Amino Acid Functionalized Metal-Organic Framework by Soft Coupling-Deprotection Sequence

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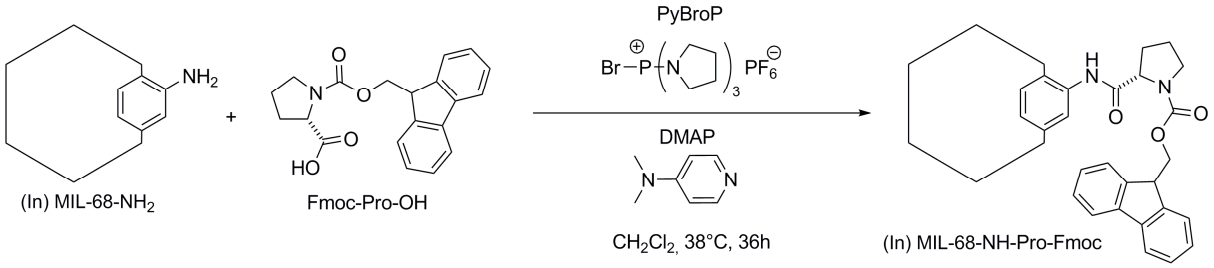
Supporting Information

1. General remarks

All reactions are carried out in anhydrous solvents. The (In) MIL-68-NH_2 is synthesized and activated according to our previously reported procedure.[1] All other reagents are commercially available (Sigma-Aldrich) and are used without further purification. NMR spectra are recorded on a Brüker 250 MHz spectrometer. Chemical shifts are reported in parts per million (ppm) referenced to the appropriate solvent peak. The following abbreviations are used to describe peak patterns when appropriate: s = singlet, d = doublet, q = quadruplet, m = multiplet. Coupling constants, *J*, are reported in Hertz unit (Hz). The XRD measurements on the materials are carried out by powder X-ray diffraction (PXRD) using a Bruker D5005 diffractometer equipped with a secondary graphite monochromator and a scintillation counter. N_2 isotherms at 77K are performed using a BELSORP-max (BEL Japan). The thermogravimetric analyses have been carried out on a SETARAM type Setsys Evolution 12 apparatus (heating rate of 2 °C min-1) under a pure air flow coupled with a mass spectrometer PFEIFFER, type Omnistar. Electro-spray mass spectroscopy is performed in positive-ion mode on a MicroTOF-Q BRUKER mass spectrometer.

2. Typical peptide coupling procedure



In a 7 mL glass vial, 0.36 mmol of PyBroP (180 mg), 0.6 mmol of DMAP (78 mg) and 0.33 mmol of the *N*-Fmoc-protected amino acid are dissolved in 5 mL of anhydrous dichloromethane. The solution is stirred at 25°C for two hours. Then, 100 mg of (In) MIL-68-NH_2 (c.a. 0.3 mmol -NH_2) are added and the suspension is allowed to react under vigorous stirring for 36 hours at 38°C. The resulting suspension is centrifuged and the solid washed with dichloromethane (3 x 5 mL) to give the desired product as a fine off-white powder after drying under vacuum. Following this procedure, around 10 % of the amino groups are converted into the corresponding amide according to ^{1}H NMR analysis. No amino acid remains inside the MOF, however NMR spectra show DMAP signals at ~ 8.20, 6.96 and 3.18 ppm which remain even after several washings.

(In) MIL-68-NH-(L)-Pro-Fmoc : Yield = 9.6 %, ^{1}H NMR (250 MHz, [D6]DMSO-DCl-D_2O) δ 9.14 (1H, d, *J* = 19.8 Hz), 8.21 (6H, d, *J* = 7.5 Hz, DMAP), 8.07 (1H, d, *J* = 8.2 Hz), 7.68-7.90 (14H, m), 7.17-7.43 (14H, m), 7.08 (10H, d, *J* = 8.1 Hz), 6.96 (7H, d, *J* = 7.5 Hz, DMAP + 1H), 4.12-4.31 (4H, m), 3.41 (2H, m), 3.17 (12H, s, DMAP), 1.75-2.07 (4H, m) ppm.

(In) MIL-68-NH-(D)-Ala-Fmoc : Yield = 10%, ^{1}H NMR (250 MHz, [D6]DMSO-DCl-D_2O) δ 9.10 (1H, s), 8.19 (10H, d, *J* = 6.8 Hz, DMAP), 8.06 (1H, d, *J* = 8.5 Hz), 7.83-7.95 (11H, m), 7.61-7.75 (12H, m), 7.31-7.42 (13H, m), 6.95 (10H, d, *J* = 7.0 Hz, DMAP), 4.24-4.28 (3 H, m), 4.09-4.12 (1H, m), 3.17 (30H, s, DMAP), 1.34 (3H, d, *J* = 7.2 Hz) ppm.

