Electronic Supplementary Information

Protection strategies for directionally-controlled synthesis of previously inaccessible Metal-Organic Polyhedra (MOPs): The case of carboxylate- and amino-functionalized Rh(II)-MOPs

Jorge Albalad,[a] Arnau Carné-Sánchez,[a*] Thais Grancha,[a] Laura Hernández-López[a] and Daniel Maspoch[ab*]

a Catalan Institute of Nanoscience and Nanotechnology (ICN2), CSIC and The Barcelona Institute of Science and Technology, Campus UAB, Bellaterra, 08193 Barcelona, Spain.

b ICREA, Pg. Lluís Companys 23, 08010 Barcelona, Spain

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S1. Materials and Methods

Rhodium acetate, 5-amino-1,3-benzenedicarboxylic acid, di-*tert*-butyl dicarbonate (Boc_2O), 1,3,5-benzenetricarboxylic acid, $SOCl_2$, 2-(trimethylsilyl)ethanol, anhydrous pyridine, trifluoroacetic acid and tetrabutylammonium fluoride (1.0 M in THF) were purchased from Sigma-Aldrich Co. Solvents at HPLC grade were purchased from Fischer Chemical. All the reagents and solvents were used without further purification unless otherwise specified. Deionized water was obtained with a Milli-Q® system (18.2 MΩ·cm).

^{1}H NMR spectra were acquired in a Bruker Avance III 400SB NMR spectrometer. Mass spectrometry (MALDI-TOF) experiments were run in an Applied Biosystems 4700 Proteomics Analyzer operating in positive-ionization mode. UV−Vis spectra were measured in an Agilent Cary 4000 at room temperature (ca. 25 °C). FTIR spectra were recorded in transmission mode on a Bruker Tensor 27 IR equipped with a Golden Gate diamond ATR cell. Elemental analysis measurements were performed using a Flash EA 2000 CHNS, Thermo Fisher Scientific analyser. Thermogravimetric analyses were performed under nitrogen flow using a Pyris TGA8000 with a heating rate of 5 °C min^{-1}. Powder X-ray Diffraction (PXRD) patterns were recorded on an X'Pert PRO MPD analytical diffractometer (Panalytical) at 45 kV, 40 mA using Cu K_α radiation (λ = 1.5419 Å). Nitrogen and CO_2 adsorption isotherms were measured at 77 K and 298 K respectively using an Autosorb-IQ-AG analyzer.

S2. Synthetic Procedures

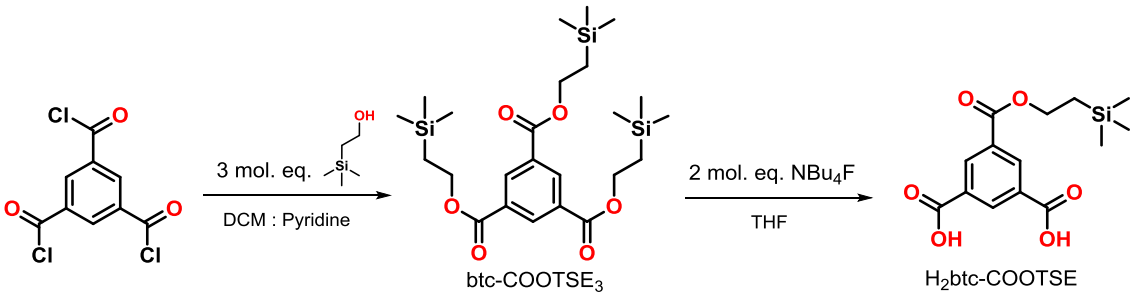
Synthesis of non-protected Blank Tests:

BT_Rh-btc: 20 mg of $Rh_2(acetate)_4 \cdot 2MeOH$ (0.04 mmol), 42 mg of 1,3,5-benzenetricarboxylic acid (0.19 mmol), and 25 mg of Na_2CO_3 (0.2 mmol) were dispersed in 2 mL of DMA. The mixture was transferred to a scintillation vial and heated at 100 °C for 48 h. A green dispersion was obtained and the solid was separated by centrifugation, washed with water, DMA and diethyl ether and dried *in vacuo* to afford BT_Rh-btc as a green powder.

BT_Rh-NH_2bdc: In a typical procedure, 20 mg of $Rh_2(acetate)_4 \cdot 2MeOH$ (0.04 mmol), 36 mg of 5-aminoisophthalic acid (0.19 mmol), and 25 mg of Na_2CO_3 (0.2 mmol) were dispersed in 2 mL of DMA. The mixture was transferred to a scintillation vial and heated at 100 °C for 48 h. A purple dispersion was obtained and the solid was separated by centrifugation, washed with water, DMA and diethyl ether and dried in vacuo to afford BT_Rh-NH_2bdc as a dark purple powder.

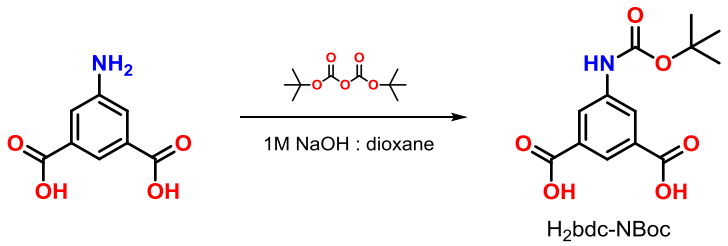
Synthesis of protected organic linkers

5-((2-(trimethylsilyl)ethoxy)carbonyl)isophthalic acid **(H_2btc-COOTSE):**



1,3,5-benzenetricarboxyl trichloride was synthesized *in situ* by reacting 1,3,5-benzenetricarboxylic acid with $SOCl_2$. 531 mg (2.0 mmol) of 1,3,5-benzenetricarbonyl trichloride and 730 µL (9.0 mmol) of pyridine were dissolved in 20 mL of dichloromethane. 860 µL (6.0 mmol) of 2-(trimethylsilyl)ethanol were added slowly, and the mixture was stirred at room temperature for 8 hours. The solution was then poured into 100 mL of chloroform, and washed subsequently with a 1 M NH_4Cl aqueous solution, 1 M HCl and water. The organic layer was recovered, dried over $MgSO_4$ and evaporated in vacuum to afford the tri-protected intermediate tris(2-(trimethylsilyl)ethyl)benzene-1,3,5-tricarboxylate (**btc-$COOTSE_3$**). In a second step, 892.9 mg (1.75 mmol) of btc-$COOTSE_3$ were dissolved in 7 mL of tetrahydrofuran. 3.5 mL (3.5 mmol, 2 mol. eq.) of tetrabutylammonium fluoride (1.0M solution in THF) were added stepwise in two additions (1.75 mL each) over a period of 5 hours. Then, the obtained yellowish solution was allowed to stir overnight at room temperature. 90 mL of diethyl ether were added, and a white precipitate formed. 20 mL of 1M HCl were added and the mixture was strongly shaked until no residual precipitate was observed. The organic phase was extracted, washed twice with water, dried over $MgSO_4$ and evaporated under vacuum to afford **H_2btc-COOTSE** as a white powder. No extra purification steps were required for the MOP synthesis.
^{1}H NMR (400 MHz, DMSO-d_6): δ = 8.65 (3H, m); 4.44 (2H, t); 1.14 (3H, t); 0.08 (9H, s). ESI-TOF (m/z) = 309.08 ([L-$COOEtTMS_1$ – H]$^-$

5-((*tert*-butoxycarbonyl)amino)isophthalic acid (H_2bdc-NBoc):



H_2bdc-NBoc

H_2bdc-NBoc was synthesized adapting a literature procedure.[1] 1.80 g (10.0 mmol) of 5-aminoisophtalic acid were dissolved in 20 mL of 1M NaOH and cooled to 0 °C. A solution of 2.40 g (11.0 mmol) of di-*tert*-butyl dicarbonate (Boc_2O) disolved in 20 mL of 1,4-dioxane was added dropwise to the former over 2 hours, and stirred at room temperature overnight. The solvent was subsequently evaporated to half of its initial volume by rotatory evaporation, and the product was precipitated with a 20% $KHSO_4$ aqueous solution up to pH = 3. **H_2bdc-NBoc** was filtered off, washed with water and dried under vacuum.
^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.77 (1H, s br); 8.30 (2H, s); 8.07 (1H, s); 1.49 (9H, s).

Synthesis of protected Metal-Organic Polyhedra

COOTSE-RhMOP: 20 mg of Rh_2(acetate)$_4$·2MeOH (0.04 mmol), 71 mg of H_2btc-COOTSE (0.2 mmol) and 25 mg of Na_2CO_3 (0.2 mmol) were dispersed in 2 mL of DMA. The mixture was then transferred to a scintillation vial and heated at 100 °C for 48 h. A deep green solution was obtained and separated from the residual solids by centrifugation. 20 mL of water were added to the supernatant in order to precipitate the crude product, which was separated by centrifugation, washed with water and dried under vacuum at 85 ºC. Further purification was achieved by sequential washing steps with diethyl ether until no residual linker signals were observed in ^{1}H NMR.
^{1}H NMR (400 MHz, Acetone-d_6): δ = 8.85 (1H, Ar), 8.45 (2H, Ar), 4.35 (2H, CH_2), 1.28 (2H, CH_2), 0.05 (9H, TMS).

NBoc-RhMOP: 100 mg of Rh_2(acetate)$_4$·2MeOH (0.2 mmol), 323 mg of H_2bdc-NBoc (0.98 mmol), and 123 mg of Na_2CO_3 (1.0 mmol) were dispersed in 7 mL of DMA. The mixture was transferred to a scintillation vial and heated at 100 °C for 48 h. A deep green solution was obtained and separated from the residual solids by centrifugation. The supernatant was then precipitated with 150 mL of diethyl ether, washed with a 0.3 M NaOH aqueous solution, water and diethyl ether and dried in vacuo to afford **NBoc-RhMOP** as a blue powder.
^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.24 (1H, NH), 8.40 – 8.05 (3H, Ar), 1.41 (9H, *tert*-Bu).

Deprotection of Metal-Organic Polyhedra

COOH-RhMOP: 50.0 mg (0.0053 mmol) of COOTSE-RhMOP were dissolved in 10 mL of wet tetrahydrofuran. 162 µL (0.162 mmol) of tetrabutylammonium fluoride (1.0 M solution in THF) were added slowly, and the mixture was allowed to stir overnight at room temperature, obtaining a blue precipitate. The supernatant was discarded, and the solid was washed with THF and Et_2O three times. After that, the product was dissolved in 5 mL of water and further precipitated with a dropwise addition of 1M HCl. The solid was recovered by centrifugation, washed with water and dried under vacuum. Further washing and solvent exchange steps with THF and Acetone were performed to the vacuum-dried material.
^{1}H NMR (400 MHz, DMSO-d_6): δ = 13.35 (1H, COO*H*); 8.51-8.33 (3H, Ar).

