Supporting Information

One-Step Encapsulation of Ortho-Disulfides in Functionalized Zinc MOF. Enabling Metal-Organic Frameworks in Agriculture.

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Experimental procedures

**Synthesis of 2,2'-disulfanediylbisaniline (DiS-NH$_2$) and disulfanediylbis(2,1-phenylene) diacetate (DiS-O-Acetyl).** The method described by Mejías et al. was employed$^4$.

**Synthesis of MOF@ DiS-NH$_2$ and MOF@DiS-O-Acetyl.** The method is a modification of that reported by Liédana$^{13}$. DiS-NH$_2$ (0.4 mmoles) was dissolved in MeOH (30 mL) together with Zn(NO$_3$)$_2$ (1 mmol). This mixture was added dropwise to a solution of 2-methylimidazole (10 mM) in MeOH. The mixture was stirred at room temperature for 2 h. The resulting solution was centrifuged at 15000 rpm for 15 min and the supernatant was removed. The solid precipitate was washed three times with distilled water and dried in a vacuum oven (35 ºC) overnight. Samples were stored at –20 ºC under a nitrogen atmosphere.

**Electron microscopy studies.** Samples for scanning electron microscopy were prepared by depositing a tiny portion of the solid directly onto a 3 mm, lacey-carbon coated 200 mesh copper grid.

The large area views of the samples were recorded using the scanning transmission electron microscopy (STEM) detector installed on an FEI Nova NanoSEM 450 scanning electron microscope. Bright-field (BF), dark-field (DF), and high-angle annular dark-field (HAADF) images were recorded using the annular-type detector installed on this microscope.

Ultra-high resolution scanning transmission electron microscopy (STEM) studies were performed on a double Aberration-Corrected (AC) FEI Titan Cubed Themis 60-300 microscope operated at 300 kV. The equipment was also equipped with a Super X-G2 X-ray high sensitivity energy-dispersive spectrometer, thus providing a tool to simultaneously combine spectroscopy and image signals.
XEDS analysis was performed by acquiring collections of 80 × 80 pixel XEDS maps of the C (0.277 keV), N (0.392 keV), O (0.523 keV), Zn (8.639 keV) and S (2.307 keV) signals. To improve visualization, the element maps were postfiltered using Average 3, as provided in Velox software.

Due to the high sensitivity of the MOF structures under the electron beam, atomically resolved images were acquired using iDPC imaging. By using the HAADF and FEI DF4 (four segments) detectors, 2048 × 2048 HAADF and iDPC images were recorded simultaneously using a convergence angle of 18.6 mrad and a camera length of 285 mm to optimize the collection of both types of signal. To limit the damage by the electron beam, a fast image recording protocol was used and this combined a beam current of 0.5 pA and a 2.5 μs dwell time.

**NMR studies.** A $^1$H-NMR release study was carried out at 25 ºC using D$_2$O as solvent with an Agilent INOVA spectrometer at 499.719 MHz. Spectra of MOF@DiS-NH$_2$ were collected every 30 mins. The residual peak for water was referenced to δ 4.79 ppm.

**Functionalization of MOF@ DiS-NH$_2$ and MOF@DiS-O-Acetyl with 2-hydroxypropyl-$\beta$-cyclodextrin.** Samples were dispersed in 2 mL of different solutions of HP-$\beta$-CD (0.6, 0.2, 0.4 and 0.02 mg/mL). The new solution was shaken during 24 hours and they were then centrifuged at 10000 rpm during 15 minutes. The supernatant was removed and samples were dried overnight in a vacuum oven (35 ºC). Samples were stored at –20 ºC in a nitrogen atmosphere.

**$\zeta$-Potential measurements.** The stabilities of the encapsulated systems were assessed by measuring the Zeta potential. A Malvern Instruments Zsizer nano system and disposable
folded capillary cells DTS 1070 were employed. Functionalized MOFs with different concentrations of HP-β-CD (0.6, 0.2, 0.4 and 0.02 mg/mL) were analyzed for each sample at 25 °C and pH 7.0. Each value is an average of 100 measurements.

**HPLC quantification method and analysis.** Calibration curves for DiS-NH2 and DiS-O-Acetyl were obtained in MeOH at eight concentrations (300, 200, 100, 50, 25, 10, 5 and 1 ppm). VWR Hitachi HPLC equipment was employed, with a diode array as detector (254 nm) and Phenomenex® column with a 5 μm pore size. Goodness of fit values for DiS-NH2 and DiS-O-Acetyl were 0.9985 and 0.9988, respectively. The gradient method is shown in Table S1 for DiS-NH2 and Table S2 for DiS-O-Acetyl. The retention time, area, mean area and standard deviation for each compound are shown in Table S3 and Table S4.

