Electronic Supplementary Material (ESI) for Catalysis Science & Technology.

Supporting Information

Catalytic activity of CuGHK peptide-based porous material

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S1. GENERAL CONSIDERATIONS: STARTING MATERIALS AND CHARACTERIZATION

S1.1. Materials and reagents

All the general reagents and solvents were commercially available and used as received. $Cu(OAc)_2 \cdot xH_2O$, benzaldehyde, propanal, cyclohexanone and nitromethane were purchased from Sigma-Aldrich. The Glycyl-L-Histidyl-L-Lysine 98% (GHK) ligand was purchased from Ark Pharm.

S1.2. Physical and chemical characterization

PXRD patterns of the CuGHK peptide MOF were collected in a PANalytical X'Pert PRO diffractometer using copper radiation (Cu K_α) with an X'Celerator detector, operating at 40 mA and 45 kV. Profiles were collected in the $2º < 2\theta < 90º$ range with a step size of 0.013. IR spectra of solids were collected using a Shimadzu Fourier Transform Infrared Spectrometer, FTIR-8400S, fitted with a Diamond ATR unit. XPS measurements were performed on a SPECS spectrometer equipped with a Phoibos 150 MCD–9 analyzer using non–monochromatic Mg KR (1253.6 eV) X–ray source working at 50 W. Microscopy images were obtained with a Hitachi S4800 SEM-FEG (scanning electron microscopy- field emission gun) equipment, with an accelerating voltage of 20kV.

S1.3. Computational details

The simulations were accomplished using Materials Studio (MS) 2017 R2. Our study combines two modules: Adsorption Locator (simulation module involves the greatest success at (Monte Carlos, MC) method in statistical mechanics) and Forcite (module of the classical molecular mechanics (MM) and molecular dynamics (MD). Starting with the experimental determined unit cell of CuGHK peptide MOF (CCDC 931607), the solvents were removed, and atomic positions were relaxed with MM method, using charges of the atoms obtained via Q_{eq} calculations and the UFF4MOF force field.[1], [2] The resulting structure was used in this study.

To study the adsorption process, an all-atoms flexible model was used to model each molecule (benzaldehyde and nitromethane), however el CuGHK peptide was considered as rigid structure. Adsorption data of benzaldehyde and nitromethane for single and mixtures were computed by GCMC simulations with Adsorption Locate module.

To study the structural flexibility upon adsorption and to ensure a proper host-guest interaction we used MD simulations, as implemented in the Forcite module at 298K for 100ps, with five benzaldehyde and ten nitromethane molecules in which all the atoms were free to move in the canonical ensemble.

S2. SYNTHESIS AND CHARACTERIZATION

Synthetic procedure of CuGHK: The synthesis of the peptide-MOF was based on a reported method.[3] In the first place, an aqueous solution of $Cu(OAc)_2 \cdot xH_2O$ was formed by dissolving 45 mg (0.25 mmol) of $Cu(OAc)_2 \cdot xH_2O$ in 900 µL of water. This solution was added to 88 mg (0.26 mmol) of GHK. To this mixture, 3.8 mL of EtOH were added and it was left stirring at room temperature for 5 min. After that, 1.2 mL of EtOH was added and the mixture was let stand at room temperature for 24h, followed by another addition of 3 mL of EtOH. After 48 h, the product was filtrated and washed with EtOH.

XRD characterization: For the in-situ capillary XRD measurements of MOF in the presence of the substrates, 10 mg of CuGHK were introduced in a glass capillary. Then, 50 µL of benzaldehyde or nitromethane were added with the help of a syringe and let stand with the MOF for several hours. The capillary was sealed and introduced in the XRD diffractometer for the analysis of the diffraction pattern (see Figure S1).