NH_2-RhMOP. NBoc-RhMOP could be quantitatively deprotected both in solid and solution fashions, hereafter referred as Thermolabile Deprotection and TFA Deprotection, respectively.

Thermolabile Deprotection of NBoc-MOP. 25 mg of NBoc-RhMOP were charged into a ceramic pan and charged into a Thermogravimetric Analizer oven. The material was then heated at 150 ºC for 6 hours or until a mass plateau was achieved (expected: 25% weight loss). The sample was then recovered, washed with methanol and acetone and dried under vacuum.

TFA Deprotection of NBoc-MOP. 20 mg of NBoc-RhMOP were dispersed into 2 mL of dichloromethane. 36 µL of trifluoroacetic acid (9 mol. eq.) were added and the slurry was stirred at room temperature overnight. The solid was then separated by centrifugation, neutralized with a trimethylamine solution in acetone (44 µL in 2 mL x3), and washed with methanol and acetone.
^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.60 – 6.95 (3H, Ar); 5.35 (2H, NH_2).

Characterisation

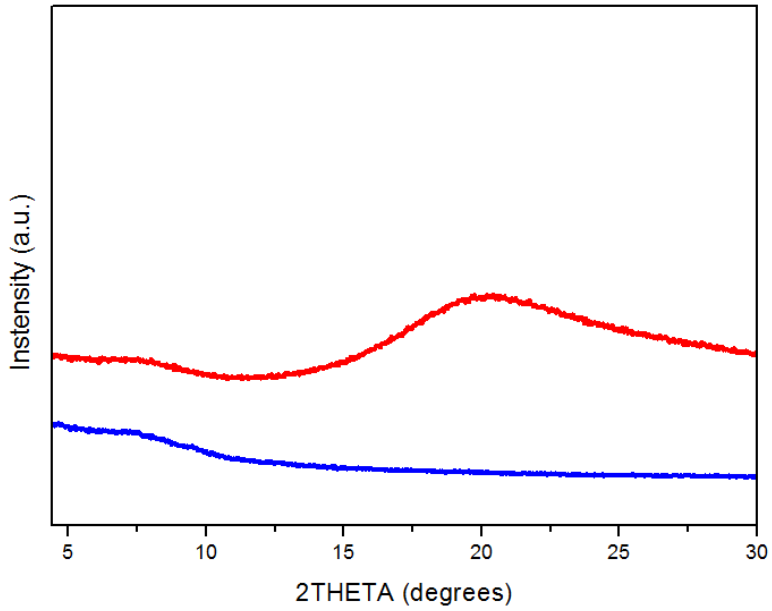


Figure S1. PXRD patterns of BT_Rh-NH_2bdc (blue) and BT_Rhbtc (red).

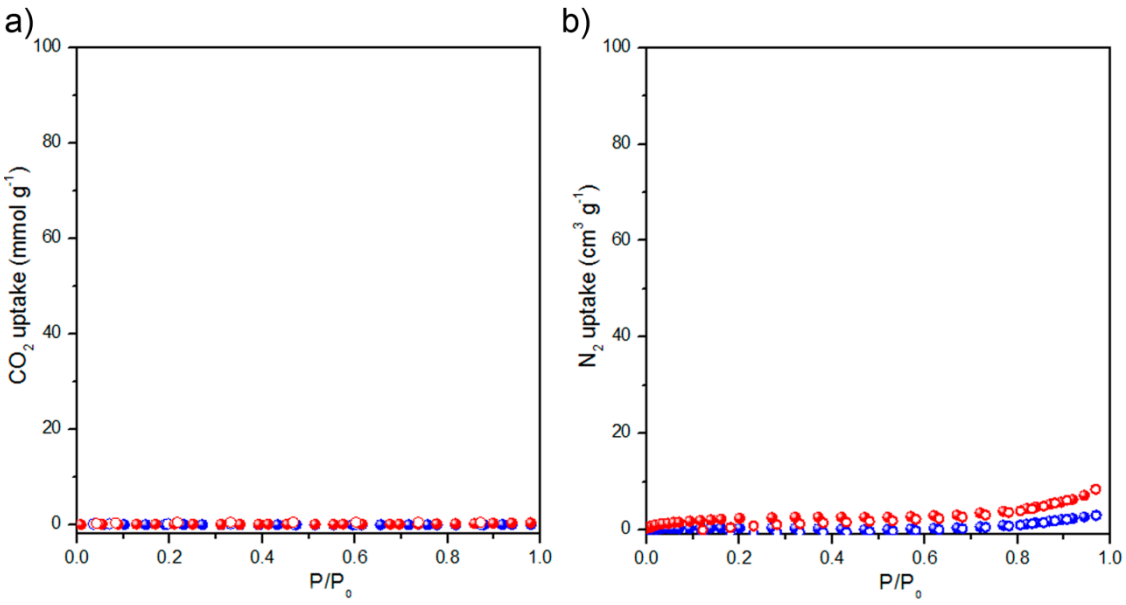


Figure S2. a) CO_2 adsorption isotherm at 295 K and b) N_2 adsorption isotherm at 77 K with BET linear fit of BT_Rh-NH_2bdc (blue) and BT_Rhbtc (red).

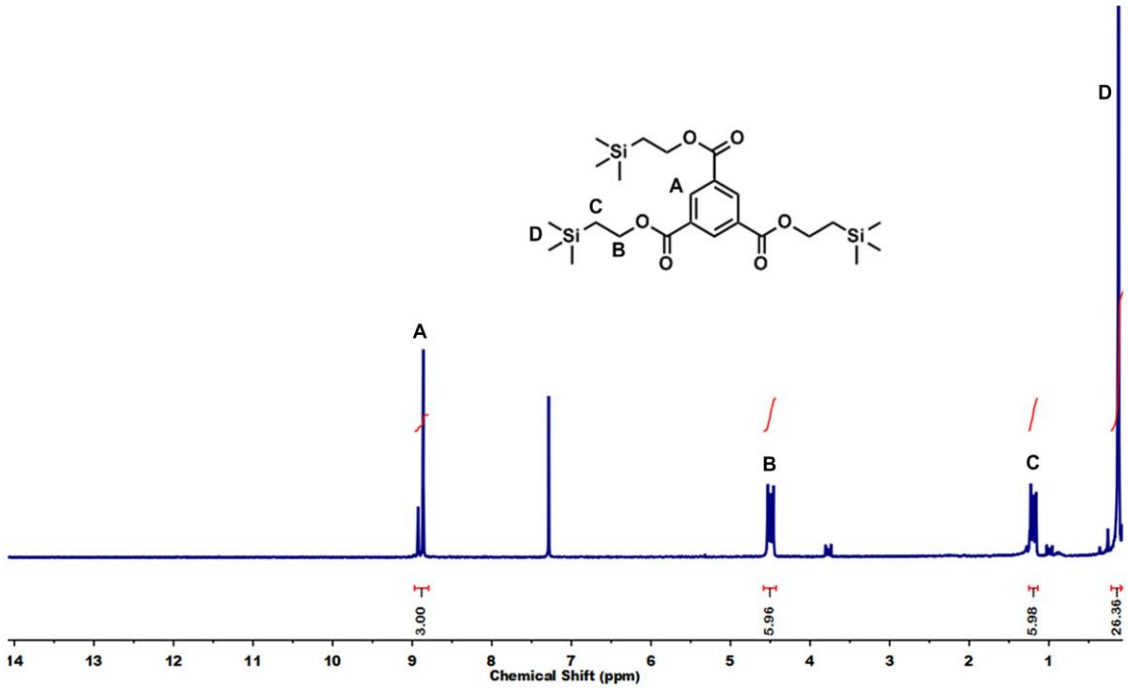


Figure S3. ^{1}H NMR spectrum of the tri-protected intermediate btc-COOTSE$_3$ in $CDCl_3$. TMS signal (D) is not fully integrable due to the presence of TMS as an internal reference in deuterated solvents.

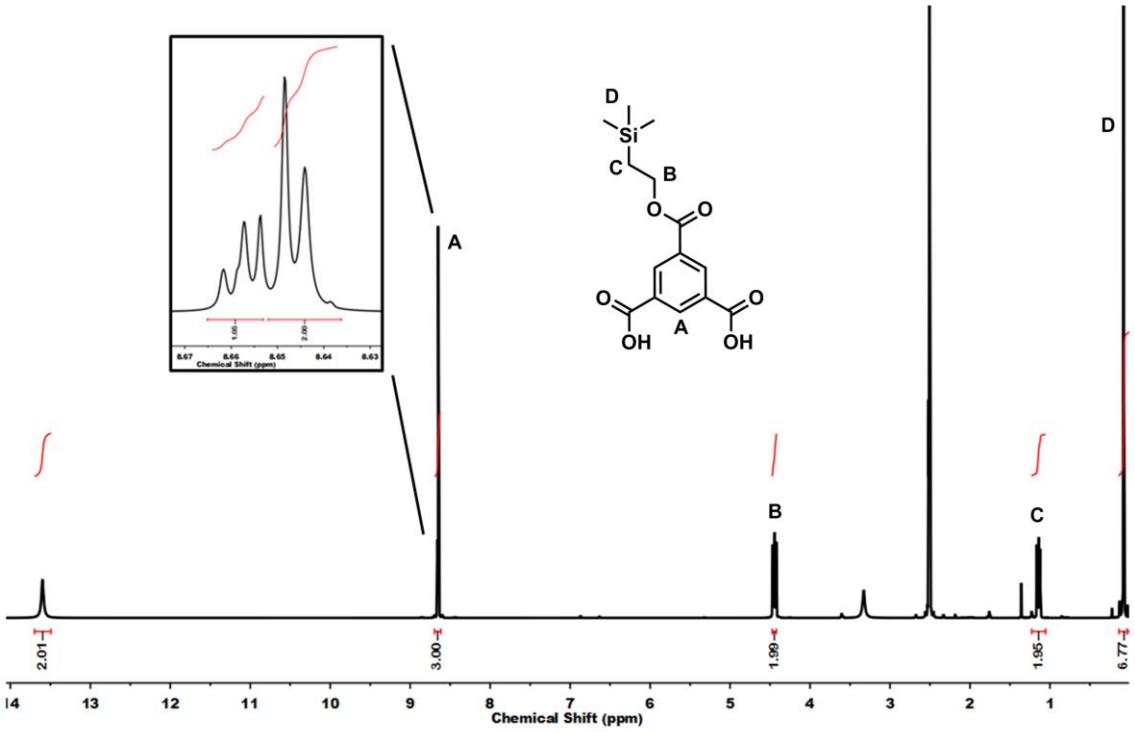


Figure S4. ^{1}H NMR spectrum of the mono-protected linker H_2btc-COOTSE in DMSO-d_6. TMS signal (D) is not fully integrable due to the presence of TMS as an internal reference in deuterated solvents.

