

Zirconia-Based Magneto Plasmonic Nanocomposites: A New Nanotool for Magnetic Guided Separations with SERS Identification.

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1- Synthesis of Bisphosphonic acid

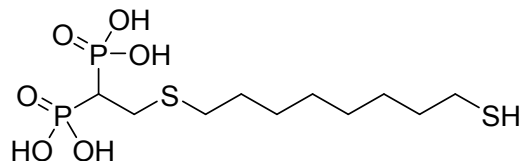


Chart S1: Molecular structure of (2-((8-mercaptooctyl)thio)ethane-1,1-diyl)bis(phosphonic acid) (BPODE).

1.1 General

The synthesis of the bisphosphonic acid were followed with TLC Polygram[®] Sil G/UV254, 0.25 mm thickness. ¹H NMR, ¹³C NMR, ³¹P NMR and 2D spectra were recorded with a Bruker Avance 300 and Ascend 400 spectrometers, working at 300-400 MHz for ¹H, 75-100 MHz for ¹³C and 121-161 MHz for ³¹P, respectively. Resonance frequencies are referred to tetramethyl silane and 85% H₃PO₄.

Reagents and solvents with high purity degree purchased by the providers were used as given. Otherwise, they were purified following the procedures reported in literature.¹ Anhydrous solvents were prepared by adding activated 3 Å molecular sieves to the solvent under inert atmosphere. Molecular sieves were activated shortly before the use by continuous heating under vacuum. Flash chromatography were performed with silica gel Merk 60, 230-400 mesh, following procedures reported in the literature.²

1.2 Experimental

Vinylidene Bisphosphonate Tetraethyl Ester (VBP)

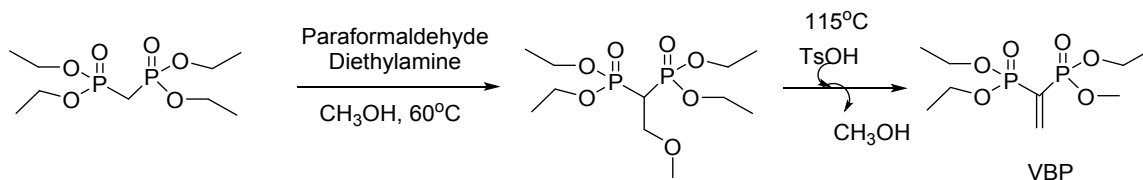


Figure S1: synthesis of VBP.

In a 500 mL round bottomed flask, paraformaldehyde (3.18 g, 106 mmol) and diethylamine (2.2 mL, 21mmol) were dispersed in 60 mL of methanol and the flask was topped with a reflux condenser. The apparatus was purged with nitrogen and the suspension refluxed until clearness. The resulting solution was cooled to room temperature. Then tetraethyl (methylene) bisphosphonate (5 ml, 20 mmol) was added dropwise into the cooled solution and then reflux for overnight. After that the completeness of the intermediate reaction was verified by ^1H & ^{31}P NMR analysis. Then the solution was concentrated under rotavapor and the crude solution was diluted with methanol (30 mL) and then concentrated. The concentrated solution was diluted with toluene and concentrated again. Then the solution was dissolved in anhydrous toluene and p-toluene sulfonic acid (15 mg, 0.09 mmol) was added to the solution. A pressure-equalizing dropping funnel filled with activated 3 Å molecular sieves was placed over the flask and topped with a reflux condenser. The apparatus was purged with nitrogen and the suspension refluxed for 24 hours. The completeness of the reaction was verified by ^1H & ^{31}P NMR analysis. The resulting solution was cooled to room temperature and concentrated under rotavapor. Then the residue was dissolved in CH_2Cl_2 , washed twice with H_2O , dried with NaSO_4 , and finally CH_2Cl_2 was removed from mother liquor with rotavapor. The product was obtained as light-yellow oil (5.3 g, 17.6 mmol, 90% yield). ^1H NMR (400 MHz, Chloroform-*d*) δ 6.88 (dd, J = 71.6, 9.3 Hz, 2H), 4.17 – 3.89 (set of m, 8H), 1.24 (t, J = 7.1 Hz, 12H). $^{31}\text{P}\{^1\text{H}\}$ NMR (162 MHz, Chloroform-*d*) δ 12.93 (s, 2P). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.29 (s), 132.17 (t, J = 166.6 Hz), 62.78 (t, J = 2.8 Hz), 16.38 (t, J = 3.3 Hz) ppm.

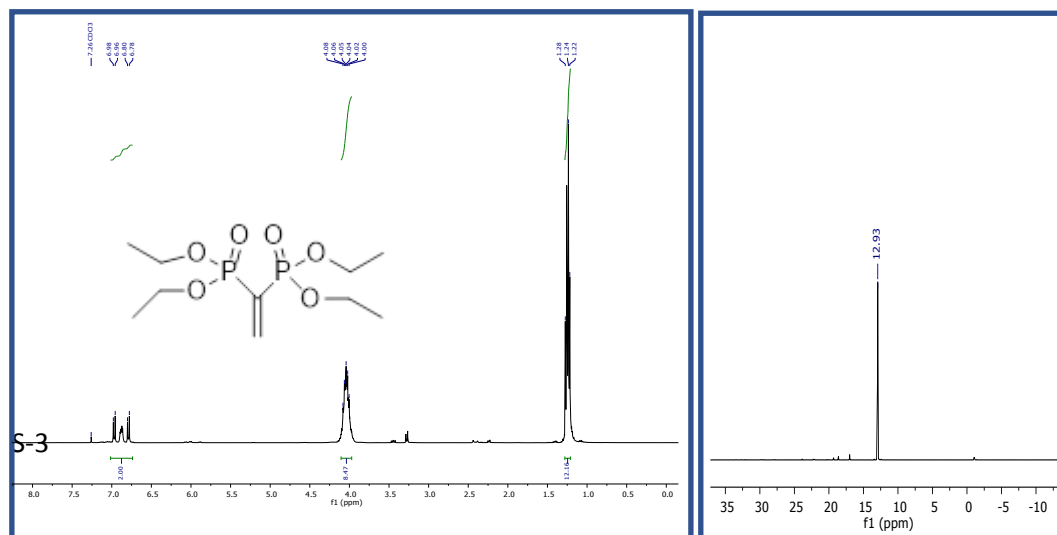


Figure S2: ^1H -NMR (left) and ^{31}P $\{^1\text{H}\}$ -NMR (right) of VBP

1.3 Tetraethyl 2-(octamethylene dimercaptan) ethane-1,1 diydiphosphonate (BPOMD)

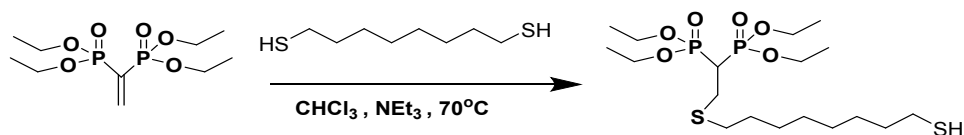


Figure S3: Synthesis of BPOMD.