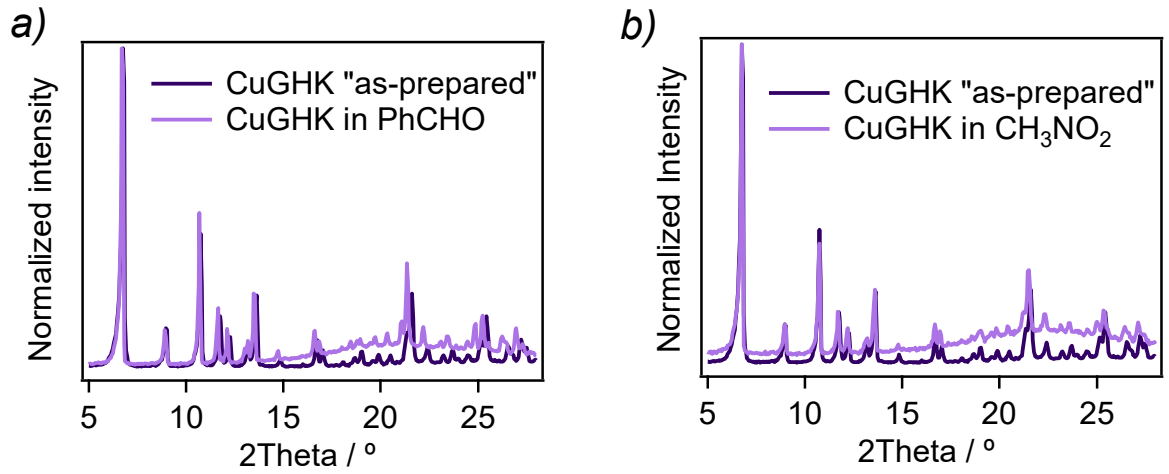

Figure S1. Capillary XRD measurements of CuGHK soaked in pure benzaldehyde (a) or nitromethane (b).