**Water solubility measurements.** To analyze the solubility enhancement, MOF@DiS-NH2 and MOF@DiS-O-Acetyl were dispersed in distilled water and shaken with a vortex. After 24 h, the samples were analyzed by HPLC applying the quantification method described previously in order to ascertain the levels of disulfides that could be solubilized. The percentages shown in Tables 1 and 2 (Results and discussion) are the results obtained after applying Equation 1. All of the information related to the the HPLC analysis for the water solubility of the free compounds is provided in Table S5.

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\text{Solubility enhancement (\%)} = \frac{\text{Water solubility when encapsulated}}{\text{Water solubility of free compound}} \cdot 100 \quad (\text{Eq. 1})
\]

**Encapsulation efficiency.** The encapsulation percentage was evaluated by the standard method reported in literature[^4]. Organic solvents and ultrasound were applied to break the MOF structure and release all the encapsulated compound. The calculations were carried out using Equation 2. The information on the encapsulation percentage is provided in Table S6.
Encapsulation efficiency (%) = \frac{[\text{Bioactive compound} \text{ encapsulated}]}{\text{Total [Bioactive compound] employed in synthesis}} \cdot 100 \quad (\text{Eq. 2})

**Etiolated Wheat Coleoptile Bioassay.** The experiments were carried out following the procedure reported in the literature\([23]\) with some modifications. MOF@DiS-NH$_2$, MOF@DiS-O-Acetyl, DiS-NH$_2$, DiS-O-Acetyl and Empty-MOF were added without predissolution in dimethyl sulfoxide (DMSO), but diluted in an aqueous phosphate-buffered saline solution (PBS) containing 2% sucrose at pH 7.0 or pH 5.6 and the corresponding concentrations of the bioactive compound (10, 30, 100, 300 and 1000 μM). The concentrations of the bioactive compound encapsulated within the MOFs were recalculated by applying the encapsulation percentage obtained for every ortho-disubstituted disulfide compound. A 10 mM buffer solution was used to avoid osmotic stress.

**Phytotoxicity Bioassay.** The selection of target plants was based on an optimization process carried out in our search for weed species\([24]\) with some modifications. The monocotyledons barnyardgrass (E. crus-galli L.) and annual ryegrass (Lolium rigidum), and the dicotyledon redroot pigweed (Amaranthus retroflexus L.) were selected. Bioassays were conducted using Petri dishes (50 mm diameter) with one sheet of Whatman No. 1 filter paper as a support. Germination and growth were conducted in aqueous solutions at controlled pH by using $10^{-2}$ M 2-[N-morpholino]ethanesulfonic acid (MES) and 1 M NaOH (pH 6.0). The compounds to be assayed were dissolved in water only and these solutions were diluted with buffer so that test concentrations for each compound ($10^{-3.3} \times 10^{-4}$, $10^{-4.3} \times 10^{-5}$ and $10^{-5}$ M) were achieved. Four replicates were used for each weed species, each containing 20 seeds. Treatment, control or internal reference solution (1 mL) was added to each Petri dish. After adding the seeds and aqueous solutions, Petri dishes were sealed with Parafilm® to ensure closed-system models. Seeds were further incubated at 25 °C in a Memmert ICE 700
controlled environment growth chamber. The photoperiod was 16/8 h light/dark for barnyardgrass, annual ryegrass and redroot pigweed. Bioassays took 8 days. After growth, plants were frozen at −10 °C for 24 h to avoid subsequent growth during the measurement process. Evaluated parameters (germination rate, root length, and shoot length) were recorded using a Fitomed system[25], which allowed automatic data acquisition and statistical analysis using its associated software. Data were analyzed statistically using Welch’s test, with significance fixed at 0.01 and 0.05. Results are presented as percentage differences from the control. Zero represents control, positive values represent stimulation, and negative values represent inhibition.
Figure S1. XRD comparison between empty MOF and MOF@DiS-NH$_2$ at the same temperature.

Figure S2. XRD comparison between synthesis temperature of MOF@DiS-NH$_2$ at 25°C and 130°C.
Figure S3. EDS spectra corresponding to the MOF@DiS-NH₂ and functionalized MOF@DiS-NH₂ samples.
Figure S4. $^1$H-NMR kinetic study to analyze the integral value during time, with overlapped data from different time points.
Figure S5. Degraded MOF@DiS-NH$_2$ after nine moth of storage.

Table S1. HPLC method employed in calibration curve and quantification of DiS-NH2

| Time (min) | MeOH (%) | H$_2$O (%) | Flow (mL/min) |
|------------|----------|------------|--------------|
| 0.0        | 75.0     | 25.0       | 1.00         |
| 15.0       | 75.0     | 25.0       | 1.00         |
| 16.0       | 100.0    | 0.0        | 1.00         |
| 20.0       | 100.0    | 0.0        | 1.00         |
| 22.0       | 75.0     | 25.0       | 1.00         |
| 25.0       | 75.0     | 25.0       | 1.00         |
**Tables S2.** HPLC method employed in calibration curve and quantification of DiS-O-Acetyl

