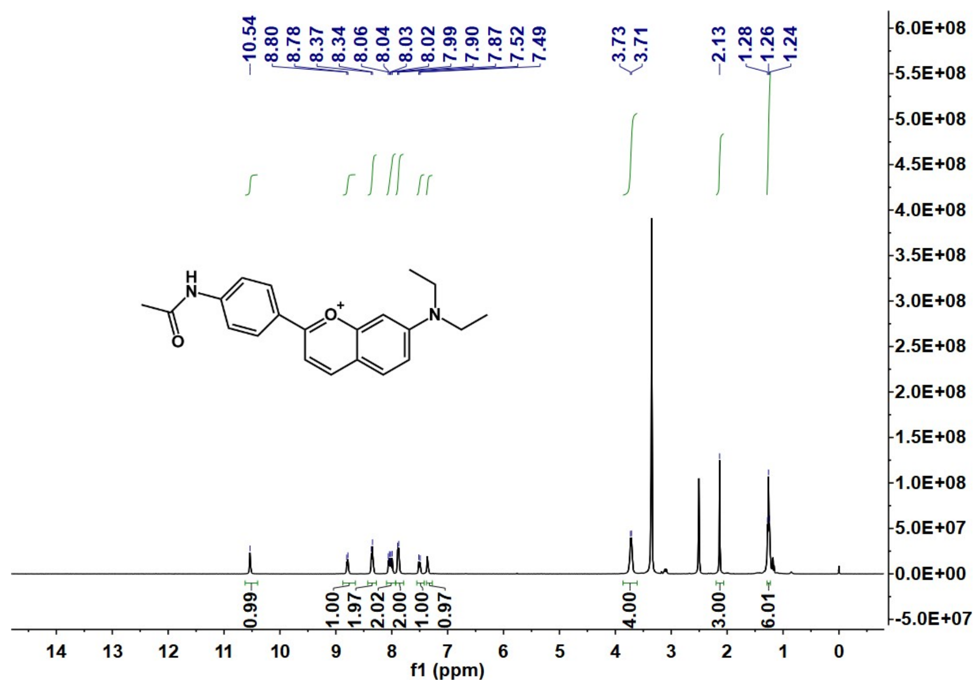


Figure S7. ^{1}HNMR spectrum of compound rSO_2-3 (400 MHz, DMSO-d_6).

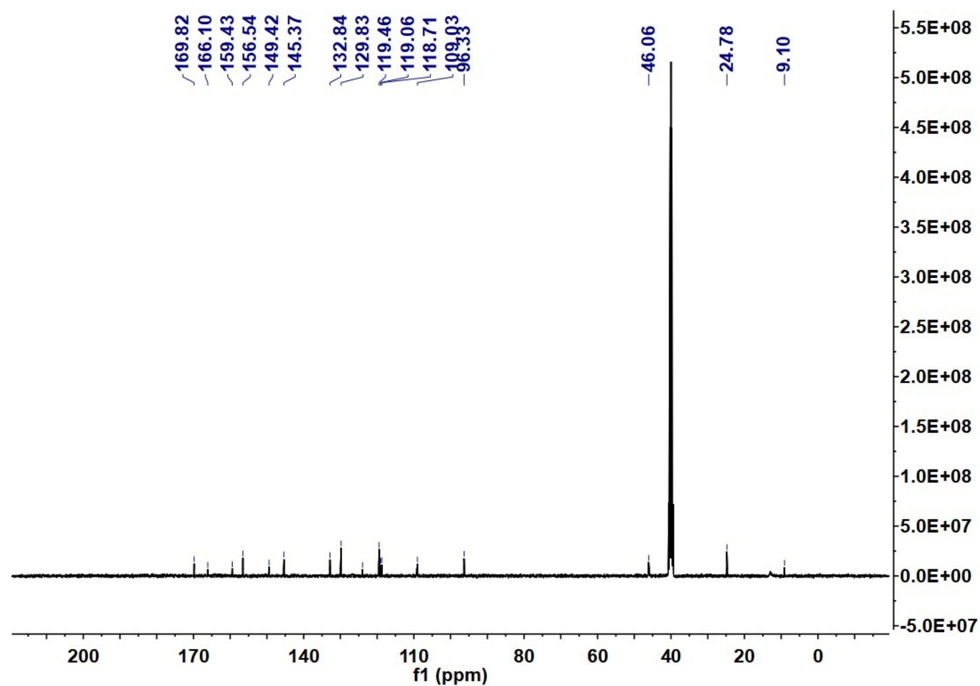
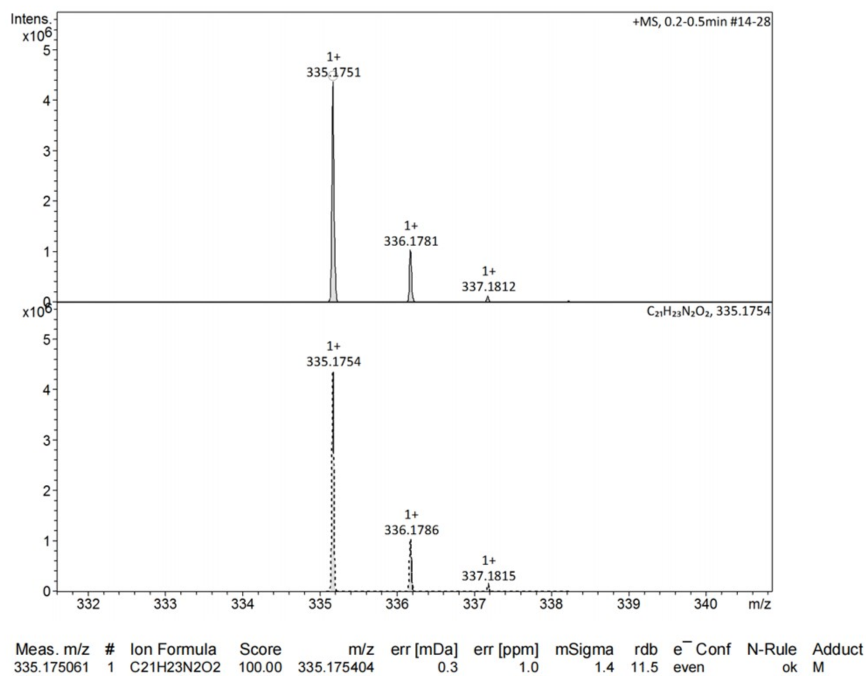


Figure S8. ^{13}CNMR spectrum of compound rSO_2-3 (400 MHz, DMSO-d_6).



Meas. m/z	#	Ion Formula	Score	m/z	err [mDa]	err [ppm]	mSigma	rdb	e⁻ Conf	N-Rule	Adduct
335.175061	1	C21H23N2O2	100.00	335.175404	0.3	1.0	1.4	11.5	even	ok	M

Figure S9. ESI-HRMS spectrum of compound rSO_2-3.