In a 100 mL round bottom flask, vinylidene bisphosphonate tetraethyl ester (VBP, 500 mg, 1.67 mmol) was dispersed in 2.5 mL CHCl₃. Then 1,8 octane dithiols (297 μL , 1.67 mmol) and triethyl amine (12 μL , 5% in mol) were added to the solution. The apparatus was purged with nitrogen and the reaction mixture was refluxed for overnight. The resulting solution was cooled to room temperature and concentrated under rotavapor. The crude was dissolved in 10 mL CH₂Cl₂ and washed with deionized H₂O (2x 25 mL). The organic phase was dried with NaSO₄ and precipitate was filtered. Then CH₂Cl₂ solvent was removed with rotavapor. The product was obtained as colorless liquid (766 mg, 1.60 mmol, 96% yield). ^1H NMR (400 MHz, Chloroform-*d*) δ 4.24 – 4.09 (set of m, 8H), 3.00 (td, J = 16.0, 5.6 Hz, 2H), 2.59 – 2.43 (set of m, 5H), 1.56 (set of m, 4H), 1.39 – 1.23 (set of m, 21H). $^{31}\text{P}\{^1\text{H}\}$ -NMR (162 MHz, Chloroform-*d*) δ 21.72 (s, 2P). $^1\text{H}\{^{31}\text{P}\}$ - NMR (400 MHz, Chloroform-*d*) δ 4.24 – 4.09 (set of m, 8H), 3.00 (d, J = 5.9 Hz, 2H),

2.57 – 2.44 (set of m, 5H), 1.63 – 1.49 (set of m, 4H), 1.39 – 1.23 (set of m, 21H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 62.96 (d, $J = 6.6$ Hz), 62.80 (d, $J = 6.7$ Hz), 39.18 (t, $J = 131.5$ Hz), 34.04 (s), 33.20 (s), 29.44 (s), 29.15 (s), 28.99 (s), 28.83 (s), 28.33 (s), 27.85 (t, $J = 4.9$ Hz), 24.67 (s), 16.45 (d, $J = 6.2$ Hz).

