

SUPPORTING INFORMATION

Being Two is Better than One — Catalytic Reductions with Dendrimer Encapsulated Copper- and Copper-Cobalt - Subnanoparticles

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1. General experimental details

Unless otherwise stated, all starting materials were obtained from commercial suppliers and used as received. Solvents were HPLC grade and used as received. ¹H-NMR spectra were recorded on a 500 MHz NMR (Bruker) apparatus. Chemical shifts are reported in ppm downfield of TMS (tetramethylsilane) using the resonance of the deuterated solvent as internal standard (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet).

Gas chromatography-mass spectrometry (GC-MS) was performed on an Agilent 6890 A (G1530A) gas chromatograph coupled with an Agilent mass selective detector 5973 Network. The temperature program was 1 min at 100 °C, then ramp of 50 K/min to 300 °C, then 10 min at 300 °C.

Scanning Transmission Electron Microscopy (STEM) was performed using a FEI 80-300 Titan microscope with correction for spherical aberration (Cs) of the condenser lens system. The studies were carried out at 300 kV acceleration voltage in the scanning transmission electron microscopy (STEM) mode. Images were recorded using annular dark field STEM and the composition was investigated using energy dispersive x-ray spectroscopy and electron energy loss spectroscopy.

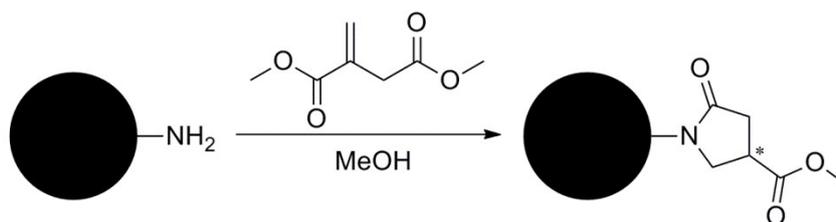
The effective hydrodynamic radii in size average by number was measured by DLS on a Zetasizer Nano ZS instrument. The standard deviations of 10 individual measurements (each 14 runs) are indicated.

UV/Vis spectra were obtained on a Varian Cary 50 Bio UV/Visible spectrophotometer, scanning with a scan rate of 600 nm/min. The spectra were corrected by subtraction of a reference solvent spectrum.

For HPLC-MS analysis a Dionex Ultimate 300 PLC connected to an ESI-MS (MSQ Plus Mass Spectrometer, Dionex) was used, all measurements were performed on a Phenomenex Kinetex 5 μ m C18 100 Å column (50 x 2.1 mm) thermostated to 42 °C with a column oven. As eluent system water and acetonitrile (containing 0.1 % (v/v) formic acid) was used, starting with 5 % acetonitrile until 0.5 min, then gradient from 5 % to 35 % for 0.7 min, then gradient 35 % to 100 % over 3 min, finally plateau of 100 % acetonitrile. The flow rate was set to 0.5 mL/min (300 bar). Absorption was followed using 215 nm as wavelength. The injection volume was 2 μ l, containing approximately 1 mg/mL dissolved in 5 % acetonitrile and 95 % water.

2. Preparation of dendrimers:

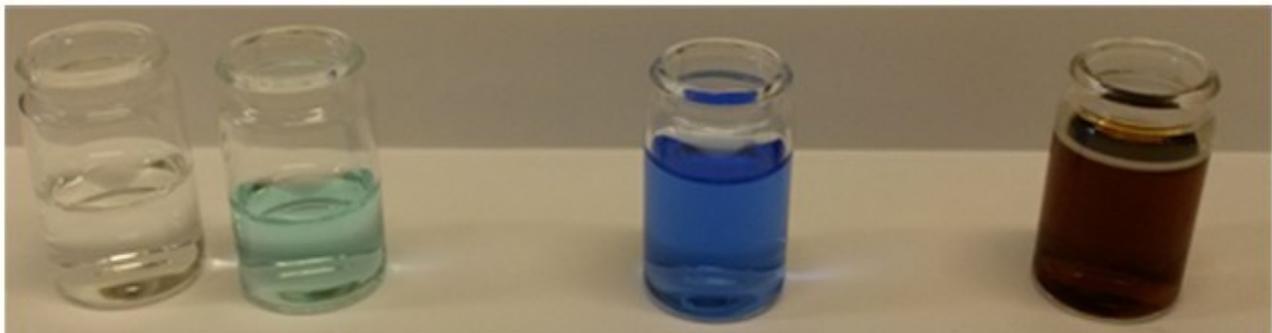
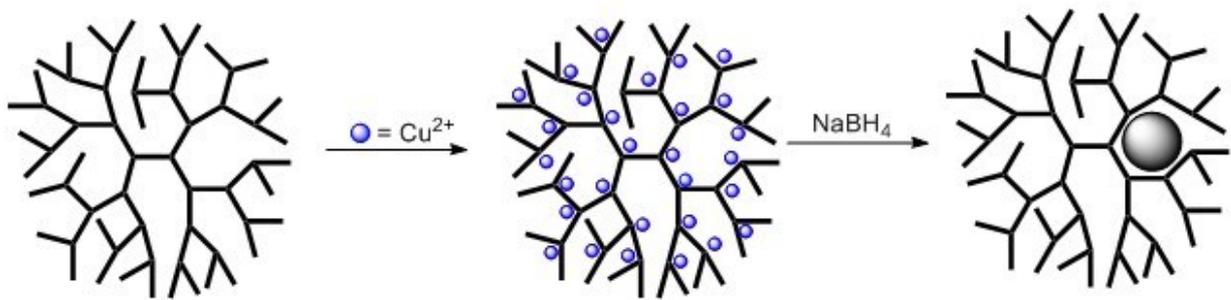
Amino-terminated PAMAM-dendrimers (G1-G5) synthesized according to [1] were functionalized with the 4-carbomethoxy pyrrolidone surface group by reaction with dimethyl itaconate in methanol.^[2,3] A 15 w/w% solution of dendrimer was added slowly to a 70 w/w% solution of dimethyl itaconate in methanol (1.05 equivalents per amino functionality), while cooling with a water/ice bath. Upon completion of the addition the reaction mixture was left in the cooling bath to slowly heat to ambient temperature (Scheme 1).