| Time (min) | MeOH (%) | H₂O (%) | Flow (mL/min) |
|------------|-----------|---------|---------------|
| 0.0        | 65.0      | 35.0    | 1.00          |
| 15.0       | 65.0      | 35.0    | 1.00          |
| 16.0       | 100.0     | 0.0     | 1.00          |
| 20.0       | 100.0     | 0.0     | 1.00          |
| 22.0       | 65.0      | 35.0    | 1.00          |
| 25.0       | 65.0      | 35.0    | 1.00          |
Table S3. HPLC results of calibration curve to DiS-NH₂

| Concentration (ppm) | Retention Time (min) | Area       | Mean Area | S.D     |
|---------------------|----------------------|------------|-----------|---------|
| 300                 | 4.753                | 1247283    |           |         |
|                     | 4.74                 | 1257116    | 1248497   | 8080    |
|                     | 4.733                | 1241093    |           |         |
|                     | 4.733                | 893470     |           |         |
| 200                 | 4.74                 | 871821     | 881620    | 10969   |
|                     | 4.747                | 879568     |           |         |
|                     | 4.74                 | 416831     |           |         |
| 100                 | 4.74                 | 407984     | 417035    | 9155    |
|                     | 4.747                | 426291     |           |         |
|                     | 4.733                | 194977     |           |         |
| 50                  | 4.747                | 204190     | 196623    | 6893    |
|                     | 4.733                | 190702     |           |         |
|                     | 4.733                | 111340     |           |         |
| 25                  | 4.733                | 107797     | 109561    | 1772    |
|                     | 4.733                | 109547     |           |         |
|                     | 4.733                | 42715      |           |         |
| 10                  | 4.733                | 40976      | 40907     | 1843    |
|                     | 4.72                 | 39030      |           |         |
|                     | 4.74                 | 19829      |           |         |
| 5                   | 4.733                | 17491      | 18804     | 1195    |
|                     | 4.713                | 19092      |           |         |
| 1                   | out of range         |            |           |         |
Table S4. HPLC results of calibration curve to DiS-O-Acetyl

| Concentration (ppm) | Retention Time (min) | Area       | Mean Area   | S.D   |
|---------------------|----------------------|------------|-------------|-------|
| 1000                | 10.253               | 8364882    |             |       |
|                     | 10.24                | 8482460    | 8457856     | 83439 |
|                     | 10.247               | 8526227    |             |       |
|                     | 10.267               | 3983322    |             |       |
| 500                 | 10.273               | 3888501    | 3937577     | 47498 |
|                     | 10.26                | 3940907    |             |       |
|                     | 10.273               | 1639626    |             |       |
| 200                 | 10.28                | 1680953    | 1653165     | 24067 |
|                     | 10.267               | 1638917    |             |       |
|                     | 10.273               | 794043     |             |       |
| 100                 | 10.28                | 815979     | 786036      | 34647 |
|                     | 10.253               | 748086     |             |       |
|                     | 10.267               | 438523     |             |       |
| 50                  | 10.267               | 452160     | 436529      | 16717 |
|                     | 10.287               | 418905     |             |       |
|                     | 10.253               | 82185      |             |       |
| 10                  | 10.253               | 86514      | 82785       | 3469  |
|                     | 10.3                 | 79655      |             |       |
| 5                   |                      |            | out of range|       |
| 1                   |                      |            | out of range|       |

Table S5. HPLC results of water solubility measurements of free bioactive compounds

| Sample (ppm)       | Injection | Area     | Real Concentration after Calibration Curve (ppm) | Water Solubility (mg/L) |
|--------------------|-----------|----------|--------------------------------------------------|-------------------------|
| Dis-NH₂ (1000)     | 1         | 177959   | 36.01                                            | 36.47 ± 0.89            |
|                    | 2         | 185430   | 37.50                                            |                         |
|                    | 3         | 177498   | 35.91                                            |                         |
| DiS-O-Acetyl (1000)| 1         | 146572   | 20.42                                            | 19.47 ± 0.86            |
|                    | 2         | 134859   | 19.24                                            |                         |
|                    | 3         | 129922   | 18.75                                            |                         |
Table S6. HPLC results of encapsulation percentages inside the MOFs

| Sample (ppm)   | Injection | Area    | Real Concentration after Calibration Curve (ppm) | Encapsulation (%) | Encapsulation Mean (%) |
|----------------|-----------|---------|--------------------------------------------------|-------------------|------------------------|
| Dis-NH₂ (1000) | 1         | 4211176 | 426.88                                           | 42.69             |                        |
|                | 2         | 4228353 | 428.59                                           | 42.86             | 42.80 ± 0.10           |
|                | 3         | 4226953 | 428.45                                           | 42.85             |                        |
| DiS-O-Acetyl (1000) | 1  | 1621114 | 167.87                                           | 16.79             |                        |
|                | 2         | 1605627 | 166.32                                           | 16.63             | 16.71 ± 0.08           |
|                | 3         | 1613515 | 167.11                                           | 16.71             |                        |