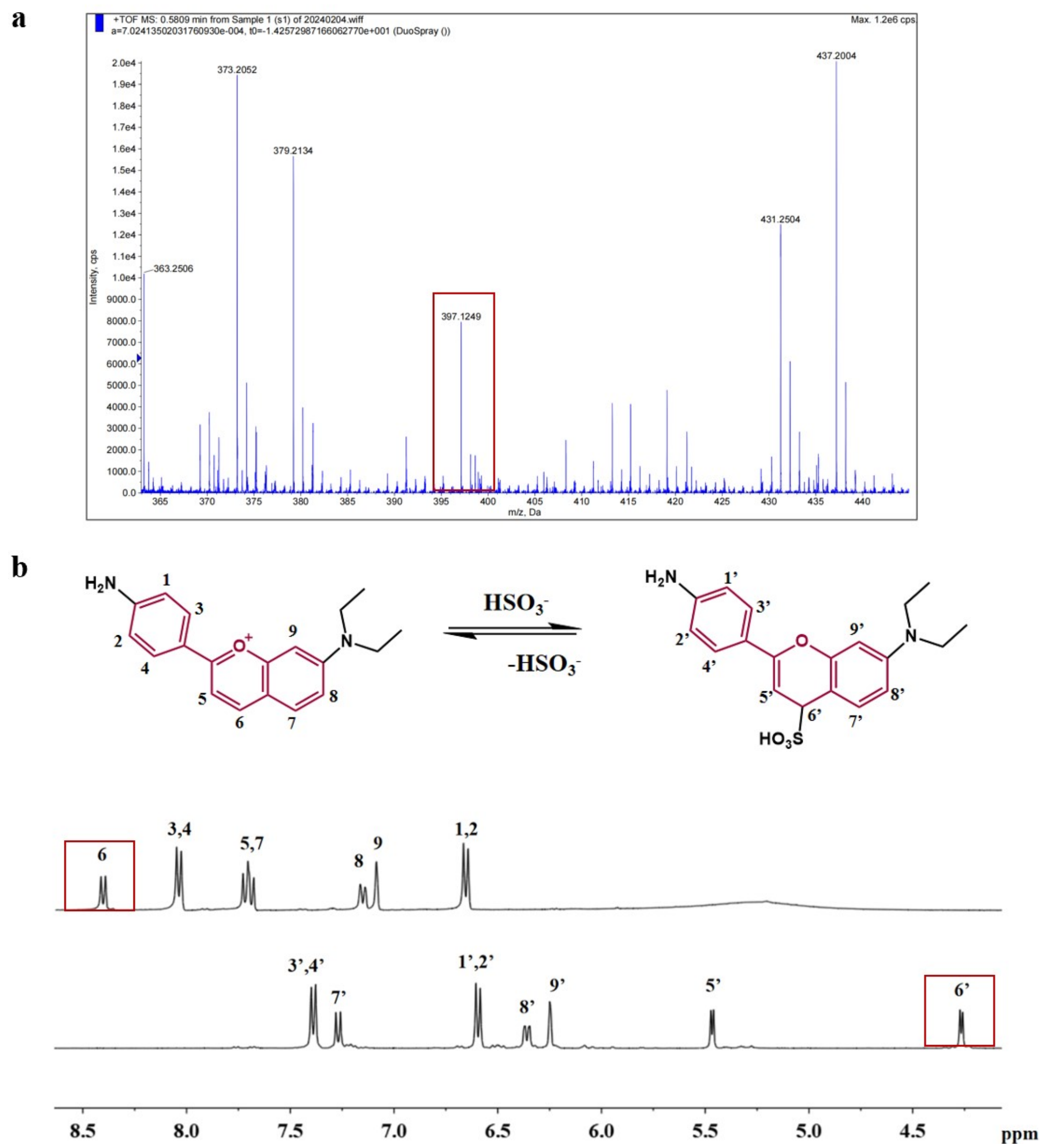


Figure S10. a) Mass spectrometry: calcd for $C_{19}H_{22}N_2O_4SNa$ m/z $[M+Na]^+$ = 397.1198; b) ^1H NMR spectroscopy of the products after the reaction of $rSO_{2-}2$ with sulfite.

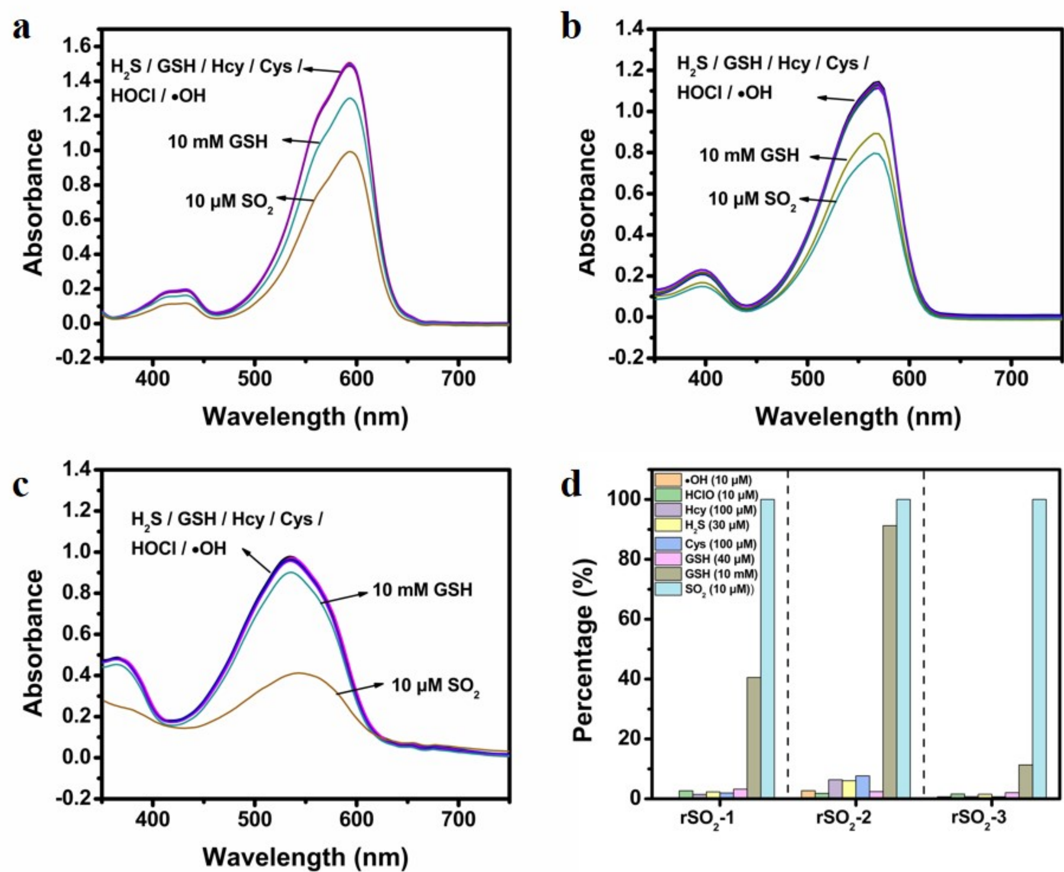


Figure S11. UV-Vis spectra before and after the addition of SO_2 and various interfering substances in the solution of rSO_2-1 (a), rSO_2-2 (b), rSO_2-3 (c): •OH (10 μM), HClO (10 μM), Hcy (100 μM), H_2S (30 μM), Cys (100 μM), GSH (40 μM), GSH (10 mM), SO_2 (10 μM). d) Analysis of the percentage changes in absorbance in (a), (b), (c).

