Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Productive encounter: Molecularly imprinted nanoparticles prepared using magnetic templates

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Experimental section

Materials

Colloidal silica MEK-ST (D = 15-20 nm) was obtained from Nissan Chemical as a 30 wt % dispersion in methylethylketone. Ellman's Reagent, hydrazine, 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride, N-hydroxysuccinimide, $FeCl_3$, Fmoc-L-Phe-OH, tetraethyl orthosilicate (TEOS), 3-aminopropyldimethylethoxysilane (APDMS), 3-aminopropyltrimethoxysilane (APTMS), 4-cyano-4-(thiobenzoylthio)pentanoic acid) (CPDB), ethylene glycol dimethacrylate (EGDMA), methacrylic acid (MAA), glycerol, triethylamine and ethyl chloroformate were obtained from Sigma Aldrich (Steinheim, Germany). Concentrated hydrochloric acid, sodium hydroxide, dichloromethane (DCM), methanol (MeOH) and DMSO came from Applichem (Darmstadt, Germany) whereas $FeSO_4{\cdot}7H_2O$, DMF and toluene came from Acros Organics (Geel, Belgium). Acetonitrile (ACN) was obtained from Merck (Darmstadt, Germany). EGDMA and MAA were passed through a column of activated basic alumina to remove inhibitor and stored at - 20 °C before polymerization. L-and D- phenylalanine anilide (L-PA, D-PA) were synthesized following a previously described procedure.[1]

Apparatus and methods

HPLC: The HPLC measurements were carried out on Hewlett-Packard HP 1100 instruments (Agilent Technologies, Waldbronn, Germany).

Elemental analysis: Carbon, nitrogen and sulphur contents were determined by elemental analysis at the Department of Organic Chemistry, Johannes Guttenberg Universität Mainz using a Heraeus CHN-rapid analyser (Hanau, Germany).

FT-IR spectroscopy: This was performed using a TENSOR 27 (Bruker) in the attenuated total reflection mode (ATR).

TEM: The transmission electron micrographs were recorded using a energy filter transmission electron microscope (Philips CM200).

TGA: Thermogravimetric analysis was carried out using a TGAQ50 (TA instruments, Eschborn, Germany). The sample (10-15mg) was placed in a platinum pan, which is suspended in a sensitive balance together with the reference pan. The sample was then heated in a furnace with at a heating rate of 20 ^{0}C/min, under N_2 atmosphere.

Dynamic light scattering and Z-potential measurements

Particle sizes were measured with a Zetasizer Nano-ZS particle-size analyser from Malvern Instruments Ltd (UK). The obtained particles (2mg) were dispersed in isopropanol (SiNPs) or water (magNPs) to a concentration ~ 10 µg mL^{-1} and sonicated for 20 min, then an aliquot of the dispersion of NPs (1 mL) was filtered through a 0.45µm syringe filter and analysed by DLS at 25°C.

Energy Dispersive X-ray analysis: This was performed using a SEM Hitachi S 4500 at the Fachbereich, Technische Chemie, Universität Dortmund. It is an inelastic emission process and the mechanism of signal generation is the decay of excited states by photons. Each atom emits X-ray photons with specific/characteristic energy and the technique is used for qualitative analysis.

Synthesis of magnetic core nanoparticles (magNP) according to Ma et al.

A slightly modified version of the procedure reported by Ma et al was followed.[2] $FeSO_4{\cdot}7H_2O$ (6 g) and anhydrous $FeCl_3{\cdot}$(7 g) were dissolved in water (200 mL) under N_2 with vigorous stirring at 85 °C. An aqueous solution of 25% ammonia (15 mL) was then quickly added leading to a change of color from orange to black due to the precipitation of the magnetite nano-particles. The solution was stirred for 30 min at elevated temperature and then allowed to cool down to room temperature. Afterwards, the magnetic particles were collected using a magnet and washed with 3 x 50 mL water and in a final step with 50 mL 0.2 M NaCl solution. The particles were finally dried at 80°C under vacuum leading to 11 g of dry magNP.

Synthesis of magnetic core silica shell nanoparticles (magNP@SiO_2) according to Taylor et al.

Following the procedure reported by Taylor et al.[3], dry magNP (2 g) was dispersed in 50 mL water by sonication. The particles were collected by a magnet and subsequently dispersed in a 10% (v/v) aqueous solution of TEOS (230 mL). After addition of glycerol (200mL) the pH was adjusted to 4.6 with glacial acetic acid. The dispersion was then heated to 90°C under N_2 atmosphere and stirred using an over head stirrer for 2 hours. After washing with water (3x200 mL) and ethanol (3x100 mL), the particles were dried in a vacuum oven at 40°C leading to 2 g of dry magNP@SiO_2.

Aminofunctionalization of magNP@SiO_2 (magNP-NH_2)

magNP@SiO_2 (1 g) was dispersed in a solution (30 mL) of ethanol/water (1/1, v/v) by sonication for 30min. 3-aminopropyltrimethoxysilane (APTMS) (4 mL) was added to the dispersion under N_2 atmosphere and the dispersion stirred at 40 °C overnight. The dispersion was thereafter cooled to room temperature and the particles collected with a magnet and washed with ethanol, and three times with deionized water. Finally, the particles were dried under vacuum at 60°C leading to 1 g of dry magNP-NH_2. The presence of free amine groups on the particles was confirmed by the ninhydrine test (Ruhemann's purple).

Immobilization of L-phenylalanine on magNP-NH_2 (magNP-L-Phe)

Fmoc-Phe-OH (1.9 mg) was converted to the active ester by dissolving it in 10 mL phosphate buffer (50mM, pH 7.5) followed by addition of EDC (5 mM) and N-hydroxysuccinimide (10 mM). The reaction was allowed to proceed for 15 min followed by addition of 500 mg of magNP-NH_2. The dispersion was sonicated for 10 min and was thereafter incubated over night at room temperature. Fmoc deprotection was achieved by treating the particles in 20% piperidine in DMF (5 x 5 mL). The resulting fulvene-piperidine adduct was quantifed by measuring the absorption of the supernatants at 301 nm. This measurement was used to estimate the loading of L-Phe on the magnetic particles. In paralell, fluorescence of the supernatants was measured using an excitation wavelength of 300 nm and detecting the emission at 400 nm.

Synthesis of RAFT modified silica core particles (SiNP-RAFT)

A slightly modified version of the procedure reported by Li et al. was followed,[4] A suspension (25 mL) of colloidal silica nanoparticles (7.5 g, SiNP) in methyl ethyl ketone was added to a three-necked round-bottom flask together with 3-aminopropyldimethylethoxysilane (0.62 g, 3.7 mmol) and dried THF (40 mL). The reaction mixture was heated at 85 °C under N_2 protection overnight. Thereafter the mixture was cooled to room temperature and was then precipitated into a large amount of hexane (500 mL). The particles (SiNP-NH_2) were recovered by centrifugation at 3000 rpm for 15 min and redispersed in acetone (40 mL) followed by reprecipitation in hexane (300 mL). The aminofunctionalized particles were dispersed directly into THF (70 mL) for subsequent coupling of the RAFT agent.