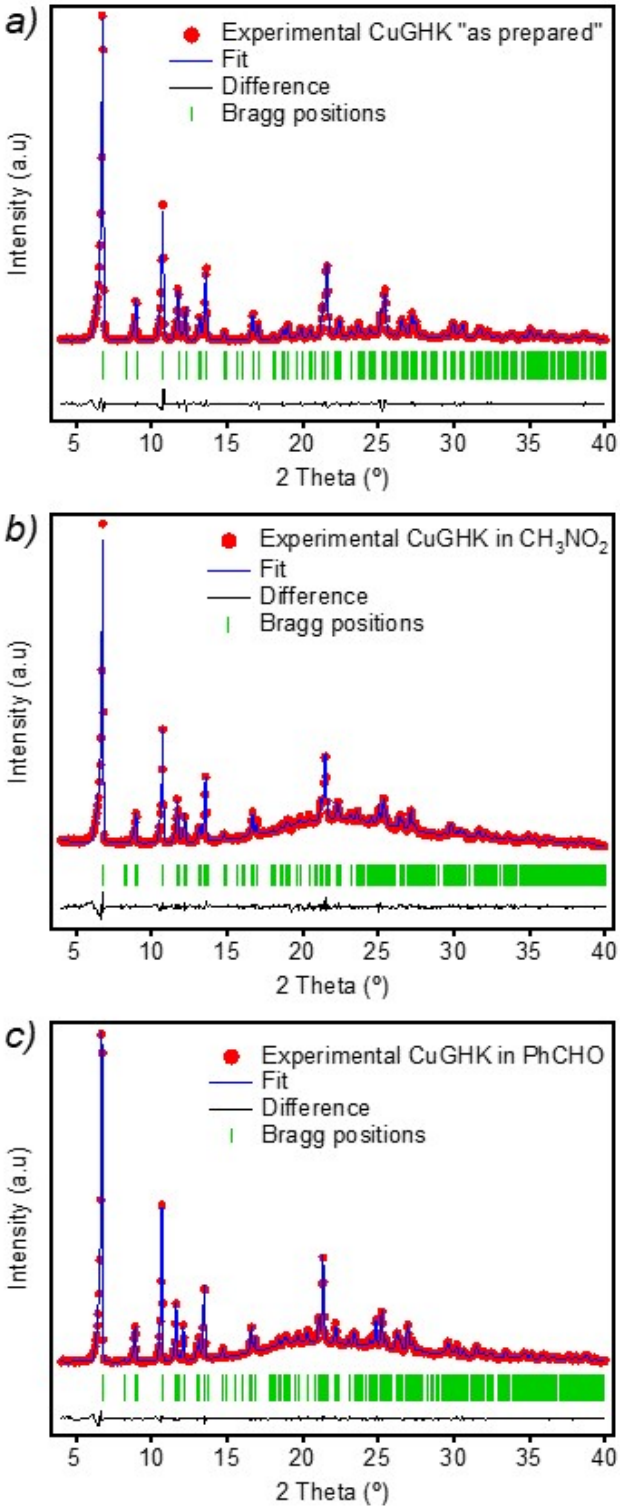

Figure S2. Le Bail refinement of the experimental diffraction pattern of CuGHK "as prepared" (a) CuGHK in nitromethane (b) and CuGHK in benzaldehyde (c).

Table S1. Parameters of the Le Bail refinement

	a=b(Å)	c (Å)	V (Å^3)	R_e (%)	R_p (%)	R_{wp} (%)	gof
CuGHK "as prepared"	14.97477	25.99237	5828.627	3.01	4.65	6.34	2.10
CuGHK in CH_3NO_2	15.07391	25.76168	5853.636	3.31	3.64	4.79	1.45
CuGHK in PhCHO	15.18618	25.80761	5951.752	2.88	2.78	3.96	1.37

Table S2. Effect of benzaldehyde and nitromethane on d-spacing of CuGHK

CuGHK "as-prepared"		**CuGHK in PhCHO**		**Δd (PhCHO)/Å**	**CuGHK in CH_3NO_2**		**Δd (CH_3NO_2)/Å**
2θ/º	d/ Å[a]	2θ/º	d/ Å[a]		2θ/º	d/ Å[a]	
6.75	13.08	6.70	13.18	0.10	6.75	13.08	0.00
8.96	9.86	8.91	9.92	0.06	8.96	9.86	0.00
10.74	8.23	10.69	8.27	0.04	10.74	8.23	0.00
11.74	7.53	11.64	7.60	0.06	11.69	7.56	0.03
12.27	7.21	12.11	7.30	0.09	12.21	7.24	0.04
13.63	6.49	13.48	6.56	0.07	13.58	6.52	0.02
16.73	5.29	16.63	5.33	0.03	16.68	5.31	0.02
21.62	4.11	21.35	4.16	0.05	21.51	4.13	0.02
25.45	3.50	25.24	3.53	0.03	25.34	3.51	0.01
27.24	3.27	26.97	3.30	0.03	27.13	3.28	0.01

[a] Calculated from the Bragg equation d = n·λ/ 2·senθ (θ in radians, λ = 1.5406 Å, n = 1).

S3. CATALYTIC TESTS

In a typical experiment, nitromethane (80 µl, 1.5 mmol) and benzaldehyde (20 µl, 0.2 mmol) were added to the MOF catalyst (10 mg, 0.02 mmol). The reaction mixture was stirred in a glass flask for 48 h at room temperature under neat conditions, while the consumption of the starting material in the supernatant was monitored by GC-FID (Gas Chromatography-Flame Ionization Detector). Identification of the reaction products was achieved by comparing the retention times in GC-FID with commercial products but also by H-NMR and GC-MS analysis. For the recycling test, the used catalyst was isolated from the reaction mixture by centrifugation (3000 rpm, 10 min) and washed with ethanol (2 x 0.5 ml) until the supernatant was the pure solvent, as confirmed by GC-FID. The recovered catalyst was dried and reused under the same reaction conditions. For the hot filtration test, the used catalyst was isolated from the reaction mixture by centrifugation (3000 rpm, 10 min) and the reaction was followed without the catalyst under the same conditions.