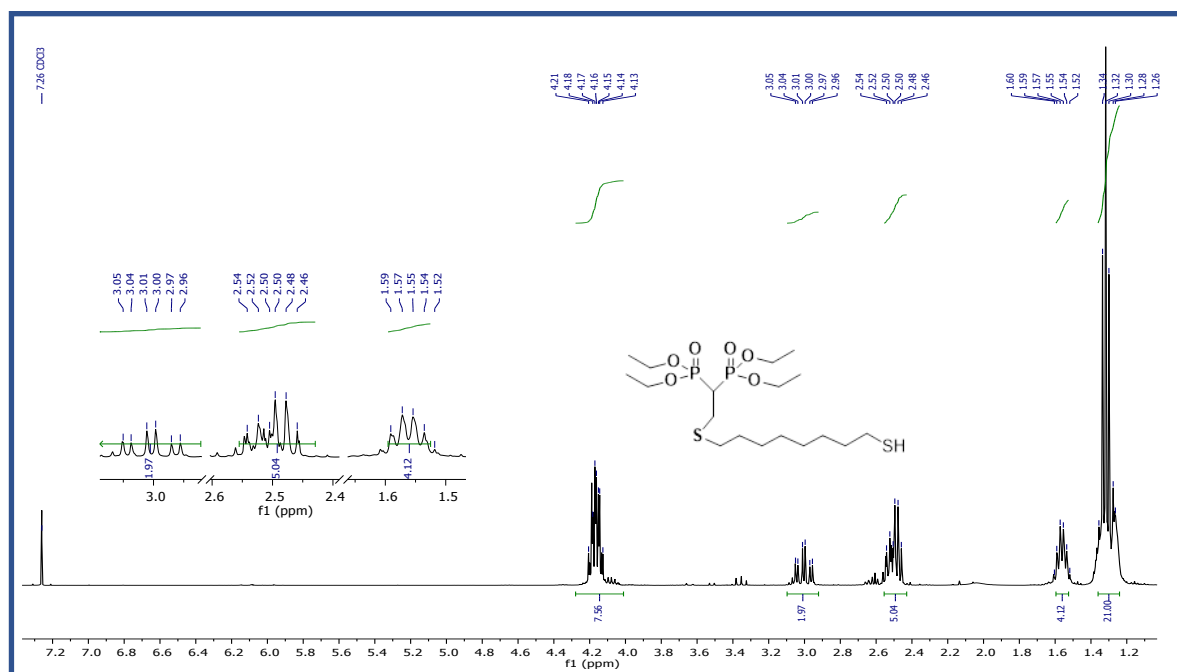


Figure S4: ^1H -NMR of BPODE ester

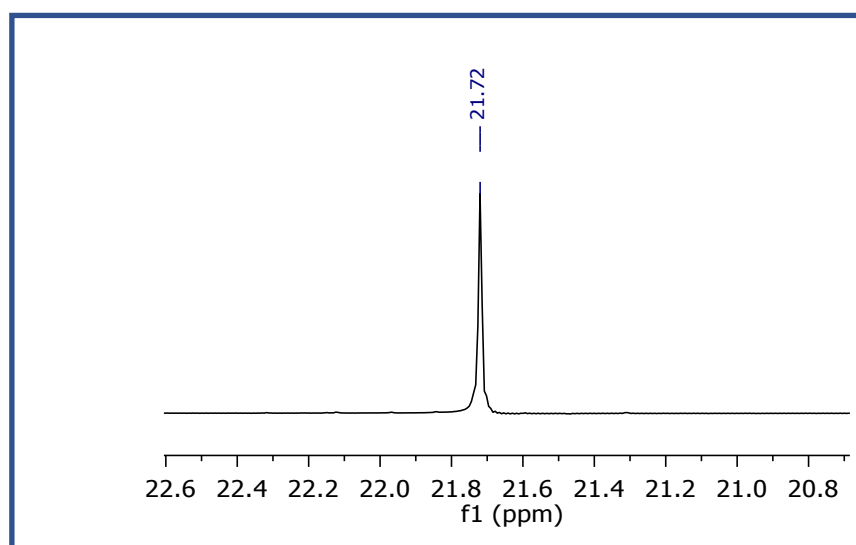


Figure S5: $^{31}\text{P}\{^1\text{H}\}$ -NMR of BPODE ester

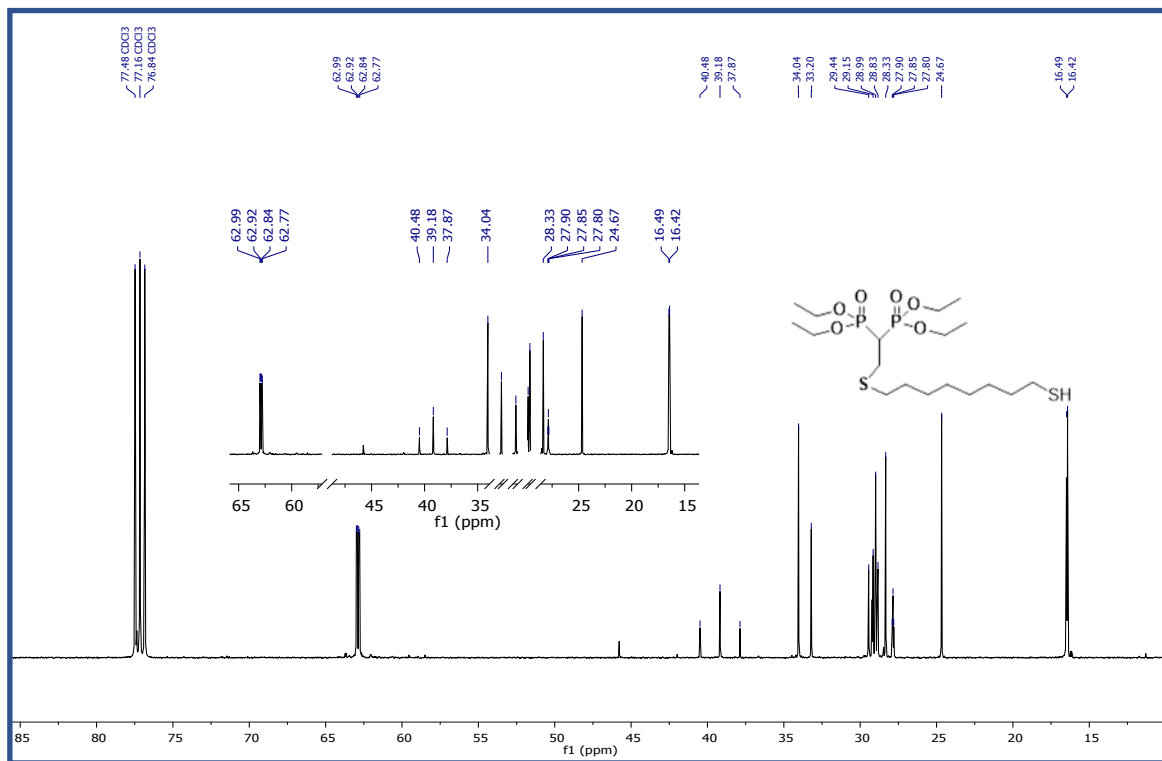


Figure S6: $^{13}\text{C}\{^1\text{H}\}$ -NMR of BPODE ester

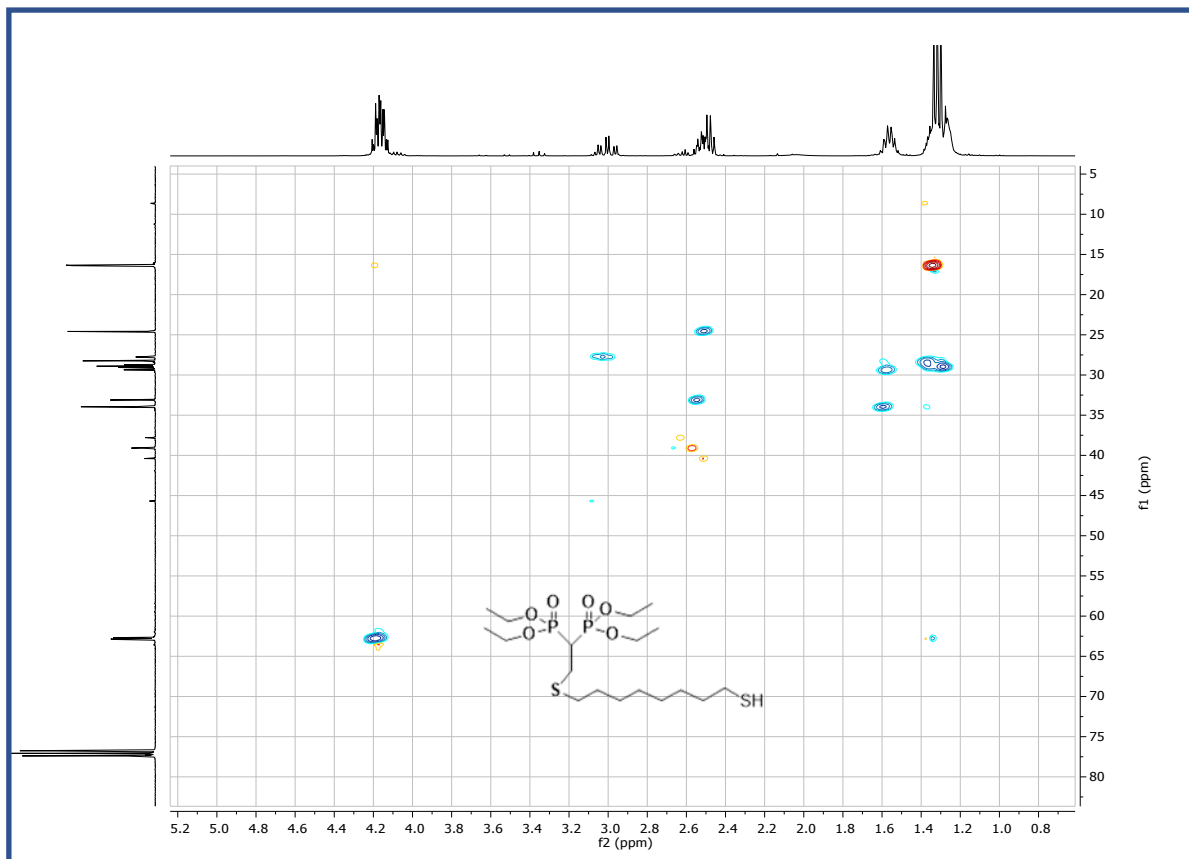


Figure S7: 2D NMR- HSQC of BPODE ester

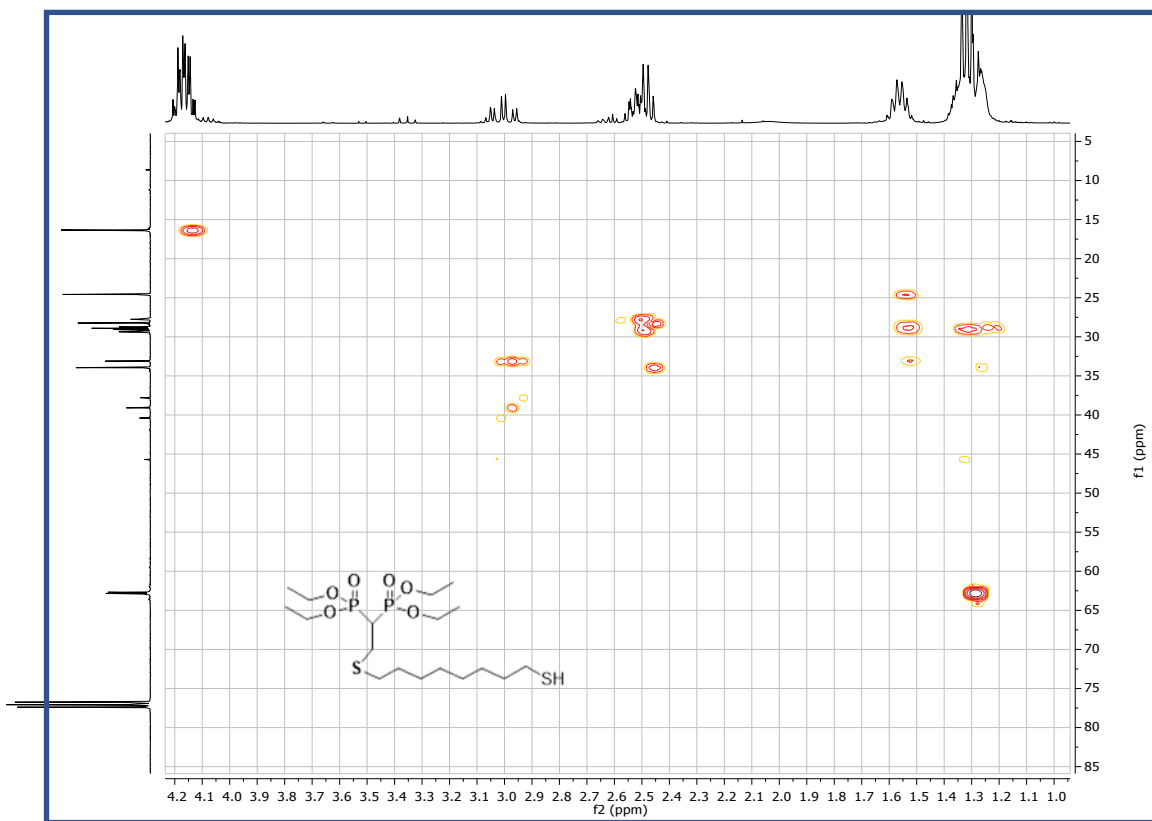


Figure S8: 2D NMR- HMBC of BPODE ester

1.4 2-(octamethylene dimercaptan) ethane-1,1- diyl diphosphonic Acid (BPODE)