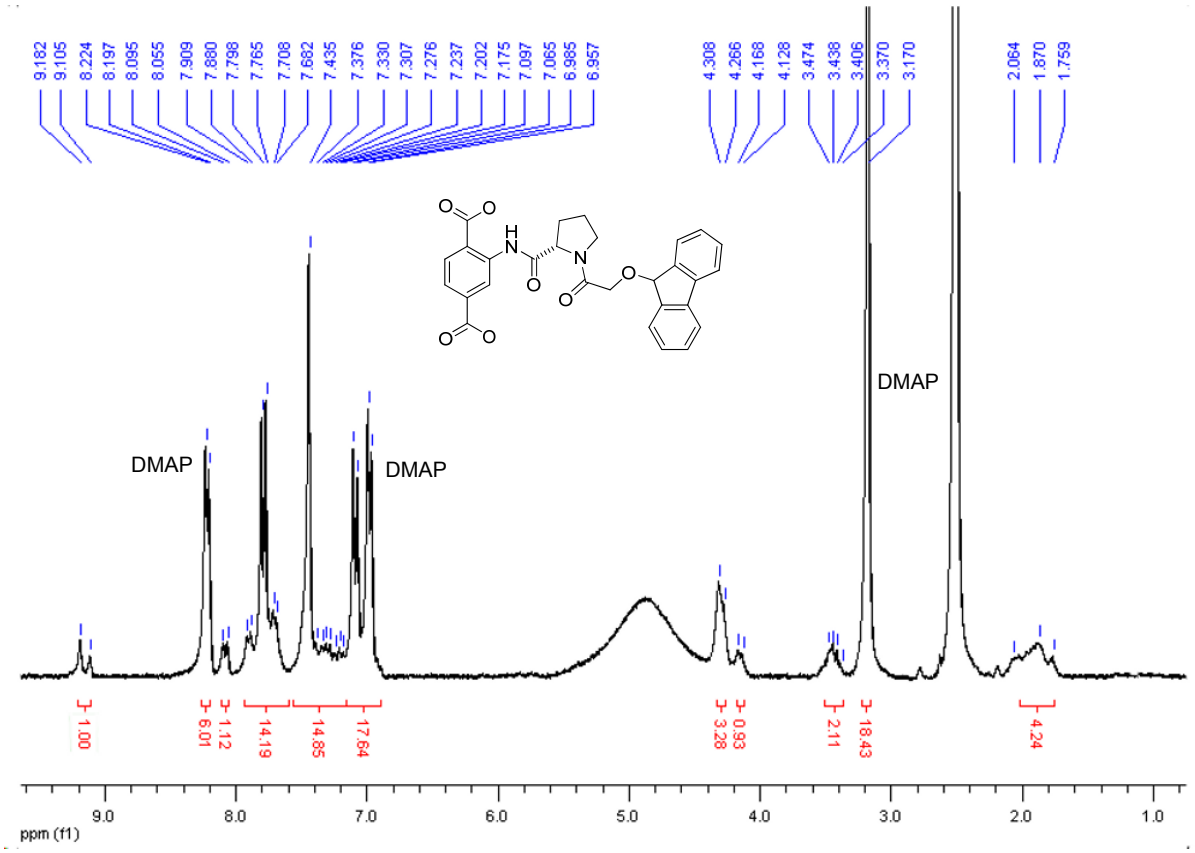


Figure S1. ^{1}H NMR spectrum of digested (In) MIL-68-NH-(L)-Pro-Fmoc (ca. 10% modified).

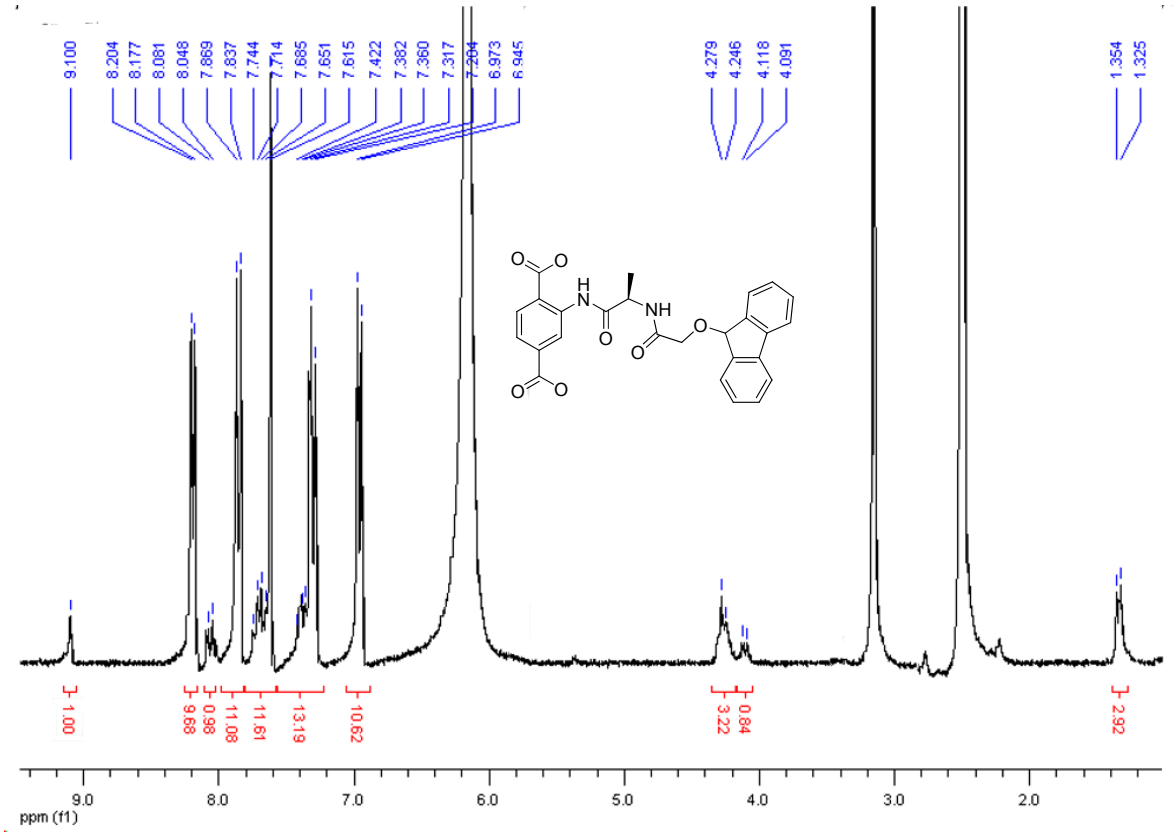
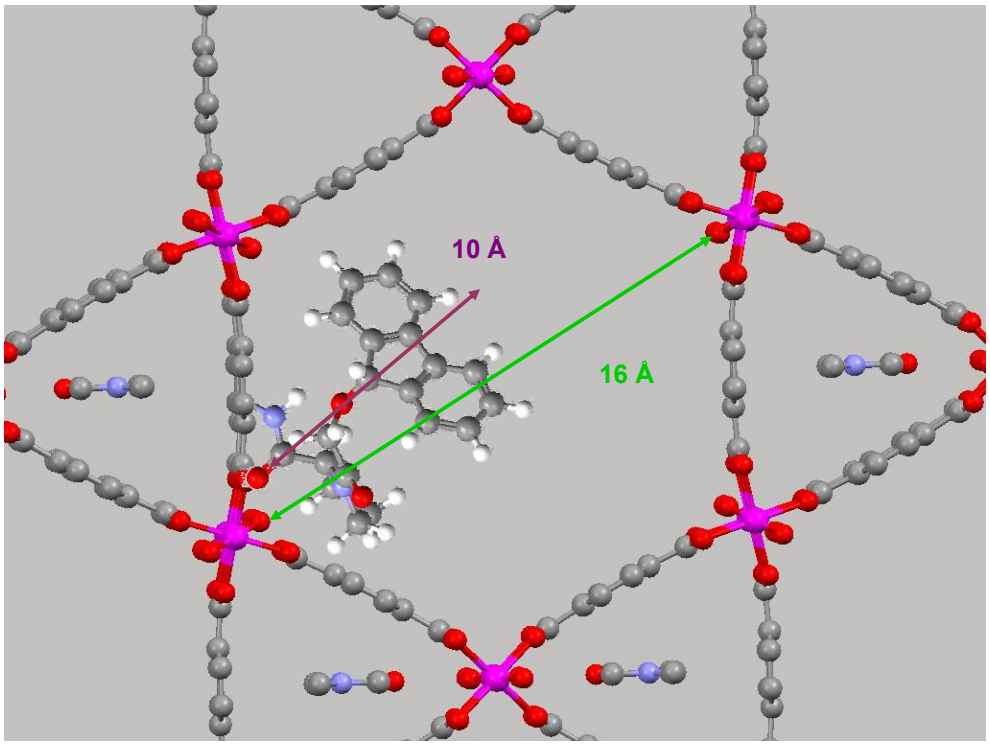
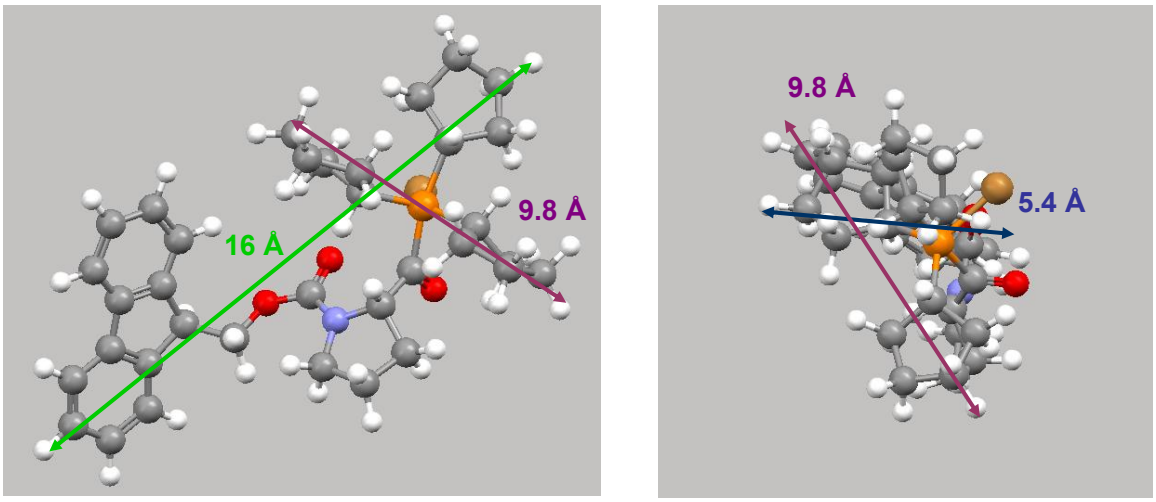