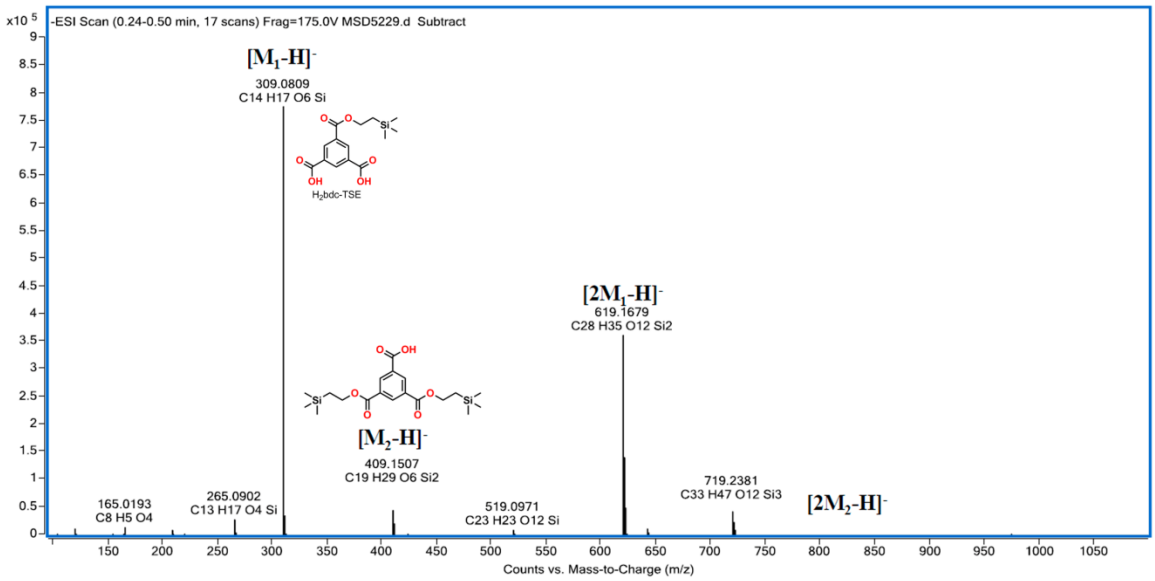


Figure S5. ESI-MS spectrum of H_2btc-COOTSE. Residual traces (<5%) of mono-deprotected linker can be observed.

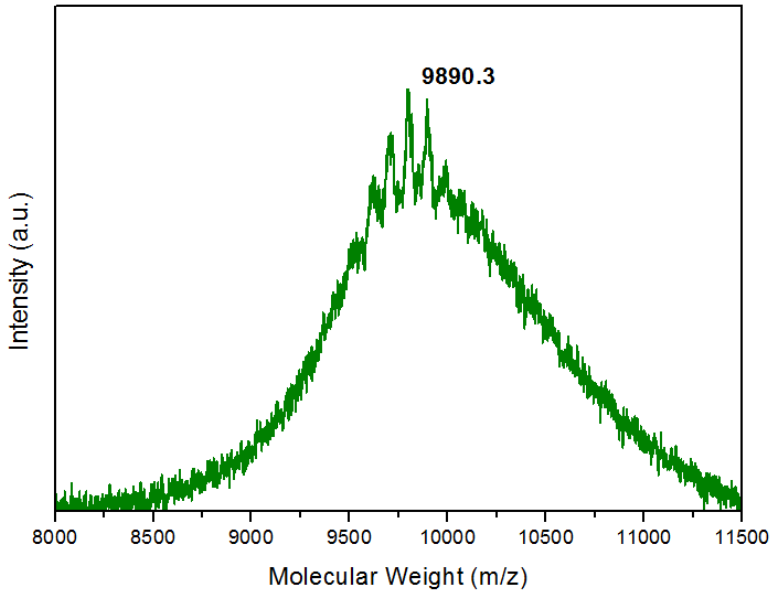


Figure S6. MALDI-TOF spectra of COOTSE-RhMOP in acetone. The weight corresponding to the formula $[Rh_{24}(TSE\text{-}bdc)_{24} + H^+]^+$ has been highlighted: expected = 9891.5; found = 9890.3.

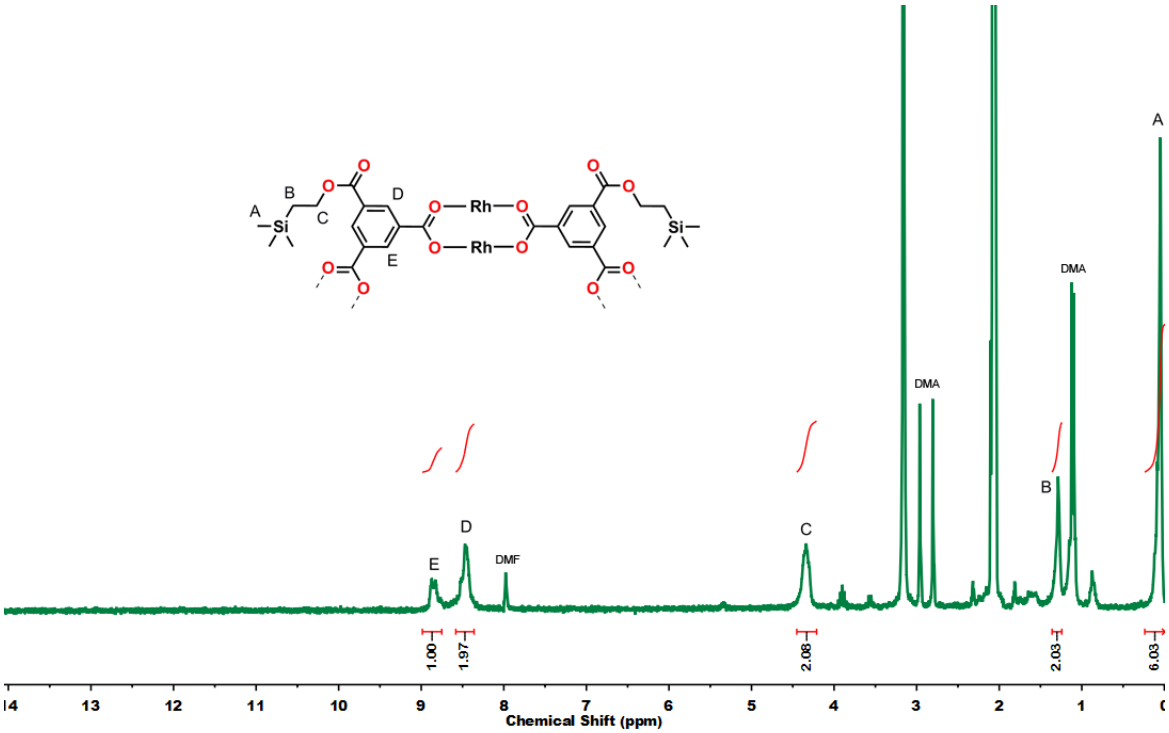


Figure S7. ^{1}H NMR spectrum of COOTSE-RhMOP in acetone-d_6. TMS signal (A) is not fully integrable due to the presence of TMS as an internal reference in deuterated solvents. The chemical shift of the signals is shifted compared with the free linker. No residual H_2btc-COOTSE peaks are observed.

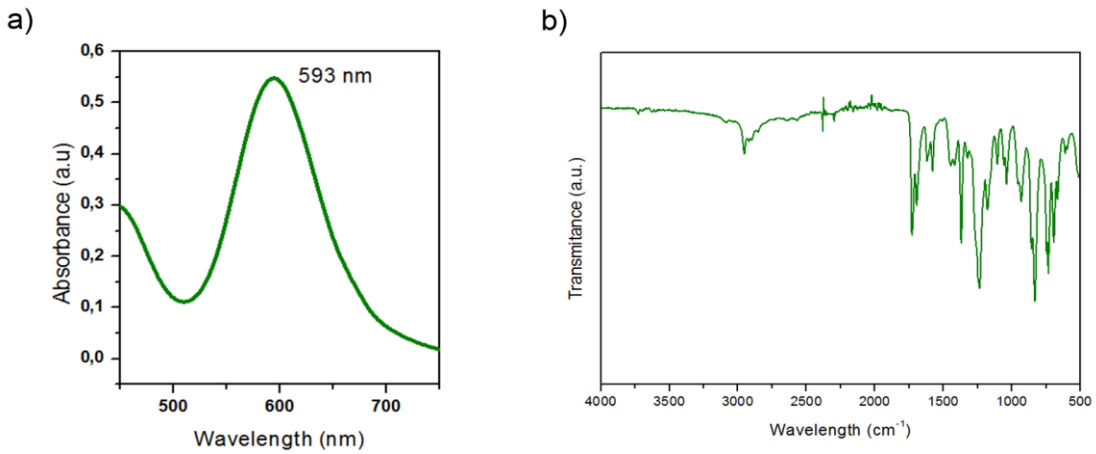


Figure S8. a) UV-Vis spectrum of COOTSE-RhMOP in acetone (0.30 mM). λ_{max} is centered at 593 nm. b) FTIR spectrum of COOTSE-RHMOP.