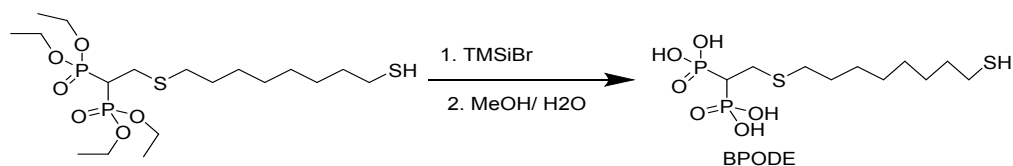


Figure S9: Synthesis of BPODE

In a 100 mL round bottom flask equipped with magnetic stirring bar tetraethyl 2-(octamethylene dimercaptan) ethane-1,1-diyl diphosphonate (500 mg, 1.05 mmol) was added in 4 mL $C_2H_4Cl_2$ solvent. Then bromotrimethylsilane ($Si(CH_3)_3Br$, 2.03 mL, 15.75 mmol) was added quickly to the solution. The mixture was refluxed under nitrogen atmosphere for an hour and a half. Then the flask was putted into high vacuum with N_2 for 1 h. Then vacuum was removed and solvent mixture (10 ml MeOH + 1 mL distilled water) was added to the flask and the reaction mixture was left stirred for 1h. After that, the solvent was remover with rotavapor. The product was obtained as colorless liquid (365 mg, 0.99 mmol, 95% yield). 1H NMR (400 MHz, $DMSO-d_6$) δ 2.84 (td, $J = 15.8, 5.9$ Hz, 2H), 2.66 (t, $J = 7.1$ Hz, 2H), 2.53 – 2.43 (m, 2H), 2.19 (tt, $J = 22.9, 5.8$ Hz, 1H), 1.64 – 1.54 (set of m, 2H), 1.49 (p, $J = 6.8$ Hz, 2H), 1.38 – 1.19 (set of m, 9H). $^{31}P\{^1H\}$ NMR (162 MHz, $DMSO-d_6$) δ 18.97. $^1H\{^{31}P\}$ NMR-(400 MHz, DMSO) δ 2.98 (d, $J = 5.9$ Hz, 2H), 2.84 (m, 2H), 2.71 – 2.54 (m, 3H), 1.59 (m, 4H), 1.27 (m, 9H). ^{13}C NMR (101 MHz, $DMSO-d_6$) δ 35.84 (s), 29.36 (s), 28.61 (s), 28.50 (s), 28.15 (s, $J = 9.3$ Hz), 27.40 (t, 4.9 Hz), 23.69 (s).