Figure S2. ^{1}H NMR spectrum of digested (In) MIL-68-NH-(D)-Ala- Fmoc (ca. 10% modified).

According to calculation made using ChemOffice 2008 (Cambridgesoft) and Mercury (CCDC), only one Fmoc-protected proline moiety can enter into the MIL-68 cavity. The yields obtained are in line with these findings.

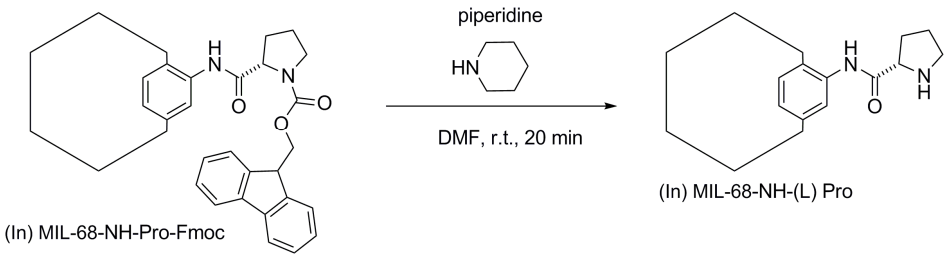


Sketch of the Fmoc-Proline placed into the MIL-68 cavity with respective sizes.



Sketch of different views of the PyBroP-activated Fmoc-Proline with respective sizes.

3. Typical deprotection procedure (Fmoc removal)



In a 7 mL glass vial, 100 mg of either (In) MIL-68-NH-(L)-Pro-Fmoc or (In) MIL-68-NH-(D)-Ala- Fmoc are suspended in 5 mL of anhydrous DMF. Then 0.5 mL of piperidine are added and the suspension is allowed to react under vigorous stirring for 15 minutes at room temperature. The resulting suspension is centrifuged and the solid washed with DMF (3 x 5 mL). The resulting solid is then allowed to soak in water for 48 hours to give the desired product as a fine off-white powder after drying under vacuum. Following this procedure, the Fmoc group is removed quantitatively according to ^{1}H NMR analysis.

(In) MIL-68-NH-(L)-Pro : ^{1}H NMR (250 MHz, [D6]DMSO-DCl-D_2O) δ 8.60 (1H, s), 8.01 (1H, d, J = 8.2 Hz), 7.82 (10H, d, J = 8.3 Hz), 7.53 (9H, s), 7.20 (9H, d, J = 8.3 Hz), 4.52 (1 H, m), 3.24 (2H, m), 1.92-2.13 (4H, m) ppm.