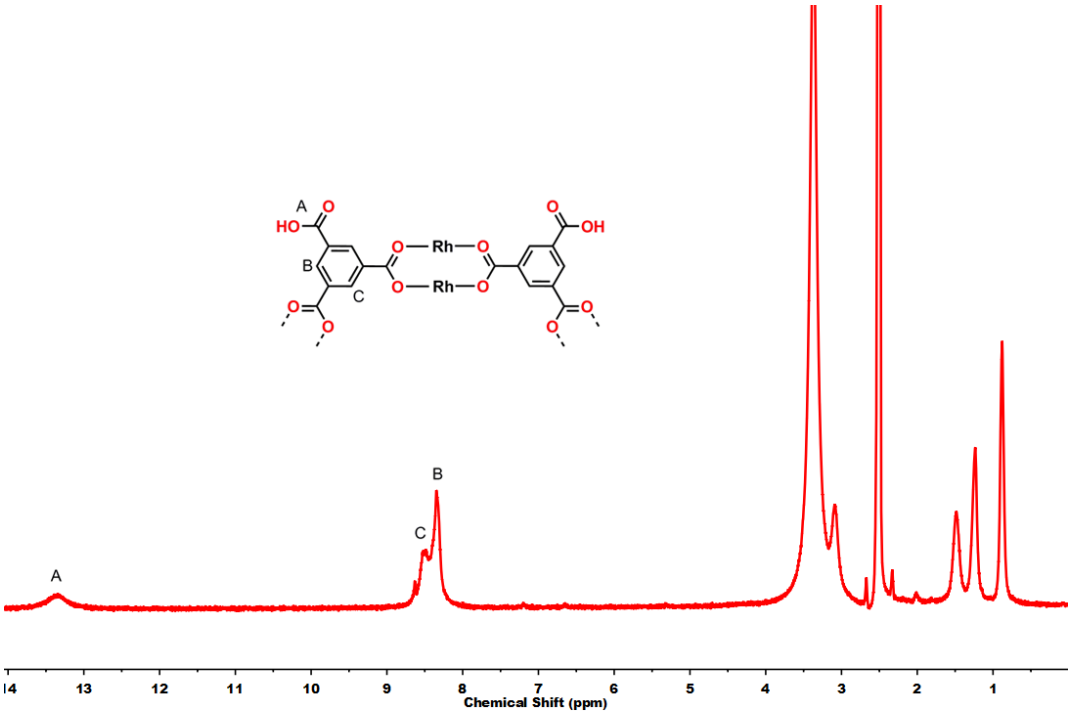


Figure S9. ^{1}H NMR spectrum of COOH-RhMOP in DMSO-d_6. COOH signal is observable at 13.4 ppm, with no residual TSE signals present.

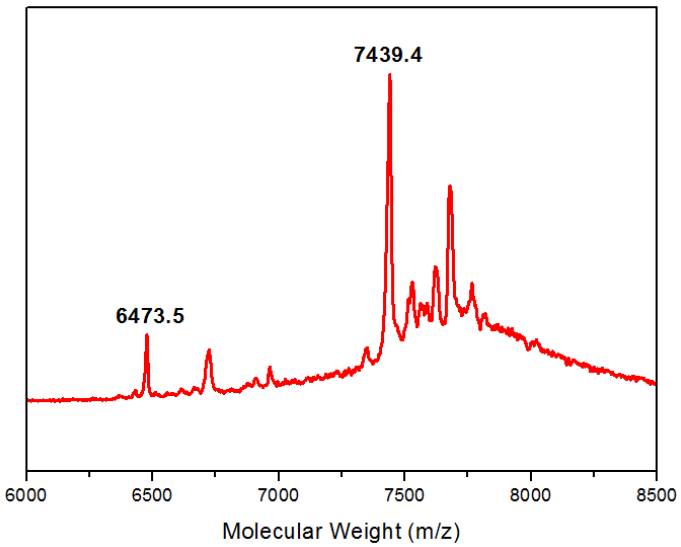


Figure S10. MALDI-TOF spectra of COOH-RhMOP in DMF. The weight corresponding to the formula $[Rh_{24}(COOH\text{-}bdc)_{24} + H^{+})]^{+}$ has been highlighted: expected = 7441.5; found = 7439.4. The weight corresponding to the formula $[Rh_{24}(COOH\text{-}bdc)_{24} - 22CO_2 + H^{+}]^{+}$ has been highlighted: expected = 6473.3; found = 6473.5.

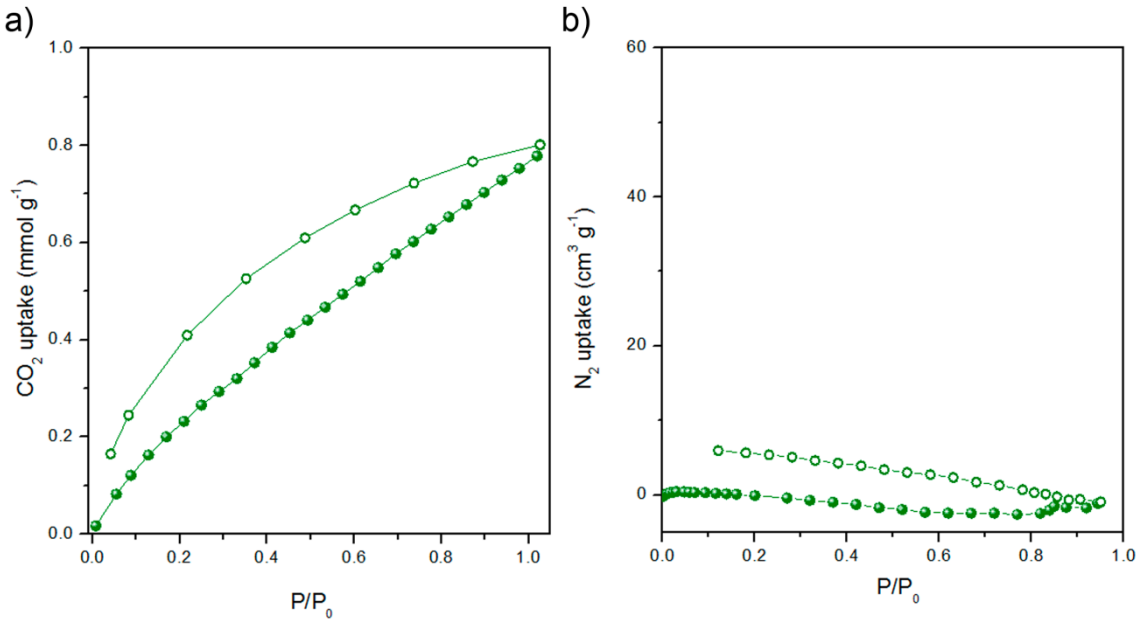


Figure S11. a) CO_2 adsorption isotherm at 295 K and b) N_2 adsorption isotherm at 77 K with BET linear fit of COOTSE-RhMOP

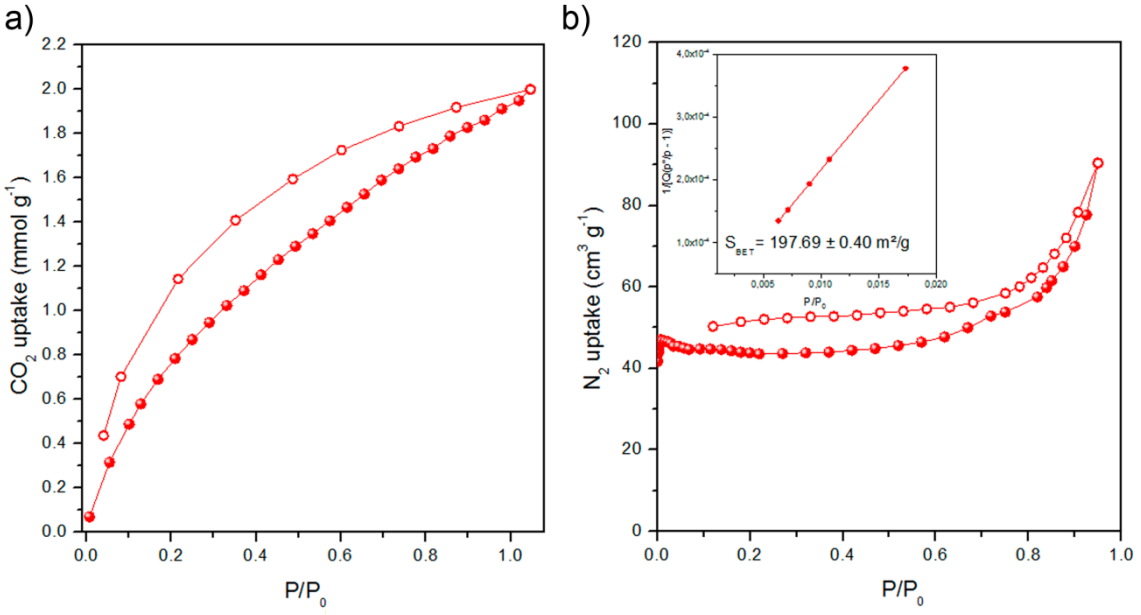


Figure S12. a) CO_2 adsorption isotherm at 295 K and b) N_2 adsorption isotherm at 77 K with BET linear fit of COOH-RhMOP

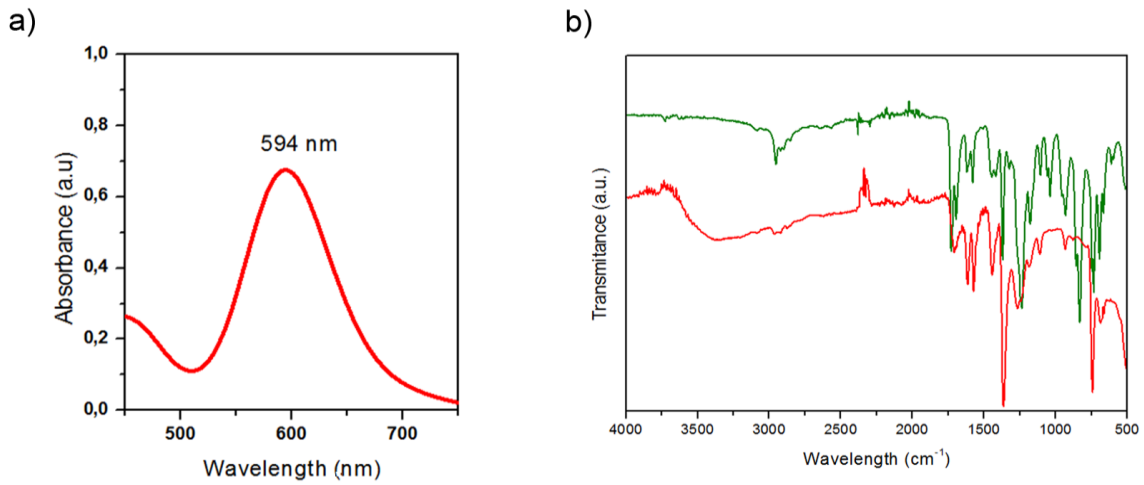


Figure S13. a) UV-Vis spectrum of COOH-RhMOP in DMF (0.30 mM). λ_{max} is centered at 594 nm. b) FTIR spectra of COOH-RhMOP (red) in comparison with COOTSE-RhMOP (green).