CPDB (0.74 g, 2.65 mmol), ethylchloroformate (254 µL, 2.65 mmol) and triethylamine (TEA) (370 µL, 2.65 mmol) were dissolved in dry THF (50 mL) under nitrogen in a three-necked round bottom flask. The solution was purged with N_2 and cooled in an ethanol-liquid nitrogen bath at -78 ºC. After stirring for 40 min the temperature was adjusted to -10 °C and a suspension of amino functionalized silica core particles (7.18 g; 2.65 mmol of amino groups) in THF (65 mL) was added and the reaction allowed to proceed over night. Thereafter the particles were precipitated in hexane (500 mL) and collected by centrifugation (3500 rpm, 15 min). They were subsequently redispersed in acetone (80 mL), precipitated again in 300 mL of hexane, centrifugated at 3500 rpm during 15 min, and redispersed in 100 mL THF. The resulting nanoparticles (SiNP-RAFT) were dried under vacuum at room temperature (6.8 g, 91% yield).

Synthesis of core shell MIPs using soluble L-PA as template (SiNP-MIP1)

RAFT modified core particles (SiNP: 400mg corresponding to 33 µmol RAFT groups) were suspended in a prepolymerization mixture containing L-PA (12 mg, 50 µmol), MAA (34 µL, 404 µmol) and EGDMA (381 µL, 2020 µmol) dissolved in 15 mL of dry toluene. Nonimprinted particles were produced identically but leaving out L-PA (SiNP-NIP1). The polymerization mixture was subjected to three freeze-thaw cycles under nitrogen where after the initiator ABDV (2.75 mg, 11.0 µmol) was added. This corresponds to a molar ratio of RAFT/initiator of 3. Polymerization was initiated at 50°C and allowed to proceed for 22h. Template removal was then carried out by incubating the particles four times with MeOH 80%, Formic acid 15%, 5% H_2O (15 mL) leaving the suspension to incubate 1h followed by centrifugation at 5000 rpm. The final step washing was carried out with pure methanol (15 ml) for 30 min. Thereafter the particles were dried under vacuum at 40 ºC resulting in 730mg (87%) of SiNP-MIP1 and 750mg (89%) of SiNP-NIP1. All the supernatants were collected and analyzed by reverse phase HPLC for the presence of template (see below).

Synthesis of core shell MIPs using magNP-L-Phe as template (SiNP-MIP2)

A suspension of RAFT modified core particles (SiNP-RAFT: 100mg), MAA (8.6µL), EDMA (95µL) in 3 mL of dry toluene was added to magNP-L-Phe (50 mg), previously dispersed in toluene by sonication. The polymerization mixture was subjected to three freeze-thaw cycles under nitrogen where after the initiator ABDV (0.9mg) was added. This corresponds to a ratio of RAFT/initiator of 3. Polymerization was initiated at 50°C and allowed to proceed for 22h. After polymerization the particles were collected by magnet and washed by intermittent magnetic separation with toluene (3 mL) followed by five times with MeOH 80%, Formic acid 15%, 5% H_2O (3 mL). Each elution step was accompanied by sonication of the suspension for 15min. The supernatants containing the free SiNP-MIP2 were collected and pooled followed by isolation of the particles by centrifugation. In order to clean them from small traces of remaining magNP-L-Phe, they were washed by intermittent magnetic separation with 1) 1M HCl (3 mL) over night resulting in a color change from brownish to pink; 2) three times with water (3 mL) until pH was neutral and 3) MeCN (3 mL) and thereafter dried under vacuum at 40°C. This resulted 17 mg of dry particles (ca 9 % gravimetric yield).

Batch binding tests of NPs for their affinity for L-PA and D-PA.

Dry template free polymer (10 mg) was weighed into 10 separate HPLC vials followed by addition of solutions (1.0 mL) of D- or L-PA (1.0 mM) in acetonitrile (the test was downscaled for samples available in limited quantities). The vials were sealed and their contents allowed to equilibrate overnight at room temperature with gentle shaking. After 15 h incubation at room temperature the supernatants were sampled (30 µL) and the aliquots diluted in 270 µL water and transferred to HPLC vials for measurement of unbound solute concentration by reversed phase HPLC. The HPLC system consisted of an Agilent HPLC 1100 series instrument (Agilent) equipped with a UV-DAD detector and an autosampler. The column was a reversed phase (C18) column (Phenomenex Luna C-18, 150 × 4.6 mm), the mobile phase: MeOH/H2O: 62/38 (0.2% TFA) ,flow rate : 1.0 mL/min, the injection volume was 10 µL and the detection performed by UV absorbance at 265 nm. The resulting peak areas were used to calculate the amount of bound analyte on the polymer (in µmol/g of polymer). The binding results are averages of two independent experiments.

Aminolysis of RAFT groups of SiNP-MIP1 and SiNP-NIP1

To enable an easy quantification of the particles in solution, they were subjected to aminolysis by butylamine to give free thiol groups on the surface.[5] SiNP-MIP1 and SiNP-NIP1 (50 mg, corresponding to ca 4 µmol RAFT groups) were dissolved in THF (1 mL) containing 20 µL of aqueous $Na_2S_2O_4$. The reaction mixture was purged of oxygen by either bubbling with N_2 for 10 min or by three successive freeze-pump-thaw cycles. Butylamine (40 µL, 0.4 mmol) was then added, and the reaction was stirred for 3 h under N_2. Upon the addition of butylamine, an immediate color change from pink to yellow was observed. The resulting product was then washed with THF (2x) and methanol (1x) and was then collected by centrifugation and dried under vacuum at 40 ^{o}C (42 mg, 84 % mass yield).

Magnetic affinity enrichment of SiNP-MIP1 and rapid particle assay using Ellman's reagent

To a suspension of aminolyzed SiNP-MIP1 or SiNP-NIP1 (1 mg/mL) in MeCN (500 µL), magNP-L-Phe (50 mg) was added. The suspension was thereafter incubated under gentle shaking overnight. Thereafter, the magnetic fraction was isolated by magnet and the supernatant was collected. This procedure was followerd by three washing steps with MeCN (3 x 500µL) and three elution steps (3 x 500µL) with (80% MeOH; 15% formic acid; 5% H2O). The concentrations of SiNP-MIP1 or SiNP-NIP1 in each supernatant was determined using Ellman’s assay in a microplate formate. In short, this was performed by adding an aliquot of the sample (80µL) to sodium phosphate buffer (40 mM, 2 mM EDTA, pH 7.6, 138 µL) in a microplate. Finally, Ellman’s reagent (DTNB in DMSO (0.1M); 2µL) was added and the absorption at 412 nm was measured after 2 min incubation at room temperature.

1. C. Sulitzky, B. Rückert, A. J. Hall, F. Lanza, K. Unger and B. Sellergren, *Macromolecules*, 2002, **35**, 79-91.
2. Z.-Y. Ma, X.-Q. Liu, Y.-P. Guan and H.-Z. Liu, *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, 2006, **275**, 87–91.
3. J. I. Taylor, C. D. Hurst, M. J. Davies, N. Sachsinger and I. J. Bruce, *J Chromatogr A.* , 2000, **890**, 159-166.
4. C. Li, J. Han, C. Y. Ryu and B. C. Benicewicz, *Macromolecules*, 2006, **39**, 3175-3183.
5. D. L. Patton, M. Mullings, T. Fulghum and R. C. Advincula, *Macromolecules*, 2005, **38**, 8597-8602.