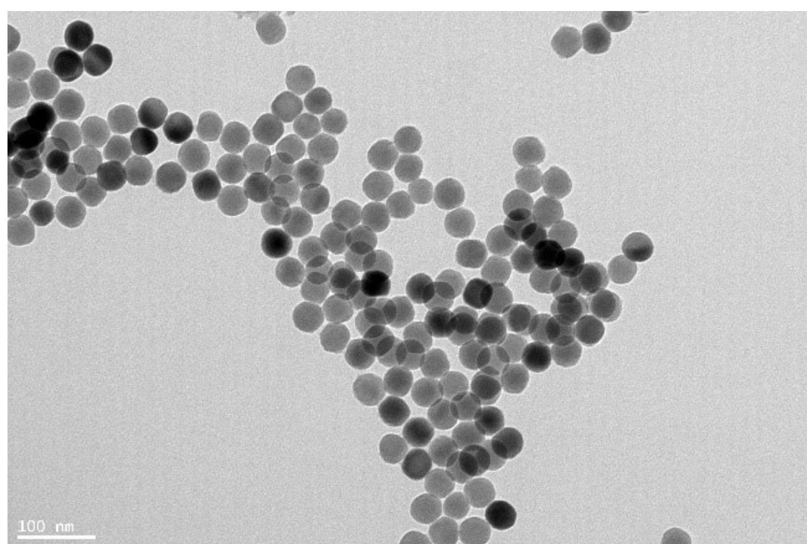


Figure S12. TEM image of UCNPs.

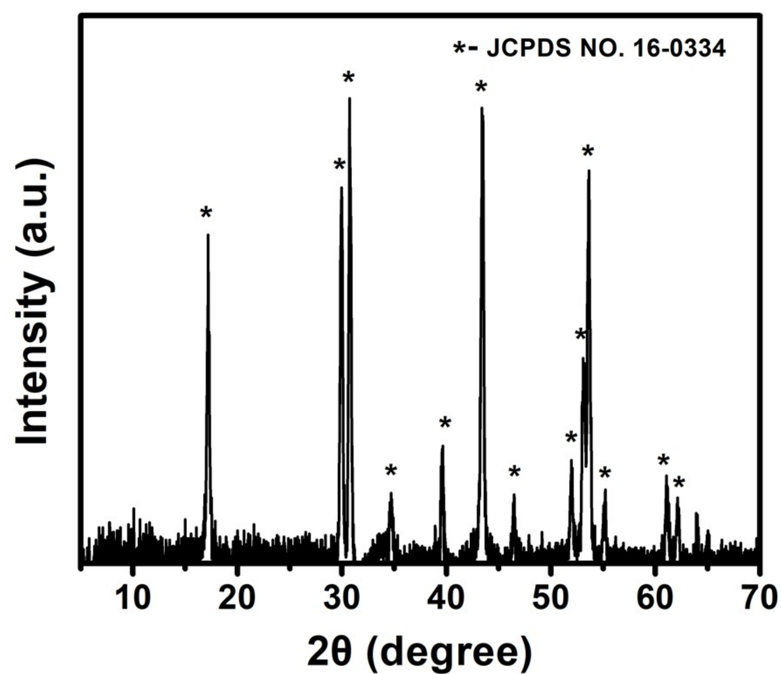


Figure S13. XRD spectrum of UCNPs.

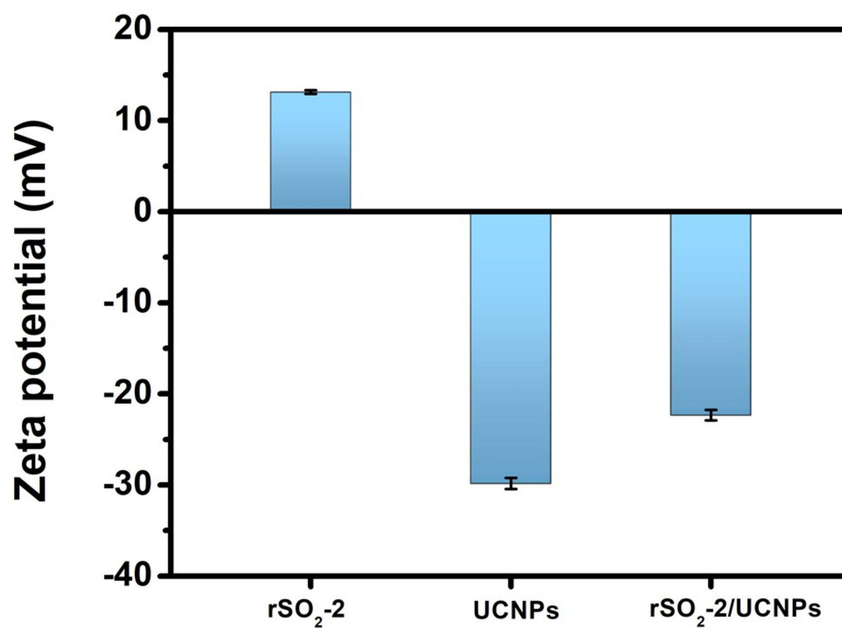


Figure S14. The Zeta potential of rSO_2-2, UCNPs, rSO_2-2/UCNPs.

Figure S15. The picture of the encapsulated titanium wire electrode within a glass capillary with an exposure length of 600 µm.

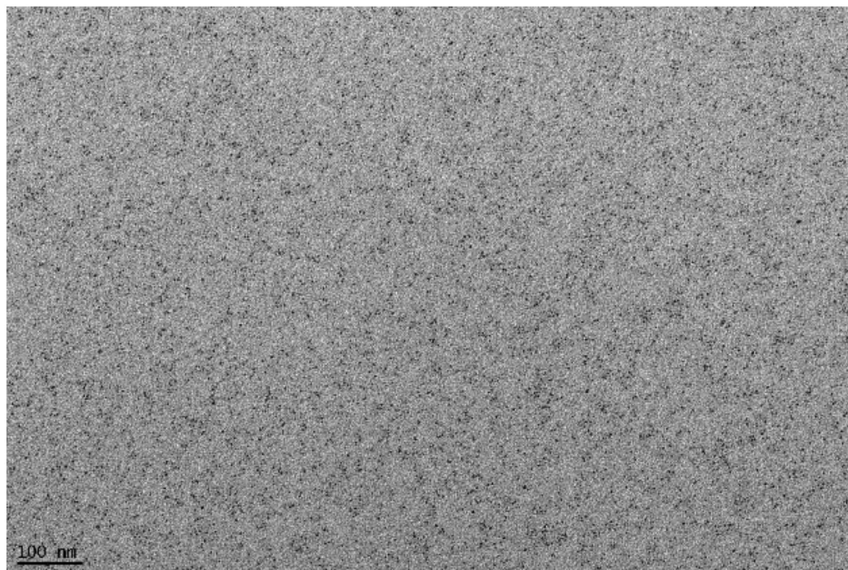


Figure S16. TEM image of CdTe QDs.