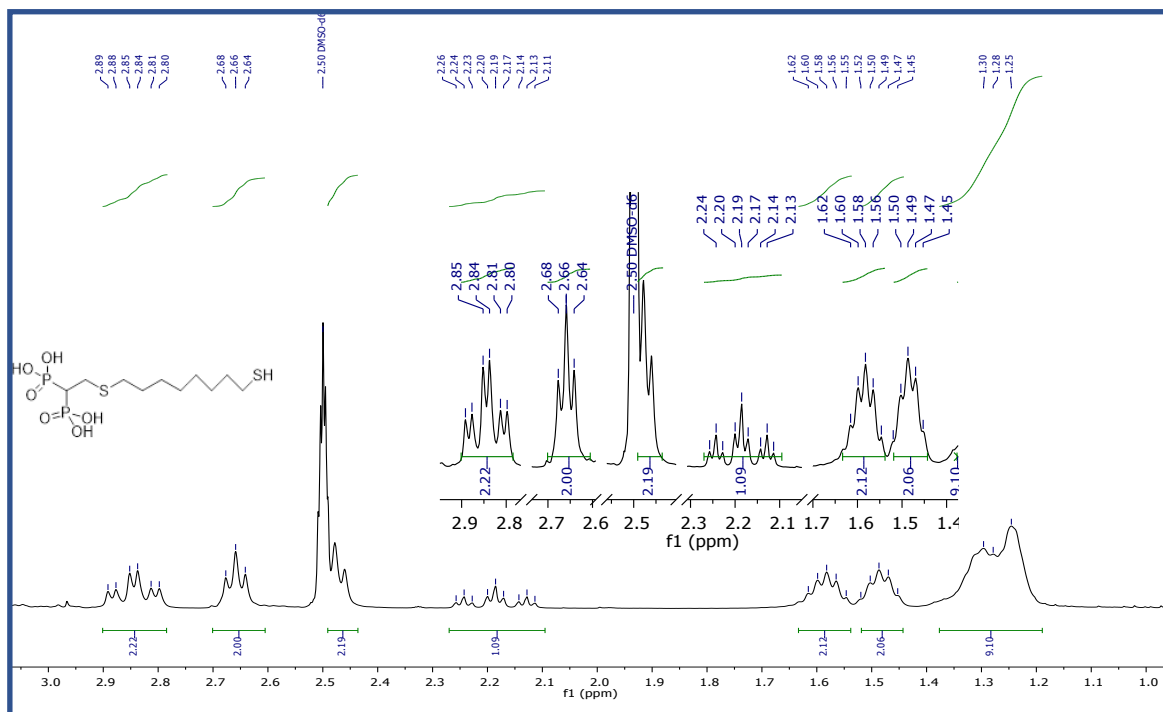


Figure S10: ¹H NMR of BPODE, 1h

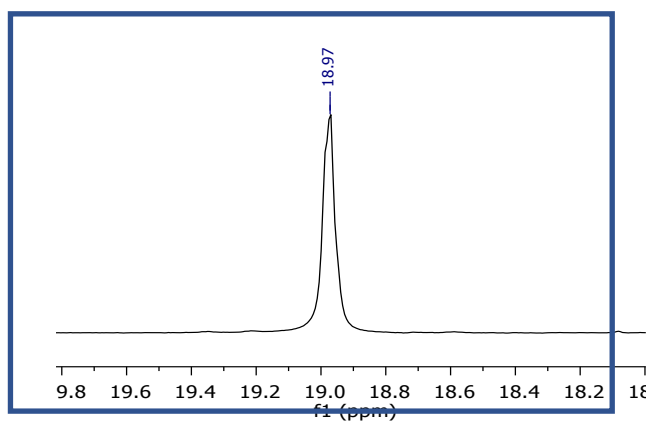


Figure S11: ³¹P{¹H}-NMR of BPODE, 1h

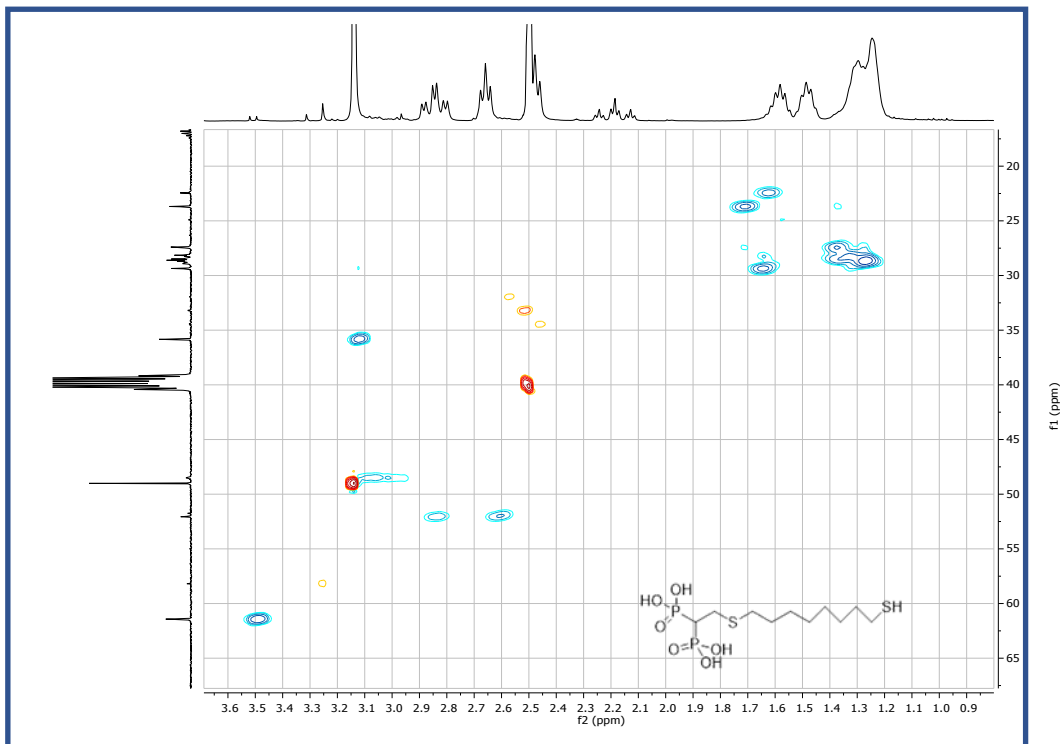


Figure S12: 2D NMR HSQC of BPODE, 1h

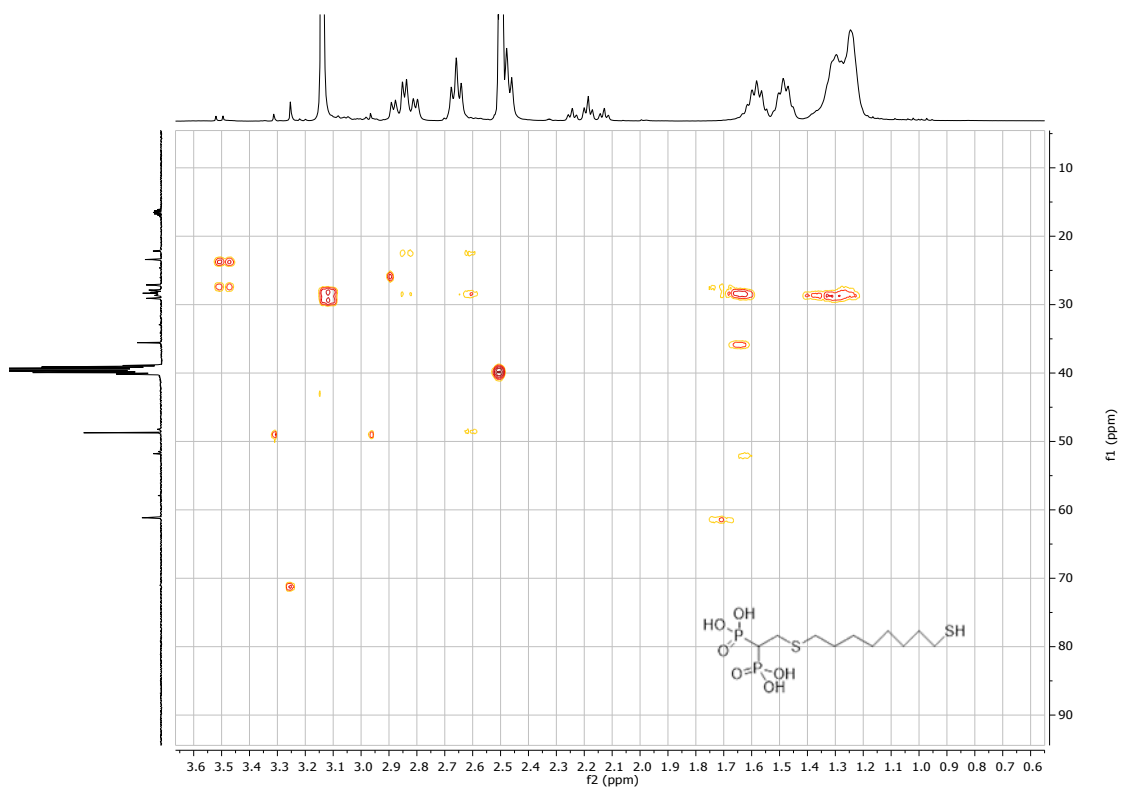


Figure S13: 2D NMR HMBC of BPODE

2- Characterization of mMZN

Units: nm	XRPD <L> _{vol}			SAXS Sphere Diam.
	t-ZrO ₂	m-ZrO ₂	CoFe ₂ O ₄	CoFe ₂ O ₄
Sample Name	t-ZrO ₂	m-ZrO ₂	CoFe ₂ O ₄	CoFe ₂ O ₄
MZN@700°C	10	21	/	/
mMZN-4	14	13	6	22
mMZN-8	11	7	18	23
mMZN-12.5	9	7	17	17

Table S1: Crystallites and particles size: t-ZrO₂ and m-ZrO₂ are tetragonal and monoclinic zirconia, respectively

	mMZn	mMZn@AuNPs
Saturation magnetization	240 10 ³ A/m (45 A·m/kg)	
Magnetic % (molar)	5%	
Zirconia density	5895 kg/m ³	
Cobalt ferrite density	5290 kg/m ³	
Hydrodynamic radius	1.0xRSEM M	1.6xRSEM
Water viscosity (T=20°C)	0.001 Pa·s	

Table S2: Parameters for the fitting of the magnetophoretic curves reported in **Figure 6** of the main text for mMZn and mMZn@AuNPs, respectively. RSEM indicates the average nanoparticle radius obtained with SEM images.

