Supporting Info

Photo-Induced Microfluidic Production of Ultrasmall Platinum Nanoparticles

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1 MATERIALS AND METHODS

Chloroplatinic acid (H_2PtCl_6 x H_2O), Polyvinylpyrrolidone (PVP average mol. Wt. 40.000), Ethanol (99.8%), and water (HPLC plus grade) were purchased from Merk and used without further purification. H_2PtCl_6 x H_2O was stored at 4°C, screened from light, as a 10 mM stock solution. The precursor solution was deaerated bubbling Argon (5.5) for 10 minutes. Vulcan XC-72R was provided by Cabot Ltd and used as received. All other chemicals were provided by Merck® and used without any further purification.

29-Thio-[3,6,9,12,15,18-hexaoxaundecanyl-β-D-galactopyranosyl)(1-4)-β-D-glucopyranoside] (3-Lac) was a generous gift from Midatech Pharma PLC (Bilbao, Spain).

XPS analyses were carried out in an ultra-high vacuum chamber system with a base pressure of 10^{-9} /10^{-10}mbar. The sample was prepared suspending the powder in 2-propanol and the solution was casted on Silicon oxide, the solvent was dried under nitrogen flux. The radiation used was a non-monochromatized Al (hv = 1486.6 eV, VSW-A10) combined with a hemispherical electron/ion energy analyser (VSW-HA100 equipped with a 16-channel detector). The operating power of the used Al X-ray source was 120 W (12 kV and 10 mA) and photoelectrons were collected normally to the sample surface, maintaining the analyser angle between the analyser axis and X-ray source fixed at 54.5°. The spectra were acquired in fixed analyser transmission (FAT) mode (pass energy of 44 eV). The XPS spectra calibration was conducted by setting the aliphatic component of C *1s* signal to 284.3 eV[1] (See Figure S5 b). The spectra were analysed using CasaXPS software, and a Shirley function was used to subtract the background. The deconvolution of XPS spectra has been performed by applying a Lorentzian Asymmetric (LA) line-shape.

Transmission Electron Microscopy (TEM) measurements and related analysis were performed on a ZEISS Libra200FE instrument, equipped with an in-column omega filter analyzer. Specimens were dispersed in 1,3-propanol, and placed in an ultrasonic bath for 15 minutes to obtain a homogeneous suspension to be drop-casted on a lacey carbon film Cu TEM grid. Samples were analyzed after drying overnight. Histograms of the particle size distribution were obtained by counting onto the micrographs at least 300 particles by iTEM software (Olympus SIS) spanning through the TEM grid and collecting several images in order to have a robust statistical data. The mean particle diameter (dm) was calculated by using the formula dm = Σdini/Σni where ni was the number of particles of diameter di.

ICP-OES analyses were carried out with Optima 8000 ICP-OES (Perkin Elmer) operating at 1500W and equipped with autosampler S10, MiraMist® Nebulizer (Perkin Elmer), and cyclonic chamber. Argon (420.069 nm) was used as the internal standard. 10 mg of material was treated with 3 mL of a mixture HCl/HNO3 (3:1) and kept at boiling temperature for three hours. After cooling, the sample was diluted with ultrapure water containing 2% HNO_3.

GC analyses were performed with a Shimadzu 2010 gas chromatograph equipped with a flame ionization detector (FID) and a 25 m (0.32 mm i.d., 0.2 μm film thickness) CP-Wax 52 CB column.
General procedure for Photo-induced Synthesis of Pt NPs:

NMR spectra were recorded at 25°C on a Bruker Avance II spectrometer operating at 500 MHz and processed with the software Topspin 4.3.0. The Pt(3-Lac) NP sample was lyophilized and redispersed in 600 μL of D2O for NMR spectroscopy. In order to quantify ligand loaded on PT-NPs, samples were analyzed by NMR using the ERETIC2 (Electronic Reference To access In vivo

Concentrations) methodology[2] . ERETIC 2 is an experimental quantitative NMR technique based on PULCON (pulse length-based concentration determination)[3], an internal standard method which correlates absolute intensities of two different spectra. A sucrose sample of known concentration (29.2 mM), under “quantitative” condition was employed as reference: probe was exactly tuned and matched, 90° pulse calibrated, D1 relaxation delay time 10 s (>5*T1), acquisition time 4 s (>T2), SW=29 ppm, NS=8.