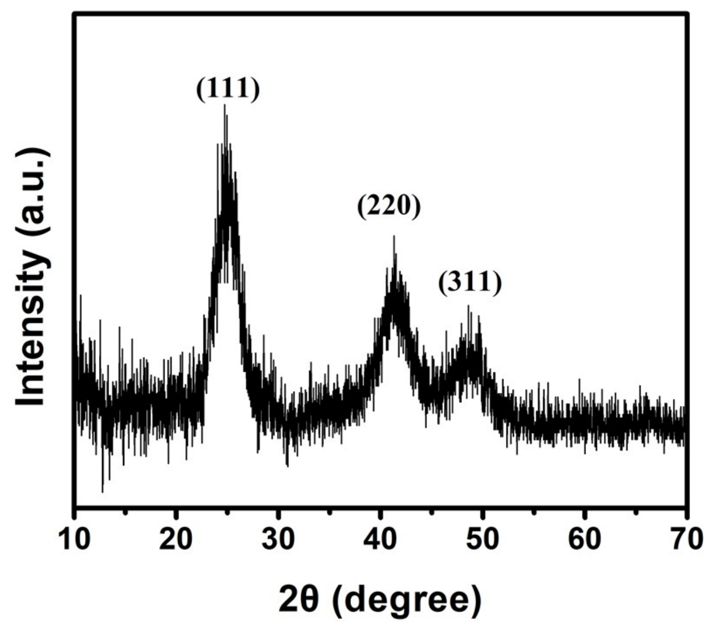


Figure S17. XRD spectrum of CdTe QDs.

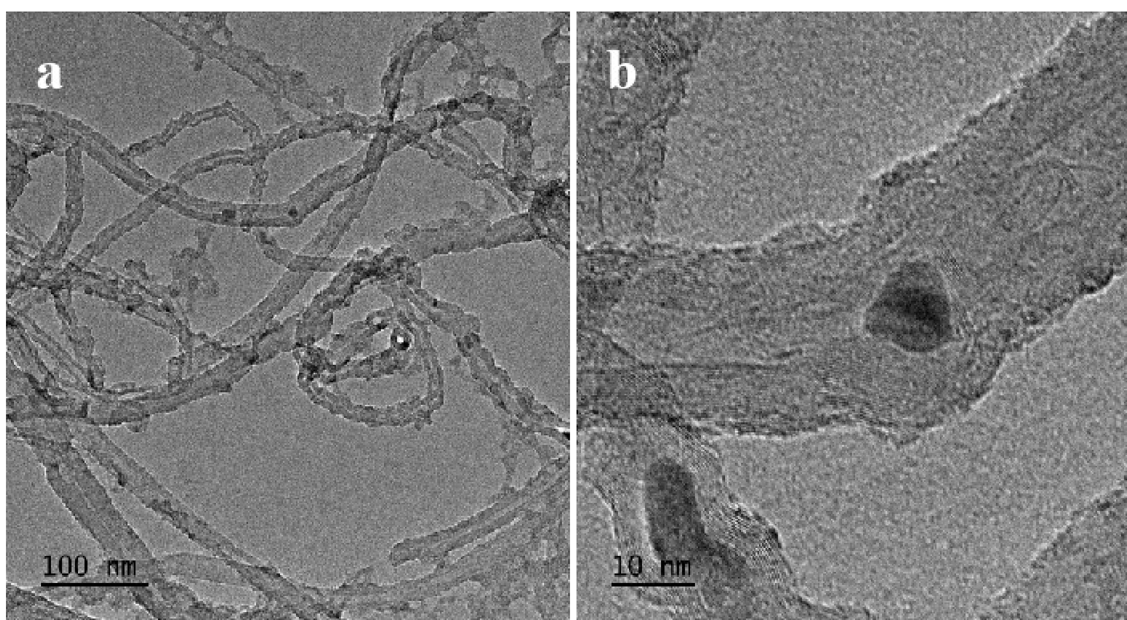


Figure S18. TEM images of CdTe-MWNTs.

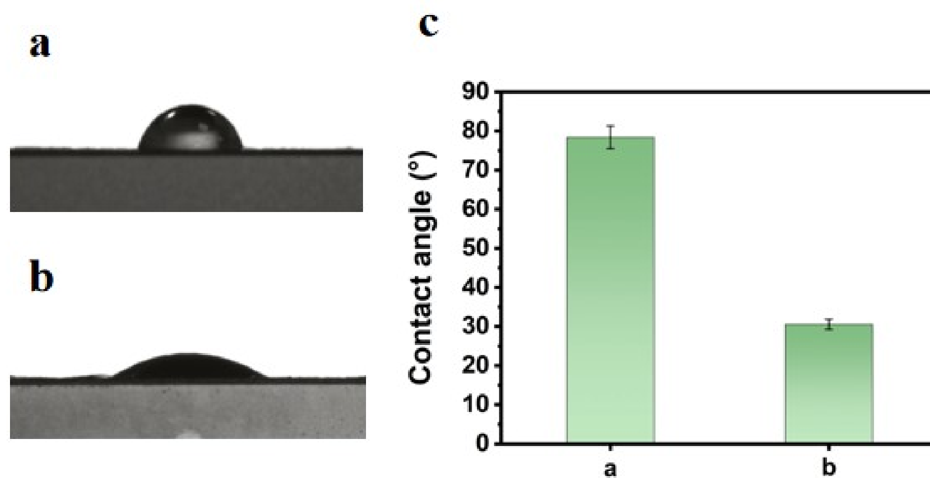


Figure S19. Water contact angles of different surfaces: (a) rSO_2-UCNPs/CdTe-MWCNTs/etched Ti sheet and (b) rSO_2-UCNPs/CdTe-MWCNTs/BSA-GA/etched Ti sheet. c) Water contact angle values obtained from (a) and (b).

