Electronic Supplementary Information

Broadened bioactivity and enhanced durability of two structurally distinct metal–organic frameworks containing Zn^{2+} ions and thiabendazole

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1. Experimental Section

1.1 Synthesis of TBZ-MOF-1:

TBZ-MOF-1 was prepared following a typical solvothermal method. A solution of zinc(II) chloride (445 mg, 3.3 mmol) and TBZ (483 mg, 2.4 mmol) in *N*,*N*-dimethylformamide (90 mL) was sealed tightly in a capped vial. The resulting solution was kept at 130 °C for 48 h in an oven and then slowly cooled to 25 °C at a rate of 2.5 °C/h to yield pale yellow crystals. Crystals suitable for X-ray diffraction analysis were directly isolated, filtered, washed with DMF and ethanol, and dried under vacuum. Yield (based on TBZ): 186.7 mg (0.24 mmol), 30.0%. Elemental Analysis $C_{30}H_{18}ClN_9S_3Zn_2$: (Calc) C, 46.98; H, 2.37; N, 16.44; (Exp) C, 46.68; H, 2.54; N, 16.24.

1.2 Synthesis of TBZ-MOF-2:

TBZ-MOF-2 was prepared following a typical solvothermal method. A solution of zinc(II) chloride (273 mg, 2.0 mmol), TBZ (403 mg, 2.0 mmol), and BDC (332 mg, 2.0 mmol) in *N*,*N*-dimethylformamide (48 mL) was sealed tightly in a capped vial. The resulting solution was kept at 130 °C for 48 h in an oven and then slowly cooled to 25 °C at a rate of 2.5 °C/h to yield yellow crystals. Crystals suitable for X-ray diffraction were directly isolated, filtered, washed with DMF and ethanol, and dried under vacuum. Yield (based on TBZ): 133.8 mg (0.31 mmol), 15.6%. Elemental Analysis $C_{18}H_{10}N_3O_4SZn$: (Calc) C, 50.30; H, 2.35; N, 9.78; (Exp) C, 49.94; H, 2.77; N, 9.68.

1.3 Single crystal XRD measurements:

Single crystal data for **TBZ-MOF-1** was recorded at the BL02B1 beamline of SPring-8 on a PILATUS 1M Cd-Te Detector (Dectris) using synchrotron radiation, while that for **TBZ-MOF-2** was recorded using a Bruker D8-Quest diffractometer equipped with a Photon-III detector with Mo-Kα radiation (λ = 0.71073 Å). The structures were solved using a direct method (SHELXT)[S1] and refined by a full-matrix least-squares method on F^2 for all reflections using the SHELXL-2016 software.[S2] Hydrogen atoms were placed using AFIX instructions, while all other atoms were refined anisotropically. Supplementary crystallographic data were deposited at the Cambridge Crystallographic Data Centre (CCDC) under the numbers CCDC- 2051988 (TBZ-MOF-1) and 2051989 (TBZ-MOF-2), respectively, and can be obtained free of charge from www.ccdc.cam.ac.uk/data_request/cif.

1.4 Elemental analysis:

Elemental analyses were performed using a MICRO CORDER JM10 elemental analyzer (J-Science Lab. Co.).

1.5 Powder XRD measurements:

The absence of impurities in TBZ-MOF-1 and TBZ-MOF-2 was investigated by powder XRD analysis conducted using a Rigaku SmartLab (Cu *K*α radiation) diffractometer (Figures S1 and S4) and Bruker D2 PHASER (Cu *K*α radiation)(Figures S9 and S10).

1.6 Solid-state ^{13}C NMR measurements:

The number of crystallographically non-equivalent carbons and the absence of impurities were investigated by solid-state ^{13}C NMR spectroscopy from −100 to 300 ppm using a JEOL JNM-ECZ500R NMR spectrometer.