^{1}H-DOSY experiments (diffusion-ordered spectroscopy) were performed on Pt(3-Lac) NP purified sample. Matrices of 16384 (t2) by 80 points (t1) were collected. The z-axis gradient strength was varied linearly from 2 to 98% of its maximum value (53 G cm^{-1}), the gradient pulse duration was 4.4 ms, and the time period between the two gradient pulses was optimized to 250 ms. Self-diffusion coefficients (D) were derived by fitting the NMR data to Stejskal and Tanner equation[4] . DOSY experiment recorded on Pt(3-Lac) NP (Figure S04) provides a translational diffusion coefficient of (5.08 ± 0.4) x 10^{-11} m^2/s.
Starting from the measured D value, the hydrodynamic radius of the functionalized nanoparticle was calculated by the Stokes−Einstein equation [1], correlating the diffusion coefficient of a molecule with its hydrodynamic radii :[5–7]

$$r_H = \frac{k_B T}{6\pi\eta D} \qquad [1]$$

where r_H is the hydrodynamic radius, k_B the Boltzmann constant, T the temperature in K, η the dynamic viscosity of D2O at 25 °C, and D the measured translational diffusion coefficient. Assuming a spherical geometry and using the diffusion measured for dioxane molecule, added to the sample as internal standard, a hydrodynamic radius of 3.7 ± 0.2 nm was derived using equation[8–10] :

$$r_H^{NP} = r_H^{diox} \times \frac{D_{diox}}{D_{NP}} \qquad [2]$$

considering r_H^{diox}=0.212 nm.

The microfluidic reactor is an FEP tube (Fluorinated ethylene propylene; 0.762 mm ID, 5 m length) coiled around a water-cooled UV lamp (125W). The UV lamp used for the microfluidic procedure was a UV high-pressure Hg 125W lamp (100V) purchased from Helios Italquarz S.r.l., Cambiago (MI), Italy. The platform is analogous to the ones described elsewhere [11]. A peristaltic pump with a constant flow rate of 0.25 mL/min ensures the reactants’ loading and suspension circulation.

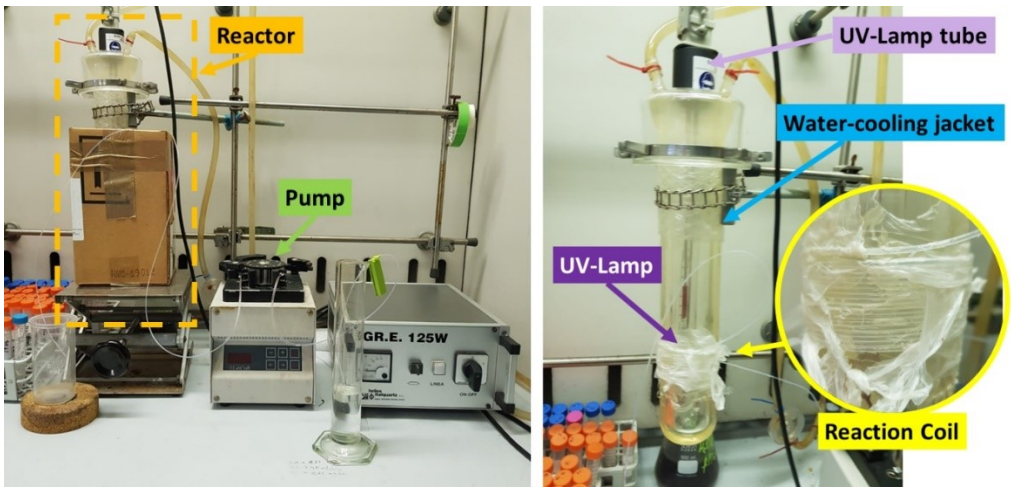


Fig S01 – General picture of the microfluidic apparatus (the circulation loop is open) and detail of the reactor area, where the tube is coiled to the water-cooled UV-lamp.