Table S1. Results from the characterisation of magnetic template particles and RAFT modified silica beads

Modified support[a]	Fe/Si (w/w)	%C	%N	%S	Ligand density[b] (mmol/g)	Area density[b] (µmol/m^2)	Coverage[c] (%)	Distance[d] (nm)
magNP-L-Phe	96/4	0.86	0.25	0.00	0.0016[e]	0.014[e]	0.2	11
SiNP-NH$_2$	-	2.10	0.81	0.00	0.37	2.00	25	0.9
SiNP-RAFT	0/100	3.33	0.69	0.56	0.080	0.44	6	1.9

a) The ligand immobilization was performed in two steps by consecutive coupling of 3-aminopropyldimethylethoxysilane (APDMS) (SiNP-NH$_2$) or 3-aminopropyltrimethoxysilane (APTMS) (magNP-L-Phe) and 4-cyanopentanoic acid dithiobenzoate (RAFT) or L-Phe on the indicated core beads as described in the experimental section. The silica core beads displayed a number average particle size of 25 nm with a polydispersity index of 0.245 and a specific surface area of 182 m^2/g whereas the magnetic core shell particles displayed an average particle size of 220nm with a polydispersity of PDI=0.245 and a specific surface area of 110 m^2/g.

b) With the exception of magNP-L-Phe, the area density (D) was calculated from the increase in carbon content after the corresponding coupling as: $D=m_X/(M_X S)$, where $m_X=X\%/(100-X\%M_w/M_X)$, M_w=molecular weight of immobilized silane (Step 1) or ligand (Step2), M_X=weight of carbon (X=C), nitrogen (X=N) or sulfur (X=S) per mole of immobilized species and S= surface area of the silica support. M_W and M_X were calculated assuming double substitution of the silane except for APDMS where only monosubstitution is possible.

c) The coverage (C) was calculated as: C=100xD/8, assuming a maximum silanol group density of 8µmol/m^2.

d) The average distance d_L (nm) between the coupled ligands assuming a random ligand distribution was calculated as: $d_L = \sqrt{\dfrac{10^{18}}{D \times 10^{-6} \times N}}$, where N is the Avogadros number.

e) The ligand density and area density were estimated from the release of fulvene-piperidine adduct upon deprotection of immobilized Fmoc-Phe.

Table S2. Results from the characterisation of imprinted and nonimprinted core shell and mesoporous beads

Polymer name[a]	%C	%N	%S	Mass loss[b] (%)	Conv.[c] (%)	d_{nom} [d] (nm)	d_{EA} [e] (nm)	d_{TGA}[f] (nm)
SiNP-MIP1	22.86	0.35	0.90	50	94	4.1	2.7	4.0
SiNP-NIP1	22.53	0.33	0.78	50	93	4.1	2.7	4.0
SiNP-MIP2	20.50	0.32	0.43	43	82	4.1	2.4	3.2

a) See experimental section for details.

b) Mass loss by thermal gravimetric analysis (TGA).

c) Gravimetric conversion: Conversion=mass loss (TGA)/mass of monomer feed.

d) Shell (film) thickness calculated assuming a homogenous liquid monomer film based on monomer feed (d_{nom}=nominal thickness), elemental analysis (d_{EA}) or mass loss (d_{TGA}) data.

The shell thickness was calculated according to (1)

1) $$d = \frac{D_{cs} - D_c}{2}$$

where D_{cs} and D_c are the average diameters of the core-shell and the core particles respectively. D_c was assumed equal to the number average particle size derived from DLS i.e. D_c=25nm, whereas D_{cs} was obtained from the average volume of the core-shell particles (V_{cs}) according to (2):

2) $$D_{cs} = \sqrt[3]{\frac{6 \times V_{cs}}{\pi}}$$

where V_{cs} in turn is the sum of the core (V_c) and shell (V_s) volume (3):

3) $$V_{cs} = V_c + V_s$$

V_c and V_s were in turn obtained from D_c and the total monomer volume (V_m) expressed in cc/g according to (4) and (5):

4) $$V_c = \frac{\pi \times D_c^3}{6}$$

5) $$V_s = \frac{10^{21} \times V_m}{N}$$

, with N being equal to the number of particles calculated from D_c and the specific surface area of the core particles (S_c=182 m^2/g) as (6):

6) $$N = \frac{10^{18} \times S_c}{\pi \times D_c^2}$$

e) The shell thickness based on elemental analysis was calculated as outlined in d) but deriving the total monomer volume (V_m) from the carbon content (%C), average monomer density (ρ) assumed equal to one and grafting density (%G) as follows:

7) $$V_m = \frac{\%G}{\rho(100 - \%G)}$$

where %G was calculated according to (8) from the nominal carbon content of the grafted polymer ($\%C_{pol}$) and the found carbon content (%C).

8) $$\%G = 100 \times \frac{\%C}{\%C_{pol}}$$

f) The shell thickness based on TGA mass loss was calculated assuming %G in equation (7) to be equal to the mass loss in %.