(In) MIL-68-NH-(D)-Ala : ^{1}H NMR (250 MHz, [D6]DMSO-DCl-D_2O) δ 8.64 (1H, s), 8.03 (1H, d, J = 8.25 Hz), 7.77 (10H, m), 7.43 (9H, s), 7.07 (9H, d, J = 8.25 Hz), 3.94 (1 H, q, J = 6.8 Hz), 1.17 (3H, d, J = 7 Hz) ppm.

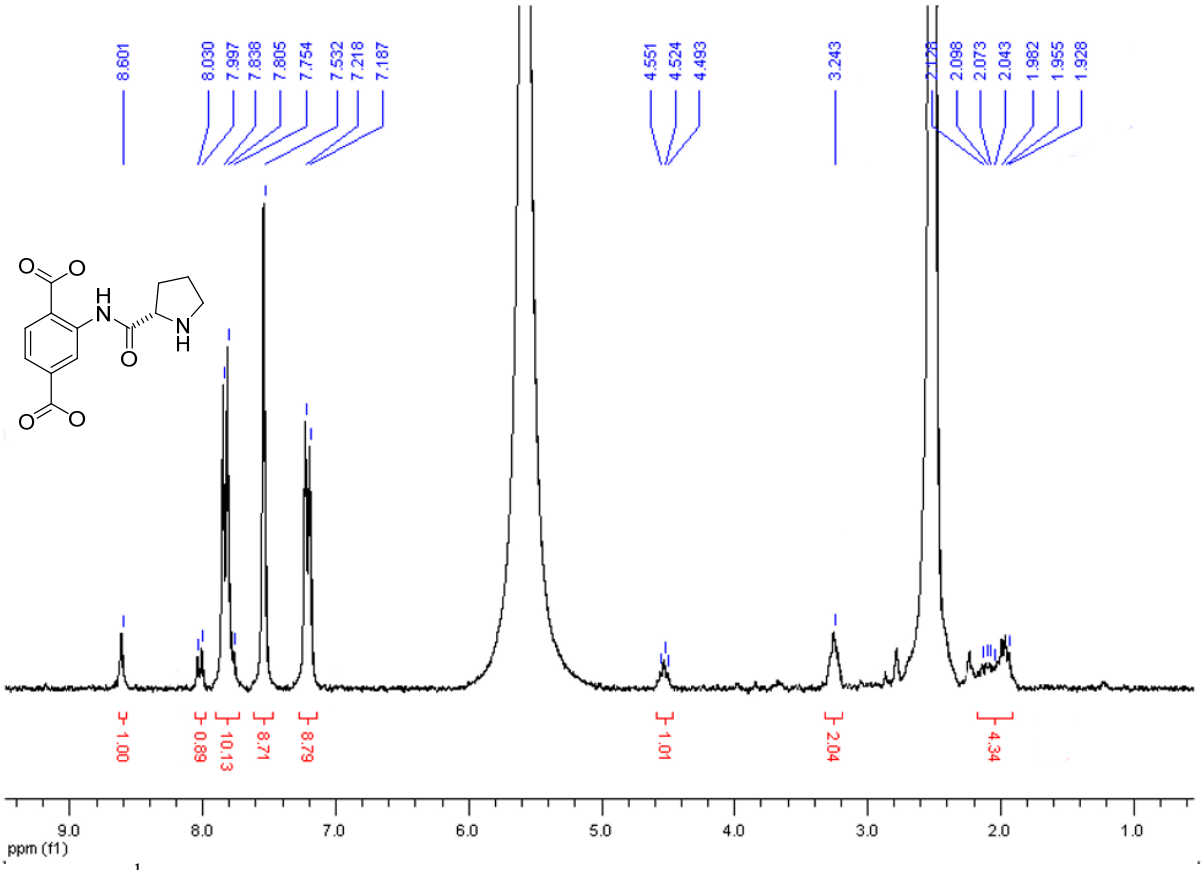


Figure S3. ^{1}H NMR spectrum of digested (In) MIL-68-NH-(L)-Pro (ca. 10% modified).