1.7 Fourier-transform infrared (FT-IR) spectra:

FT-IR spectra were recorded with a JASCO FT/IR-6300 (JASCO Int. Co., Ltd., Tokyo, Japan) using a germanium crystal attenuated total reflection (ATR) accessory under vacuum. The spectral region was 4000–600 cm^{-1} with a resolution of 4 cm^{-1}.

1.8 TGA measurements:

To confirm the thermal stability of the samples, TGA analyses were performed in air and under nitrogen using a Mettler Toledo TGA/DSC 1 instrument by heating the sample to 1000 °C at a rate of 10 °C/min.

1.9 Inductively coupled plasma optical emission spectrometry (ICP-OES):

Zinc(II) solubility in the bacterial medium (from TBZ-MOF-1 and TBZ-MOF-2 samples) was investigated using a Thermo Fisher Scientific iCAP 7600 Duo system.

1.10 High-performance liquid chromatography (HPLC):

Equilibrium solutions of the compounds filtered using sterile syringe filters (0.22 μm membrane) were analyzed by HPLC (Nexera XR system, LC-40BXR pump, and SPD-M40 detector, LabSolutions software, Shimadzu). TBZ was separated over an InertSil ODS-3 column (GL Science, 5 μm, 150 mm × 4.6 mm). HPLC analysis was conducted at 50 °C with a flow rate of 1 mL/min. UV detection at 280 nm was employed, with a mobile phase of distilled water/methanol (60:40, v/v).

2. Characterization

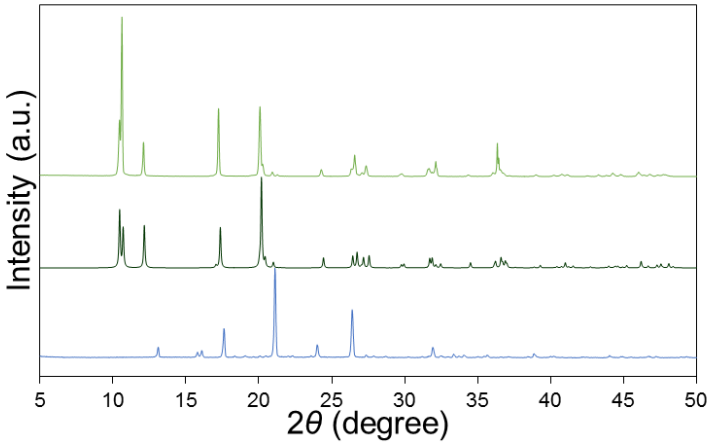

Figure S1. PXRD diffraction patterns of TBZ (bottom), the simulated diffraction pattern converted from the TBZ-MOF-1 single crystal data (middle), and PXRD diffraction patterns of TBZ-MOF-1 (top).

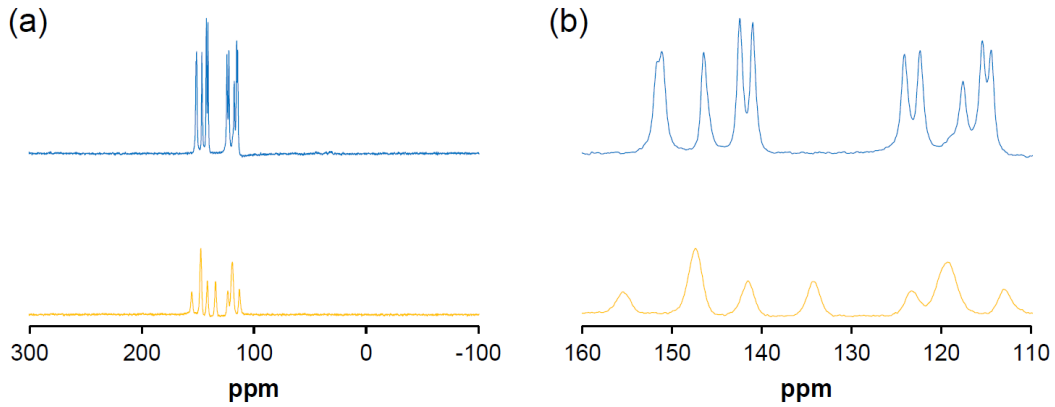

Figure S2. Solid-state ^{13}C NMR spectra: (a) full −100 to 300 ppm range and (b) magnified 110 to 160 ppm region of the TBZ (bottom) and TBZ-MOF-1 (top) spectra.