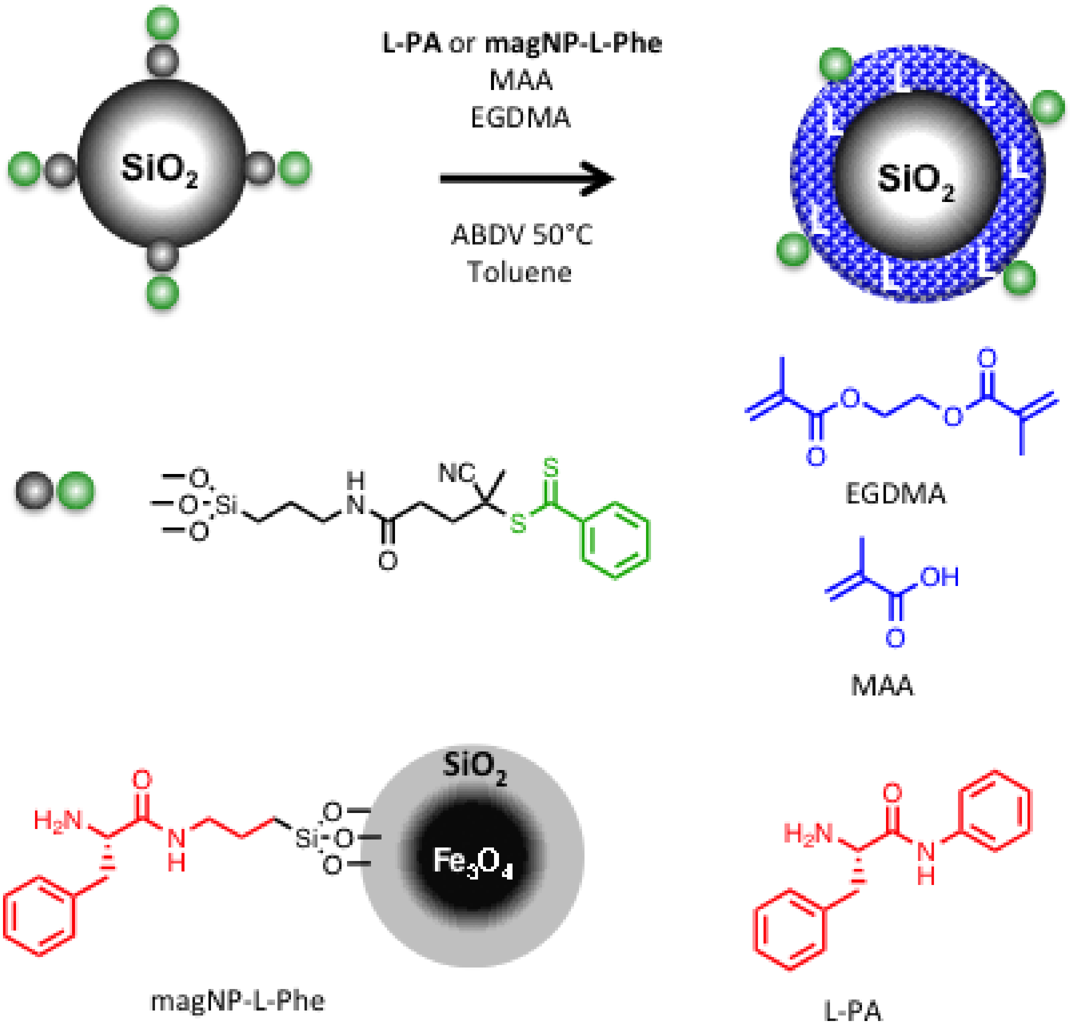
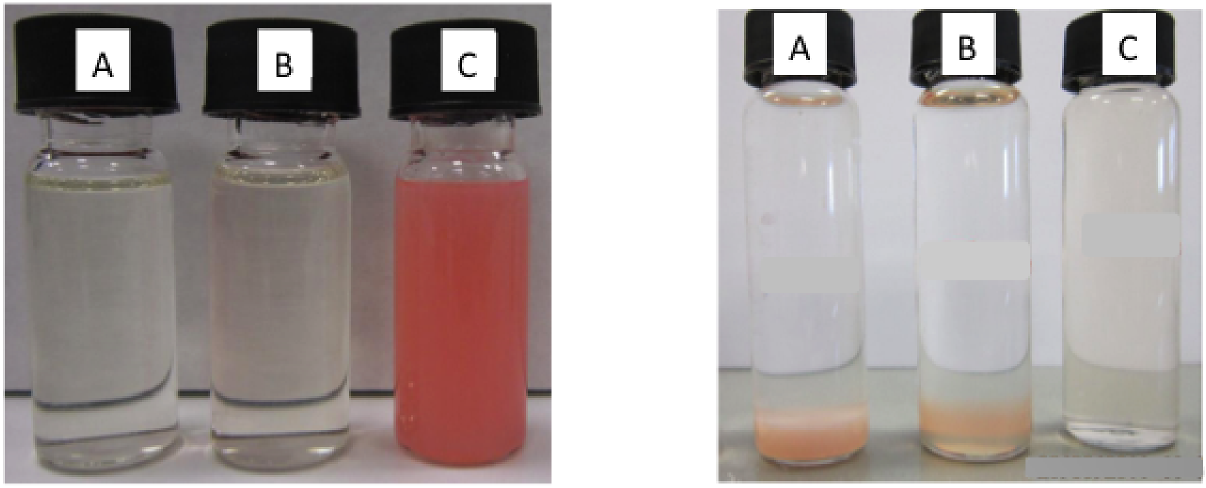
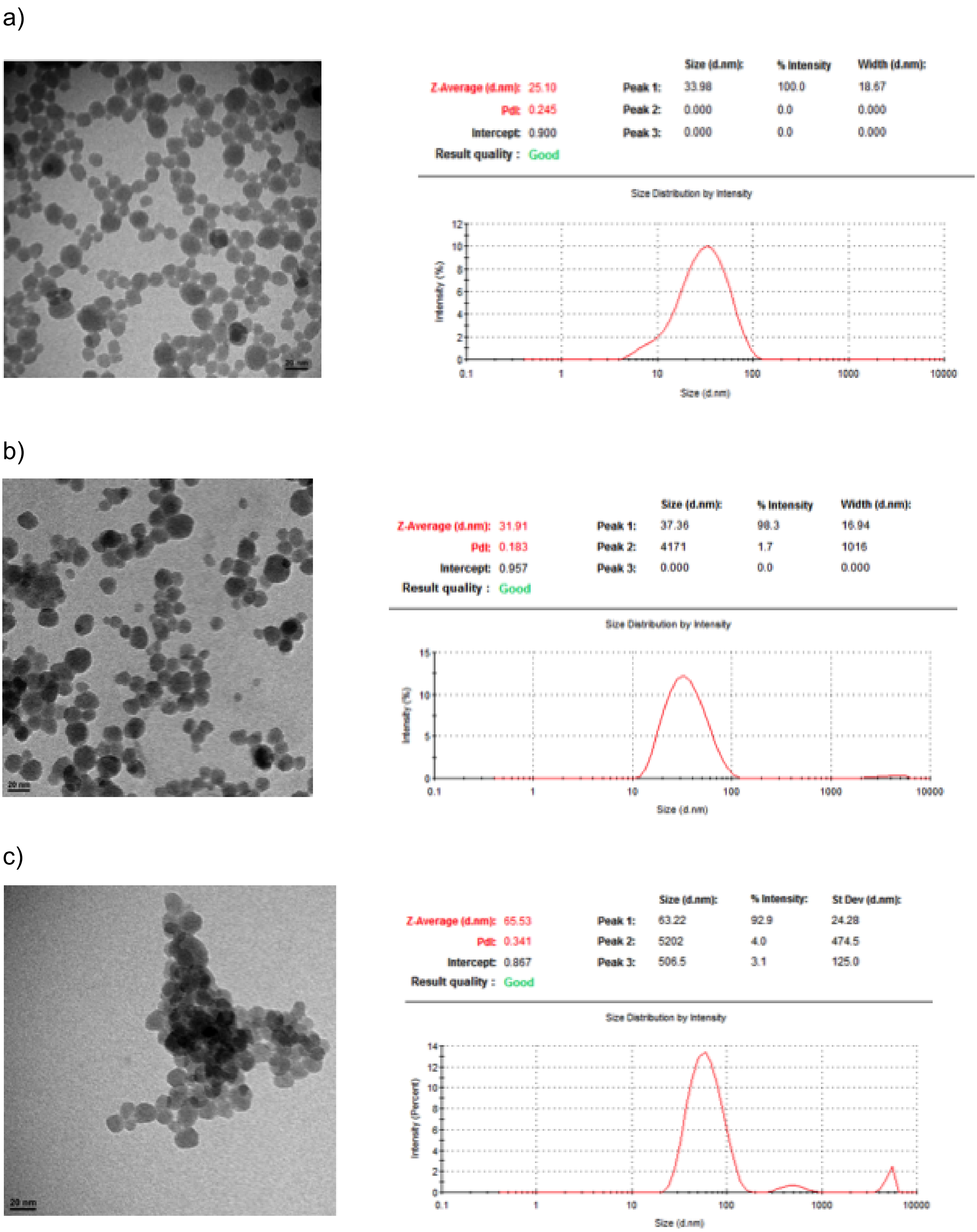


Figure S1. Procedure used to synthesise silica core-MIP shell nanoparticles.



a) b)

Figure S2**.** a) SiNP (A), SiNP-NH_2 (B) and SiNP-RAFT (C) dispersed in THF. b) SiNP-RAFT dispersed in acetone (A), toluene (B) and methanol (C).



a)

			Size (d.nm):	% Intensity	Width (d.nm):
Z-Average (d.nm):	25.10	Peak 1:	33.98	100.0	18.67
PdI:	0.245	Peak 2:	0.000	0.0	0.000
Intercept:	0.900	Peak 3:	0.000	0.0	0.000
Result quality :	Good				

b)

			Size (d.nm):	% Intensity	Width (d.nm):
Z-Average (d.nm):	31.91	Peak 1:	37.36	98.3	16.94
PdI:	0.183	Peak 2:	4171	1.7	1016
Intercept:	0.957	Peak 3:	0.000	0.0	0.000
Result quality :	Good				

c)

			Size (d.nm):	% Intensity:	St Dev (d.nm):
Z-Average (d.nm):	65.53	Peak 1:	63.22	92.9	24.28
PdI:	0.341	Peak 2:	5202	4.0	474.5
Intercept:	0.867	Peak 3:	506.5	3.1	125.0
Result quality :	Good				

c)

Figure S3. DLS (isopropanol) results and TEM images of SiNP at different stages of the surface modifications. a) SiNP, b) SiNP-NH_2 and c) SiNP-RAFT. Scale bar = 20nm.

