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Supporting Information

Hexagonal Magnetite Nanoprisms: Preparation, Characterization and Cellular Uptake

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Experimental Materials

Dopamine hydrochloride, Boc anhydride, benzyl bromide, trifluoroacetic acid, succinic acid anhydride, tetraethylene glycol, EDC, DMAP, iron(III)acetylacetonate ($Fe(acac)_3$), oleic acid, stearic acid, benzyl ether, fetal bovine serum (FBS), neocuproine, ascorbic acid, ammonium acetate, and concentrated hydrochloric acid (HCl) were purchased from Sigma-Aldrich (St. Louis, MO). RAW264.7 mouse monocyte/macrophage (Mo/Ma) cells were purchased from ATCC (Manassas, VA). RPMI were purchased from Invitrogen (Carlsbad, CA). Thiazolyl blue and sodium dodecyl sulfate were purchased from Fisher Scientific (Pittsburgh, PA). Ferrozine was purchased from Hach (Loveland, CO).

Characterization of the Hexagaonal Fe_3O_4 Nanoplatelets

The morphology of the hexagaonal Fe_3O_4 nanoplatelets is characterized by transmission electron microscopy (TEM). The TEM samples were prepared by immersing carbon-coated 200-mesh copper grids into a solution of nanoplatelets, followed by washing the grids with dropwise chloroform and drying overnight in a desiccator. The dried grids were analyzed with a Philips CM100 microscope operated at 100 kV. High-resolution TEM was recorded on FEI Tecnai F20XT, 200 kV; FEI, Hilsboro, OR. Powder X-ray diffraction (XRD) patterns were obtained on a Bruker D8 X-ray diffractometer with Cu Kα radiation. X-ray photoelectron spectroscopy (XPS) data was recorded with a Perkin–Elmer PHI 5400 electron spectrometer using acrochromatic AlKα radiation (1486.6 eV). Analysis was carried out under vacuum less than 5×10^{-9} Torr and heated to 120 ^{o}C to remove any adsorbed molecules on the surface. The XPS binding energies were measured with a precision of 0.025 eV. The analyzer pass energy was set to 17.9 eV, the contact time was 50 ms, and the area scanned was 4 mm^2.

Preparation of Hexagonal Fe_3O_4 Nanoplatelets

0.71 g of $Fe(acac)_3$ was added to a mixture of 1.27 g of oleic acid and 0.5 g of stearic acid in 10.4 g of benzyl ether. After degassing at room temperature for 1 hour, the reaction mixture was heated to 290 ^oC at the rate of 20 ^oC/min with vigorous stirring. The reaction mixture was maintained at 290 ^oC for 30 min, and then cooled to room temperature naturally. The resulted mixture was diluted with 10 mL hexane and 30 mL toluene. The nanoparticles were collected by centrifugation and further washed with chloroform. In the absence of stearic acid, under otherwise the same conditions, only Fe_3O_4 nanocubes were obtained (Figure S1)

