New Silver BioMOFs driven by 1,3,5-Triaza-7-phosphaadamantane-7-sulfide (PTA=S): Synthesis, Topological Analysis and Antimicrobial Activity

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Electronic Supplementary Information (ESI)

Electronic Supplementary Information contains materials and methods, synthesis and analytical data of **1** and **2**, supplementary Table S1 with antimicrobial and antifungal activities of **1**, **2** and the reference silver salts, and Figures S1–S4 with additional structural and topological representations.

Materials and Methods. All synthetic work was performed in air. The reagents and solvents were obtained from commercial sources and used as received, except 1,3,5-triaza-7-phosphaadamantane-7-sulfide (PTA=S) that was prepared by a published method.[S1] C, H, N, and S elemental analyses were carried out by the Microanalytical Service of the Instituto Superior Técnico. Infrared spectra (4000–400 cm^{-1}) were recorded on a BIO-RAD FTS 3000MX or Bruker IFS 1113v instrument in KBr pellets (abbreviations: vs − very strong, s − strong, m – medium, w – weak, br – broad). ESI-MS(±) spectra were run on a 500-MS LC Ion Trap instrument (Varian Inc.) equipped with an electrospray (ESI) ion source, using ca. 10^{-3} M solutions of **1** and **2** in MeCN/H_2O and MeOH/H_2O, respectively. ^1H and $^{31}P\{^1H\}$ NMR spectra were measured on a Bruker 300 AMX spectrometer at ambient temperature. ^1H chemical shifts (δ) are given in ppm relative to Me_4Si, while ^{31}P shifts are relative to external H_3PO_4 (85% in H_2O).

Synthesis and Analytical Data of 1 and 2. Compound **1**: A solution (12 mL) of PTA=S (0.2 mmol, 38 mg) in MeCN/H_2O (5:1, v/v) was added to a solution (6 mL) of $AgNO_3$ (0.2 mmol, 34 mg) in MeCN/H_2O (5:1, v/v). The obtained mixture was stirred at room temperature (r.t., ~25ºC) in air for 1 h, resulting in the formation of a white precipitate that was filtered off. The colourless filtrate was left to slowly evaporate in air at r.t. producing colourless X-ray quality single crystals, which were collected and dried in air to furnish **1** in 40% yield, based on $AgNO_3$. $S_{25}{}^{o}{}_{C}$ (in H_2O) ≈ 3 mg mL^{-1}. $C_6H_{12}AgN_4O_3PS$ (359.1): calcd. C 20.07, N 15.60, H 3.37, S 8.93; found: C 19.77, N 15.20, H 3.43, S, 8.82. IR (KBr): 2942 (w) ν_{as}(CH), 2889 (w) ν_s(CH), 1469 (w), 1378 (s, br) $\nu(NO_3)$, 1276 (m), 1235 (m), 1142 (m), 1092 (m), 1032 (w), 1010 (s), 962 (s), 943 (vs), 906 (m), 839 (w), 800 (s), 774 (m), 742 (s), 715 (vs) and 634 (s) ν(P=S), 594 (m), and 523 (m) cm^{-1}. ^1H NMR (300.13 MHz, D_2O): δ 4.47 and 4.37 (2d, 6H, J_{AB} = 13.3 Hz, NCH^AH^BN, PTA=S), 4.21 (d, 6H, $^2J_{P\text{-}H}$=7.3 Hz, PCH_2N, PTA=S). $^{31}P\{^1H\}$ NMR (121.4 MHz, D_2O, 85% H_3PO_4): δ −14.17 (s, PTA=S). ESI-MS(±) (H_2O/MeCN), selected fragments with relative abundance >20%: MS(+), *m/z*: 297 (90%) $[Ag(PTA=S)]^+$, 487 (100%) $[Ag(PTA=S)_2]^+$; MS(−) *m/z*: 231 (90%) $[Ag(NO_3)_2]^-$. The above-mentioned white precipitate can be recrystallized from MeCN/H_2O, resulting in additional crop of **1** (~10% yield).