The tubes, the connections, the valves, and the fittings are commercially available (IDEX Health & Science), and made in PEEK. The circulation loop was ensured by connecting the inlet to the outlet via a union connector or a three-way valve.

In a typical experiment, the reactant mix is composed of 0.5 mL of a solution of H_2PtCl_6 10 mM added to 4.5 mL deaerated 50% v/v ethanol/water, left in smooth agitation for 15min. 5mg of PVP is added if needed (0.1%). *Carbon-Vulcan support was dispersed in 5 mL water (1mg to obtain a 0.1% w/w Pt loading) and the Pt colloidal solution was dropped into it, keeping the whole In agitation for 12 hours after deposition.* Purification of colloidal Pt(3-lac) solution was performed by ultrafiltration using Millipore Amicon Ultra-4 Centrifugal Filter Units, cut-off 30 kDa.

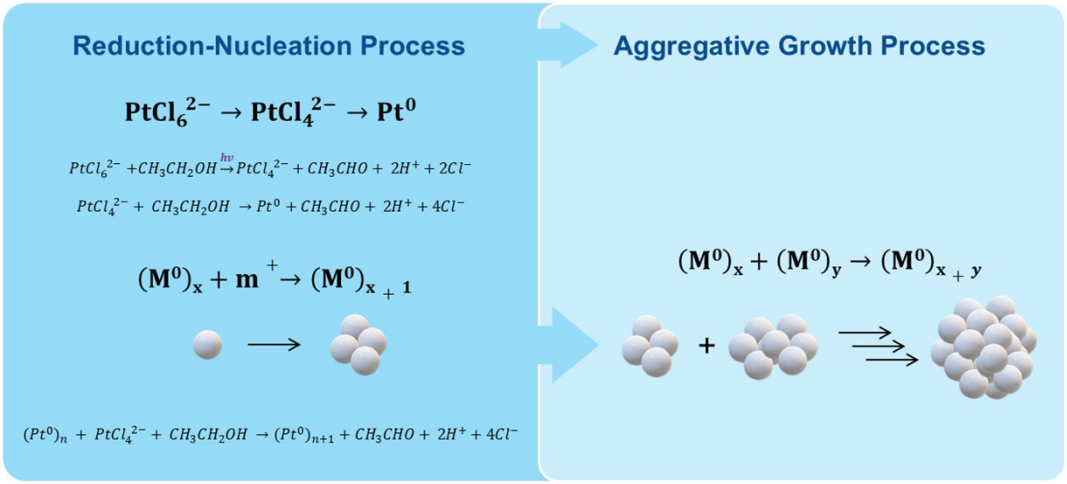
1.1 General procedure for hydrogenation of p- and o-chloronitrobenzene

Hydrogenation of halonitrobenzene was carried out in a 25-mL Schlenk flask with a magnetic stirring bar (stirring rate = 1200 rpm) and under atmospheric hydrogen pressure (0.1 Mpa) at 25 °C. Before the reaction, 10 mg of Pt catalyst (containing 1 wt.% Pt, 0.5 μmol Pt) was activated under hydrogen for 15 min, then 1.28 mmol of halonitrobenzene (202 mg for 1-chloro-4-nitrobenzene, 1-chloro-2-nitrobenzene in 5 mL CH_3OH; 259 mg for 1-bromo-4-nitrobenzen in 10 mL CH_3OH) was added to the reaction system to start the reaction. Reactants and products are identified and quantified by GC-FID via comparison with authentic compounds. Recycling reaction was performed by collecting the catalyst via centrifugation, followed by washing, drying, and reacting at identical reaction conditions to the initial one.

1.2 General procedure for hydrosilylation of 1-hexyne

Catalytic runs have been performed into Pyrex Carius tubes fitted with rotaflo taps. To certain amount of Pt/support was added via syringe 8 mmol (0.91 ml) of 1-hexyne and 2 mmol (0.31ml) of the silane. The suspension was stirred for 2 h at 70°C, filtered on celite and the filtrate evaporated under vacuum to remove the excess 1-hexyne. The crude products were analyzed by ^{1}H NMR proton signals.