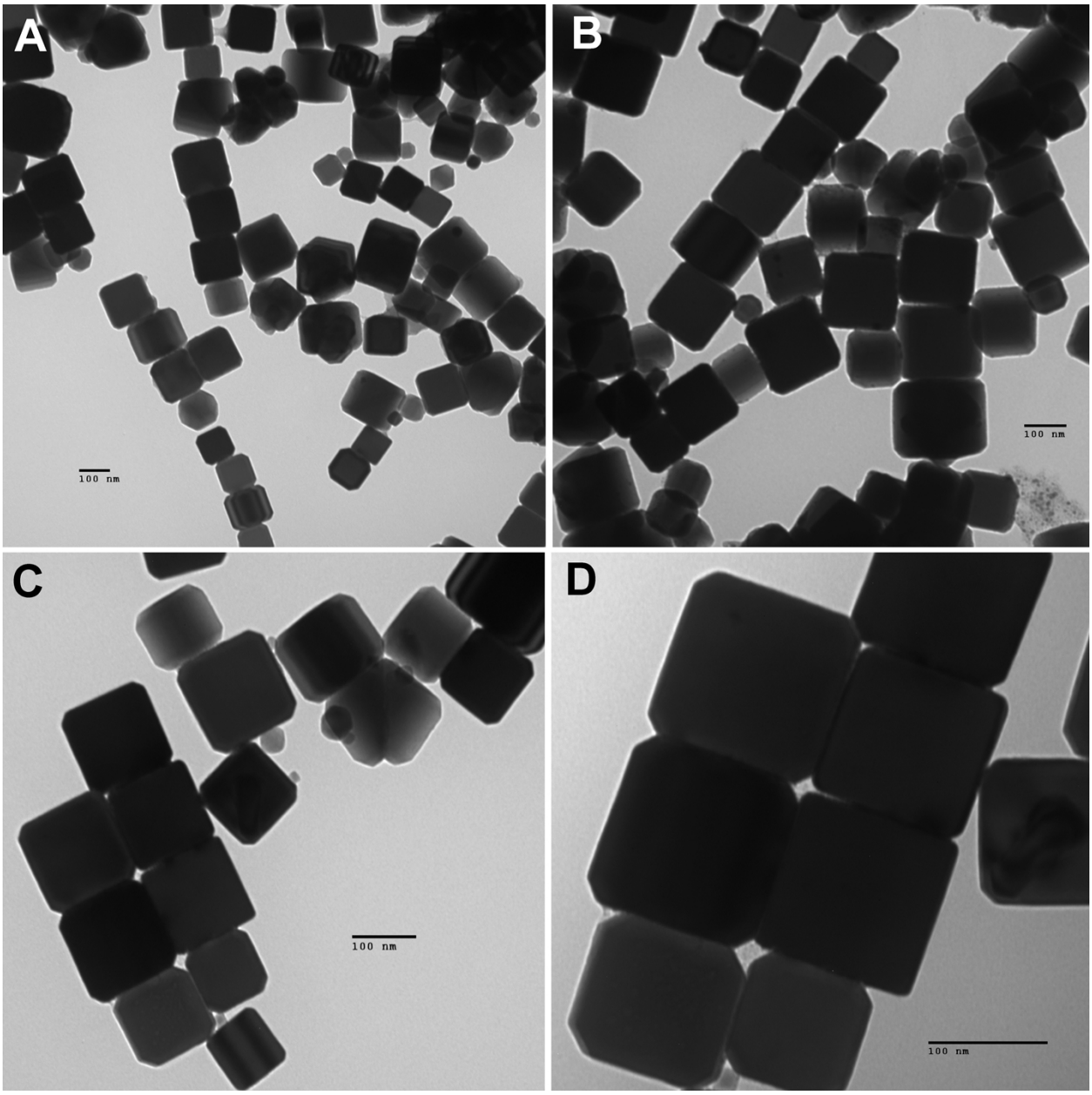


Figure S1: TEM of Fe_3O_4 nanocubes

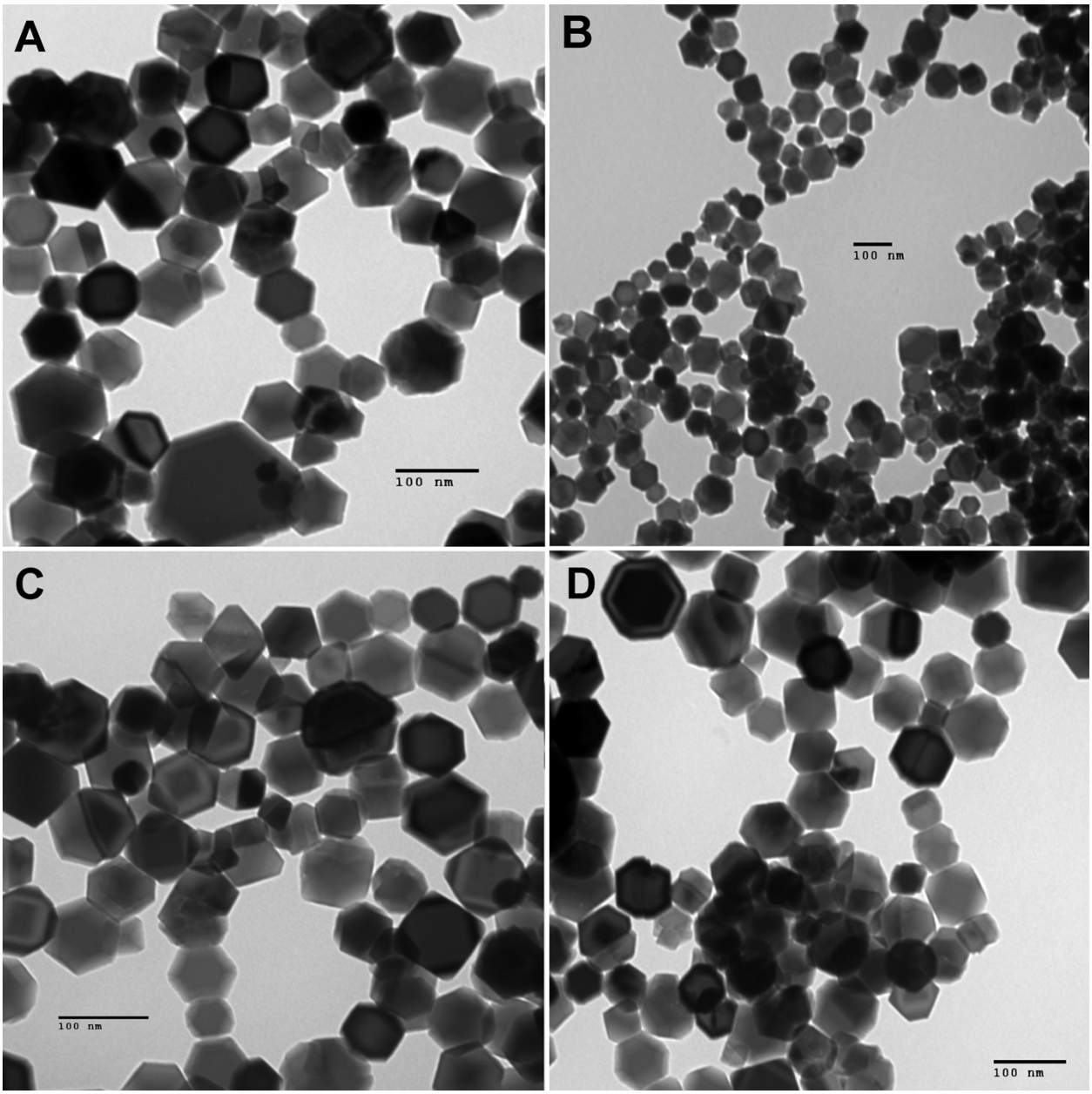
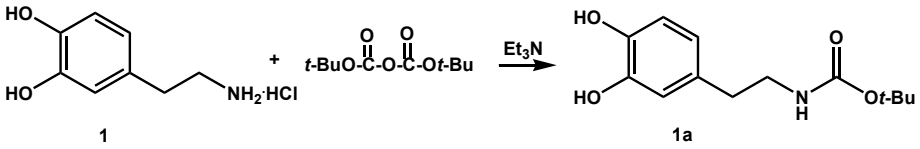


Figure S2: TEM of Fe_3O_4 HMNPs

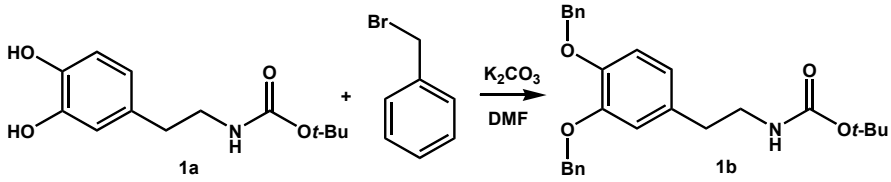
Synthesis of Dopamine Based Water Soluble Ligand 4

*N-tert-Butoxycarbonyl-3,4-dihydroxiphenylethylamine (**1a**)*



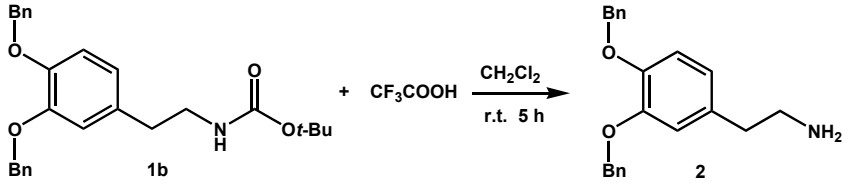
A solution of dopamine hydrochloride **1** (310 mg, 1.63 mmol) in methanol (8 mL) was stirred under N_2 for 5 minutes. TEA (1.8 mmol) was added followed by Boc-anhydride (393 mg, 1.8 mmol). The mixture was stirred under N_2 for 12 hours and the solvent was removed under reduced pressure. The remaining residue was dissolved in 40 mL CH_2Cl_2 and washed with 1 N HCl (3×5 mL) and brine (5 mL). The organic layer was dried over anhydrous Na_2SO_4. After filtration, the organic phase was kept at -5 ^oC for 3 hours. A white precipitate came out as product **1a** and collected by filtration. (98% yield). ^1H NMR (DMSO-d_6) δ: 1.73 (s, 9H); 2.48 (t, 2H); 3.02 (q, 2H); 6.40 (d, 1H); 6.54 (s, 1H); 6.61 (d, 1H); 6.83 (t, 1H); 6.85 (s, 1H); 6.76 (s, 1H).