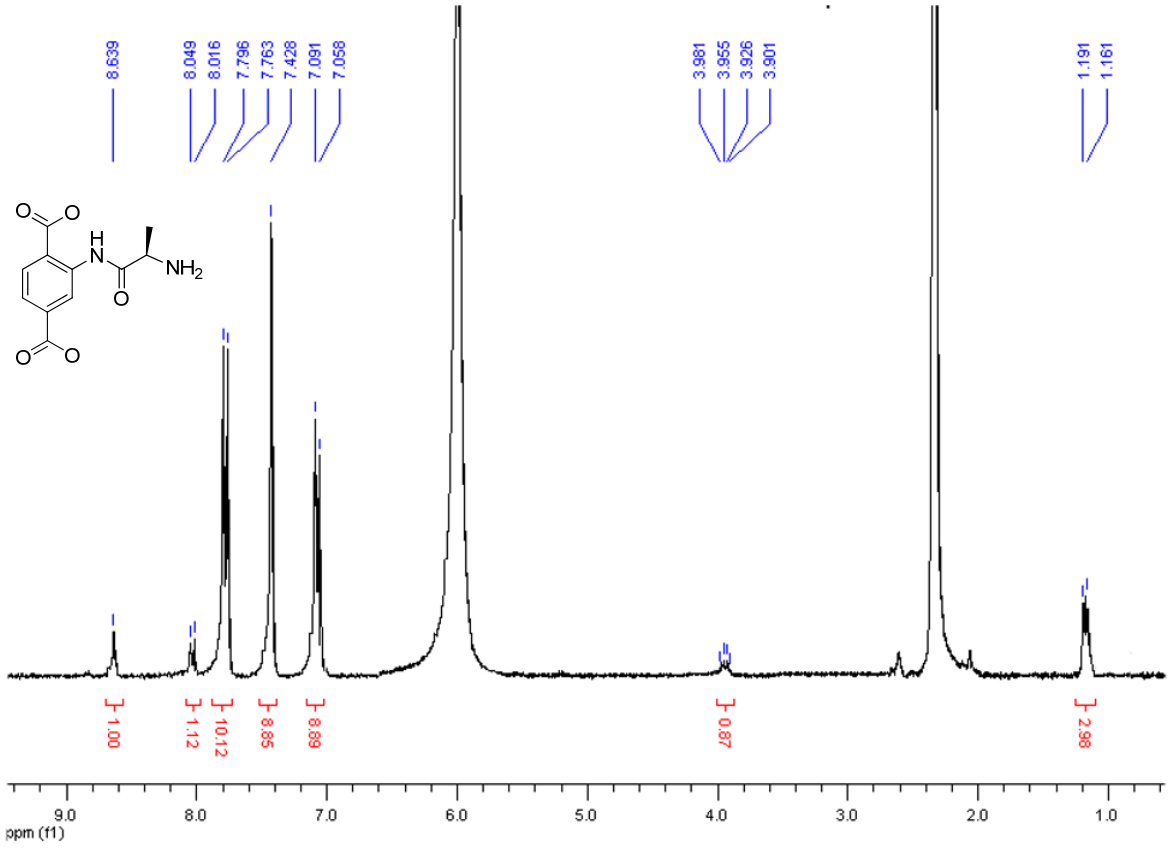


Figure S4. ^{1}H NMR spectrum of digested (In) MIL-68-NH-(D)-Ala

4. X-ray diffraction (XRD)

The XRD measurements on the materials were carried out by powder X-Ray diffraction (PXRD) using a Bruker D8 Advance Diffractometer equipped with a Lyon-Eye detector (CuKα radiation, wavelengths λ = 0.154178 nm). The XRD studies were done at room temperature.

The unit cell refinement was carried out using Topas software (Brücker) with Le Bail method.

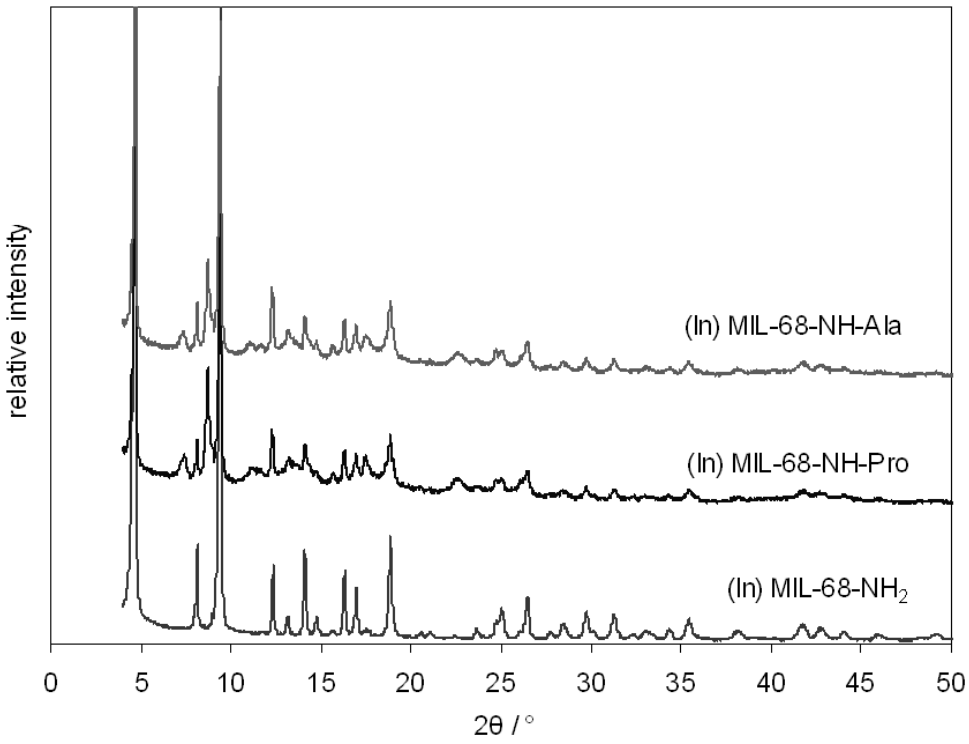


Figure S5. PXRD patterns of (In) MIL-68 samples

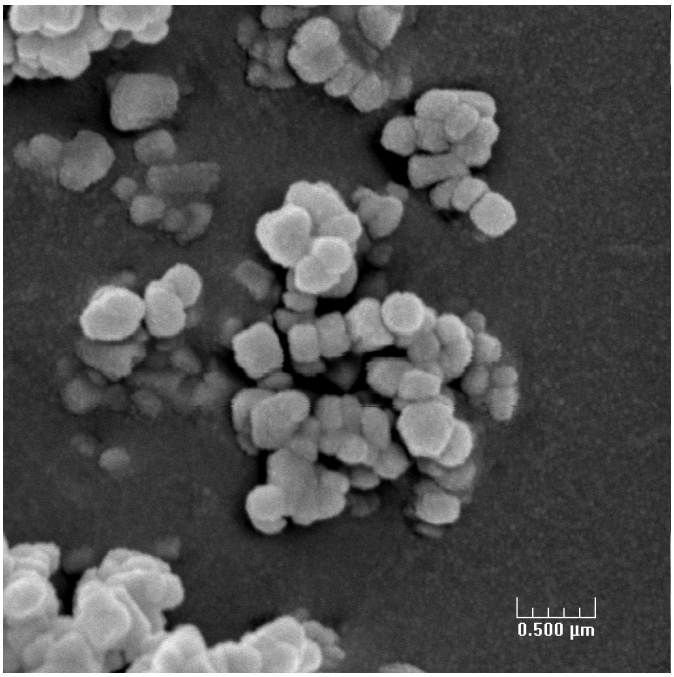


Figure S6. SEM picture of (In) MIL-68-NH_2

Starting from crystal data and structure refinement found for (In) MIL-68,[2] cells parameters are calculated for (In) MIL-68-NH_2 as followed:

Space group: Cmcm (63) orthorhombic
Unit cell dimensions: a= 21.733(4) Å
b= 37.548(9) Å
c= 7.194(1) Å
Volume: V= 5870(2) $Å^3$