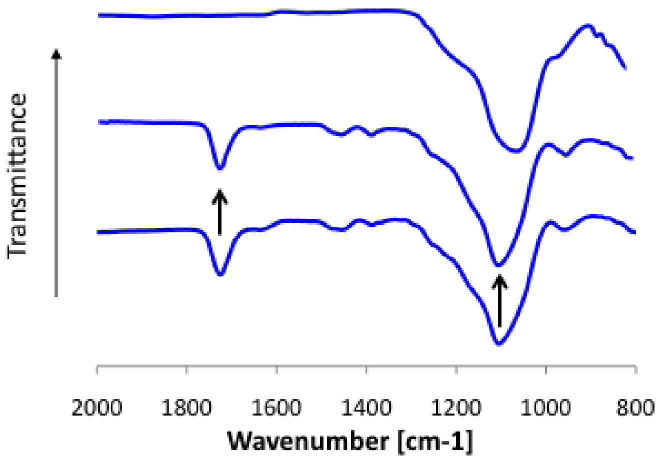
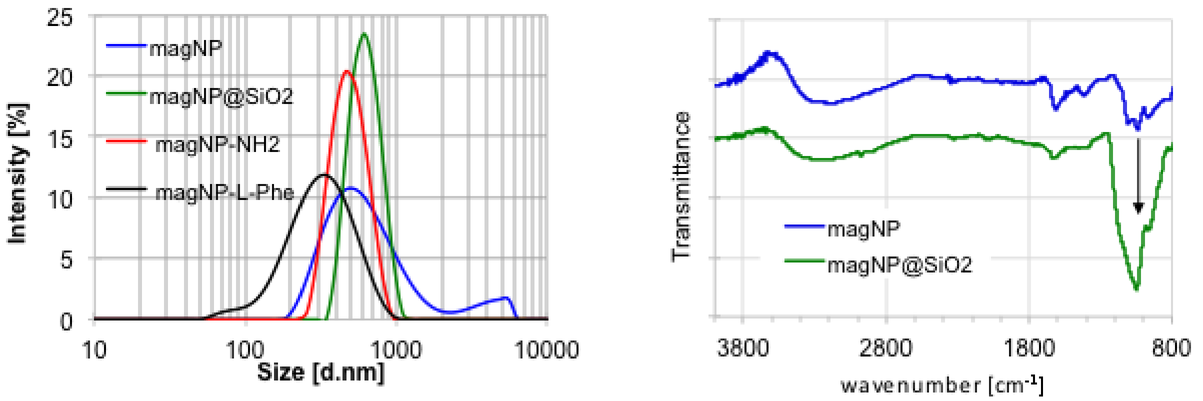


Figure S4. FTIR spectra (ATR) of from top to bottom: SiNP-RAFT, SiNP-MIP1, SiNP-MIP2. The bands corresponding to the C=O (1700 cm^{-1}) and Si-O-Si (1100 cm-1) vibrations have been indicated.



a.

b.

Figure S5. Particle size distribution (a) and FTIR (ATR) spectra (b) of magNP (blue line), magNP@SiO$_2$ (green line), magNP-NH$_2$ (red line) and magNP-L-Phe (black line). The Fe-OFe band of the core is accompanied by the Si-O-Si band at ca 1100 cm^{-1} in the IR-spectra of the magnetite particles after the application of the silica shell.

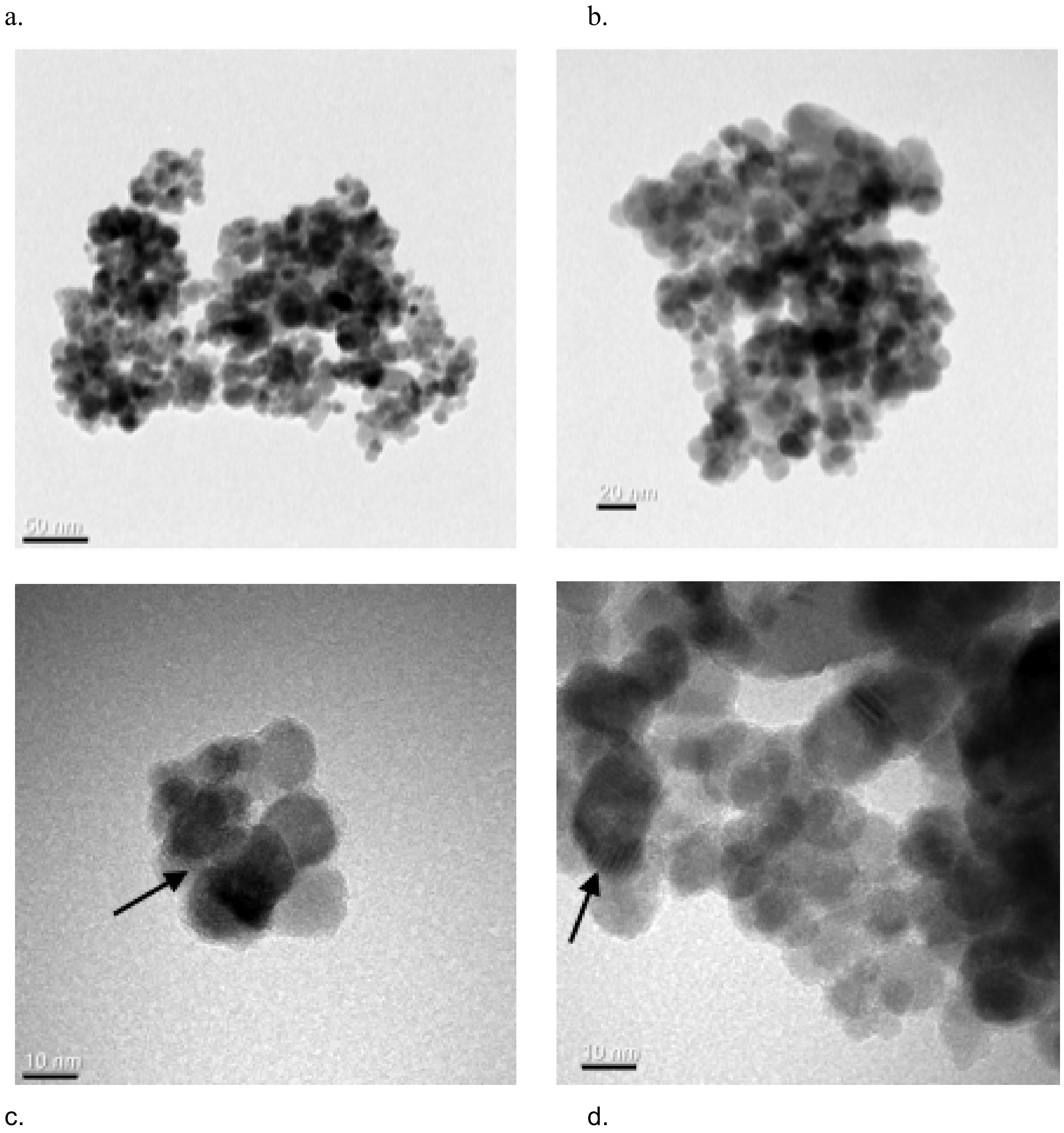
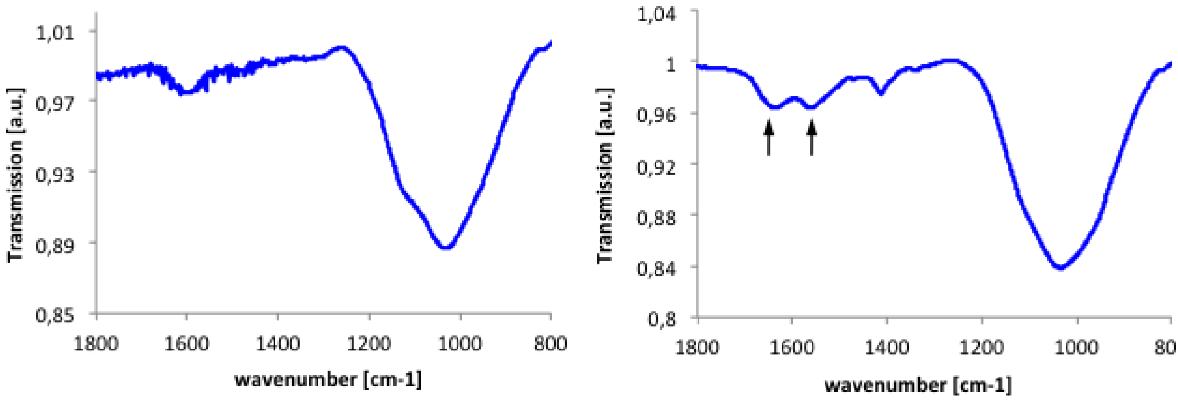