*N-tert-Butoxycarbonyl-3,4-dibenzyloxyphenylethylamine (**1b**)*



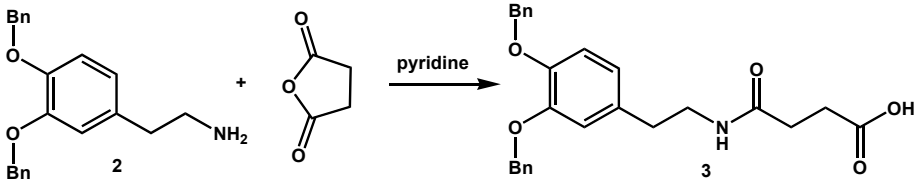
3.47 g of compound **1a** was dissolved in 100 mL DMF. 12.6 g K_2CO_3 was then added and the system was protected under N_2. 4.69 g (2 eq.) of benzyl bromide was added drop wise. The mixture was stirred at room temperature for 24 hours without light. The solid was removed by filtering through a short pad of celite and the filter-cake was washed with ether (3×100 mL). The combined filtrate and washing solution were washed with ice water (3×50 mL) and brine (15 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated to 150 mL. After resting at -5 ^oC for 5 hours, a white precipitate occurred as product **1b** and was collected by vacuum filtration. (93% yield). ^1H NMR ($CDCl_3$) δ: 1.45 (s, 9H); 2.70 (t, 2H); 3.31 (q, 2H); 4.49 (s, 1H); 5.15 (d, 4H); 6.71 (d, 1H); 6.80 (s, 1H); 6.88 (d, 1H); 7.32 (t, 2H); 7.37 (t, 4H); 7.45 (d, 4H).

*2-(3,4-Bis-benzyloxy-phenyl)-ethylamine (**2**).*



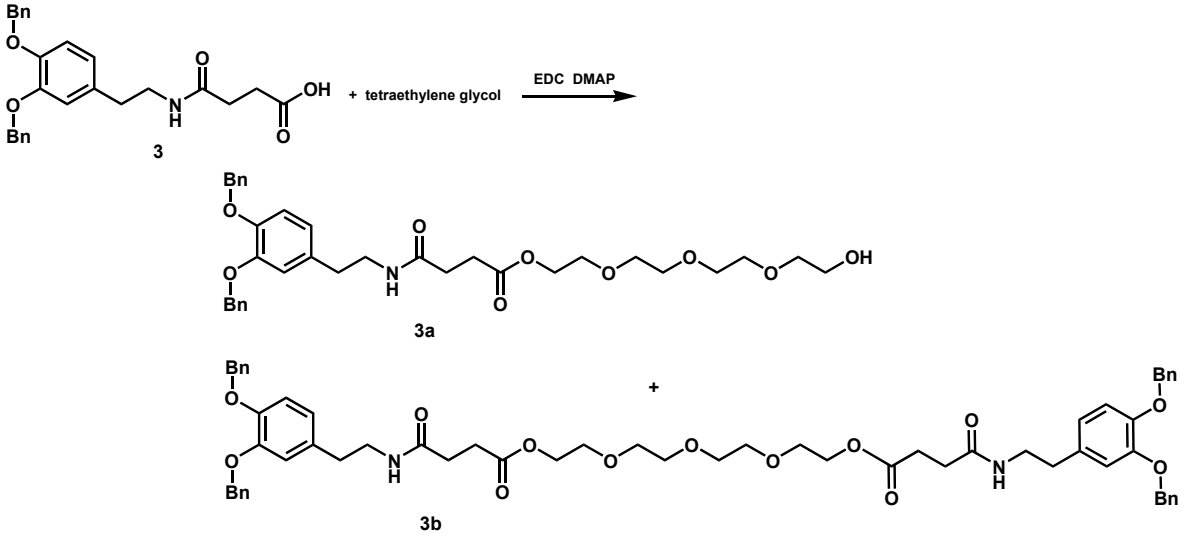
4.3g of compound **1b** was dissolved in 150 mL 5% TFA CH_2Cl_2 solution and stirred at room temperature for 5 hours. The solvent was removed in vacuum and a clear oil was obtained as the product **2**. (100% yield). ^{1}H NMR ($CDCl_3$) δ: 2.79 (t, 2H); 3.08 (m, 2H); 5.11 (s, 4H); 6.68 (d, 1H); 6.75 (s, 1H); 6.90 (d, 1H); 7.32 (t, 2H); 7.35 (t, 4H); 7.42 (d, 4H). ^{13}C NMR ($CDCl_3$) δ: 32.90; 41.85; 71.50; 72.00; 115.60; 116.25; 122.30; 127.60; 127.85; 128.35; 128.45; 128.63; 128.85; 136.70; 136.85; 148.45; 149.00; 160.88; 161.20; 161.58; 161.90.