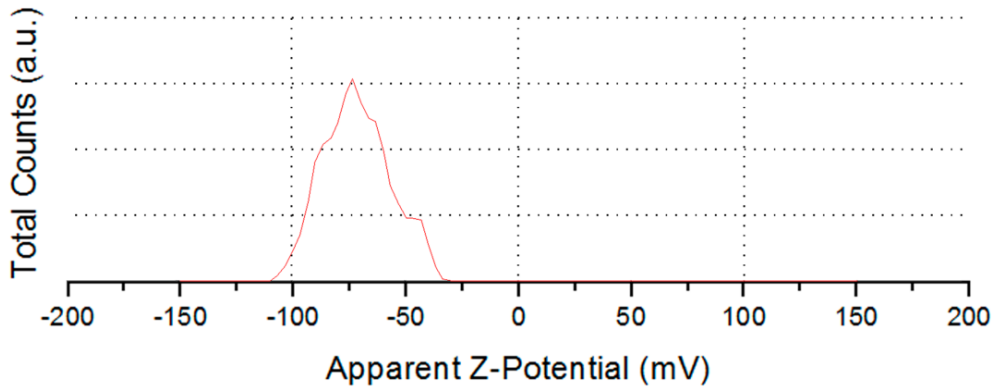


Figure S14. Z-Potential measurements of COONa-RhMOP in basic H_2O, confirming a charged specie.

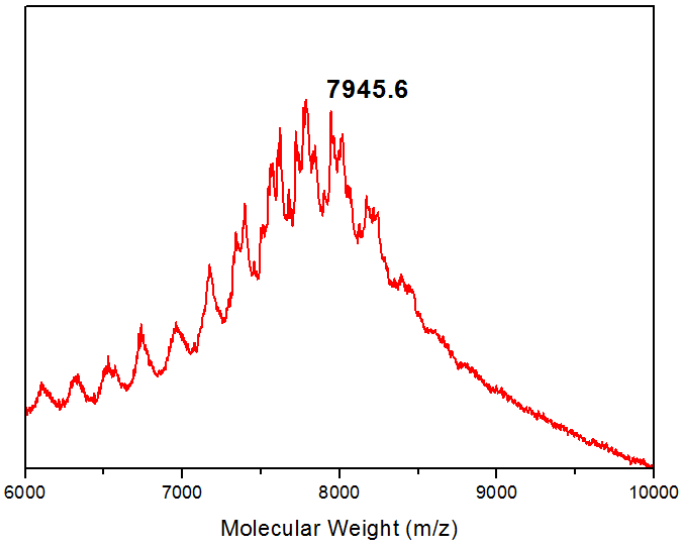


Figure S15. MALDI-TOF spectrum of COONa-RhMOP. The weight corresponding to the formula $[Rh_{24}(COONa\text{-}bdc)_{24} - 2Na^{+} + H^{+})]^{-}$ has been highlighted: expected = 7947; found = 7945.6.

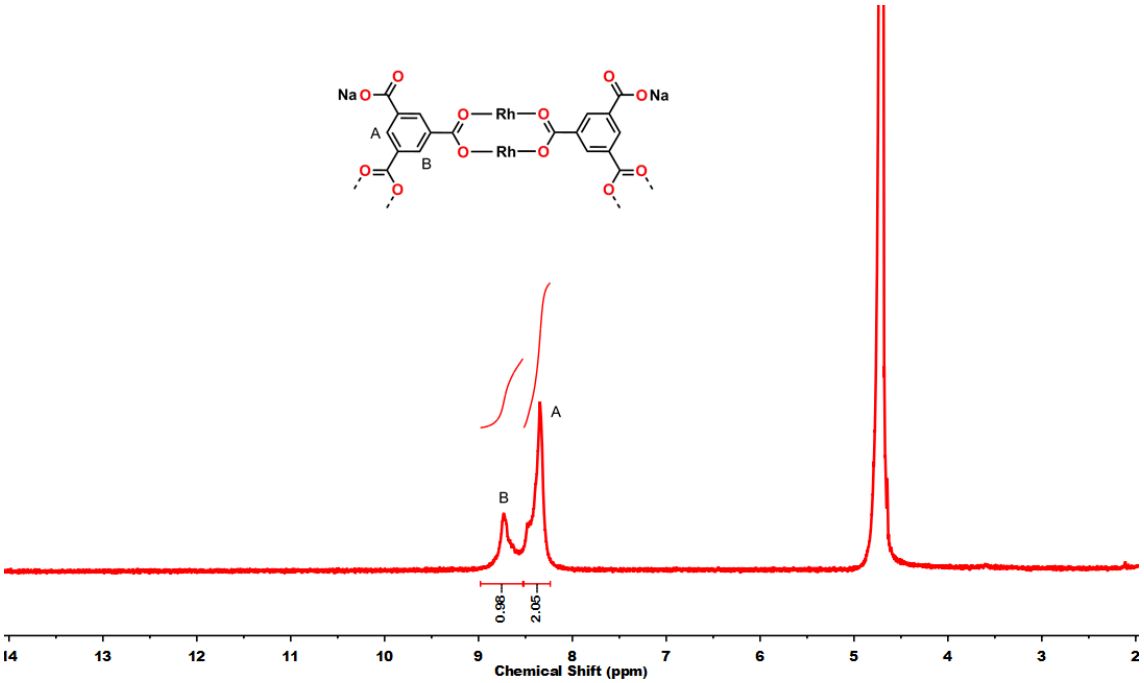


Figure S16. ^{1}H NMR spectrum of COONa-RhMOP in D_2O/NaOD (24 mol. eq. vs MOP) dissolved for 7 days.

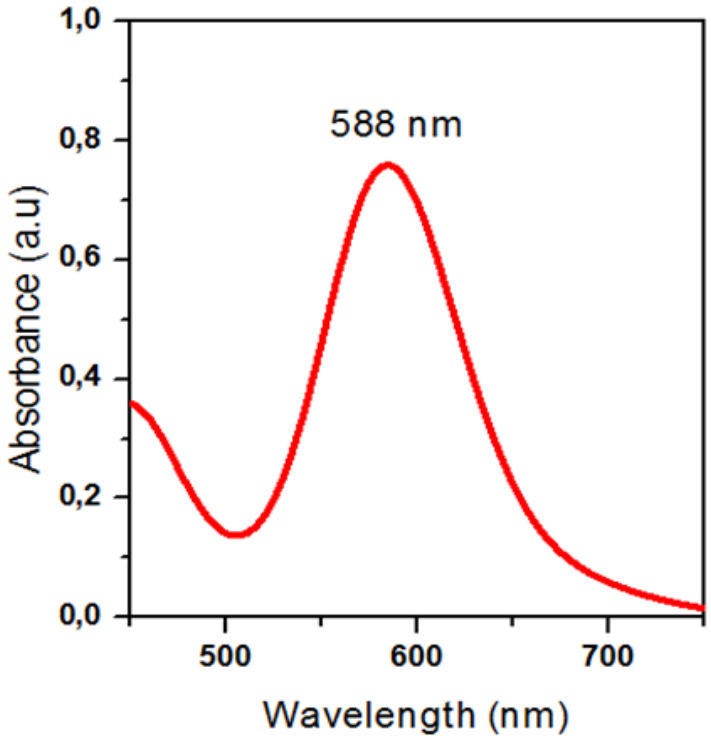


Figure S17. UV-Vis spectrum of COONa-RhMOP in H_2O (0.30 mM). λ_{max} is centered at 588 nm.

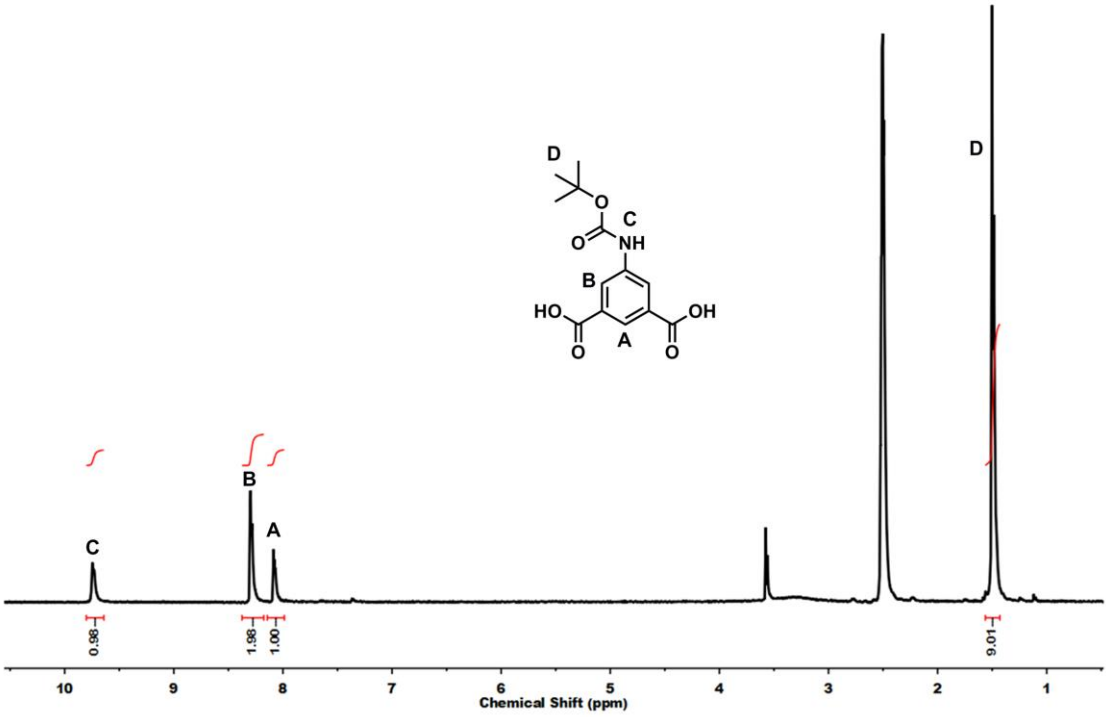


Figure S18. ^{1}H NMR spectrum of H_2bdc-NBoc in DMSO-d_6.

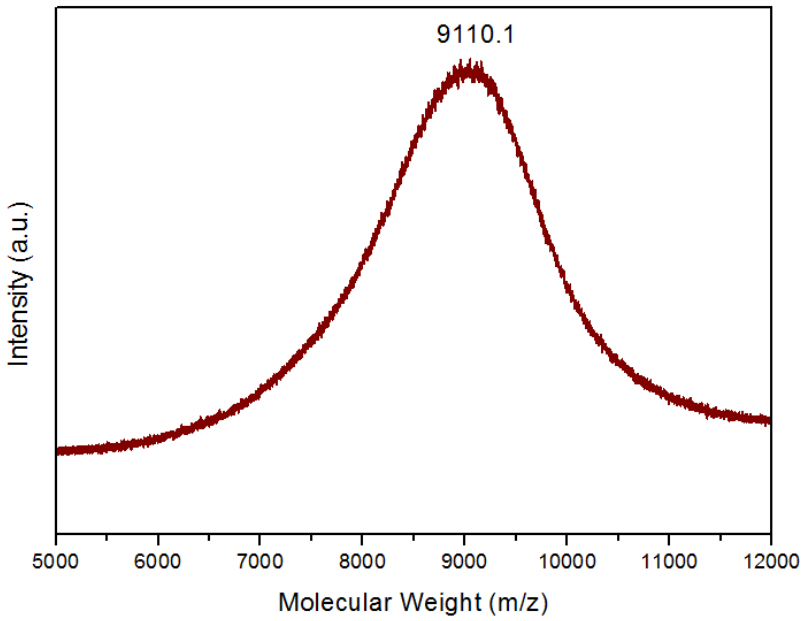


Figure S19. MALDI-TOF spectra of NBoc-RhMOP in Acetone. The weight corresponding to the formula $[Rh_{24}(NBoc\text{-}bdc)_{24} - Nboc + H^{+}]^{+} + 2H_2O$ has been highlighted: expected = 9105.4; found = 9110.1.