Figure S6. TEM-Pictures of magNP-L-Phe in water. The samples were sonicated in Millipore water and then a drop was applied on the graphene-support of the sample holder, left to dry, and subsequently analyzed by TEM. In (c) and (d), the lattice plain is indicated by arrows. The scale bar is 50 nm in the case of (a) 20 nm for (b) and 10 nm in the case of (c) and (d).



a) b)

Figure S7. FTIR (ATR) of aminofunctionalized magNP@SiO2 prior to (a) and after (b) coupling of Fmoc-L-Phe. In (b) the amide I and II bands have been indicated by arrows.

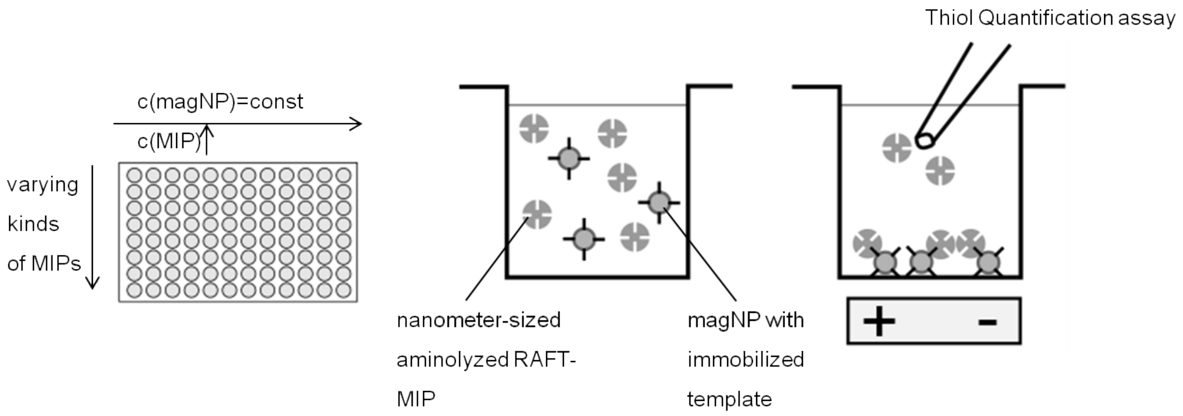


Figure S8. Principle of a binding assay between magnetic nanoparticles and aminolyzed RAFT-MIPs.

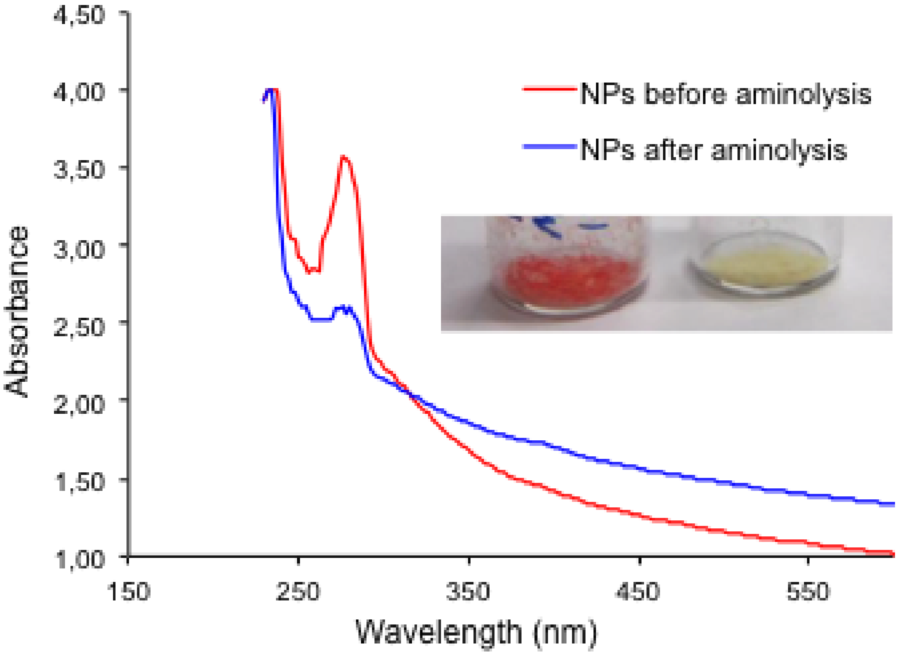


Figure S9. UV spectra of RAFT modified particles prior to (red trace) and after (blue trace) aminolysis. The inset shows the particle appearance prior to (left vial) and after (right vial) aminolysis.