1.3 . Proposed Reaction Mechanism



Scheme 1. Reaction Mechanism for the photoredution of Pt^{4+} to Pt^{0} and formation of Pt nanoparticles[12]

2 **UV-vis spectra**

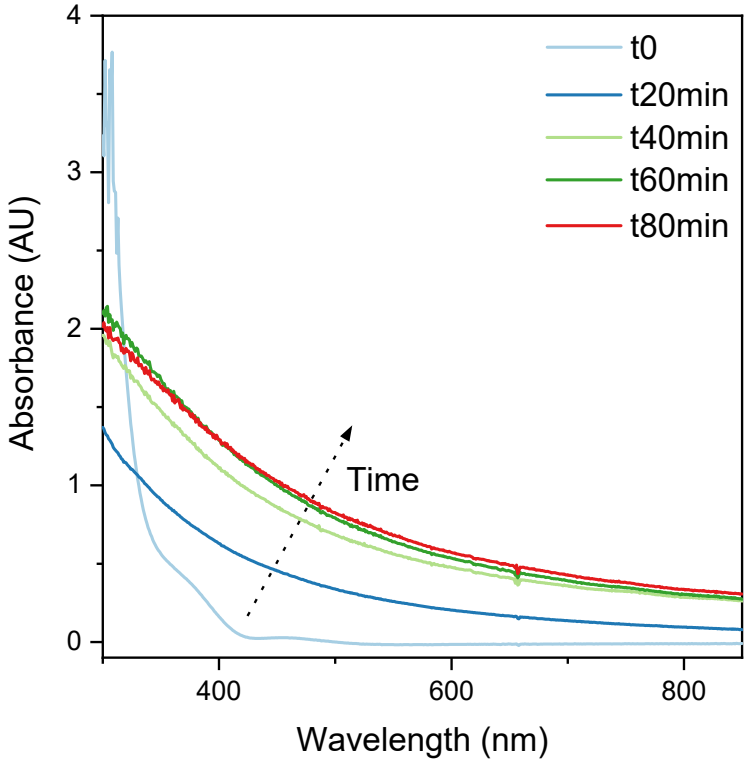


Figure S02 – UV-vis spectra of the Pt colloidal solution after every reaction cycle (20 minutes each)

3 **XPS data**

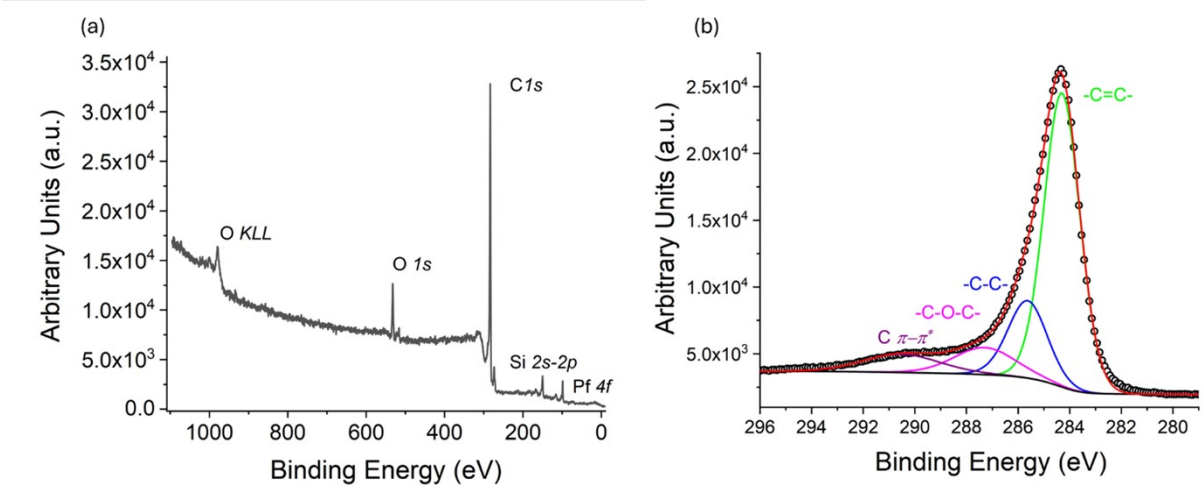


Figure S03 – (a) XPS Survey of Pt(3-Lac) NPs and (b) XPS C*1s* region with component assignment.