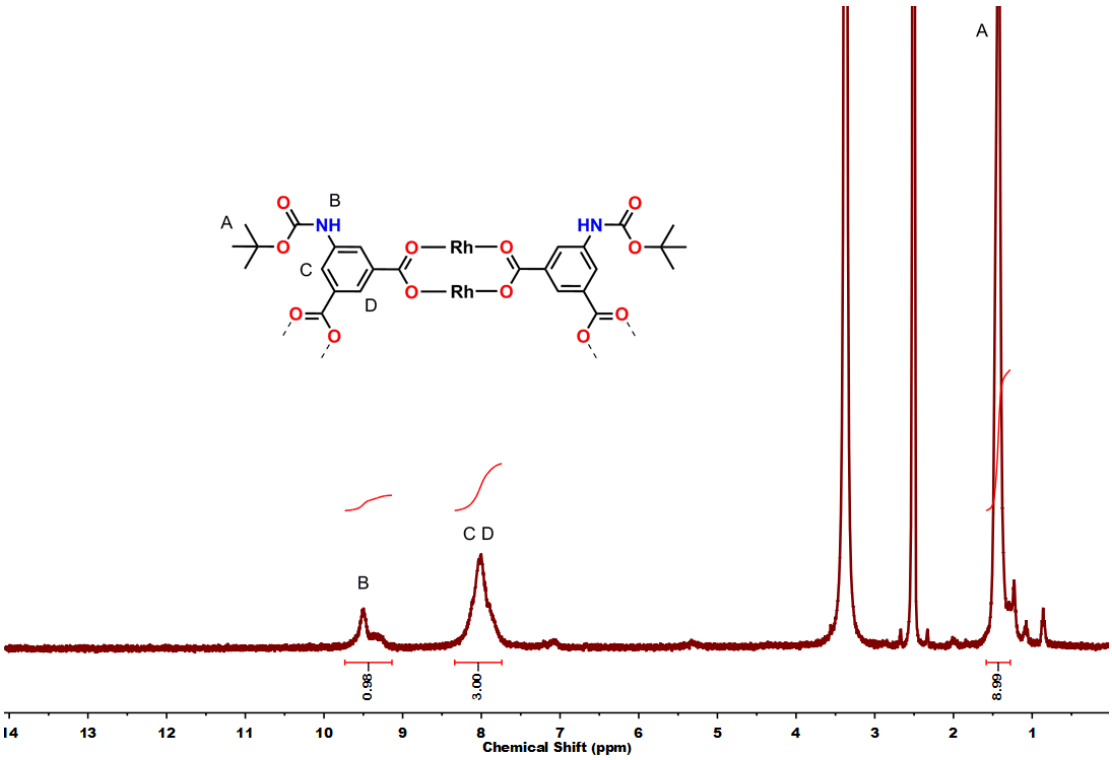


Figure S20. ^{1}H NMR spectrum of NBoc-RhMOP in DMSO-d_6. The chemical shift of the signals is shifted compared with the free linker. No residual H_2bdc-NBoc peaks are observed.

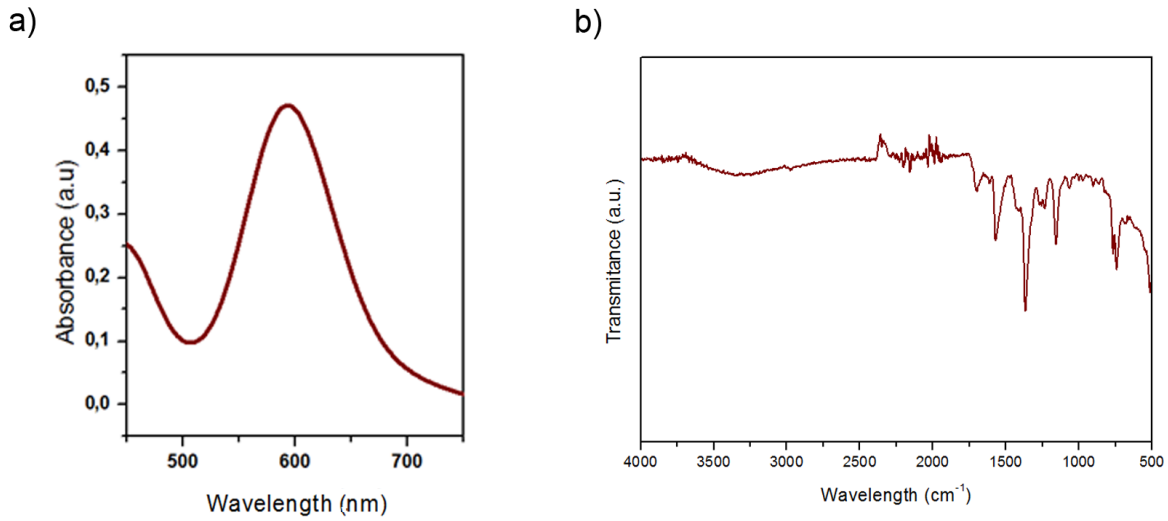


Figure S21. a) UV-Vis spectrum of NBoc-RhMOP in Acetone (0.30 mM). λ_{max} is centered at 594 nm. b) FTIR spectrum of NBoc-RhMOP.

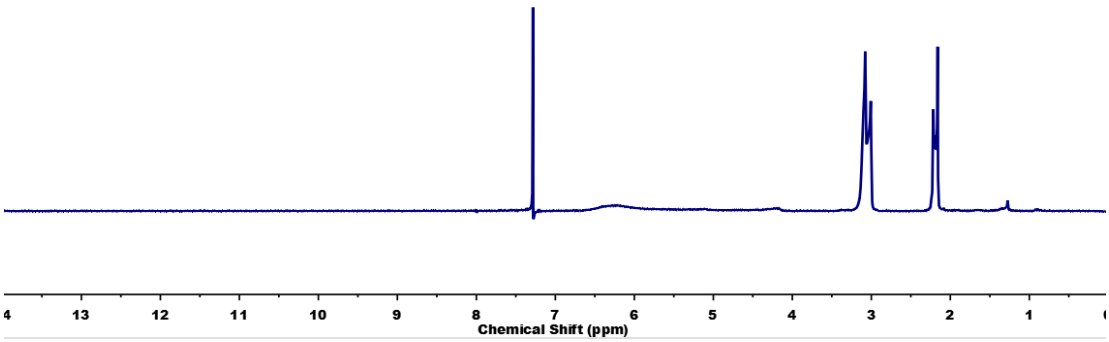


Figure S22. ^{1}H NMR of the evaporated DCM:TFA supernatant in DMSO-d_6 after the deprotection step. No H_2bdc-NH_2 signals can be observed, discarding any linker exchange process or partial degradation of the scaffold. DMA signals, coming from the MOP inner solvation, can be observed.

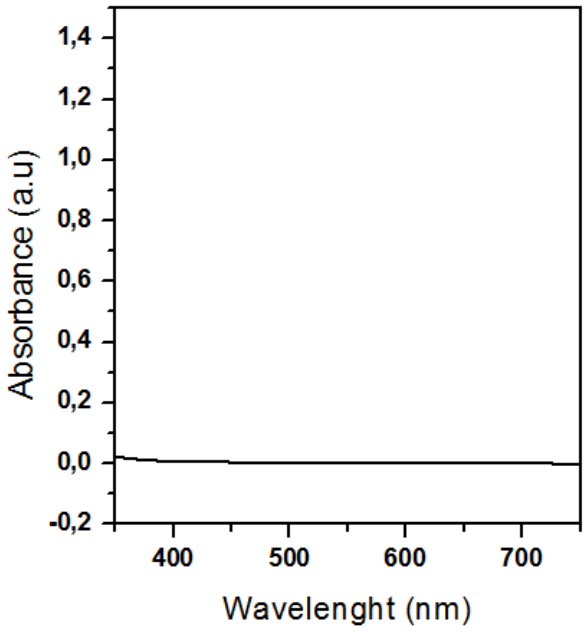


Figure S23. UV-Vis spectrum of the DCM:TFA supernatant after the deprotection step. The absence of absorption bands at the Rh-Rh expected region (594 nm) confirms that no $Rh_2(TFA)_4$ byproduct is being formed.

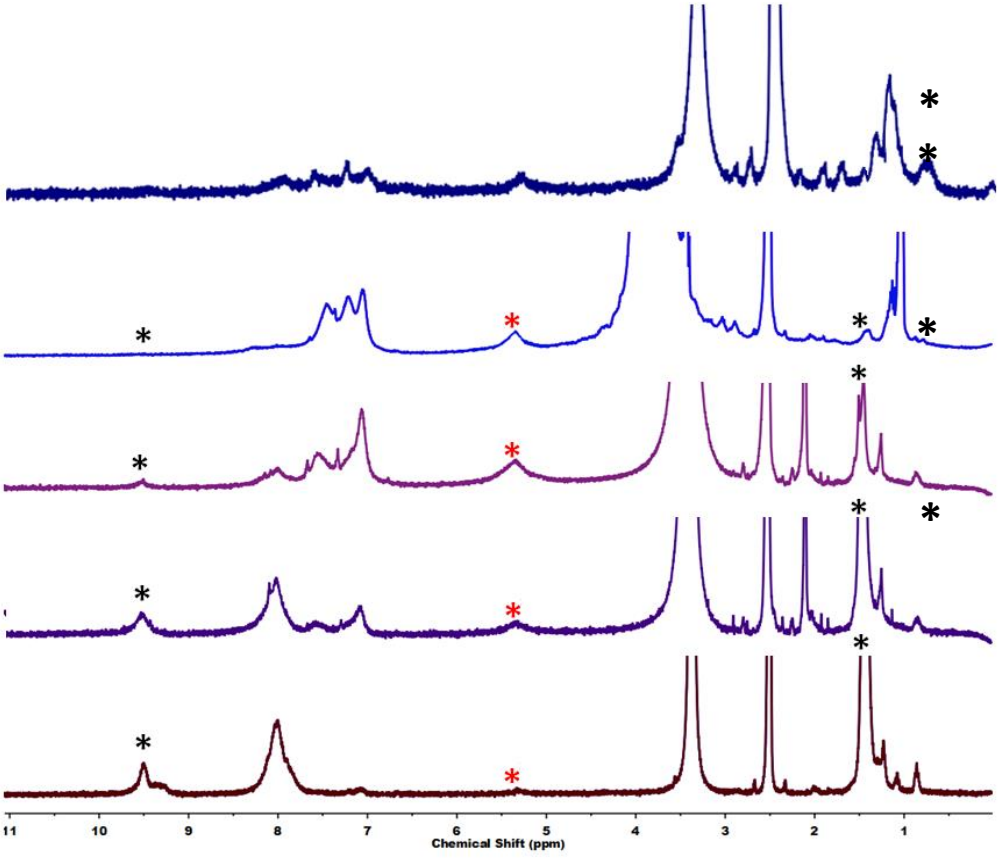


Figure S24. ^{1}H NMR spectrum of the TFA-based Deprotection strategy of NBoc-RhMOP (wine) in DMSO-d_6. After the addition of 3 mol. eq. (deep purple), 6 mol. eq. (light purple) and 9 mol. eq. of TFA (blue).