*N-[2-(3,4-Bis-benzyloxy-phenyl)-ethyl]-succinamic acid (**3**)*



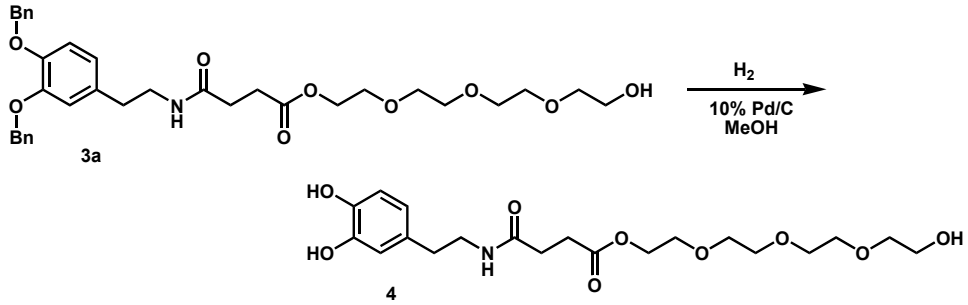
1.43 g of compound **2** and 0.43 g of succinic anhydride (1/1 ratio) were dissolved in 6 mL pyridine. The solution was stirred at room temperature for 5 hours. The solvent was removed by co-evaporation with toluene (toluene 5×5 ml). A white solid was obtained and washed with CH_2Cl_2 3 times. After drying in vacuum, 1.4 g of product **3** was obtained. (89% yield). ^{1}H NMR (DMSO-d_6) δ: 2.29 (t, 2H); 2.42 (t, 2H); 2.60 (t, 2H); 3.21 (q, 2H); 5.09 (d, 4H); 6.71 (d, 1H); 6.94 (s, 1H); 6.96 (d, 1H); 7.32 (t, 2H); 7.38 (d, 4H); 7.45 (t, 4H); 7.90 (t, 1H); 12.08 (s, 1H). MS-ESI+: m/z 434.2. Molecular weight calculated as 433.5**.**

2-(2-(2-(2-hydroxy-ethoxy)ethoxy)ethoxy)ethyl-N-[2-(3,4-Bis-benzyloxy-phenyl)-ethyl]-succinamic acid ester (3a)



0.964 g of compound **3** and 0.426g of EDC (1/1 ratio) were dissolved in 100 mL CH_2Cl_2 and stirred at room temperature for 10 minutes. 0.433 g of tetraethylene glycol was added followed by 5 mg DMAP. After stirring for 12 hours at room temperature, the organic phase was washed with 10% H_3PO_4 solution (3×10 mL), water (3×10 mL) and brine (10 mL). The organic phase was dried over anhydrous $MgSO_4$. After removing the solvent in vacuum, the residue was loaded on a column and eluted with 1/1 acetone/methylene chloride. 0.77 g of product **3a** was obtained. (79% yield). 0.21 g of side product **3b** was isolated. ^{1}H NMR for **3a** ($CDCl_3$) δ: 2.39 (t, 2H); 2.57 (t, 1H); 2.70 (q, 4H); 3.44 (q, 2H); 3.60 (t, 2H); 3.65 (broad 12H); 4.24 (t, 2H); 5.15 (d, 4H); 5.74 (t, 1H); 6.71 (d, 1H); 6.81 (s, 1H); 6.89 (d, 1H); 7.31 (t, 2H); 7.37 (t, 4H); 7.46 (d, 4H). MS-ESI+: m/z 610.4. Molecular weight calculated as 609.3. ^{1}H NMR for **3b** ($CDCl_3$) δ: 2.37 (t, 4H); 2.67 (m, 8H); 3.42 (q, 4H); 3.63 (s, 8H); 3.67 (t, 4H); 4.22 (t, 4H); 5.15 (d, 8H); 5.70 (t, 2H); 6.70 (d, 2H); 6.80 (s, 2H); 6.88 (d, 2H); 7.31 (t, 4H); 7.36 (t, 8H); 7.45 (d, 8H). MS-ESI+: m/z 1024.7. Molecular weight calculated as 1024.2.