4 Synthesis of PVP-stabilized Pt NPs and Catalytic Activity

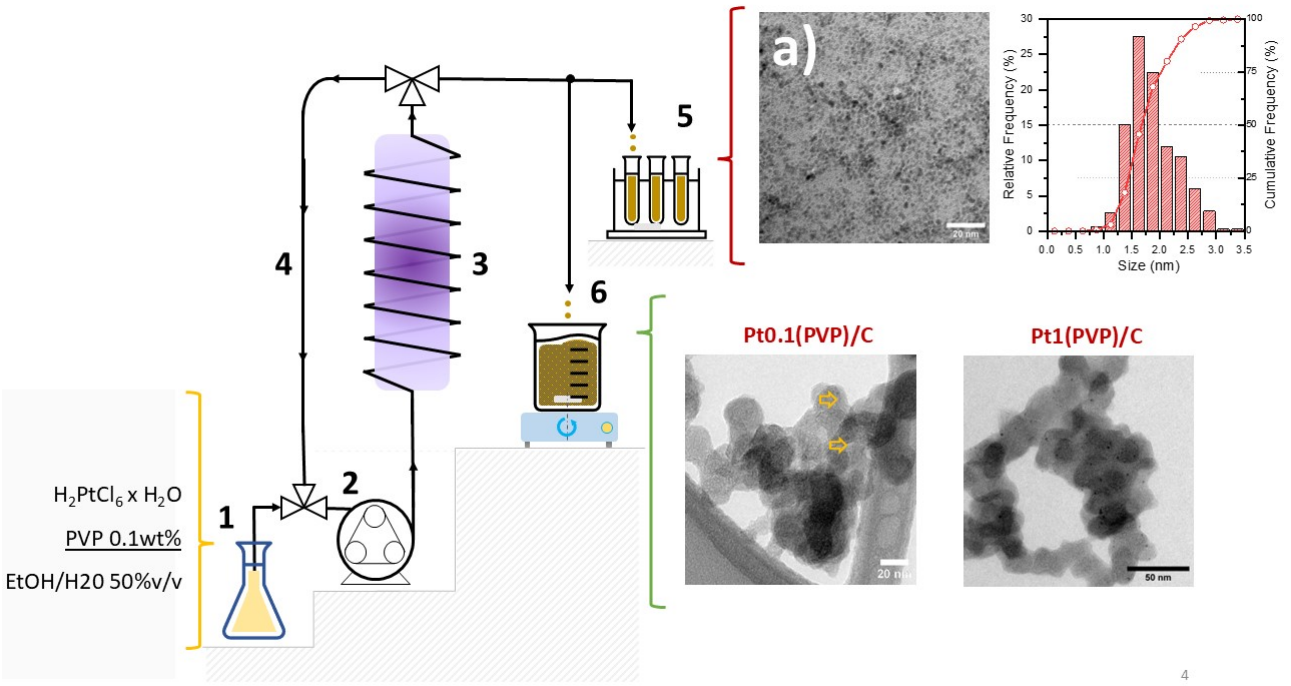
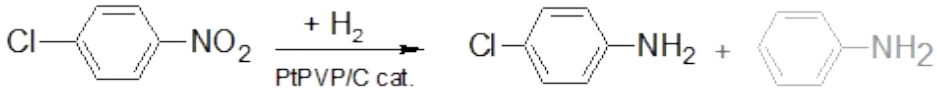


Figure S04 – Microfluidic reactor sketch for the synthesis of PVP-stabilized Pt colloidal solution and Pt(PVP)/C catalyst with 0.1% and 1% metal loading - (1) Reagent INLET, (2) pump, (3) Reactor coiled around the UV lamp, (4) circuit loop, (5) Pt(PVP) colloidal solution OUTLET and (6) direct Carbon impregnation.