Table S3. Catalytic activity of the peptide MOF in the Henry reaction.[a]

Catalyst	Benzaldehyde conversion (%)	TON ($mol_{PhCHO} \cdot mol_{Lys}^{-1}$)
CuGHK "as prepared"	23 (14)[b] (14)[c] (9)[d] (1)[e]	2
CuGHK "1st cycle"	28	2
CuGHK "2nd cycle"	22	2
CuGHK "3rd cycle"	20	2
CuGHK[f]	3	<1
CuGHK[g]	21	2
GHK	52	4
Lysine	62	4
$Cu(OAc)_2$	Non-detected	-

[a] Reaction conditions: PhCHO:MOF = 8; CH_3NO_2: PhCHO = 8; room temperature; 48h. [b] Yield after 24h. [c] o-vanillin, [d] m-tolualdehyde and [e] 2-hydroxy-3-nitrobenzaldehyde as substrates. [f] Reaction in 100 µl CH_3CN. [g] Reaction in 100 µl hexane.

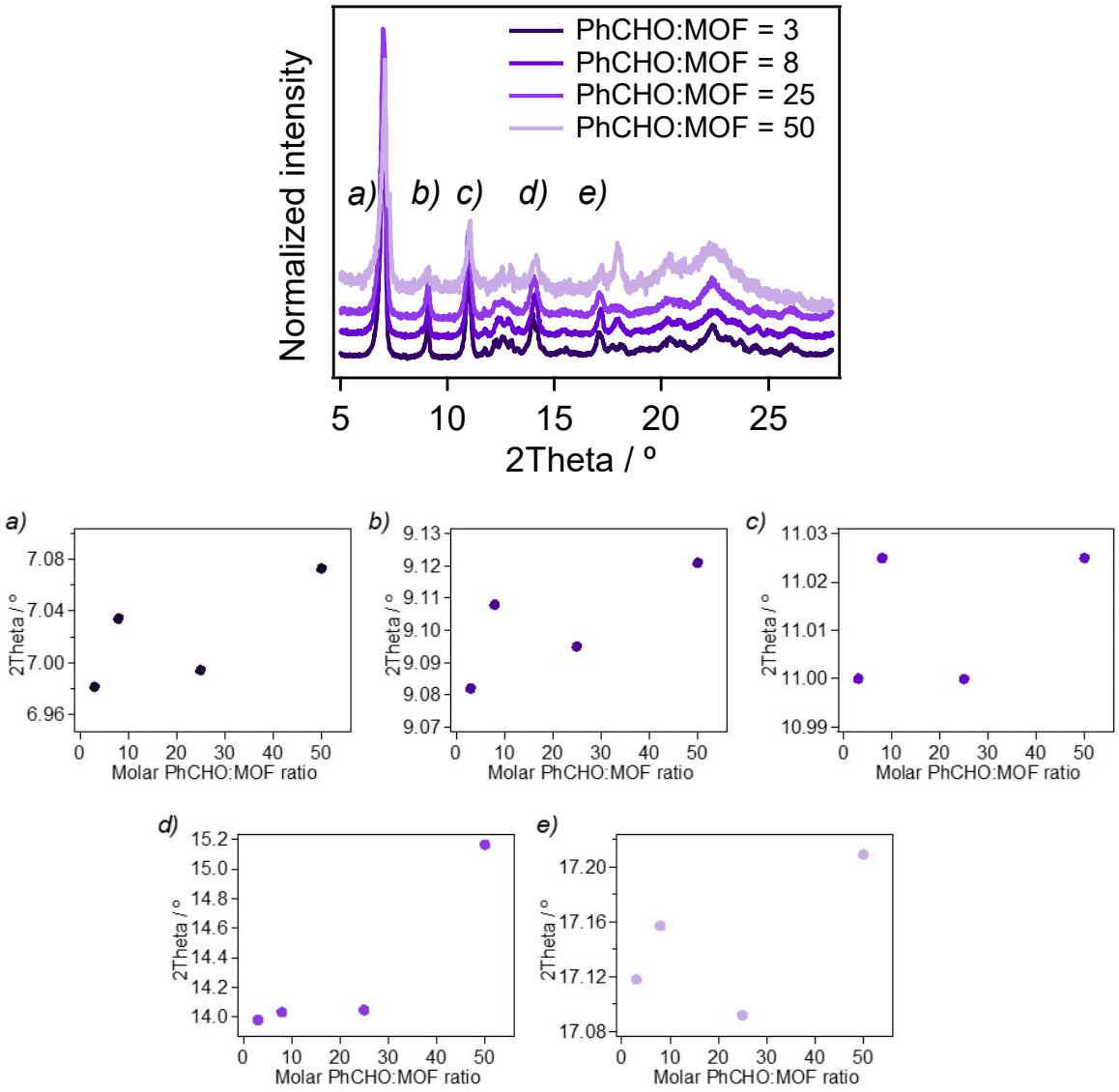

Figure S3. First five XRD peak shift (a, b, c, d and e) dependence on the PhCHO:MOF ratio for the CuGHK after 48h of Henry reaction between benzaldehyde and nitromethane at room temperature, solvent-free conditions.

Table S4. Reaction rate dependence on the temperature.

T(ºC)	t (h)	Benzaldehyde/ Cu-GHK	Nitromethane/ Benzaldehyde	Yield (%)	TON	TOF ($10^2 \cdot h^{-1}$)
20	48	50	4	1	0.5	**1.0**
30	48	50	4	3	1.5	**3.1**
40	48	50	4	6	3	**6.3**