2-(2-(2-(2-hydroxy-ethoxy)ethoxy)ethoxy)ethyl-N-[2-(3,4-dihydroxy-phenyl)-ethyl]-succinamic acid ester (4)



0.34 g of compound **3a** was dissolved in 50 mL methanol. 77 mg of Pd/C was added under N_2. After evacuating three times, 1 atm. H_2 was applied and the mixture was stirred for 24 hours at room temperature. The catalyst was removed by filtering through a short pad of celite. After removing the solvent in vacuum, 0.23 g of product **4** was obtained. (100% yield). ^{1}H NMR (DMSO-d_6) δ: 2.33 (t, 2H); 2.48 (q, 2H); 3.15 (broad multiplet, 4H); 3.41 (t, 2H); 3.49 (t, 2H); 3.51 (broad multiplet, 8H); 3.59 (t, 2H); 4.11 (t, 2H); 6.41 (d, 1H); 6.55 (s, 1H); 6.61 (d, 1H). MS-ESI$^+$: *m/z* 430.4. Molecular weight calculated as 429.4.

Surface Capping of Hexagonal Fe_3O_4 Nanoplatelets With Ligand 4

20 mg of hexagonal Fe_3O_4 nanoplatelets was dispersed in 10 mL chloroform by sonication; 35 mg of ligand **4** in 10 mL of methanol was added. The mixture was sonicated for 5 min, and then was further shaken at room temperature for 12 hours. The nanoplatelets were precipitated by centrifugation, and the free ligand **4** was removed by 6 cycles of methanol washing.

Zeta Potential Measurements

Zeta potential measurements were performed using ZetaPALS Zeta Potential Analyzer purchased by Brookhaven Instruments Corporation.[18] The HMNPs were characterized in 1 X PBS at 298K. Their concentration was 0.1mg/mL.

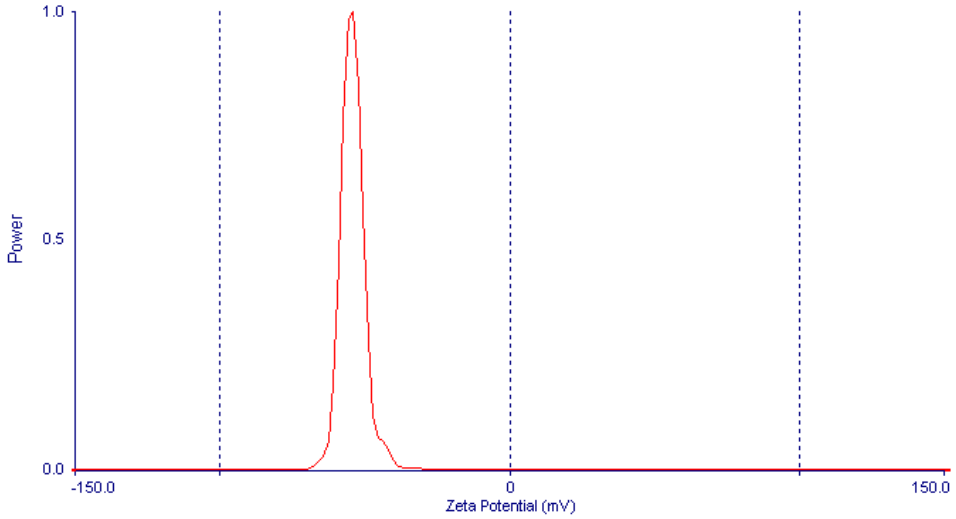


Figure S5: Zeta potential of HMNPs in 1 X PBS

Reference

18 A. S. Perera, H. Wang, M. T. Basel, M. R. Pokhrel, P. S. Gamage, M. Kalita, S. Wendel, B. Sears, D. Welideniya, Y. Liu, C. Turro, D. L. Troyer and S. H. Bossmann, *Langmuir*, 2013, **29**, 308.