Hydrogenation:



CATALYST: Pt 1.0 wt.% - PVP

Substrate	Main product	Time (min)	Conversion (%)	Selectivity (%)	Specific activity (h^{-1})
1-chloro-4-nitrobenzene	4-chloroaniline	10	14%	> 99%	2000
		25	42%	99%	2387
		50	84%	98 %	2413
		75	96%	98 %	1826

Reaction condition: temperature 25°C, 5 mL CH_3OH (10 mL CH_3OH in case of 1-bromo-4-nitrobenzene due to low solubility), 10 mg of Pt 1 wt.%, mol of substrate 1.28 mmol, 1200 rpm

Table S01. The catalytic efficiency of Pt(PVP)/C catalyst in the hydrogenation of 1-chloro-4-nitrobenzene

5 Synthesis of Glyco-stabilized Pt NPs and related NMR data

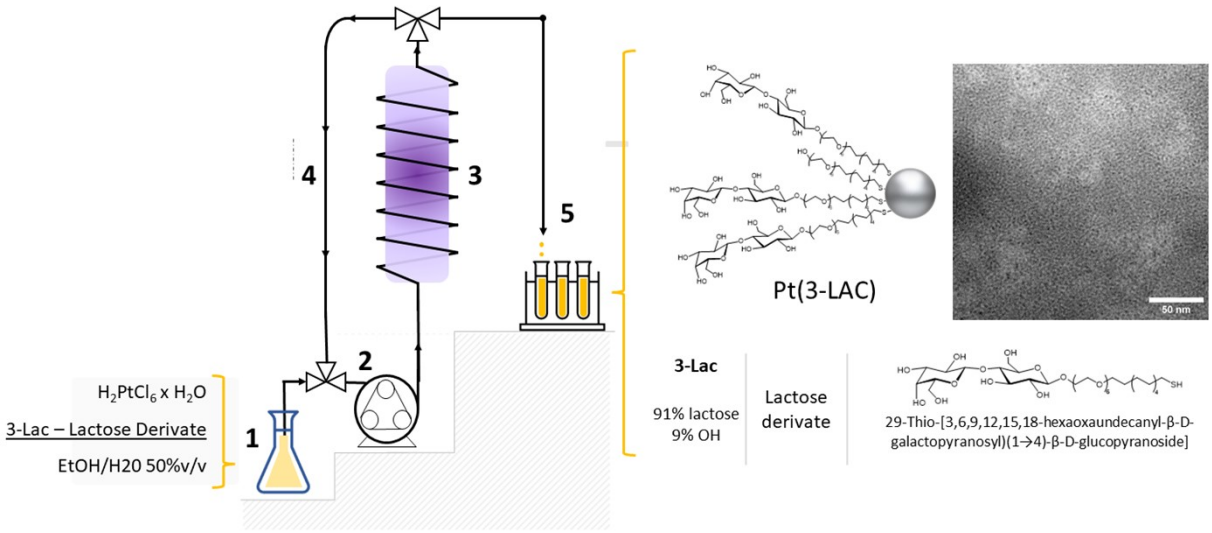


Figure S05 – Microfluidic reactor sketch for the synthesis of Glyco-Pt colloidal solution - (1) Reagent INLET, (2) pump, (3) Reactor coiled around the UV lamp, (4) circuit loop, (5) Pt(3-LAC) colloidal solution OUTLET. On the right side, the chemical formula of 3-Lac, Glycan derivative of lactose