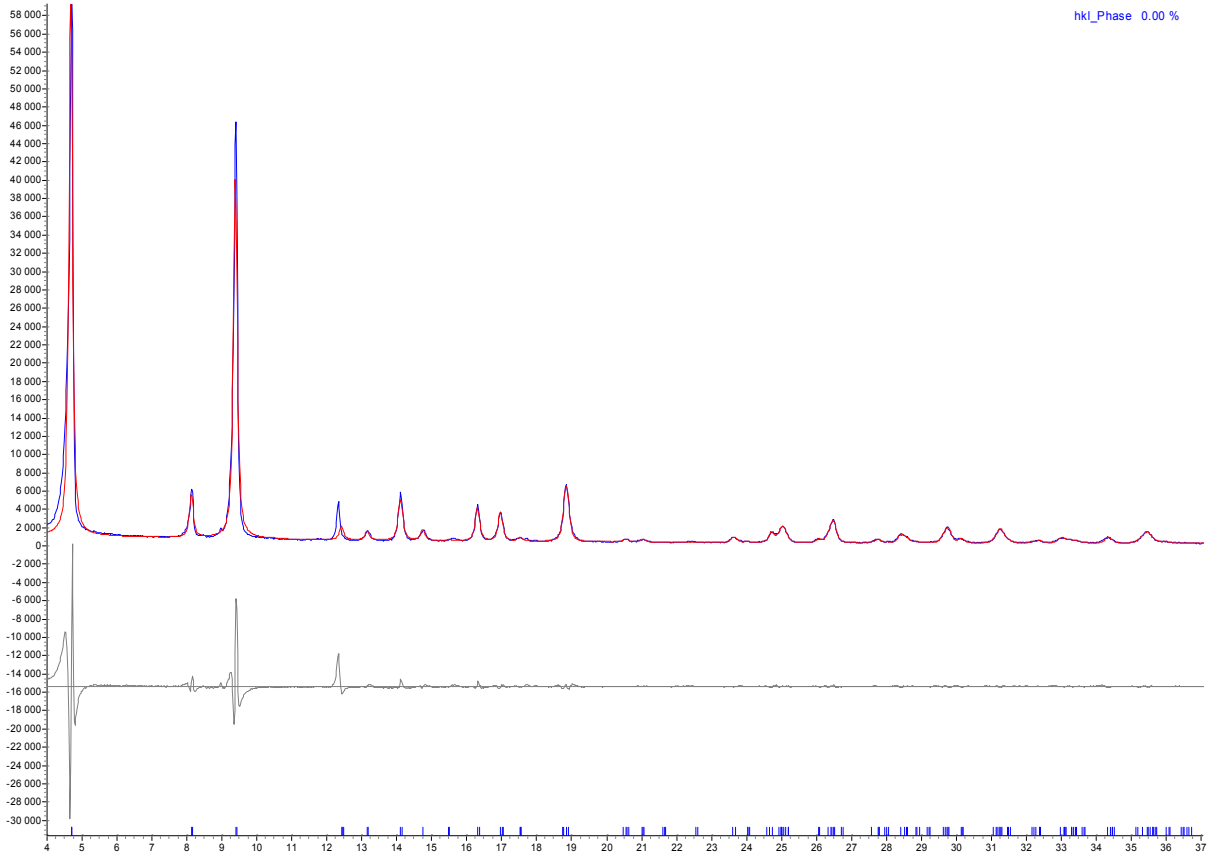


Figure S7. PXRD patterns of (In) MIL-68, measured (blue) and simulated using cell parameters (red).

Considering the minor changes into the patterns of the functionalized (In) MIL-68-NH-Pro and (In) MIL-68-NH-Ala, the new cells parameter calculated are in the orthorhombic system (space group P222):