Scheme S1 Conversion of the amine functionality to pyrrolidone.

The reaction was stirred until the Kaiser-test (ninhydrin in ethanol) was negative, usually 2-4 days depending on the generation. The functionalized dendrimer was isolated by removing the methanol, dissolving the dendrimer in a minimum amount of water and extracted multiple times with ether until any remaining dimethyl itaconate had been removed. The aqueous phase was freeze-dried to give the pure pyrrolidone-terminated PAMAM-dendrimers as white, very hygroscopic solids. Dendrimers were characterized by ¹H-, ¹³C-NMR and HPLC analysis.

3. Preparation of nanoparticles and catalytic hydrogenation procedure:



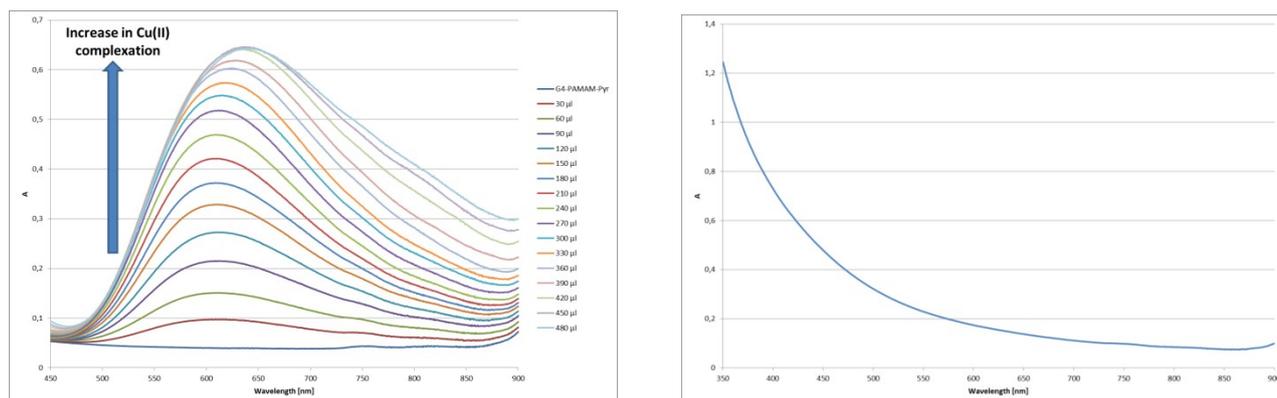
G4-Pyr

CuSO₄

Cu(II)-Dendrimer-Complex

Cu₁₈@G4-Pyr





Scheme S2 The complexation of the metal salt to the dendrimer can easily be seen by the naked eye, as demonstrated above, after reduction with NaBH_4 a change of color to brown, due to the plasmon resonance of the nanoparticles.

Cu₁₂@G3: 66 mg (6 µmol) of G3-PAMAM-Pyrrolidone dendrimer were dissolved in 5.9 mL of methanol and 1.8 mL of a 0.04 M CuSO_4 (72 µmol) solution was added. After 15 minutes complexation time the complex was reduced with 10 mg NaBH_4 (270 µmol) to Cu₁₂@G3. Any not dendrimer stabilized particles were removed by centrifugation (5min, 4000 rpm).

Cu₁₈@G4: 134 mg (6 µmol) of G4-PAMAM-Pyrrolidone dendrimer were dissolved in 5 mL of methanol and 2.7 mL of a 0.04 M CuSO_4 (108 µmol) solution was added. After 15 minutes complexation time the complex was reduced with 10 mg NaBH_4 (270 µmol) to Cu₁₈@G4. Any not dendrimer stabilized particles were removed by centrifugation (5min, 4000 rpm).