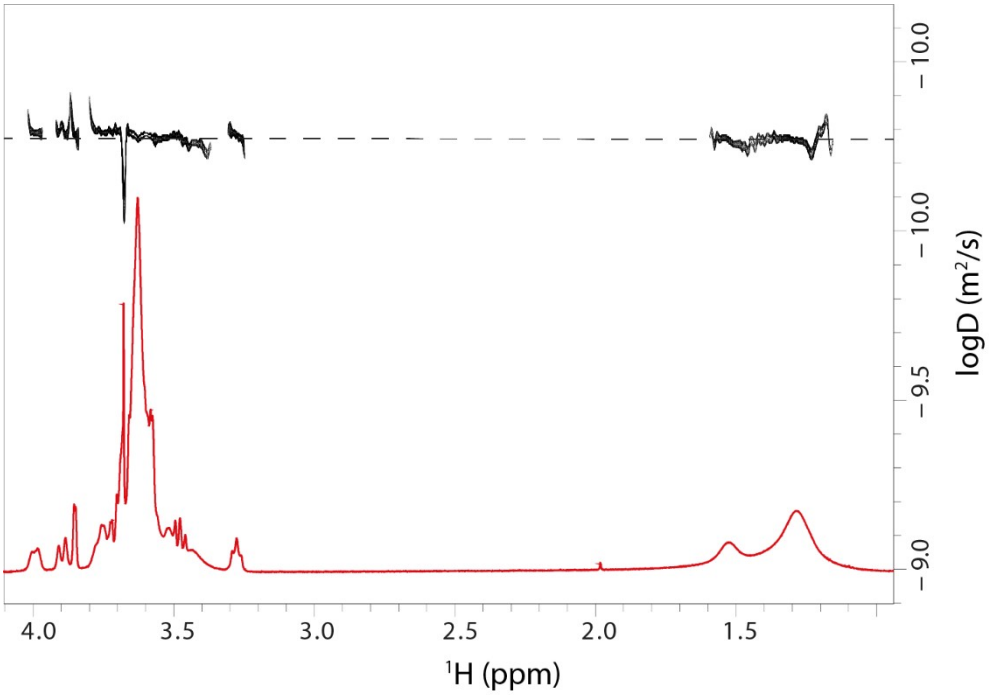


Figure S06 – NMR DOSY spectrum of Pt(3-Lac) NPs colloidal solution. The ^{1}H 1D NMR spectrum is reported in red as a reference

A **hydrodynamic radius of 3.7 ± 0.2 nm** was estimated from the **Pt NP** diffusion coefficient (D= 5.08 ± 0.4 x 10^{-11} m2/s) measured from DOSY spectrum on Pt(3-Lac) sample dissolved in D2O and recorded at 25°C on 500 MHz Bruker spectrometer.

The quantification of the bound 3-Lac ligand on Pt NPs was achieved by exploiting quantitative ^{1}H-NMR using ERETIC2 methodology[2]. Anomeric signals of lactose at 4.430 ppm (H1) and 4.377 ppm (H2), free from overlap in both unconjugated and NP bound ligand samples (Figure 3), were selected for integration andused to estimate an uploaded ligand concentration of 6.8 ± 0.1 mM; that is almost half the initial free ligand concentration (i.e. 12.65 mM).

6 References:

1 S. Sinha and M. Mukherjee, *Vacuum*, 2018, **148**, 48–53.

2 Y. Nishizaki, D. C. Lankin, S. N. Chen and G. F. Pauli, *Anal Chem*, 2021, **93**, 2733–2741.

3 G. Wider and L. Dreier, *J Am Chem Soc*, 2006, **128**, 2571–2576.

4 E. O. Stejskal and J. E. Tanner, *J Chem Phys*, 1965, **42**, 288–292.

5 D. Li, G. Kagan, R. Hopson and P. G. Williard, *J . Am. Chem. Soc.*, 2010, **131**, 5627–5634.

6 A. Einstein, *Investigations on the Theory of Brownian Movement*, Dover Publications, 1956.

7 B. E. P. Robert C. Reid, J. M. Prausnitz, *The Properties of Gases and Liquids*, 1987.

8 Á. G. Barrientos, J. M. De la Fuente, T. C. Rojas, A. Fernández and S. Penadés, *Chemistry - A European Journal*, 2003, **9**, 1909–1921.

9 L. Ragona, O. Gasymov, A. J. Guliyeva, R. B. Aslanov, S. Zanzoni, C. Botta and H. Molinari, *Biochim Biophys Acta Proteins Proteom*, 2018, **1866**, 661–667.

10 D. K. Wilkins, S. B. Grimshaw, V. Receveur, C. M. Dobson, J. A. Jones and L. J. Smith, *Biochemistry*, 1999, **38**, 16424–16431.

11 P. Perez Schmidt, K. Pagano, C. Lenardi, M. Penconi, R. M. Ferrando, C. Evangelisti, L. Lay, L. Ragona, M. Marelli and L. Polito, *Angewandte Chemie*, , DOI:10.1002/ange.202210140.

12 M. Harada and Y. Kamigaito, *Langmuir*, 2012, **28**, 2415–2428.