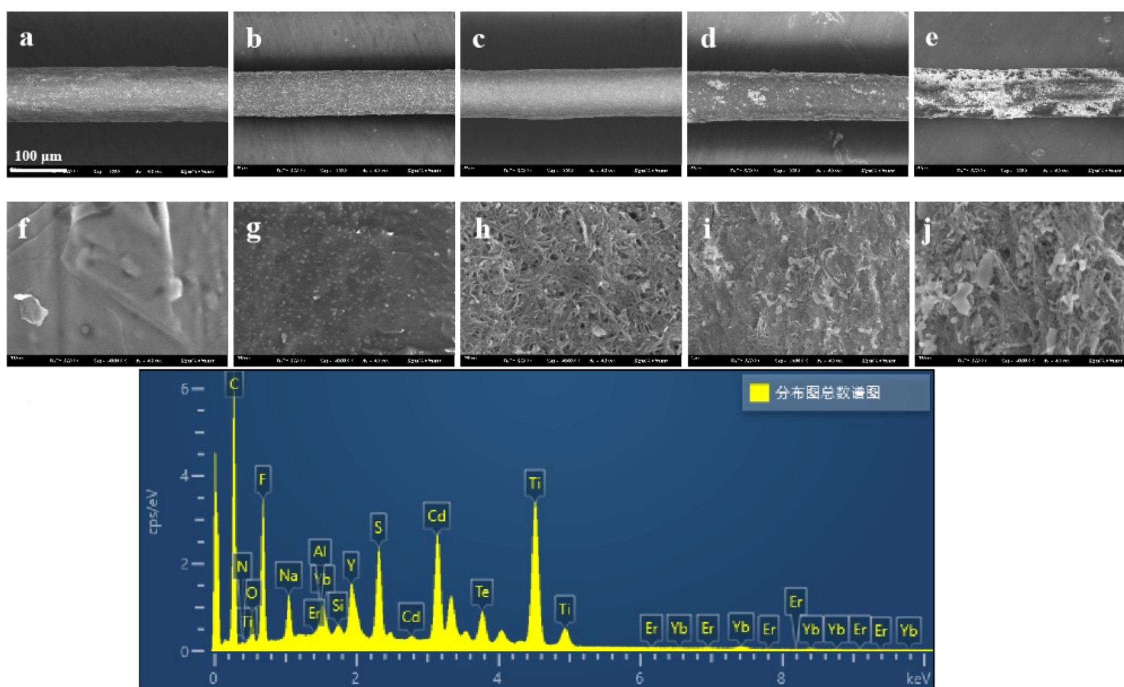


Figure S20. SEM characterization of the Ti wire (a, f), etched Ti wire (b, h), CdTe-MWNTs/TiME (c, h), rSO_2-UCNPs/CdTe-MWCNTs/TiME (d, i), rSO_2-UCNPs/CdTe-MWCNTs/BSA-GA/TiME (e, j), and the element distribution of rSO_2-UCNPs/CdTe-MWCNTs/BSA-GA/TiME.

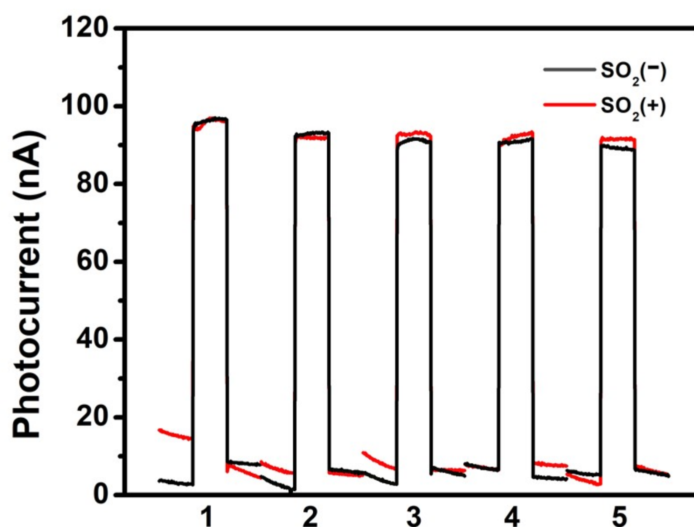


Figure S21. Photocurrents obtained with the microelectrode without rSO_2 modification for five independent experiments. The measurements were conducted in aCSF containing no SO_2 (black curve) and 50 µM SO_2 (red curve).

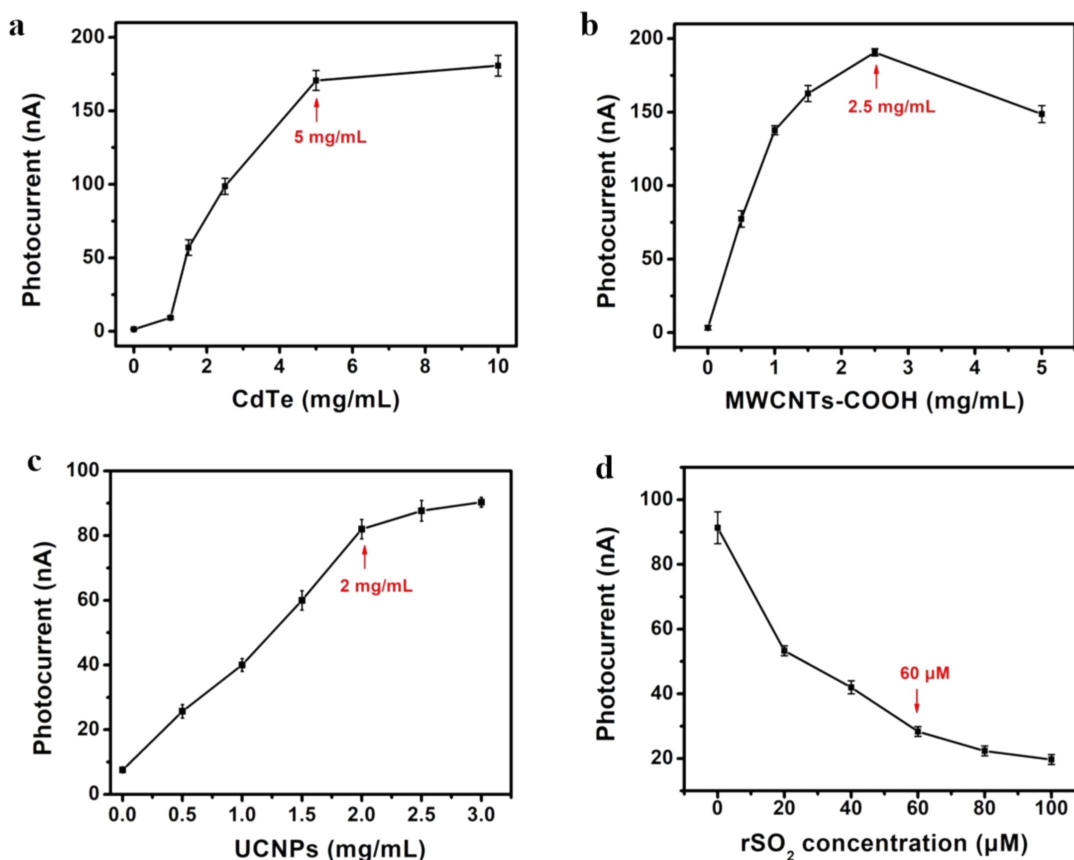


Figure S22. Influence of the CdTe concentration (a), MWNTs concentration (b), UCNPs concentration (c), rSO_2 concentration (d) on the photocurrent response of the sensor (n=3). Red font indicates the optimal condition.