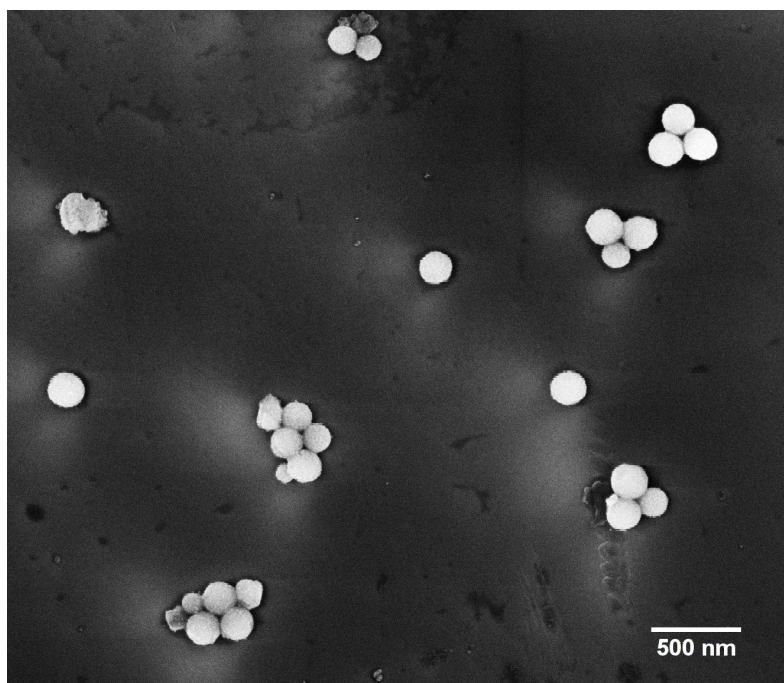


Figure S14: SEM image of MZN

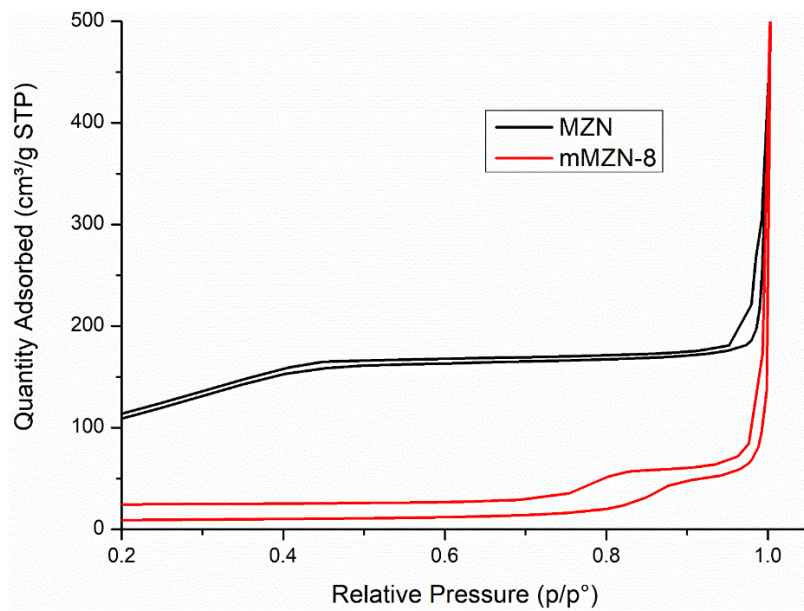


Figure S15: Comparison of N₂-physorption analysis of MZN and mMZN-8.

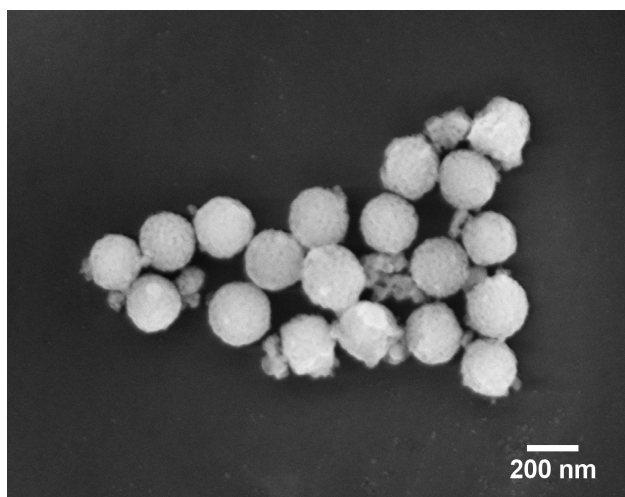


Figure S16: SEM image of mMZN-8

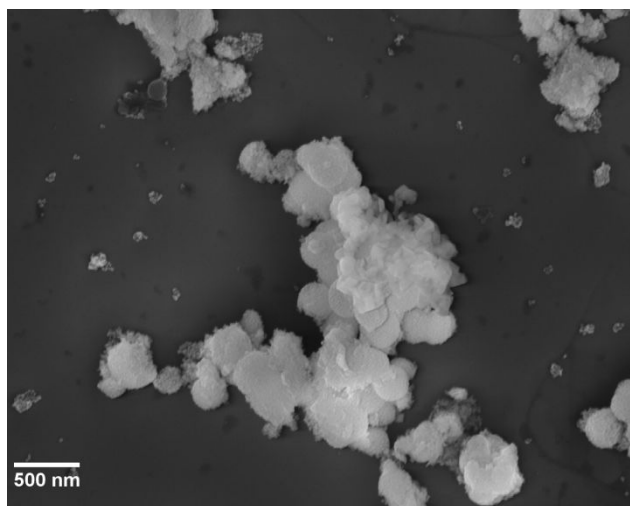


Figure S17: SEM image of mMZN-12.5

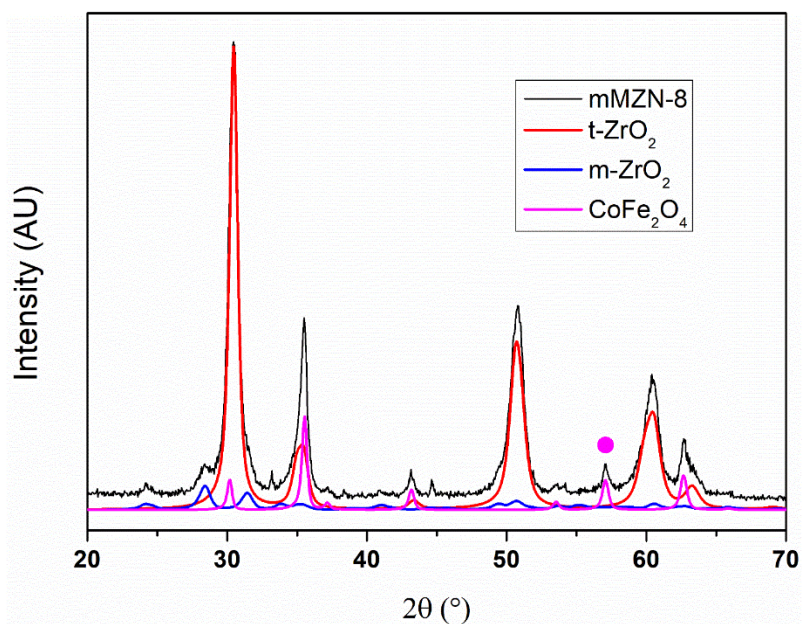


Figure S15: XRPD pattern of mMZN-8 compared to the ones related to t-ZrO₂ (ICSD # 164862), m-ZrO₂ (ICSD # 417639) and CoFe₂O₄ (ICSD # 41257), highlighted with pink dot the only peak related to cobalt ferrite not covered by the ones of zirconia.