Compound **2**: This was obtained following the procedure described for **1**, but using Ag_2SO_4 (0.1 mmol, 31 mg) instead of $AgNO_3$ and a different amount of PTA=S (0.1 mmol, 19 mg). Pale brown crystals of **2** were isolated in 50% yield, based on PTA=S. $S_{25}{}^{o}{}_{C}$ (in H_2O) ≈ 2 mg mL^{-1}. $C_{12}H_{30}Ag_4N_6P_2O_{11}S_4$ (**2**−H_2O, 1056.1): C 13.65, N 7.96, H 2.86, S 12.15; found: C 13.79, N 7.74, H 2.52, S 12.45. IR (KBr): 3401 (s, br) $\nu(H_2O)$, 2962 (w) ν_{as}(CH), 2917 (w) ν_s(CH), 1632 (m, br.) $\delta(H_2O)$, 1473 (m), 1448 (m), 1428 (m), 1368 (w), 1309 (w), 1283 (m), 1273 (m), 1232 (m), 1111 (s) and 1057 (s, br.) $\nu(SO_4)$, 1001 (m), 979 (w), 963 (w),

952 (w), 941 (w), 812 (w), 801 (w), 786 (m), 750 (m), 700 (m) and 616 ν(P=S) (s), 578 (w), and 461 (w) cm^{-1}. ^{1}H NMR (300.13 MHz, D_2O+NaOD): δ 4.48 and 4.38 (2d, 6H, J_{AB} = 13.4 Hz, NC$H^{A}H^{B}$N, PTA=S), 4.22 (d, 6H, $^{2}J_{P\text{-}H}$=7.4 Hz, PCH_2N, PTA=S). $^{31}P\{^{1}H\}$ NMR (121.4 MHz, D_2O+NaOD, 85% H_3PO_4): δ −13.71 (s, PTA=S). ESI-MS(±) (H_2O/MeOH), selected fragments with relative abundance >15%: MS(+), *m/z*: 523 (15%) $[Ag(PTA{=}S)_2(H_2O)_2]^{+}$, 487 (80%) $[Ag(PTA{=}S)_2]^{+}$; MS(−), *m/z*: 1056 (15%) $[Ag_4(PTA{=}S)_2(SO_4)_2(H_2O)_3 - H]^{-}$, 516 (30%) $[Ag_3(SO_4)_2]^{-}$, 394 (25%) $[Ag(PTA{=}S)(SO_4)]^{-}$, 97 (85%) $[HSO_4]^{-}$. As in **1**, a precipitate formed during the synthesis of **2** can be recrystallized from MeCN/H_2O, resulting in additional crop of **2** (~10% yield).

Refinement Details for X-ray Analysis. The X-ray diffraction data of **1** and **2** were collected using a Bruker AXS-KAPPA APEX II diffractometer with graphite monochromated Mo-Kα radiation. Data were collected using omega scans of 0.5º per frame, and a full sphere of data was obtained. Cell parameters were retrieved using Bruker SMART software and refined using Bruker SAINT on all the observed reflections. Absorption corrections were applied using SADABS.[S2] Structures were solved by direct methods using SIR97[S3] program and refined with SHELXL–97.[S4] Calculations were performed with the WinGX System-Version 1.80.03.[S5] All hydrogen atoms were inserted in calculated positions. In **1**, the heavily disordered nitrate anion and crystallization water molecule in the accessible voids could not be modeled satisfactorily and thus were handled with PLATON/SQUEEZE.[S6] For the compound **1**, the low value of Flack parameter [–0.002(17)] indicates that the data have enough information to allow a reliable absolute determination; since it is zero within 2su one can be sure that the absolute structure of the crystal is the one refined. For the compound **2**, that parameter was refined by means of TWIN and BASF using SHELXL to yield a value of 0.352(14). Since the crystal structure is chiral, one can consider that the crystal contains both enantiomorphs in *ca*. 0.65/0.35 proportion. Diamond and TOPOS software packages were used for structural visualization.[S7]

Procedure for Antibacterial and Antifungal Activity Studies. The following strains were employed: *Staphylococcus aureus* PCM 2054 (=ATCC 25923), *Escherichia coli* PCM 2057 (=ATCC 25922) from the Polish Collection of Microorganisms of the Institute of Immunology and Experimental Therapy in Wroclaw, as well as *Pseudomonas aeruginosa* and *Candida albicans* isolated from clinical samples in the Department of Veterinary Microbiology, University of Environmental and Life Sciences, Wroclaw (Poland). The two latter strains were identified using conventional methods and miniaturized identification systems (ID 32 C and API 20 NE [bioMérieux], respectively).

The antimicrobial and antifungal activities were evaluated by the method of serial dilutions using Antibiotic Broth ([g L^{-1} (H_2O)]: Dextrose 1.0; K_2HPO_4 3.68; Beef Extract 1.5;

Peptone 5.0; KH_2PO_4 1.32; NaCl 3.5; Yeast Extract 1.5), according to Grove and Randall.[S8] Both compounds **1** and **2** were soluble in Antibiotic Broth.