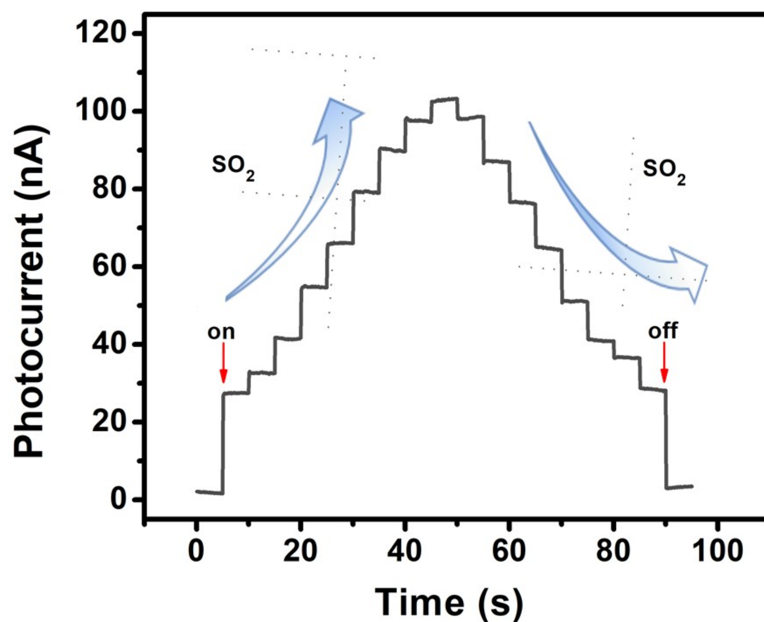


Figure S23. The photocurrent changes obtained at RPMS with continuously increasing and then decreasing concentration of SO_2.

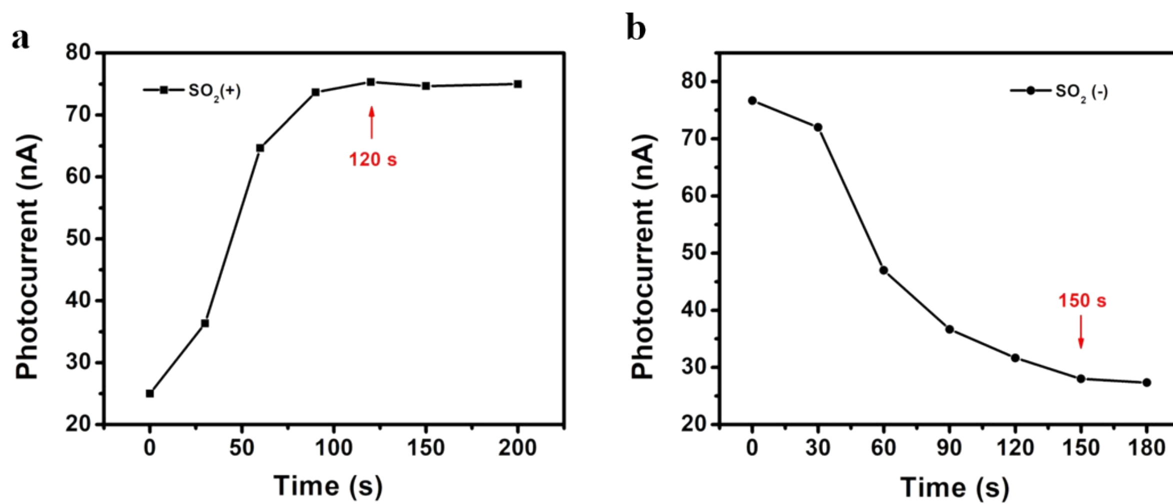


Figure S24. Time-dependent photocurrent response obtained at RPMS for addition (a) and dissociation (b) reaction (n=3). Red font indicates the time required to complete the respective reaction.

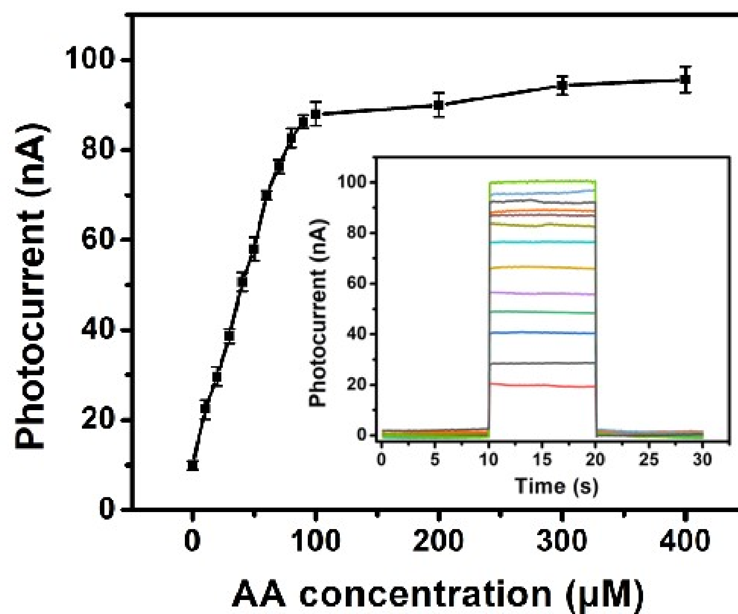


Figure S25. Influence of ascorbic acid (AA) concentration on the photocurrent response of the sensor (n=3, S.D.).

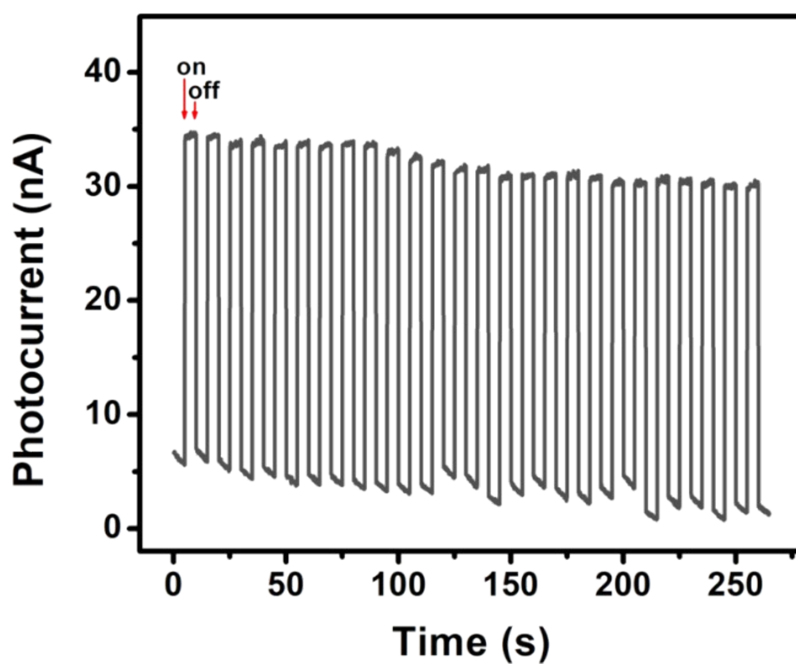


Figure S26. PEC stability of RPMS.