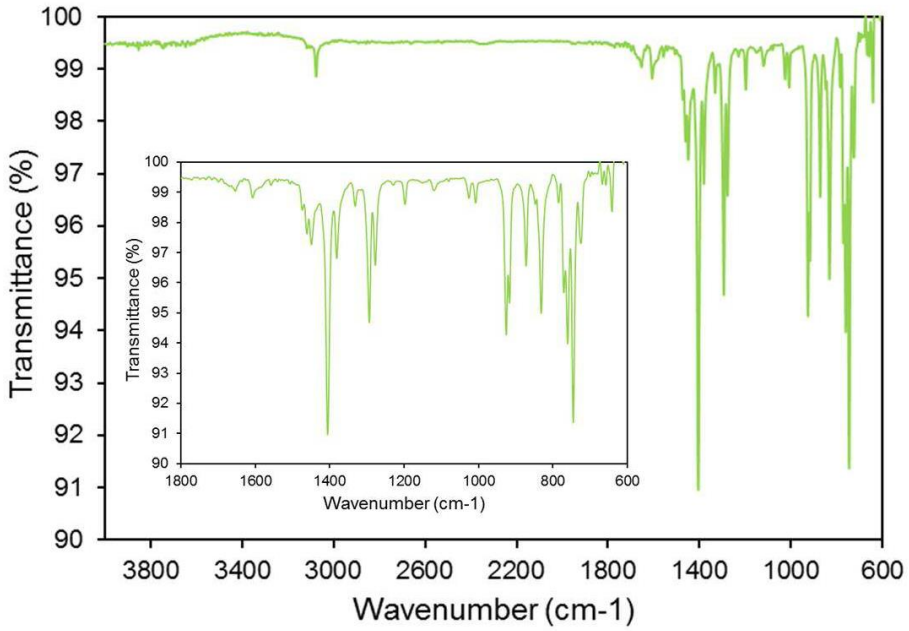

Figure S3. FT-IR spectrum of TBZ-MOF-1 with an enlarged view of the region between 600-1800 cm^{-1}.

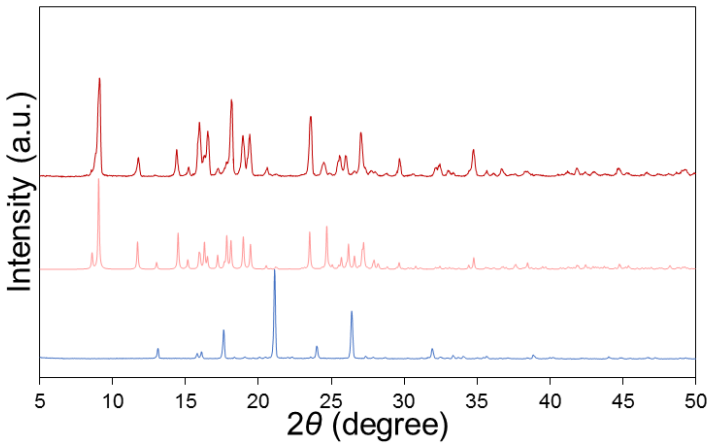

Figure S4. PXRD diffraction patterns of TBZ (bottom), the simulated diffraction pattern converted from the TBZ-MOF-2 single crystal data (middle), and PXRD diffraction patterns of TBZ-MOF-2 (top).