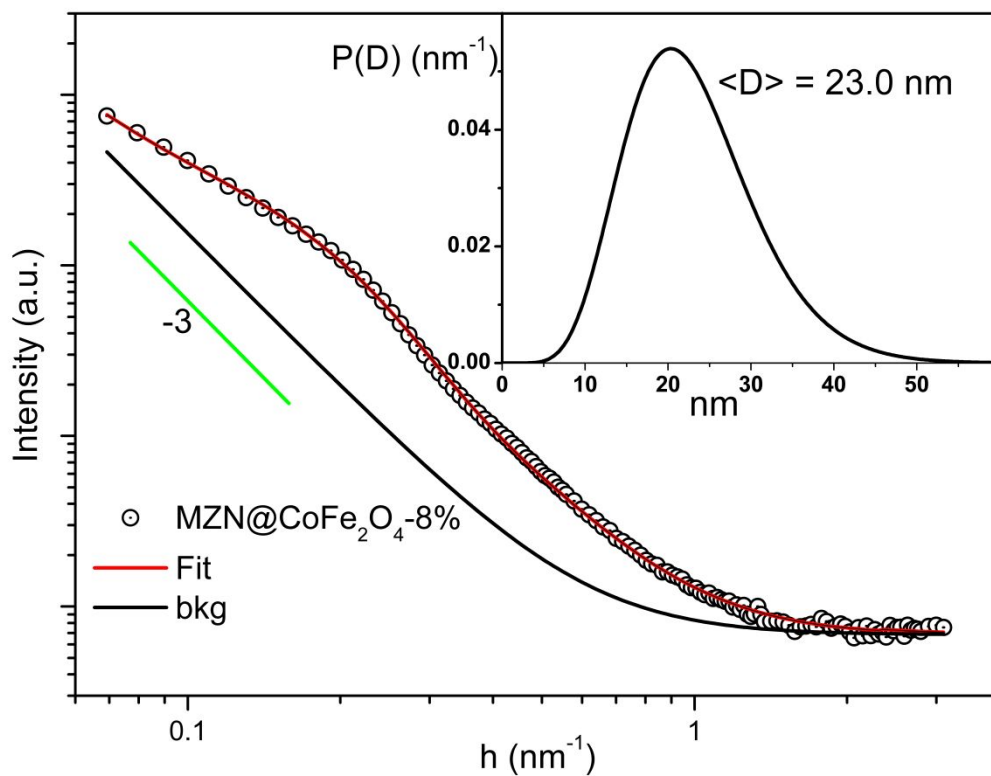


Figure S19: Fit of SAXS data with a distribution of spherical particles. Inset: Fitted size probability distribution of CoFe₂O₄ nanoparticles.

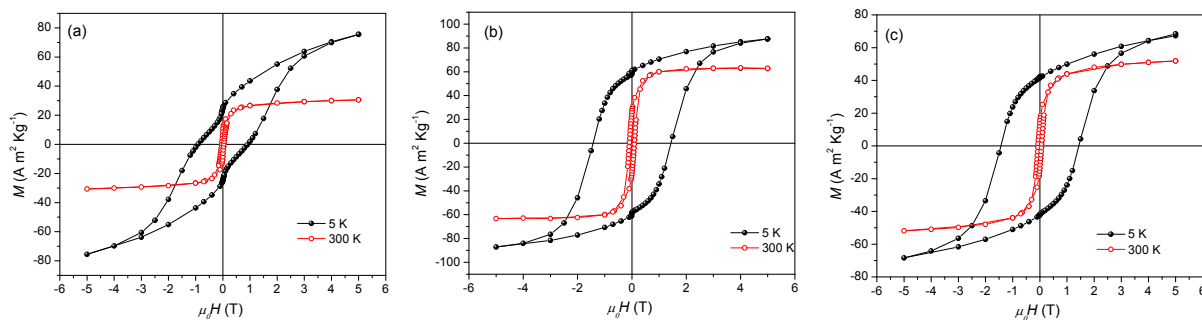


Figure S10: Hysteresis loops recorded at 5 K (full black circles) and 300 K (empty red circles) for mMZN-4 (a) mMZN-8 (b) and mMZN-12.5 (c)

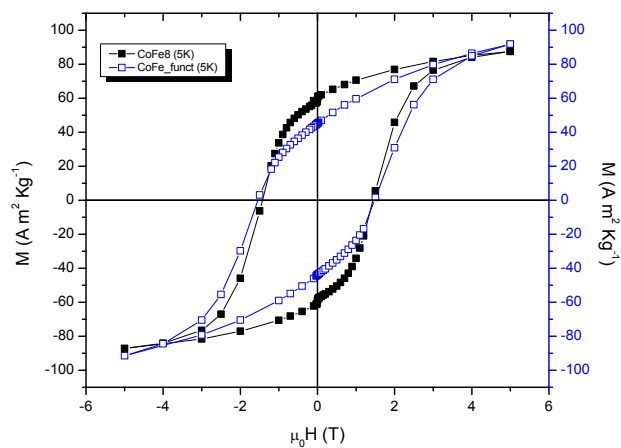


Figure S21: Hysteresis loops recorded at 5K of mMZn- 8 (black line and dots) and mMZn- 8-BPODE (blue line and dots)

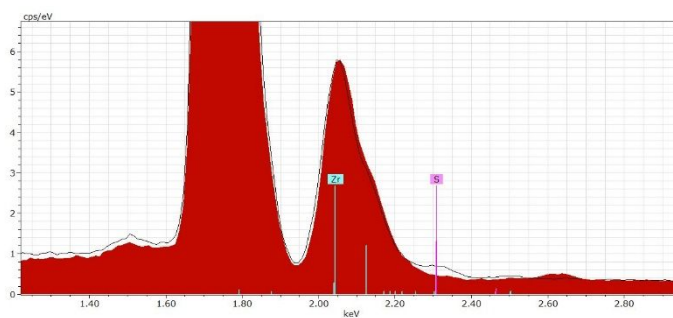


Figure S22: EDX spectra (d) of MZn-BPODE, red spectra for unmodified MZn, black line for MZn modified with BPODE.

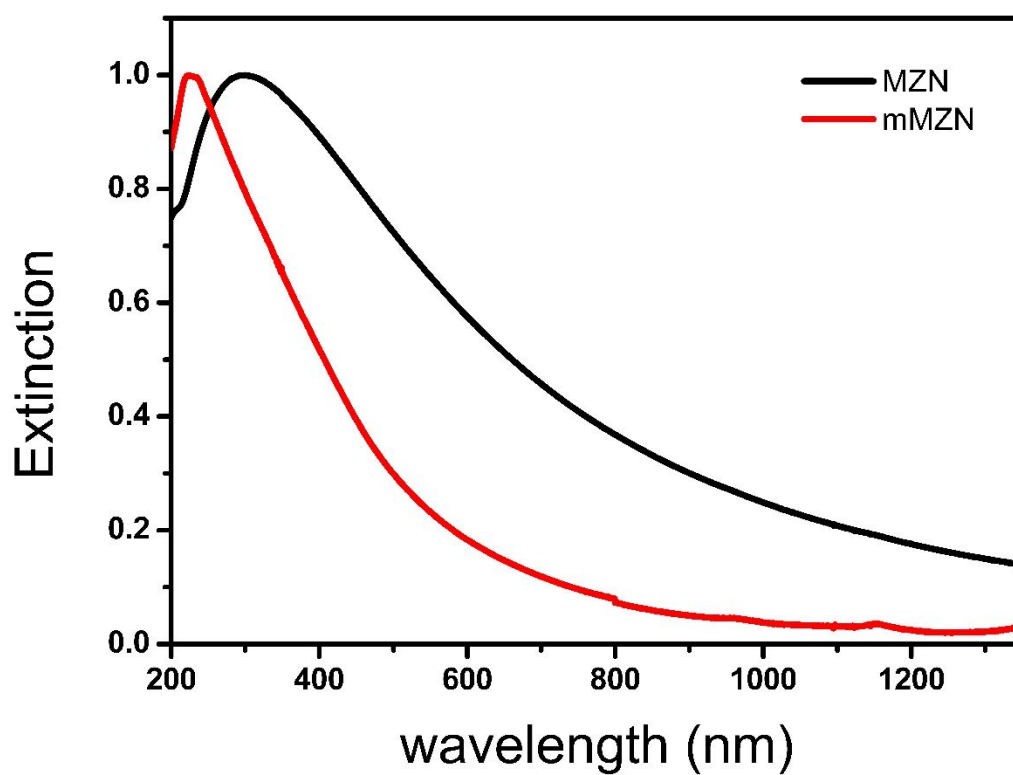


Figure S16: Extinction spectra of MZN (black line) and mMZN-8 (red line) normalized at the maximum intensity.