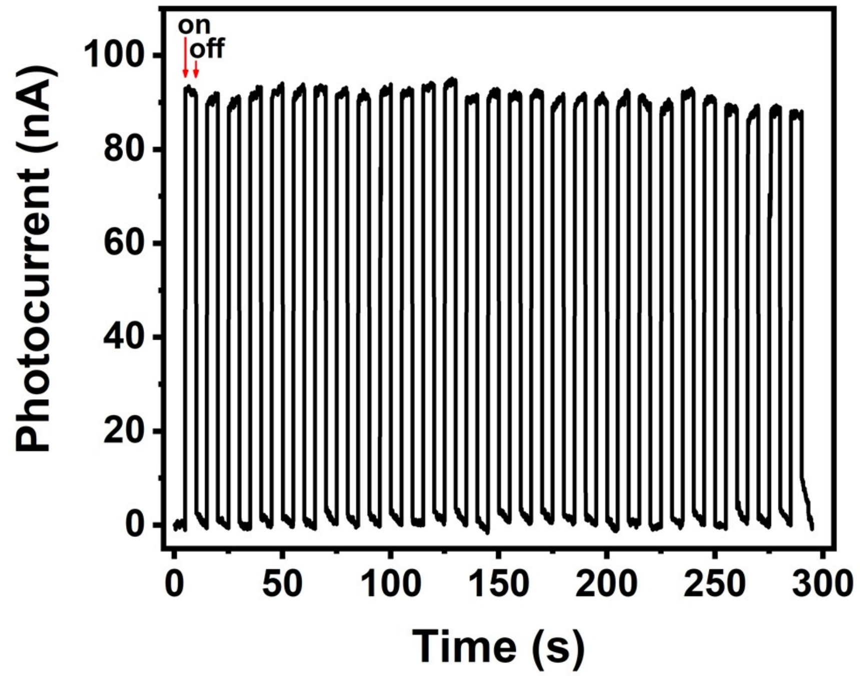


Figure S27. PEC stability of CdTe QDs upon the excitation of UCL.

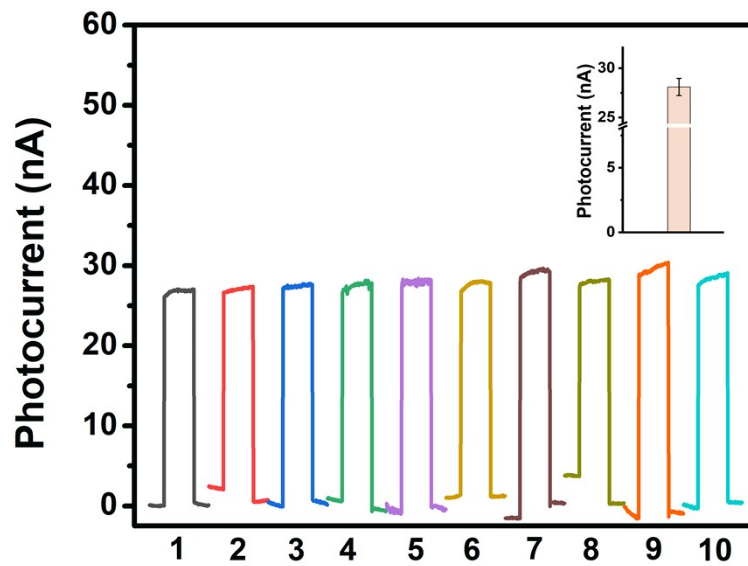


Figure S28. Reproducibility of RPMSs.

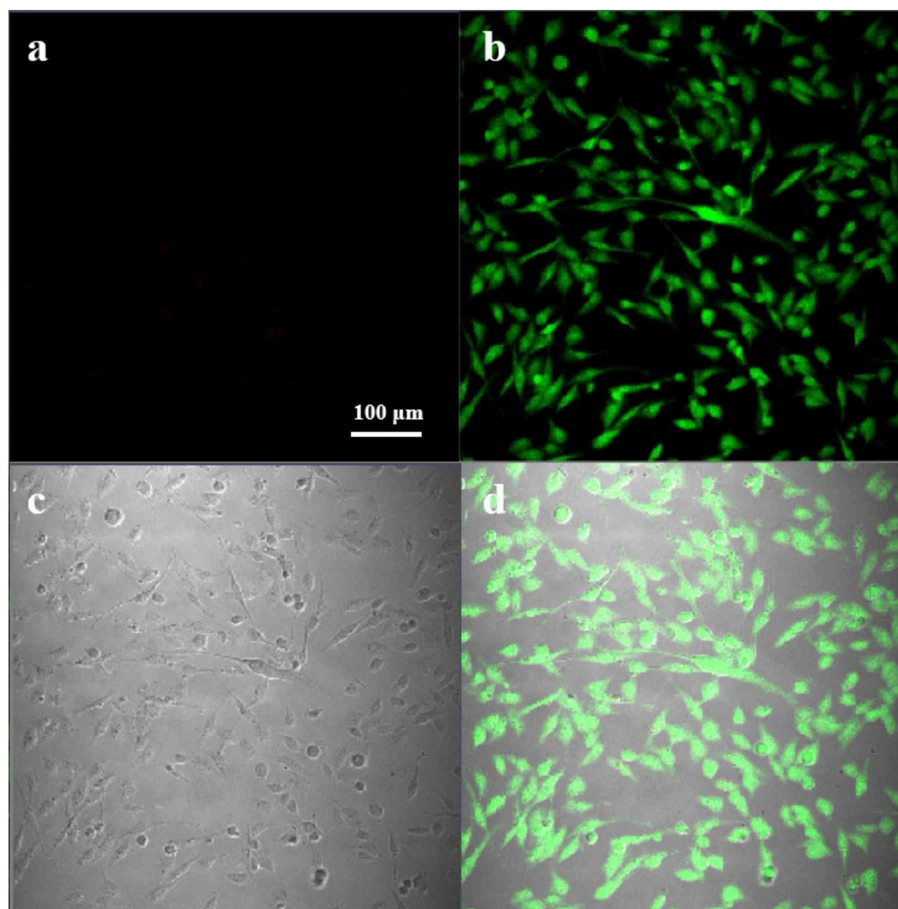


Figure S29. Confocal fluorescence (a,b) and bright field (c) images of cultured cells on the rSO_2-UCNPs/CdTe-MWCNTs/BSA-GA/etched Ti film. (d) Merged image from (a), (b) and (c). Live cells are stained green with Calcein-AM and dead cells are stained red with propidium iodide.

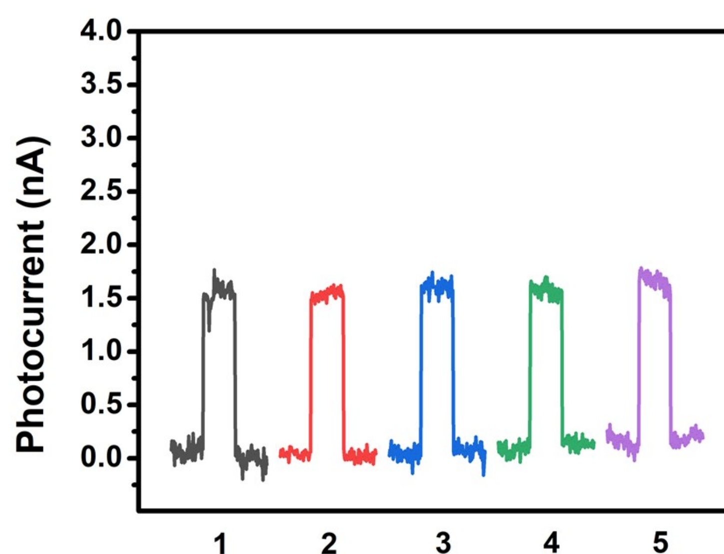


Figure S30. Photocurrent signals obtained at a single RPMS in the hippocampus of five different normal mouse brains.