Unit cell dimensions: a= 21.719(5) Å
b= 37.518(12) Å
c= 14.388(4) Å

Volume: V= 11724(6) Å^3

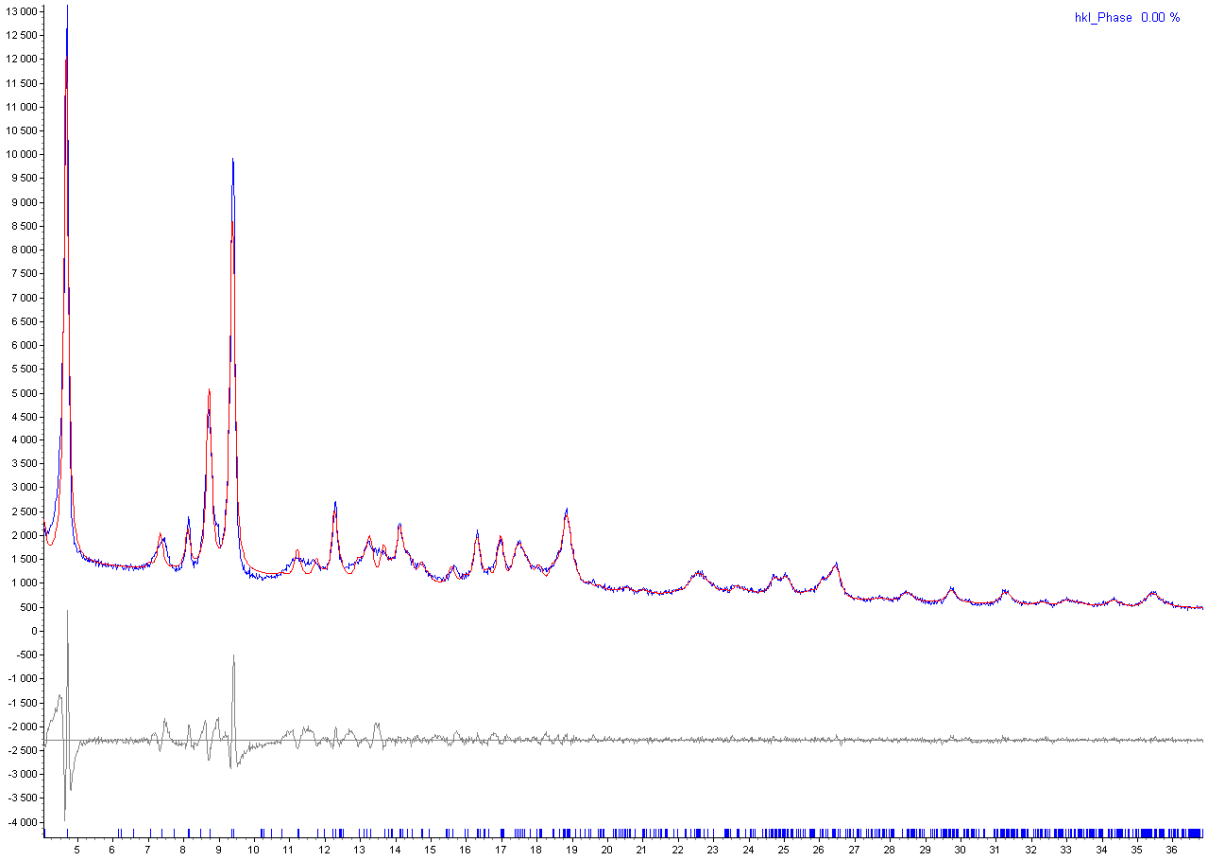


Figure S8. PXRD patterns of functionalized (In) MIL-68, measured (blue) and simulated using new cell parameters (red).

The doubling of the unit cell size shows that the 10% grafting of amino-acids does occur into the MOF framework, keeping the crystallinity.

5. Gas sorption analysis

The N_2 adsorption/desorption isotherms qt 77 K were measured on a BELSORP-MAX. The samples were outgassed under vacuum (~ 10^{-4} mbar) at 393K for 12 h before start of the measurements. The specific surface was determined by BET method.

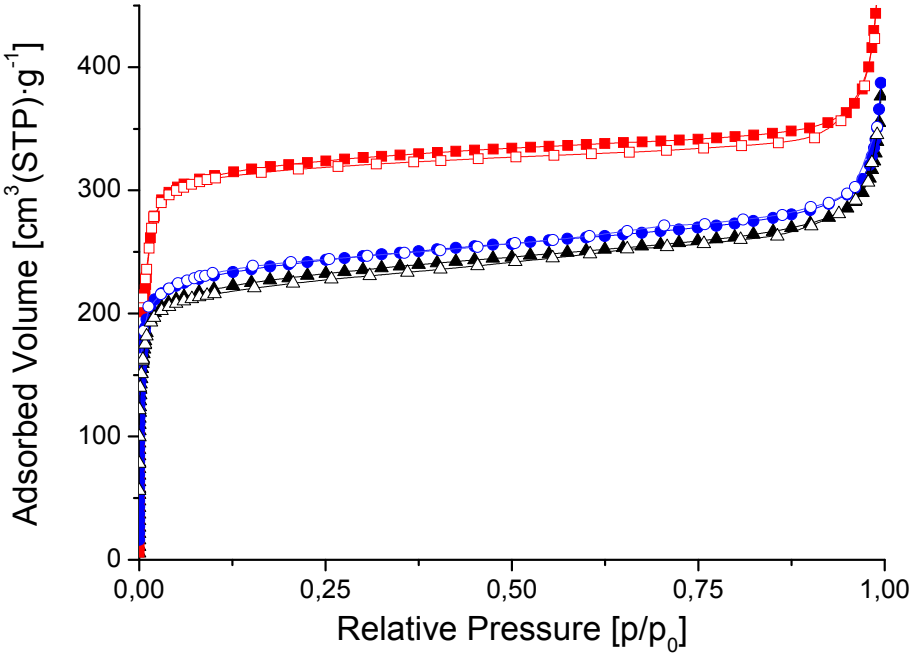


Figure S9. Nitrogen isotherms (77 K) represented as linear-linear diagrams for In-MIL-68-NH_2 (■), In-MIL-68-NH-Pro (▲) and In-MIL-68-NH-Ala (●). Close and open symbols correspond to adsorption and desorption data, respectively.

MOF	BET surface area (m^2/g)
In-MIL-68-NH2	1260
In-MIL-68-NH-Pro	768
In-MIL-68-NH-Ala	825

6. Thermogravimetric analysis

The thermogravimetric analyses have been carried out on a SETARAM type Setsys Evolution 12 apparatus (heating rate of 2 °C.min^{-1}) under a pure air flow coupled with a mass spectrometer PFEIFFER, type Omnistar.

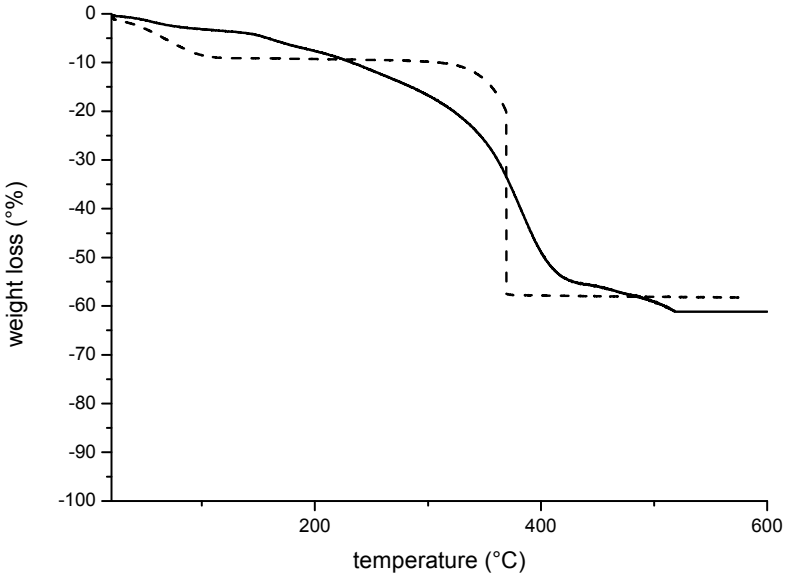


Figure S10. TGA of (In) MIL-68-NH_2 (dashed line) and (In) MIL-68-NH-Pro (solid line)

7. Mass spectrometry analysis

ESI-MS (positive ion) are performed using 1 mg of MOF sample dissolved in a HCO_2H / CH_2Cl_2 / H_2O / MeOH solution. Cations $[M+H]^+$ corresponding to the both protonated amino and functionalized linkers are detected.