An overnight culture of strain tested was diluted 1:1000 in Antibiotic Broth (AB). To a series of wells of a multiwell plate (EuroClone®, Italy) containing appropriate amounts of AB, aqueous solutions of **1** or **2** were added to obtain 0.9 mL. To each well, 0.1 mL of a microbial suspension was pipetted. The final concentrations of the compounds tested were as follows [μg mL^{-1}]: 60, 50, 40, 30, 20, 10, 9, 8, 7, 6, 5, 4, 3, 2, and 1. In addition, the antimicrobial activity of the "free" PTA=S was examined using the same method (concentration range was extended up to 600 μg mL^{-1}). Broth sterility control and (for each strain) growth controls were included. Plates were incubated at 37 ºC for 24 h. The minimum inhibitory concentration (MIC, μg mL^{-1}) was defined as the lowest concentration of the compound that fully inhibited the growth of bacteria or fungi. Turbidity of wells contents was controlled using DEN-1B densitometer (Biosan, Latvia).[S9]

The obtained results are given in Table 1, whereas Table S1 also contains the comparison of the activities of **1** and **2** with those of the reference silver salts ($AgNO_3$, Ag_2SO_4), calculated after normalization for the number of silver atoms in each compound.

Table S1. Antimicrobial and antifungal activities of **1**, **2** and reference silver salts expressed as minimum inhibitory concentration (MIC).

Entry	Strains	MIC [μg mL^{-1}][a]				Normalized MIC [*n*mol mL^{-1}][b]			
		1	**2**	**$AgNO_3$**[c]	**Ag_2SO_4**[d]	**1**	**2**	**$AgNO_3$**	**Ag_2SO_4**
1	*E. coli*	4	20	6	39	11	76	37	251
2	*P. aeruginosa*	5	20	63	–	14	76	368	–
3	*S. aureus*	20	40	63	39	56	152	368	251
4	*C. albicans*	30	>60	>1600	–	84	>227	>9417	–

[a] For PTA=S, MIC > 600 μg mL^{-1} for all strains.
[b] These MIC values [*n*mol mL^{-1}] were normalized for the number of silver atoms in each compound.
[c] Data taken from ref. 22.
[d] Data taken from ref. 23.

Supplementary References

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S9. *Antibiotics in Laboratory Medicine*, Thrupp, L. D. 2nd edn., ed. Lorian, V. p. 93. Baltimore: Williams & Wilkins, 1986.