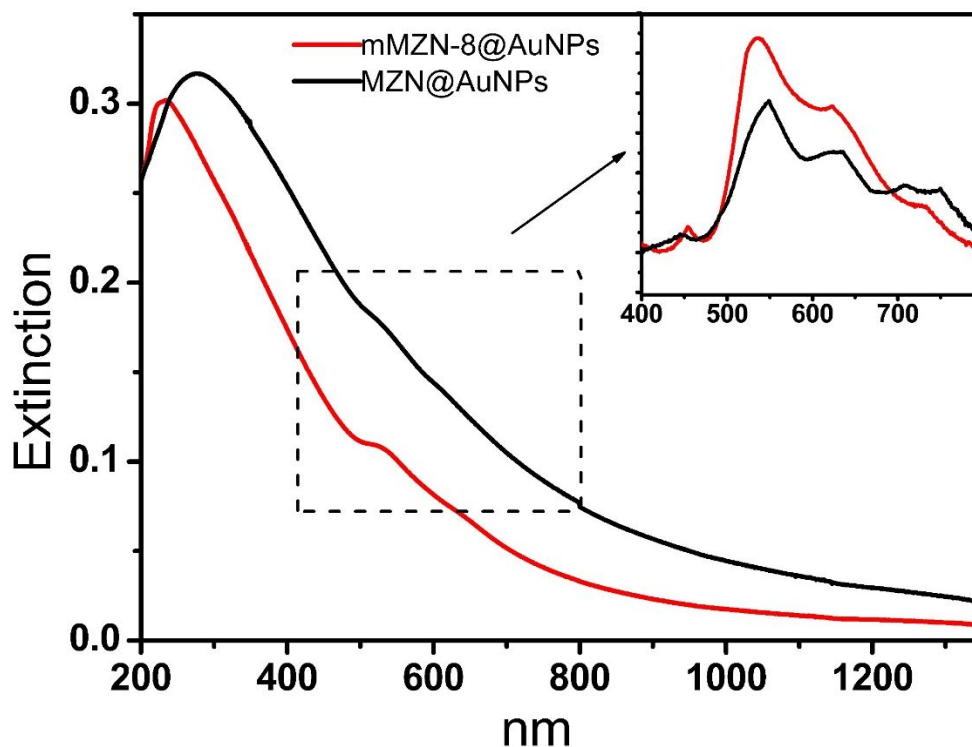


Figure S24: UV-Vis-NIR extinction spectra of MZN@AuNP (black line) and mMZN@AuNP (red line). Inset shows the spectral region from 400-800 nm after subtraction of the broad extinction of the ZrO₂ nanoparticles.

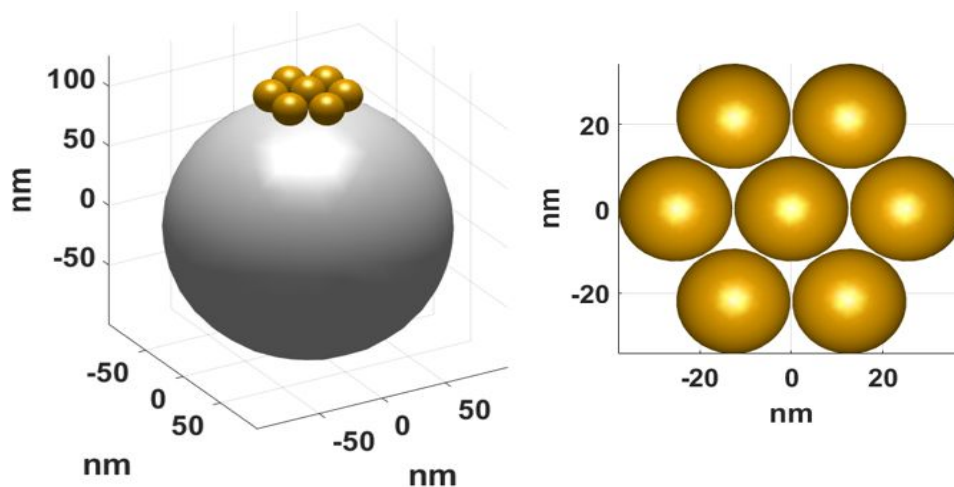


Figure S25: Model for the calculation of the extinction, scattering and absorption spectra of MZN@AuNP with a zirconia sphere with diameter of 200 nm and a 'flower' of seven AuNP of 20 nm (a). Organization of AuNP in the 'flower' (b).

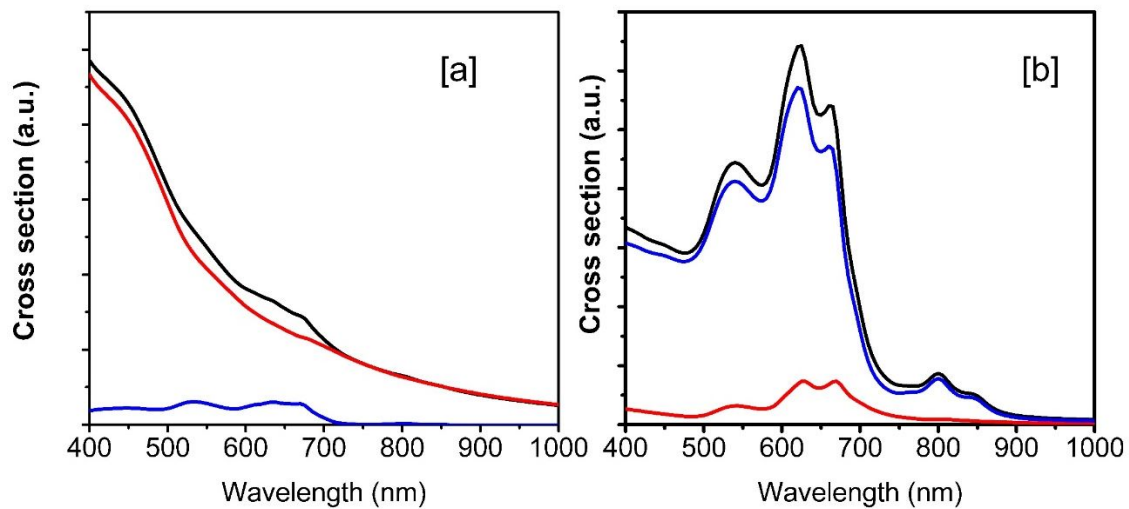


Figure S26: BEM calculation of the extinction (black lines), scattering (red lines) and absorption spectra (blue lines) of the model structure (a) and of the AuNP 'flower' only (b).