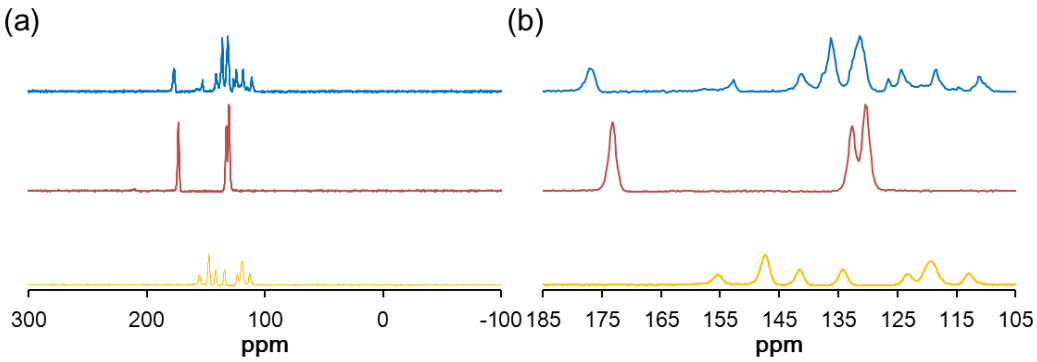

Figure S5. Solid-state ^{13}C NMR spectra: (a) full −100 to 300 ppm range and (b) magnified 110 to 160 ppm region of the TBZ (bottom), BDC (middle), and TBZ-MOF-2 (top) spectra.

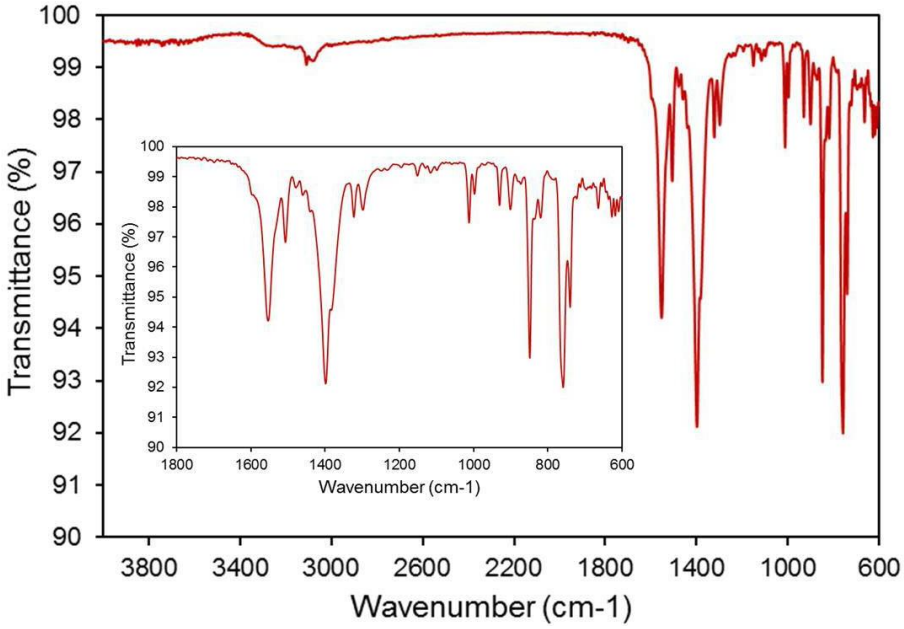

Figure S6. FT-IR spectrum of TBZ-MOF-2 with an enlarged view of the region from 600-1800 cm^{-1}.

Table S1. Crystal data and structure refinement parameters of TBZ-MOF-1 and TBZ-MOF-2.