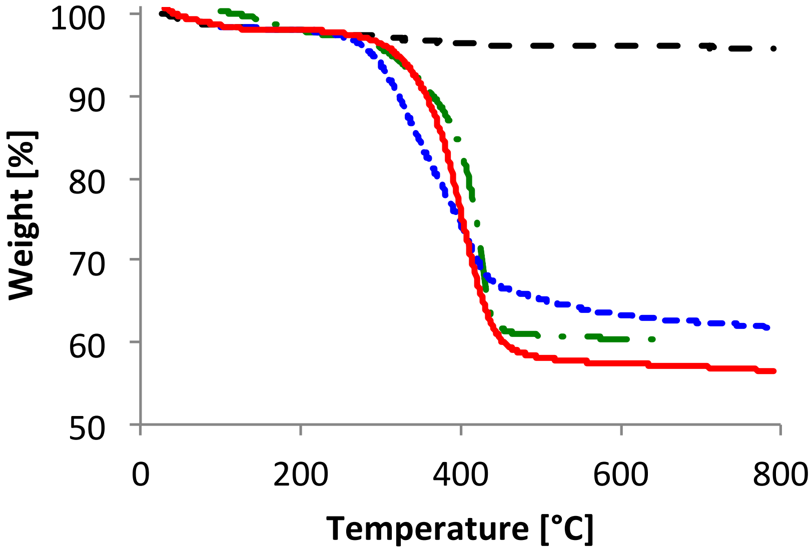
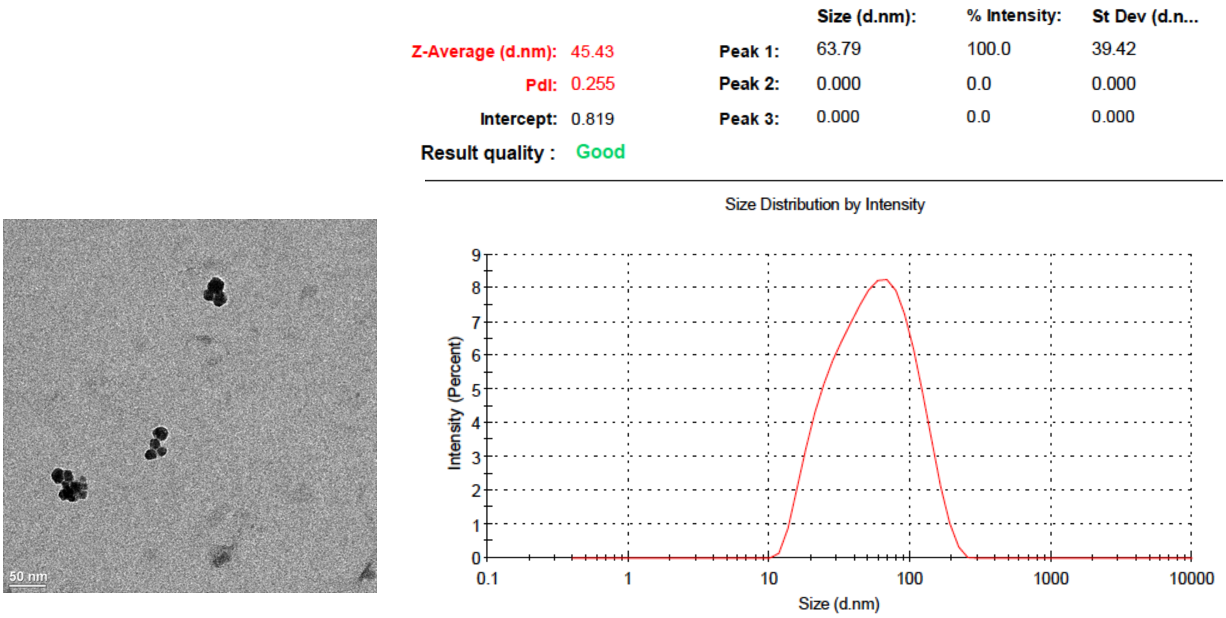


Figure S10. Thermal gravimetric analysis of magNP-L-Phe (black dashed line), crude magNP-L-Phe/SiNP-MIP2 prior to washing (green dashed line), magNP-L-Phe/SiNP-MIP2 after washing (blue dotted line) and released SiNP-MIP2 (red solid line).



Z-Average (d.nm): 45.43

PdI: 0.255

Intercept: 0.819

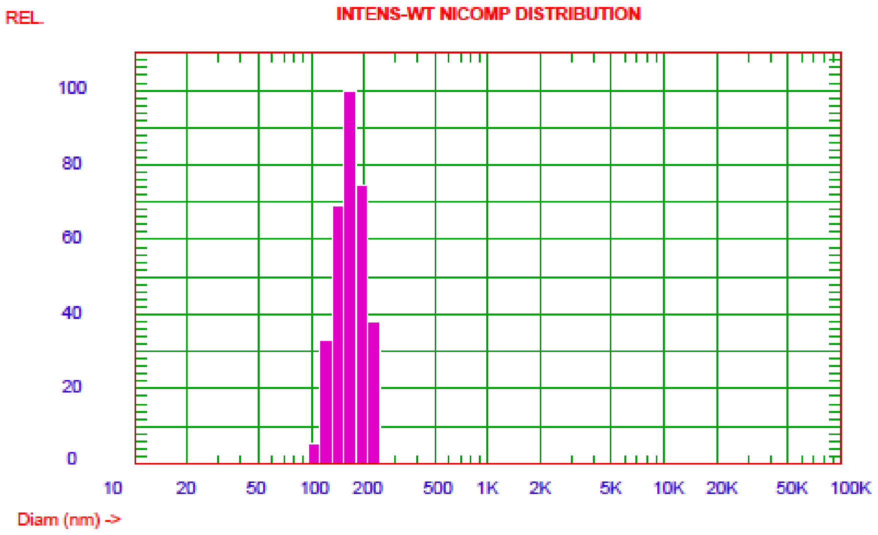
Result quality : Good

	Size (d.nm):	% Intensity:	St Dev (d.n...
Peak 1:	63.79	100.0	39.42
Peak 2:	0.000	0.0	0.000
Peak 3:	0.000	0.0	0.000

Figure S11. DLS (isopropanol) results and TEM image of SiNP-MIP2. Scale bar = 50nm.

Study of particle aggregation in a medium mimicking the prepolymerization solution