Fading NBoc signals are highlighted in black (∗) and arising NH_2 signal in red (∗). Thermolabile-deprotected NH_2-RhMOP is represented on top (navy).

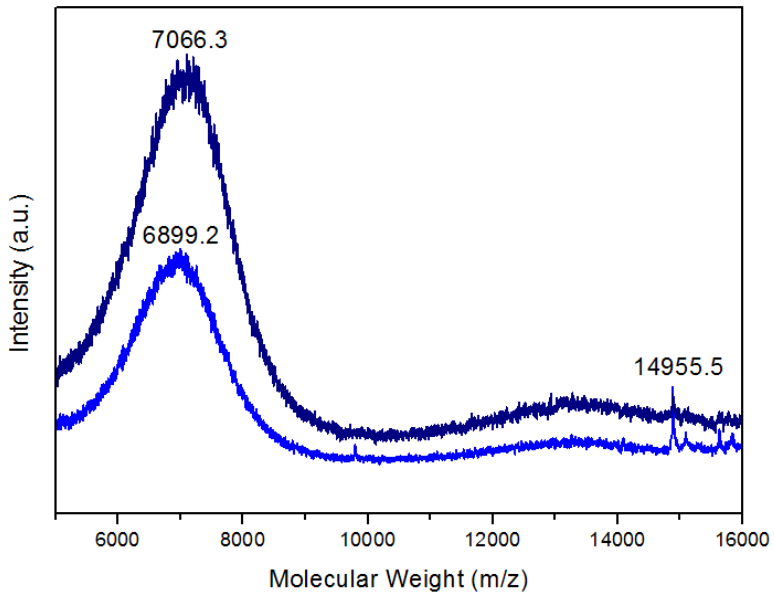


Figure S25. MALDI-TOF spectra of NH_2-RhMOP in DMSO, deprotected through the Thermolabile strategy (navy) and TFA-based strategy (blue). The weight corresponding to the formula $[Rh_{24}(NH_2\text{-bdc})_{24} + H^+]$ + DMSO (expected = 6895.3, found = 6899.2) and $Rh_{24}(NH_2\text{-bdc})_{24} + H^+]$ + 3DMSO + H_2O (expected = 7069.6, found = 7066.3) have been highlighted. Small packings of two NH_2-RhMOP units (m/z = 14,955) can start to be observed, due to the strong affinity of Rh paddlewheels for N-donor functional groups.

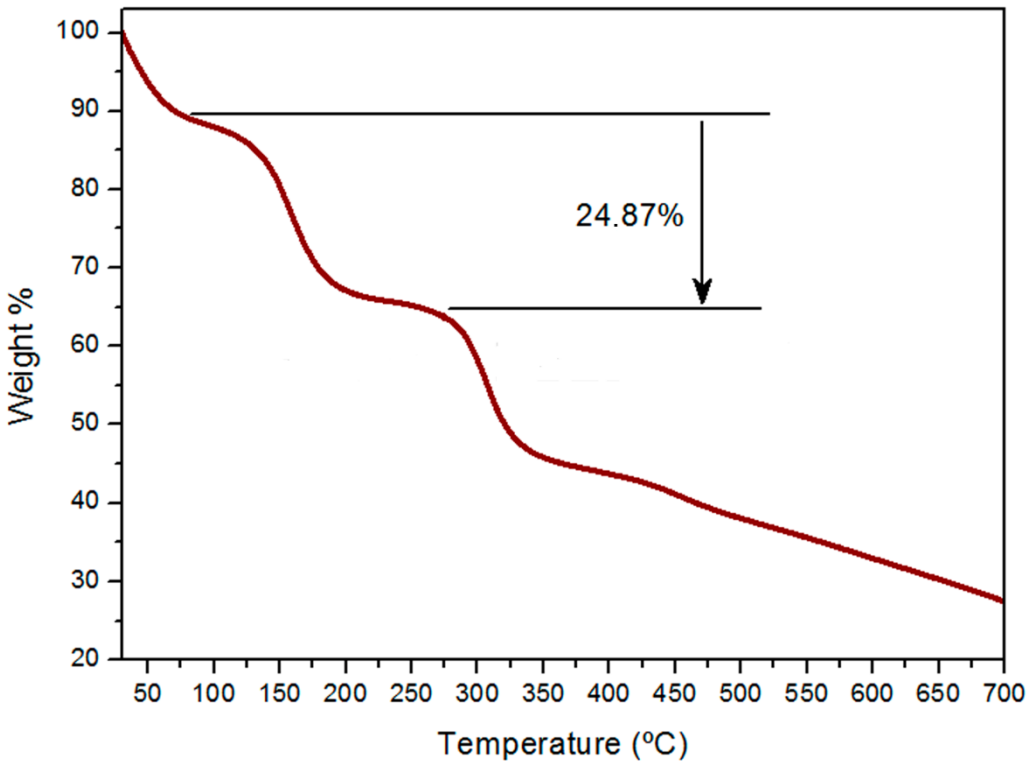


Figure S26. Thermogravimetric Analysis of NBoc-RhMOP, highlighting the 24.87% weight loss attributed to the thermolabile deprotection of 24 Boc groups (Calculated weight loss 25.1%).

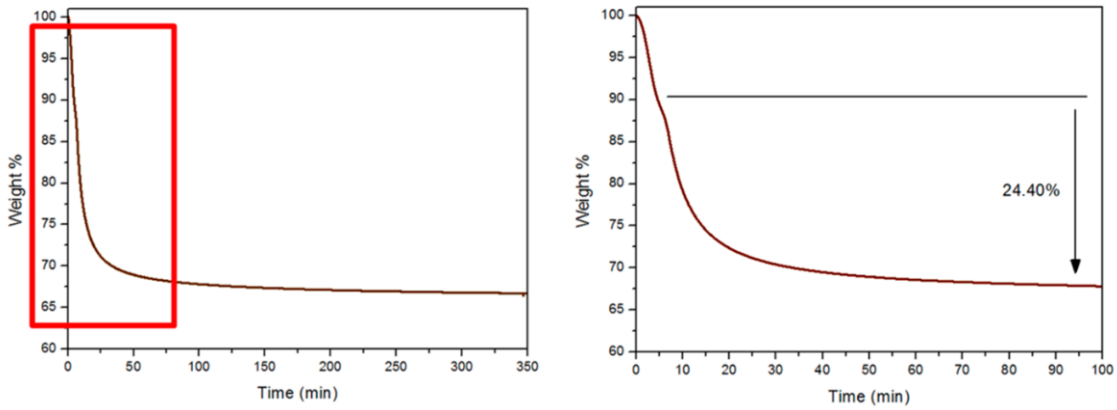


Figure S27. Isothermal Thermogravimetric Analysis of NBoc-RhMOP at 150 ºC, highlighting the stability of thematerial after the weight loss attributed to the thermolabile deprotection of 24 Boc groups.

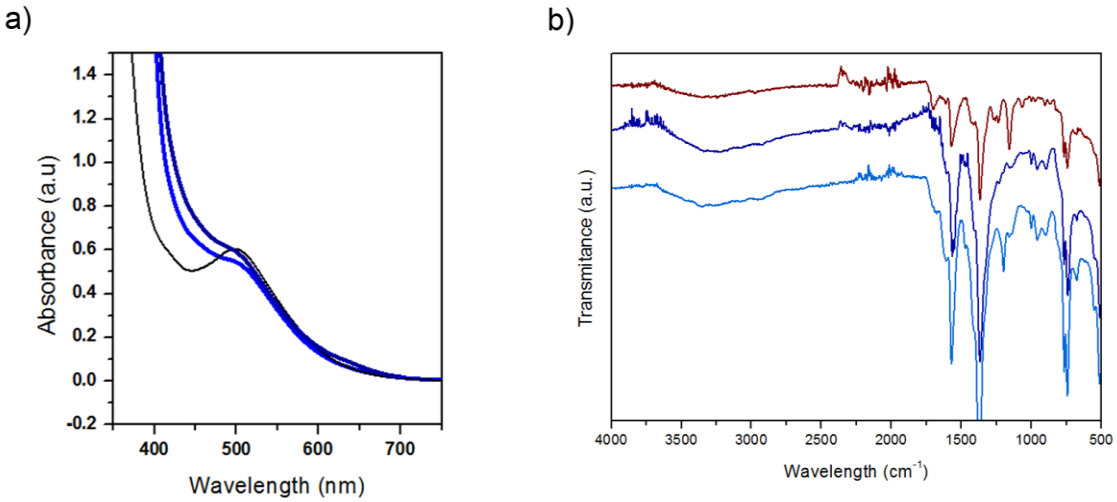


Figure S28. a) UV-Vis spectrum of NH_2-RhMOP deprotected by thermolabile (navy) or TFA (blue) in DMSO (0.30 mM). λ_{max} is centered at 501 nm. $Rh_2(Acetate)_4$ in DMSO (0.3 mM) added for reference (Black) to show the strong coordination of DMSO molecules in the axial positions of the paddlewheel.[2,3] b) FTIR spectra of NH_2-RHMOP, deprotected by thermolabile (navy) or TFA (blue) in comparison with NBoc-RhMOP (wine).