	TBZ-MOF-1	**TBZ-MOF-2**
empirical formula	$C_{30}H_{18}ClN_9S_3Zn_2$	$C_{18}H_{10}N_3O_4SZn$
formula weight	766.90	429.72
color	pale yellow	yellow
crystal system	trigonal	monoclinic
unit-cell dimensions		
(a = Å), (b = Å), (c = Å)	a = 10.3859(8)	a = 7.2558(2)
	b = 10.3859(8)	b = 20.6091(6)
	b = 24.7964(19)	b = 11.1997(4)
α (deg)	90	90
β (deg)	90	96.739(10)
γ (deg)	120	90
volume of unit cell ($Å^3$)	2316.4(4)	1663.2(9)
space group	*R*3	$P2_1/c$
Z value	3	4
D_{calc} (g/cm3)	1.649	1.716
crystal size (mm)	0.01 x 0.01 x 0.01	0.1 x 0.05 x 0.05
temp (K)	100	123
λ (Å)	0.41180	0.71073
Reflections collected	18080	42193
Independent reflections	2399	3825
Completeness (%)	99.9	99.9
Parameters	137	244
R1, wR2	0.0143, 0.0369	0.0338, 0.0790
goodness-of-fit on F^2	1.087	1.091
CCDC	2051988	2051989

Table S2. Selected distances and angles in TBZ-MOF-1.

Distance (Å)		Angle (°)	
Zn1–N1	2.255(2)	N1–Zn1–N2	76.13(6)
Zn1–N1'	2.255(2)	N1–Zn1–N2"	164.98(6)
Zn1–N1"	2.255(2)	N1'–Zn1–N2	164.99(6)
Zn1–N2	2.072(2)	N1'–Zn1–N2'	76.13(6)
Zn1–N2'	2.072(2)	N1"–Zn1–N2'	164.99(6)
Zn1–N2"	2.072(2)	N1"–Zn1–N2"	76.13(6)
Zn2–N3	2.009(2)	N3–Zn2–N3’	109.33(4)
Zn2–N3”	2.009(2)	N3’–Zn2–N3”	109.33(4)
Zn2–Cl	2.229(1)	N3–Zn2–Cl	109.61(4)

Table S3. Selected distances and angles in TBZ-MOF-2.

Distance (Å)		Angle (°)	
Zn1–N1	2.144(2)	N1–Zn1–N2	79.10(8)
Zn1–N2	2.071(2)	O1–Zn1–O2	61.02(6)
Zn1–O1	2.086(1)	O3–Zn1–O4	61.19(6)
Zn1–O2	2.205(2)	N1–Zn1–O1	103.62(7)
Zn1–O3	2.116(1)	O2–Zn1–O4	91.72(6)
Zn1–O4	2.202(2)	N2–Zn1–O3	98.04(7)

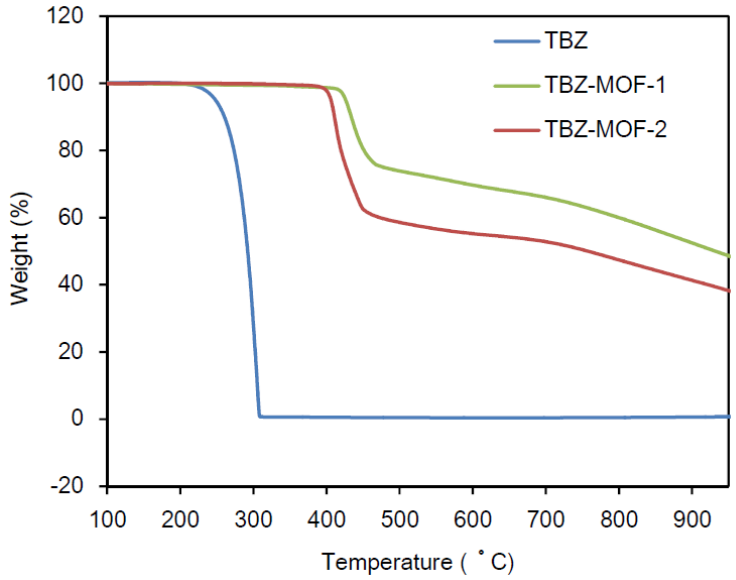

Figure S7. TGA curves for TBZ, TBZ-MOF-1, and TBZ-MOF-2 in under N_2.