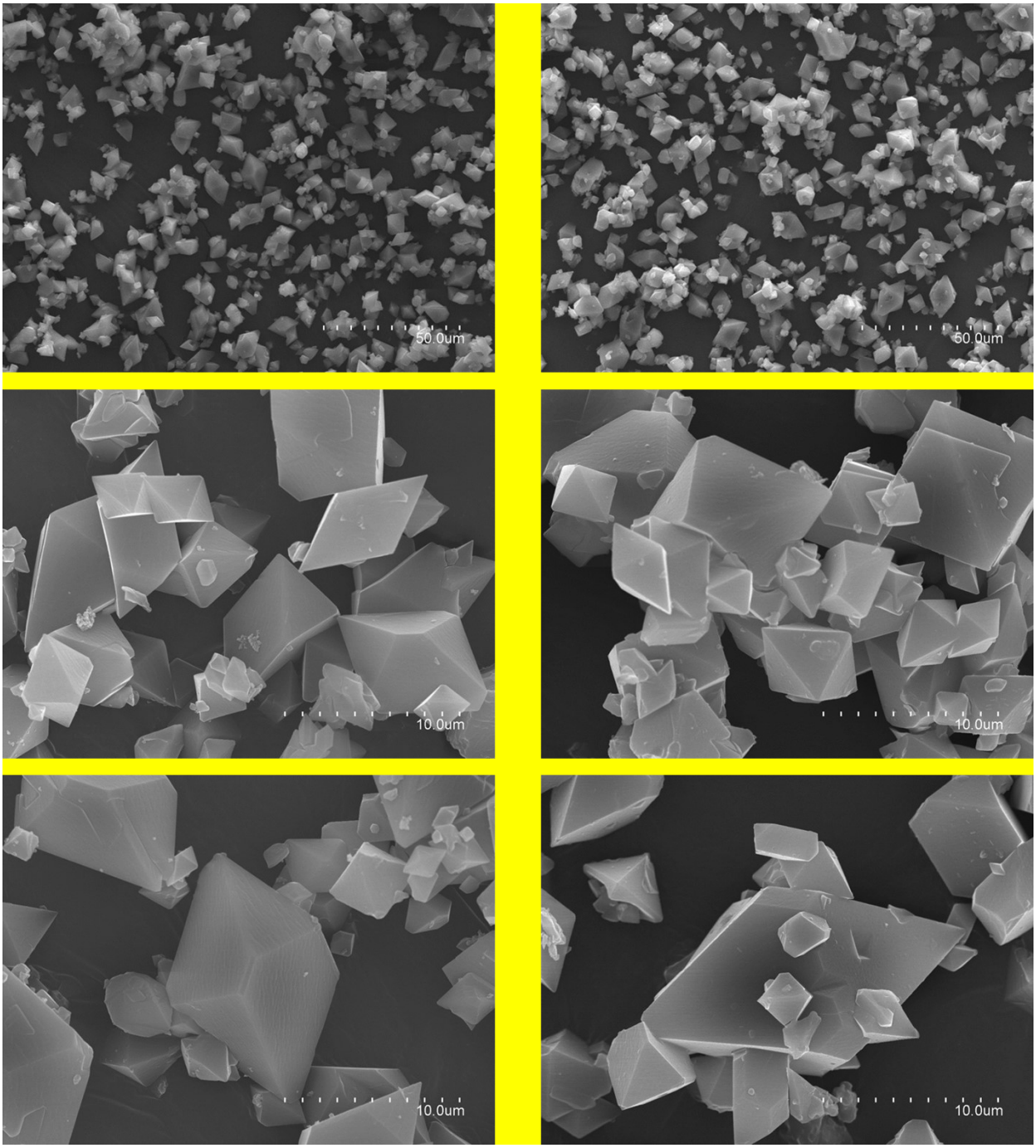

Figure S4. SEM images of CuGHK before (left) and after (right) the Henry reaction between benzaldehyde and nitromethane for 48 h under neat and room temperature conditions.

S4. BENZALDEHYDE ADSORPTION TESTS

First, we perform a GC Calibration using 5, 10, 20 and 40 µL of benzaldehyde (PhCHO) in 1mL of hexane. The A_{PhCHO} /A_{hexane} is taken as the actual concentration of benzaldehyde in g/L.

The experiments related to the adsorption of benzaldehyde on the CuGHK porous solid was carried out in the following way: A solution of 5, 10, 20 and 40 µL of benzaldehyde in 1mL of hexane, $[PhCHO]_0$ = 5, 10, 20 and 40 g/L, was added to 5 mg of the CuGHK porous peptide MOF (12 µmol Lys) in a glass vial. The mixture was stirred (300 rpm) at room temperature for 1h. After this time, the liquid supernatant was isolated by centrifugation (3000 rpm, 5 min) and the benzaldehyde, $[PhCHO]_{1h}$, was analysed by GC-FID. The amount of PhCHO adsorbed in the porous solid was calculated taking into account the initial $[PhCHO]_0$, according to:

$$\text{PhCHO uptake} = ([PhCHO]_0 - [PhCHO]_{1h}) \cdot g_{MOF}^{-1}$$

where $[PhCHO]_0$ and $[PhCHO]_{1h}$ is the detected GC signal for the initial and equilibrium solution, respectively.

Table S5. Experimental uptake of benzaldehyde in the peptide MOF.

$[PhCHO]_0$ ($g \cdot L^{-1}$)	**Uptake (molecules·unit $cell^{-1}$)**
5	1
10	4
20	8
40	11