Supplementary Figures

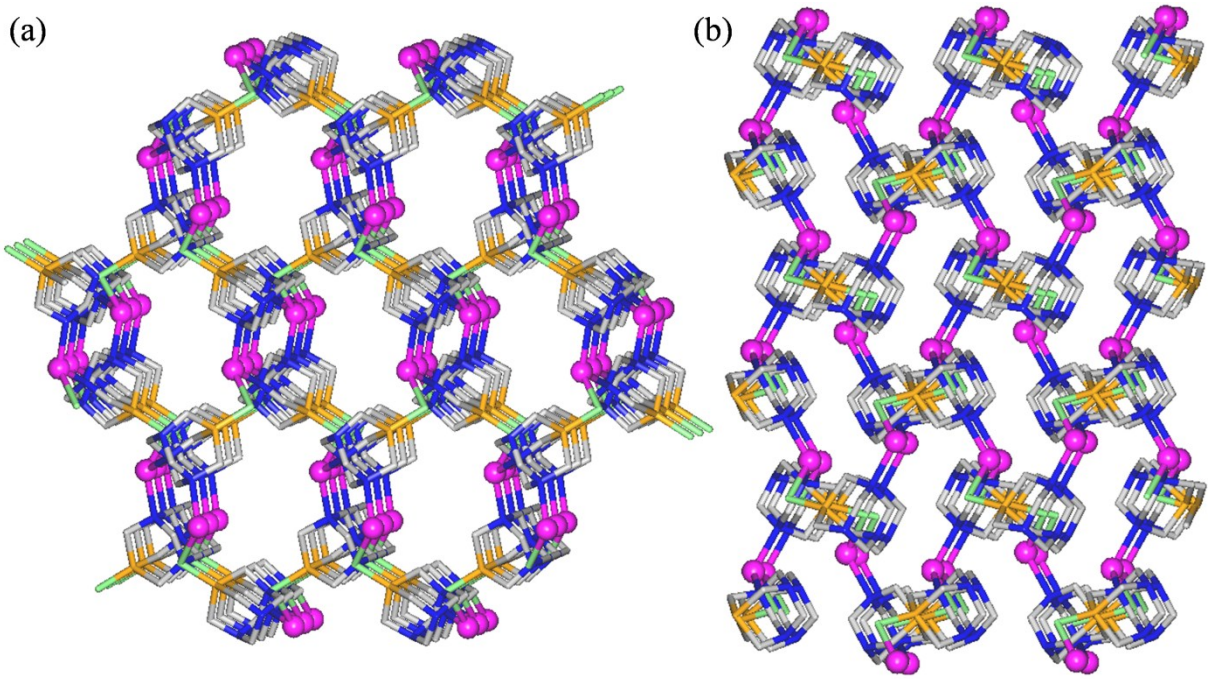

Figure S1. Structural fragments of the 3D framework of **1**: views along the *b* (a) and *c* (b) axis. Hydrogen atoms are omitted for clarity, colour codes: Ag (magenta), N (blue), P (orange), S (green), and C (grey).

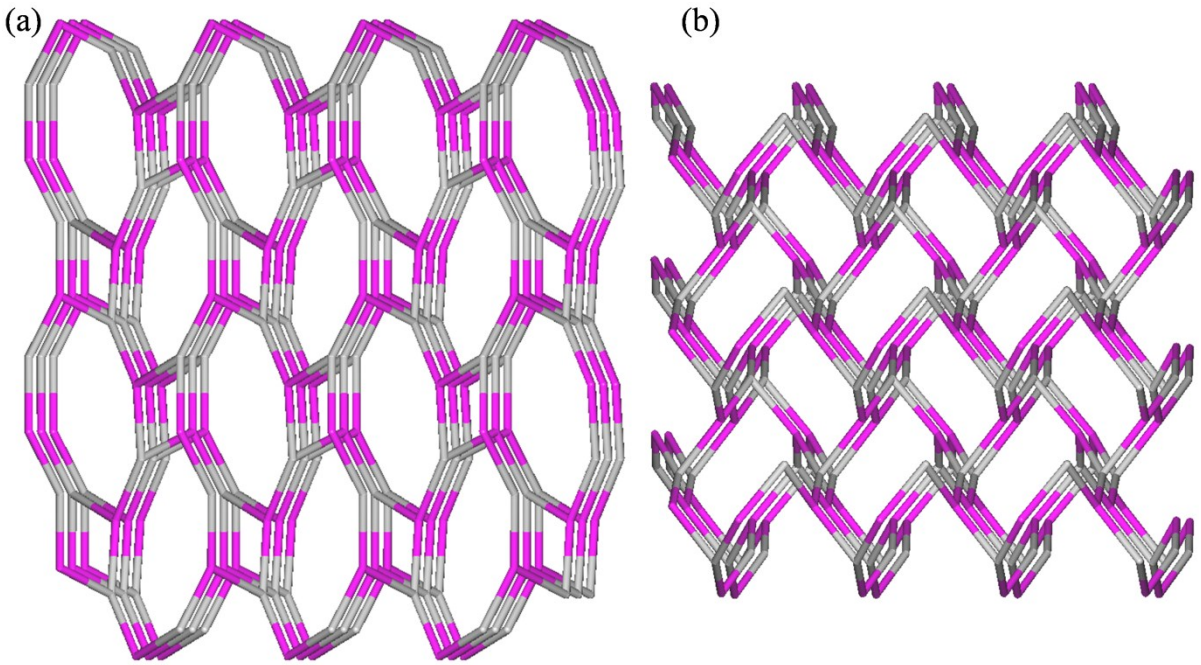

Figure S2. Topological representations of the underlying uninodal 3-connected **srs** net of **1**: views along the *b* (a) and *c* (b) axis. Colour codes: centroids of 3-connected μ_3-PTA=S nodes (grey), 3-connected Ag1 nodes (magenta).