3. Water solubility test

3.1 Details of the water solubility test:

Water solubility was measured by placing the compound (10 mg) in distilled water (50 mL) at 25 °C with continuous stirring until equilibrium was reached (24–168 h). The equilibrium concentration of free TBZ in each sample was analyzed by HPLC. The standard solution was adopted with a 25.6 ppm methanol solution obtained by diluting a 102.5 ppm methanol solution. The concentration of free TBZ in each sample was determined by comparison with the peak area of the standard solution. The concentration of TBZ alone was ~32 ppm after 24 h, which is similar to the previously reported value of 30 ppm at neutral pH.[S3]

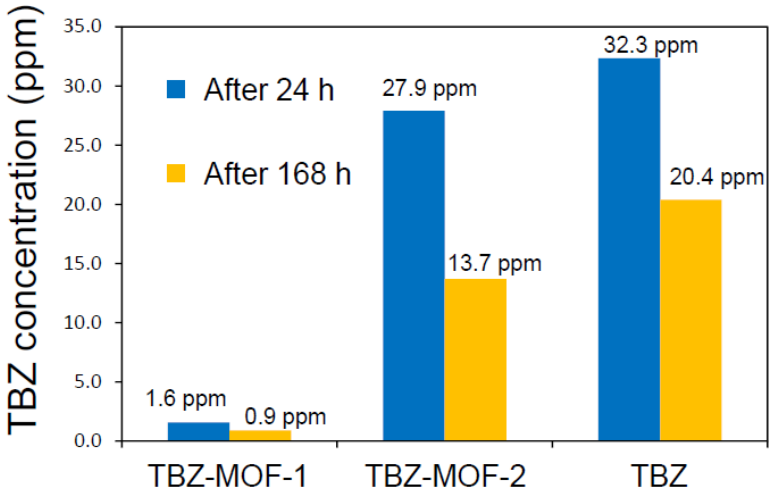

Figure S8. Water solubility of TBZ-MOF-1, TBZ-MOF-2, and TBZ (for reference) determined by HPLC. HPLC measurements were performed after immersion of the samples in water for 24 and 168 h.

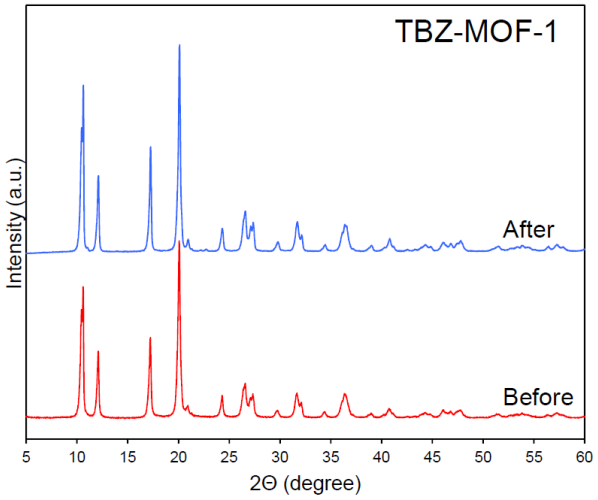

Figure S9. PXRD diffraction patterns of TBZ-MOF-1 before (red line) and after water immersion for 24h (blue line). The conditions for immersing the MOF in water are the same as for the water solubility test.

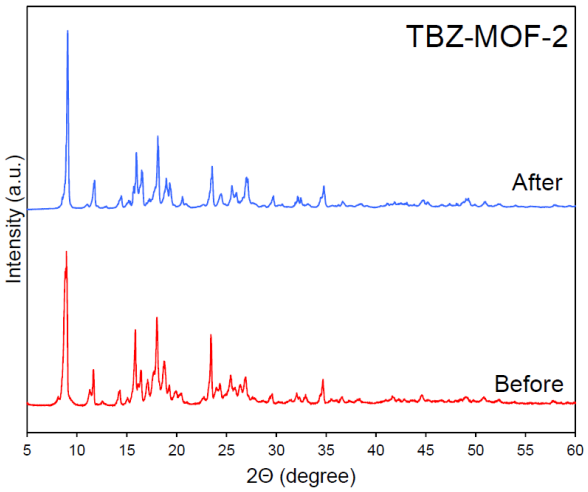

Figure S10. PXRD diffraction patterns of TBZ-MOF-2 before (red line) and after water immersion for 24h (blue line). The conditions for immersing the MOF in water are the same as for the water solubility test.