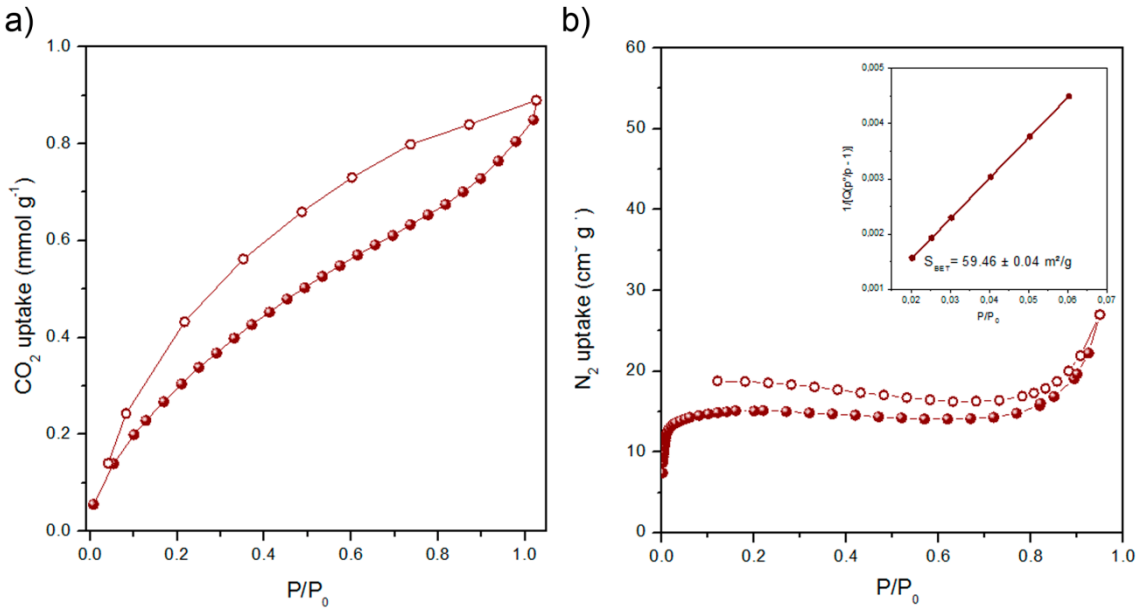


Figure S29. a) CO_2 adsorption isotherm at 295 K and b) N_2 adsorption isotherm at 77 K with BET linear fit of NBoc-RhMOP

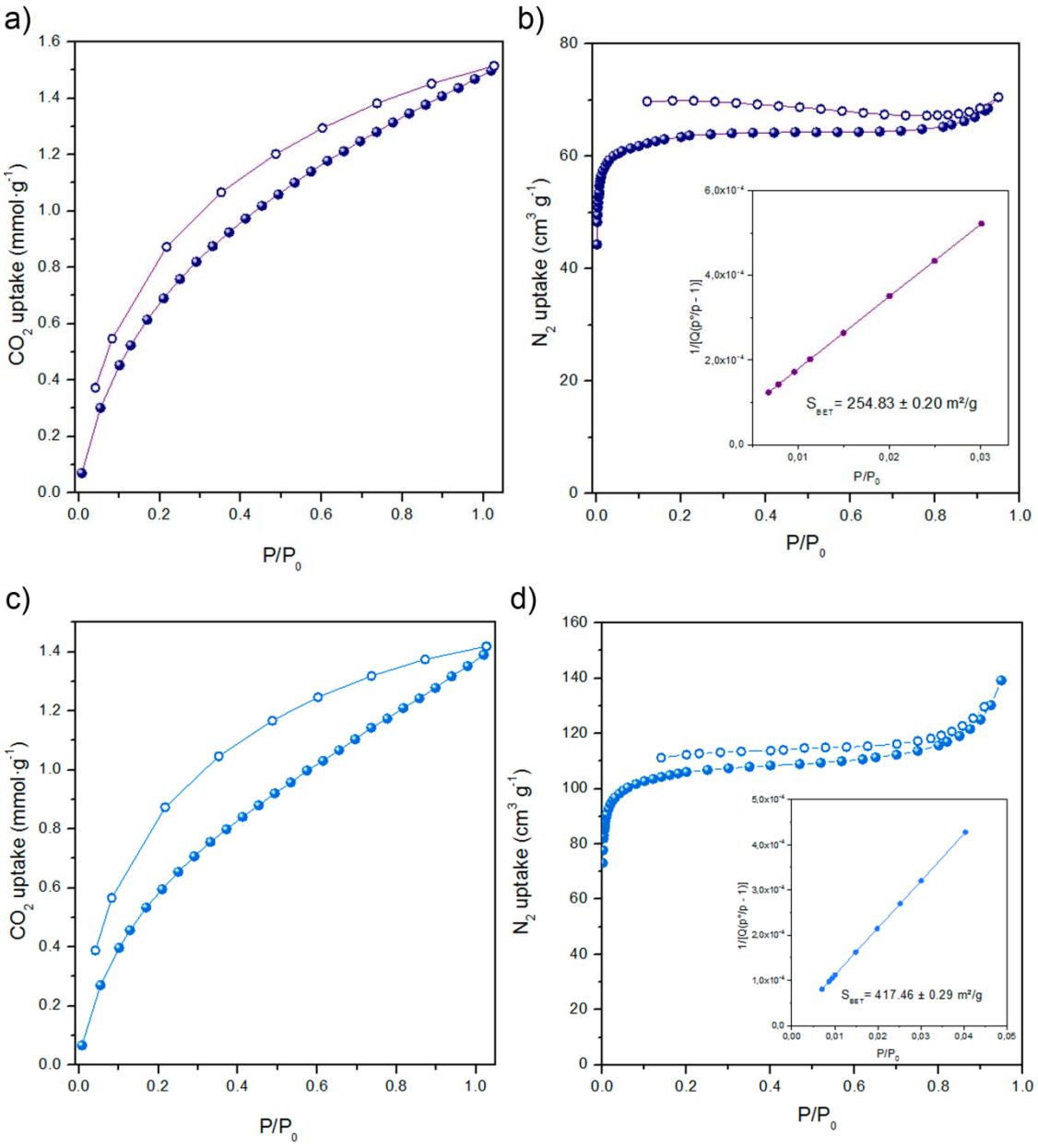


Figure S30. a,c) CO_2 adsorption isotherm at 295 K and b,d) N_2 adsorption isotherm at 77 K with BET linear fit of Thermolabile-deprotected NH_2-RhMOP (navy) and TFA-deprotected NH_2-RhMOP (blue).

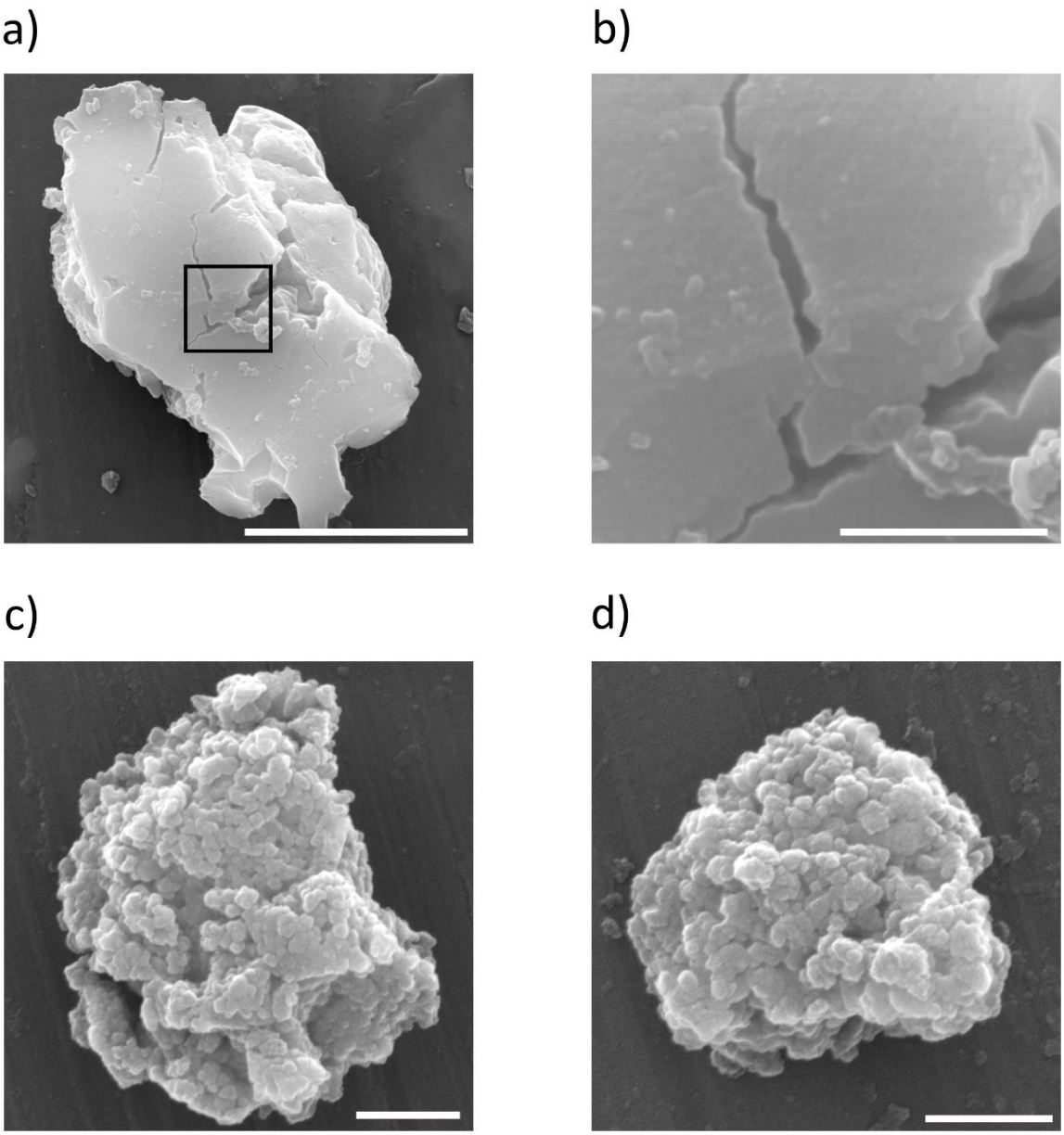


Figure S31. a,b) FESEM images of the NH_2-RhMOP obtained by the thermal treatment of the NBoc-RhMOP. b) High magnification image of the highlighted area in a). c,d) FESEM images of the NH_2-MOP obtained after deprotecting the NBoc-RhMOP with TFA. Scale bars = 5 µm (a), 1 µm (b), and 500 nm (c, d).

S4. References

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