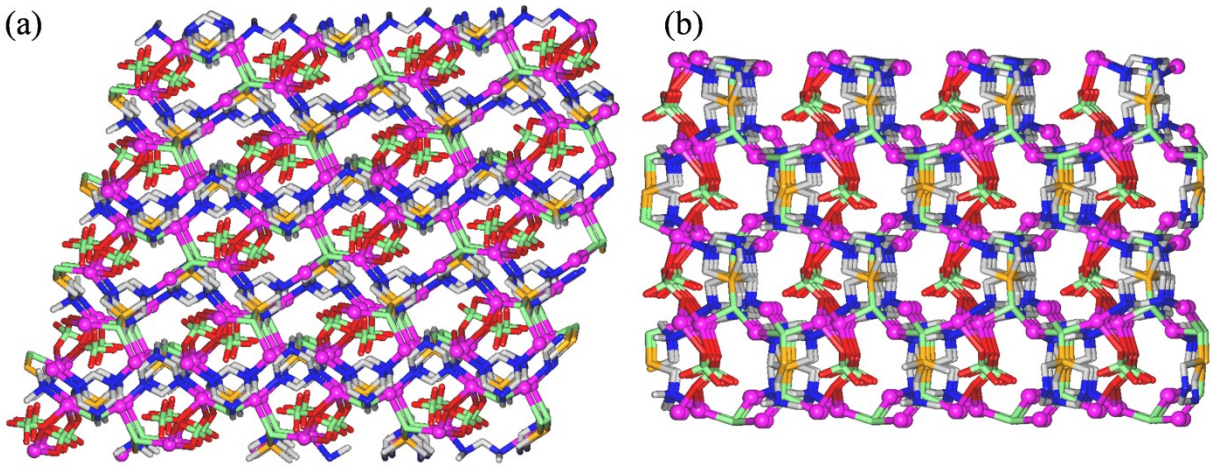

Figure S3. Structural fragments of the complex 3D framework of **2**: views along the *b* (a) and *c* (b) axis. Hydrogen atoms and H_2O molecules are omitted for clarity, colour codes: Ag (magenta), N (blue), P (orange), S (green), and C (grey).

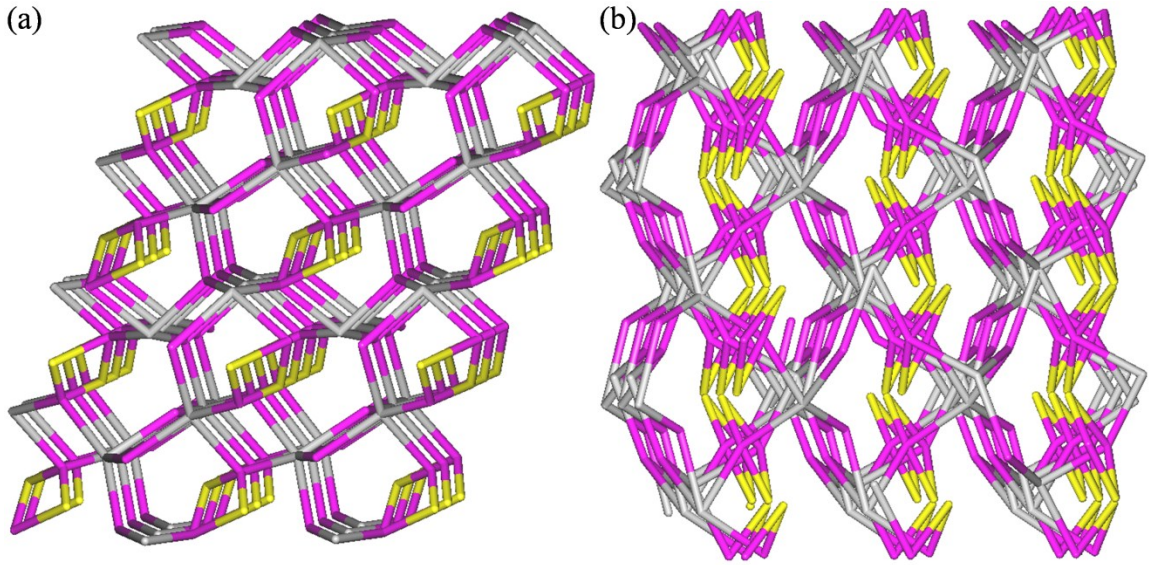

Figure S4. Topological representation of the underlying pentanodal 3,4,5-connected net of **2** with a novel topology: views along the *b* (a) and *c* (b) axis. Colour codes: centroids of 5- or 4-connected μ_5- or μ_4-PTA=S nodes (grey), 4- and 3-connected Ag1−Ag3 nodes or 2-connected Ag4 linkers (magenta), and centroids of 2-connected μ_2-SO_4 linkers (yellow).