4. Minimum inhibitory concentration (MIC) measurement

4.1 Details of the MIC tests:

The antimicrobial activities of bioactive materials were measured with a MIC (μg/mL) test using bacteria (*Escherichia coli* NBRC 3972, *Staphylococcus aureus* subsp. *aureus* NBRC 12732) and fungi (*Aspergillus niger* NBRC 105649, *Trichoderma virens* NBRC 6355).

Bacteria were cultivated on a nutrient agar slant for one week. These cultures were collected and used to inoculate 9 mL of LB broth (Miller). Bacterial cultures were incubated at 37 °C for 18 h under constant shaking at 120 rpm. Aliquots (1 mL) of these bacterial cultures was then placed in 1.5 mL microcentrifuge tubes and centrifuged at 6000 rpm for 5 min. The obtained pellets were subsequently resuspended in sterile distilled water (1 mL) and this process was repeated two more times. Enough of the final resuspended pellets were then added to sterile distilled water to obtain an absorbance of 0.09 or 0.10 at 600 nm, referred to as the optical density (OD600). Bacterial inocula were prepared by mixing the 0.09 or 0.10 OD600 bacterial suspensions (3 mL), LB broth (9 mL), and sterile distilled water (24 mL).

Bioactive materials were suspended in a surfactant solution containing 0.05% nonionic surfactant (Penerol N-100), and then diluted two times with the surfactant solution. Aliquots (80 μL) of this diluted solution containing different concentrations of bioactive materials was then added to a well of a 96-well plate and inoculated with the bacterial inocula (120 μL) prepared above.

Fungi were cultivated on a potato dextrose agar slant for one or two weeks. The surfactant solution (5 mL) was poured into each slant, and then the spores and mycelia were collected. The surfactant solution was then added to these spore and mycelia suspensions to obtain a total volume of 50 mL. An aliquot (1 mL) from each suspension was subsequently added to separate potato dextrose broths (50 mL) to prepare fungal inocula.

Bioactive materials were suspended in the surfactant solution and then diluted twice with the surfactant solution. Aliquots (40 μL) of this solution containing different concentrations of bioactive materials was added to a well in a 96-well plate and inoculated with the fungal inocula (60 μL) prepared above.

The inoculated 96-well plates were incubated for 7 days at 26 °C, and then fungal growth was assessed using a microscope. When no fungal growth was observed in the medium containing the lowest concentration of bioactive materials, the MIC was defined at this point of dilution.

5. Active species concentration tests in the MIC media

5.1 Details of active species concentration tests in the bacterial and fungal MIC media:

Active species concentration tests in the MIC media were performed by measuring saturated solutions containing the compound (10 mg) in either bacterial or fungal media (50 mL) at 25 °C with continuous stirring after 24 or 168 h. Solutions containing different concentrations of the active species were analyzed by ICP for Zn^{2+} and HPLC for TBZ.

Compositions of the media:

The bacterial MIC test medium was prepared by mixing LB broth (15 mL), sterile distilled water (45 mL), and surfactant solution (40 mL) containing 0.05% nonionic surfactant (Penerol N-100).

The fungal MIC test medium was prepared by mixing potato dextrose broth (60 mL) and the surfactant solution (40 mL).

Notes and references

S1 G. M. Sheldrick, *Acta Crystallogr. Sect. A*, 2015, **71**, 3-8.

S2 G. M. Sheldrick, *Acta Crystallogr. Sect. C*, 2015, **71**, 3-8.

S3 M. E. R. Jalil, R. S. Vieira, D. Azevedo, M. Baschini, and K. Sapag, *Appl. Clay Sci.*, 2013, **71**, 55-63.