S5. COMPUTATIONAL STUDY

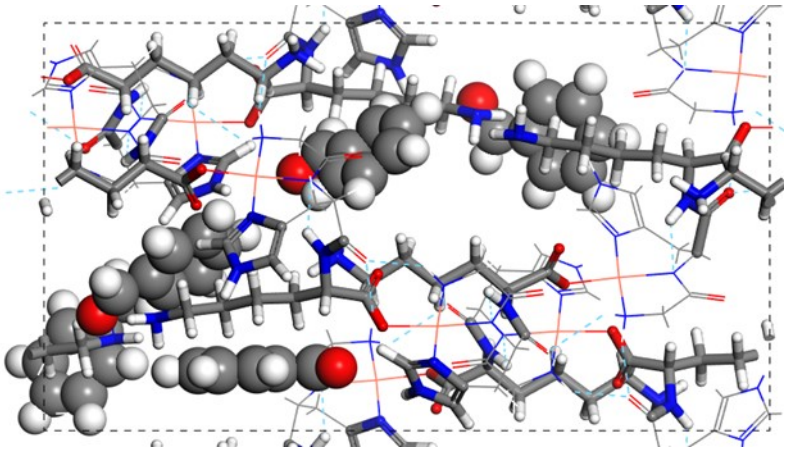

Figure S5. Docking of 5 molecules of benzaldehyde (VDW representation) on CuGHK peptide MOF (line representation) using Adsorption Locator module (MC) of Materials Studio computer program. The Lys and His residues from MOF are highlighted in stick.

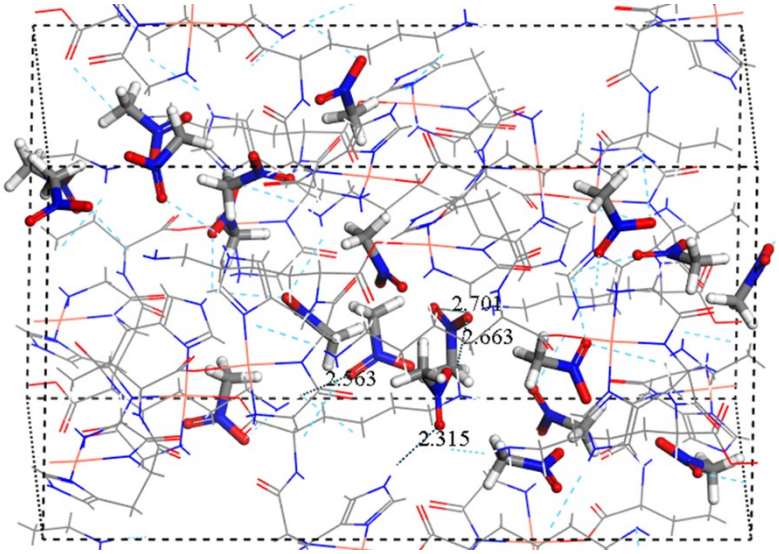

Figure S6. Docking of 20 molecules of nitromethane (stick representation) on CuGHK peptide MOF (line representation) using Adsorption Locator module (MC) of Materials Studio computer program. Interactions: nitromethane and histidine (2.3 Å) and benzaldehyde and lysine (2.6 Å) from MOF are highlighted.

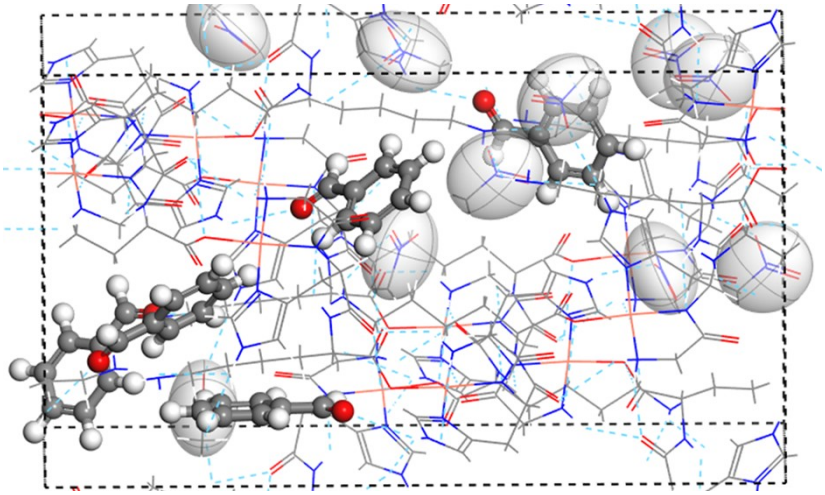

Figure S7. Docking of 5 molecules of benzaldehyde (ball and stick) and 10 molecules of nitromethane (sphere representation) on CuGHK peptide MOF (line representation) using Adsorption Locator module (MC) of Materials Studio computer program. This result was used as an input for Molecular Dynamic (MD) simulations.