We decided to compare particles dispersed in isopropanol and toluene containing acetic acid. The latter solvent was used in order to mimic the solvent conditions prevailing during polymerization, with acetic acid acting as a mimic of the acidic monomer methacrylic acid. Both magNP-L-Phe and SiNP-RAFT formed stable dispersions with no evidence of time dependent changes of the average particle size during 15 repeat measurements with 2min interval. SiNP-RAFT is more prone to aggregation which we again observed in both solvents (see Figure S12 A, D). This was particularly pronounced in toluene resulting in three populations with size averages of ca 15, 40 and 800nm. Considering magNP-L-Phe the smaller size measured in isopropanol (201nm) and toluene (242nm) versus water (281nm) probably reflects a weaker solvation in these solvents although toluene (+acetic acid) seemed to result in partial break up of aggregates with the appearance of a small population of particles smaller than 20nm. We then performed DLS on a mixture composed of roughly equal weights of the two NPs in both solvents. In both isopropanol and toluene, the position of the major peak indicated the formation of slightly larger aggregates compared to the particles alone. Hence in isopropanol the mixture resulted in a peak at 229nm (a shift of ca 28nm versus magNP-L-Phe alone) whereas in toluene the main peak was found at 308nm (a shift of ca 62nm versus magNP-L-Phe alone). In the latter case, the peak at 49nm agrees with the size of the smaller aggregates of SiNP-RAFT (Figure S12D below). Interestingly the large 800nm aggregates detected in SiNP-RAFT in toluene was not to be found in the particle mixture experiment. All in all, these observations support the proposed model where at least a portion of SiNP-RAFT aggregates with magNP-L-Phe.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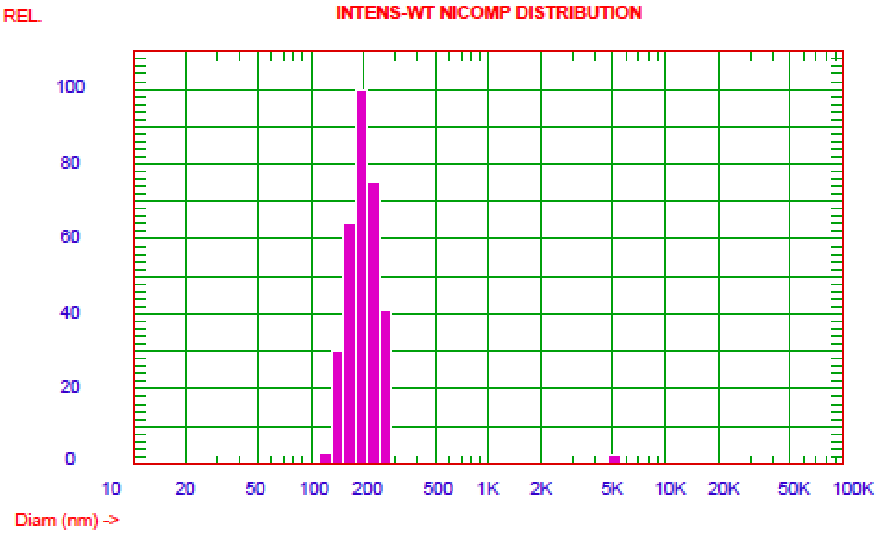
A)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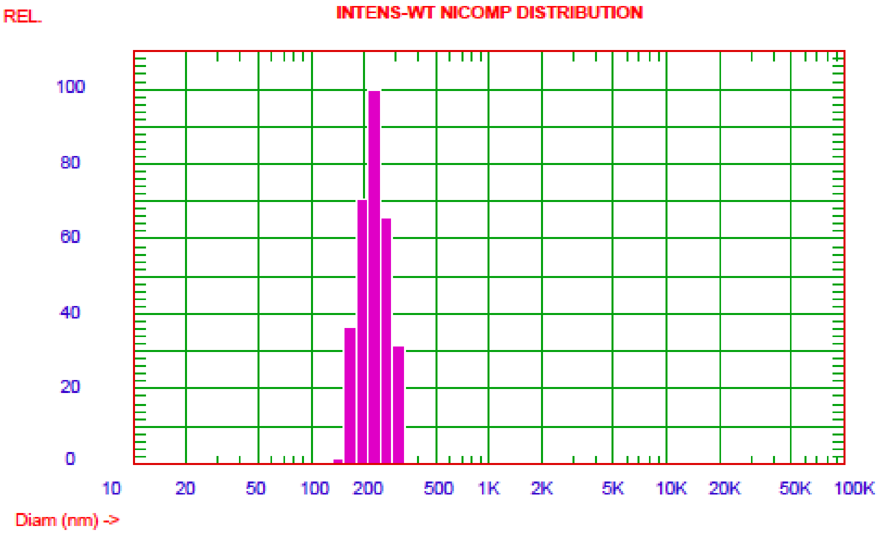
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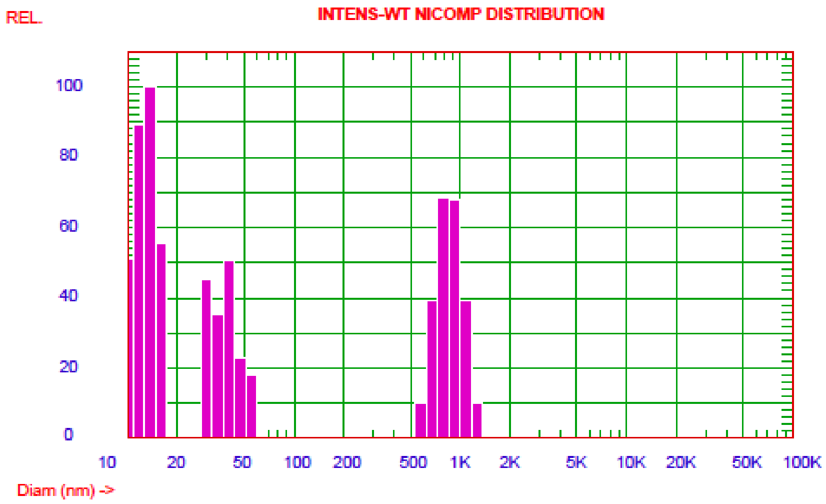
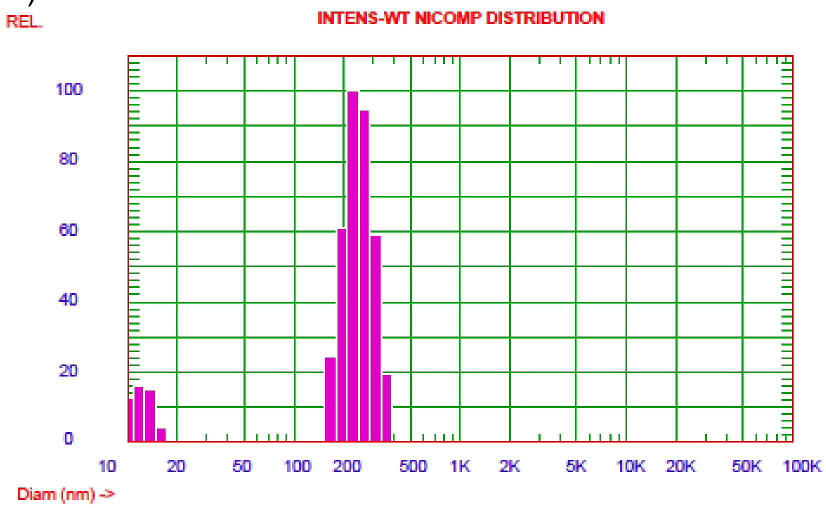
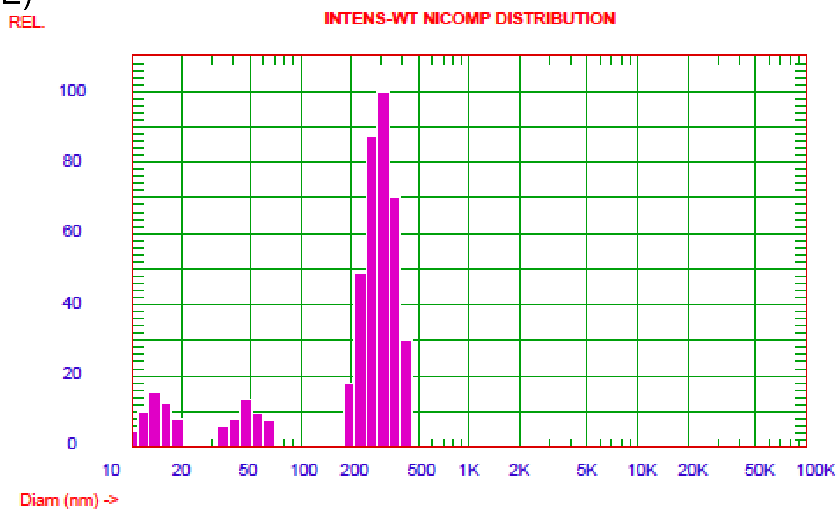
C)



D)



E)



F)

Figure S12. DLS results of dispersions of SiNP-RAFT (A, D), magNP-L-Phe (B, E) and a mixture of SiNP-RAFT and magNP-L-Phe (C, F) in i-propanol (A-C) or toluene (+ 3% (w/w) acetic acid) (D-F). The peak maxima were as follows: A: 170nm, B: 201nm, C: 229nm, D: 15nm, 40nm, 800nm, E: 14nm, 242nm, F: 14nm, 49nm, 308nm.