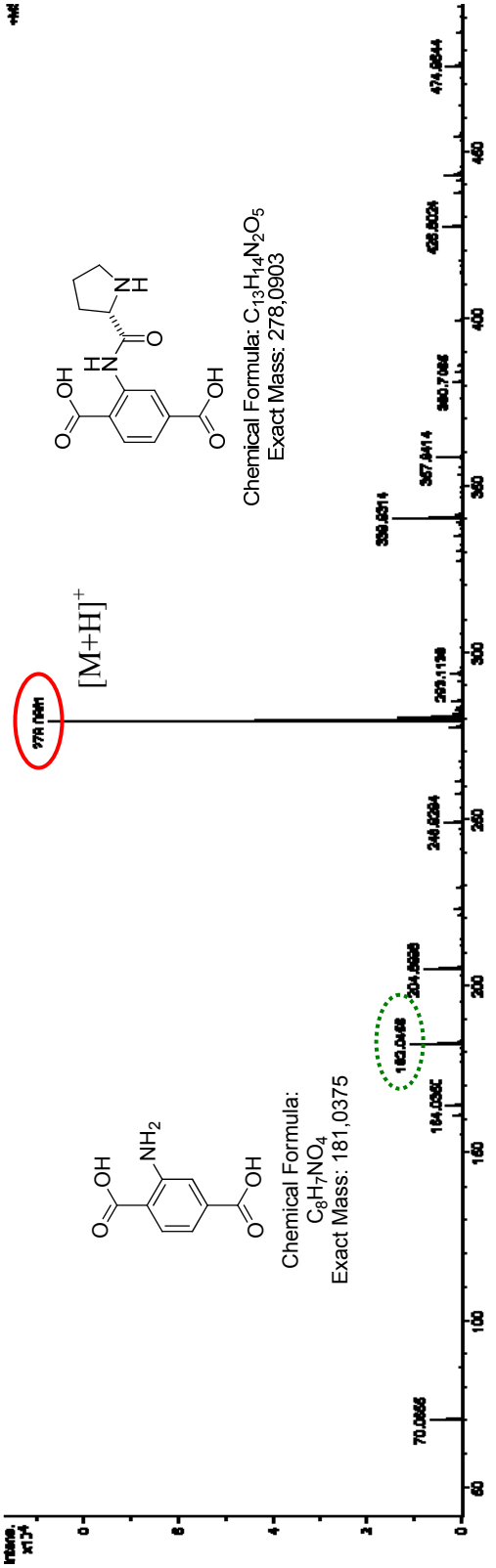


Figure S11. ESI-MS analysis of digested (In) MIL-68-NH-(L)-Pro

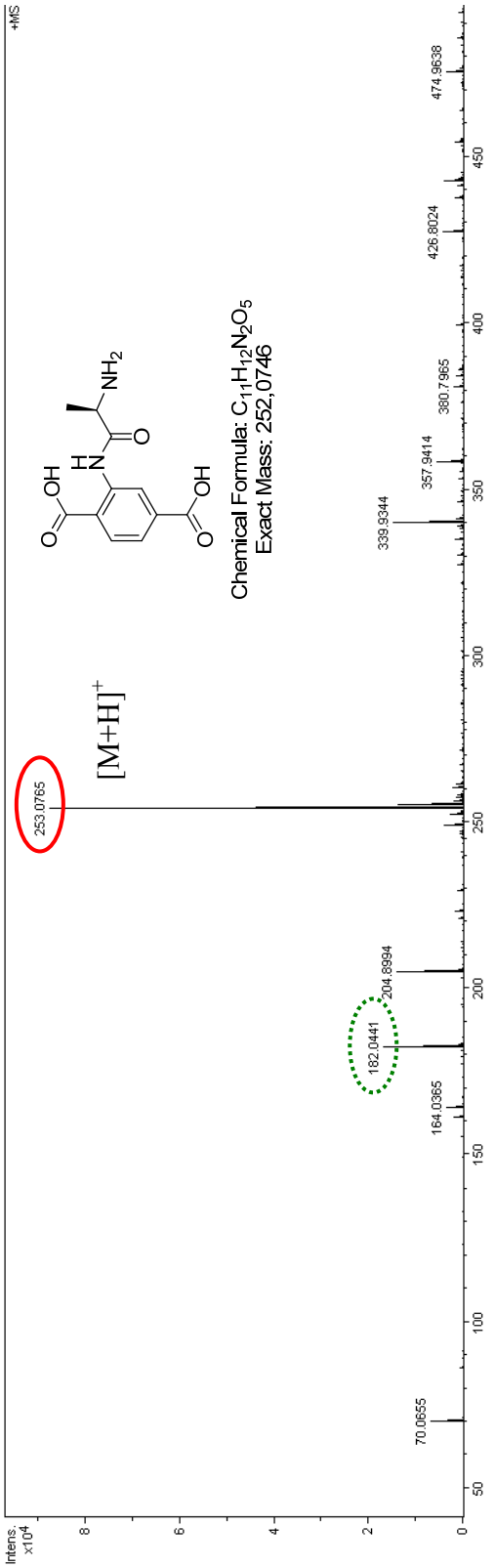


Figure S12. ESI-MS analysis of digested (In) MIL-68-NH-(D)-Ala

8. Optical rotation angles

For a typical measurement of the specific rotation, 200 mg of the MOF are dissolved in a solution of DMSO (2.9 mL) and HCl 1M (0.1 mL). The solution is then used to measure the optical rotation angle using a polarimeter.

(In) MIL-68-NH-(L)-Pro : α = - 108°
(In) MIL-68-NH-(D)-Ala : α = - 12°

9. References

[1] a) M. Savonnet, D. Bazer-Bachi, N. Bats, J. Perez-Pellitero, E. Jeanneau, V. Lecocq, C. Pinel, D. Farrusseng, *J. Am. Chem. Soc.* **2010**, *132*, 4518; b) M. Savonnet, D. Farrusseng, *PCT Appl. WO2011048284*, **2011**

[2] C. Volkringer, M. Meddouri, T. Loiseau, N. Guillou, J. Marrot, G. Ferey, M. Haouas, F. Taulelle, N. Audebrand, M. Latroche, *Inorg. Chem.* **2008**, *47*, 11892.