S6. MECHANISTIC HYPOTHESIS

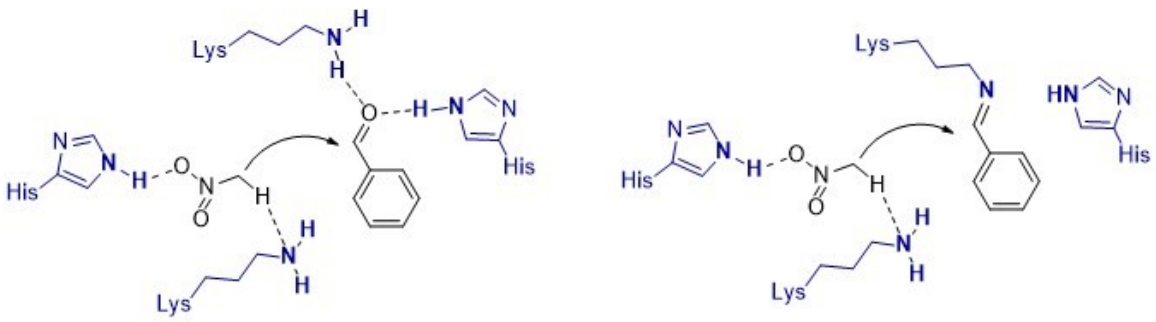

Figure S8. Possible interactions of the substrates at the MOF peptide "enzyme-like" pockets involving the activation of nitromethane and benzaldehyde by histidine and lysine amino acid residues acting as acid-base and/or nucleophilic catalytic sites.

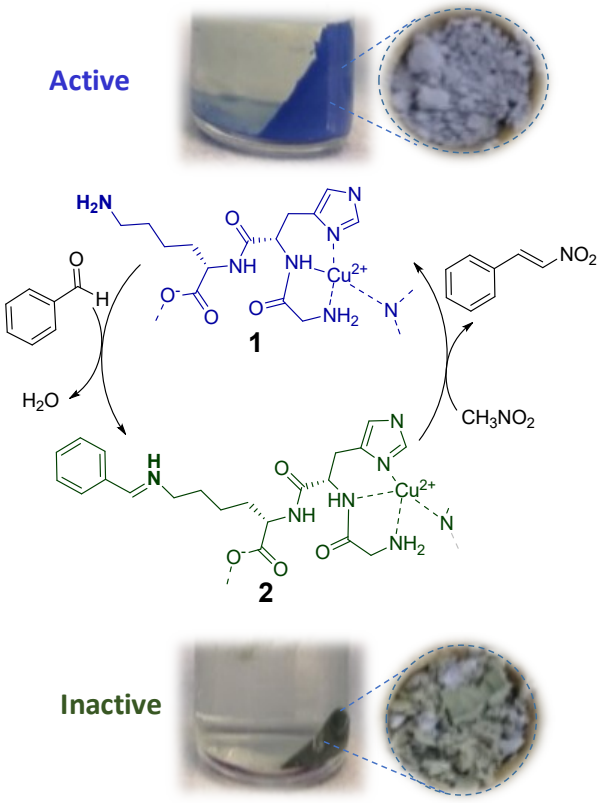

Figure S9. Tentative mechanism involving the free (top) and bonded to benzaldehyde (bottom) amino, together with the MOF after the reaction using benzaldehyde: MOF of 3 (top) or 25 (bottom).

S7. REFERENCES

[1] M. A. Addicoat, N. Vankova, I. F. Akter, T. Heine, *J. Chem. Theory Comput.* **2014**, *10*, 880-891.

[2] D. E. Coupry, M. A. Addicoat, T. Heine. *J. Chem. Theory Comput.* **2016,** *12*, 5215-5225

[3] C. Martí-Gastaldo, J. E. Warren, M. E. Briggs, J. A. Armstrong, K. M. Thomas, M. J. Rosseinsky, *Chem. Eur. J.* **2015**, *21*, 16027-16034.