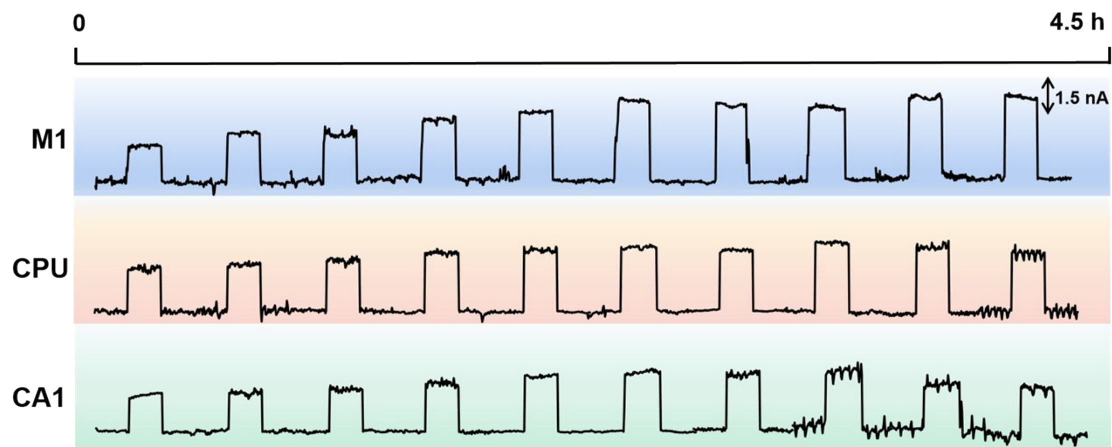


Figure S31. Time-dependent PEC signals obtained with RPMS in CA1, M1 and CPU regions of epileptic mice.

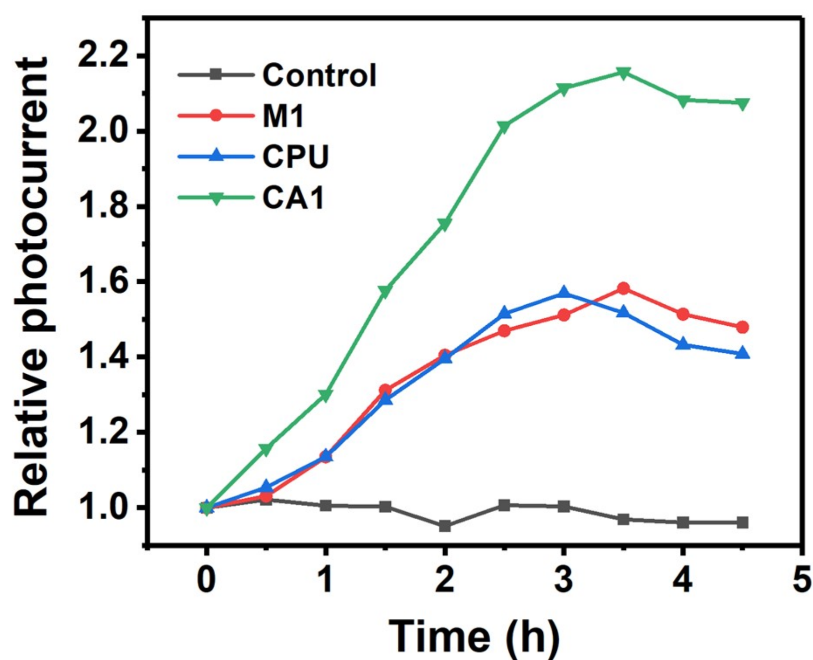


Figure S32. PEC signals obtained with RPMS in CA1, M1 and CPU regions of epileptic mice varied with time going. (plotting from the data in Figure 3f and S29)

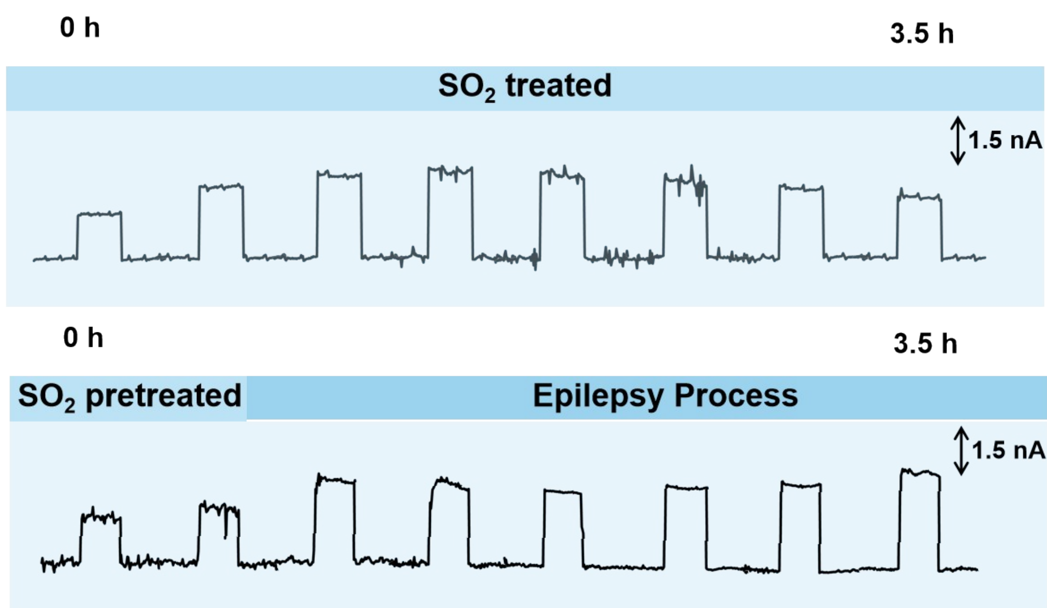


Figure S33. Photocurrent response obtained at RPMS in CA1 region of live mice brain with SO_2 treatment (a) and epilepsy with SO_2 pretreatment (b).

Reference

[1] X. Liu, T. Xiao, F. Wu, M.-Y. Shen, M. Zhang, H.-h. Yu, L. Mao, **Angew. Chem. Int. Ed.** 2017, 56, 11802-11806.

[2] H. Dong, Q. Zhou, L. Zhang, Y. Tian, **Angew. Chem. Int. Ed.** 2019, 58, 13948-13953.

[3] X. Ye, X. Wang, Y. Kong, M. Dai, D. Han, Z. Liu, **Angew. Chem. Int. Ed.** 2021, 60, 11774-11778.

[4] J. Sabaté del Río, O. Y. F. Henry, P. Jolly, D. E. Ingber, **Nat. Nanotechnol.** 2019, 14, 1143-1149.