Cu₃₂@G4: 270 mg (6 µmol) of G5-PAMAM-Pyrrolidone dendrimer were dissolved in 2.9 mL of methanol and 4.8 mL of a 0.04 M CuSO_4 (192 µmol) solution was added. After 15 minutes complexation time the complex was reduced with 10 mg NaBH_4 (270 µmol) to Cu₃₂@G5. Any not dendrimer stabilized particles were removed by centrifugation (5min, 4000 rpm).

Procedure for Cu_m@G_n catalyzed hydrogenations: The Cu_m@G_n as catalyst did not require inert atmosphere during the reaction. 1.5 mmol of the starting material was dissolved in 15 mL methanol and 25 mg (0.45 eq) NaBH_4 was added, followed by the addition of a methanol solution containing 0.4 mol% of Cu_m@G_n. Additional portions of NaBH_4 (25 mg, 0.45 eq.) were added in the time interval of 5 minutes. The reactions were monitored using GC-MS and ¹H-NMR. The monitoring-samples were prepared by quenching a 200 µL samples of the reaction mixture with 2M H_2SO_4 and extraction with CDCl_3 for ¹H-NMR and GC-MS analysis.

Cu₆Co₆@G3: 66 mg (6 μmol) of G3-PAMAM-Pyrrolidone dendrimer were dissolved in 5.9 mL of methanol and 1.8 mL of a 0.02 M CuSO₄ and 0.02 M CoCl₂ (36 μmol CuSO₄, 36 μmol CoCl₂) solution was added. After 15 minutes complexation time the complex was reduced with 10 mg NaBH₄ (270 μmol) to Cu₆Co₆@G3. Any not dendrimer stabilized particles were removed by centrifugation (5min, 4000 rpm).

Cu₉Co₉@G4: 134 mg (6 μmol) of G4-PAMAM-Pyrrolidone dendrimer were dissolved in 5 mL of methanol and 2.7 mL of a 0.02 M CuSO₄ and 0.02 M CoCl₂ (54 μmol CuSO₄, 54 μmol CoCl₂) solution was added. After 15 minutes complexation time the complex was reduced with 10 mg NaBH₄ (270 μmol) to Cu₉Co₉@G4. Any not dendrimer stabilized particles were removed by centrifugation (5min, 4000 rpm).

Cu₁₆Co₁₆@G5: 270 mg (6 μmol) of G5-PAMAM-Pyrrolidone dendrimer were dissolved in 2.9 mL of methanol and 4.8 mL of a 0.02 M CuSO₄ and 0.02 M CoCl₂ (96 μmol CuSO₄, 96 μmol CoCl₂) solution was added. After 15 minutes complexation time the complex was reduced with 10 mg NaBH₄ (270 μmol) to Cu₁₆Co₁₆@G5. Any not dendrimer stabilized particles were removed by centrifugation (5min, 4000 rpm).

Procedure for Cu_mCo_m@Gn catalyzed hydrogenations: All reactions were carried out under inert nitrogen atmosphere, ambient pressure and room temperature. 1.5 mmol of the starting material was dissolved in 15 mL methanol and 40 mg (1.06 eq.) NaBH₄ was added, followed by the addition of a methanol solution containing 0.4 mol% of Cu_mCo_m@Gn. Additional portions of NaBH₄ (40 mg, 1.06 eq.) were added in the time interval of 5 minutes. The reactions were monitored using GC-MS and ¹H-NMR. The monitoring-samples were prepared by quenching a 200 μL samples of the reaction mixture with 2M H₂SO₄ and extraction with CDCl₃ for ¹H-NMR and GC-MS analysis.

4. Dynamic light scattering

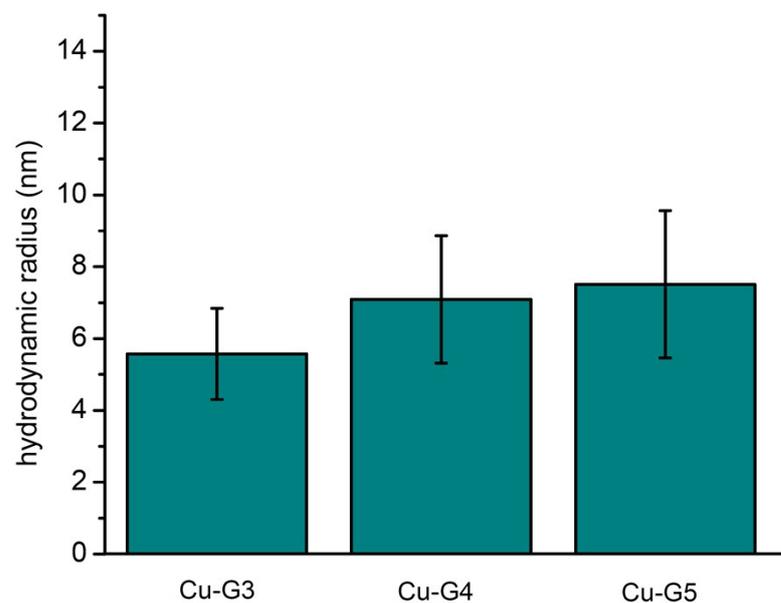
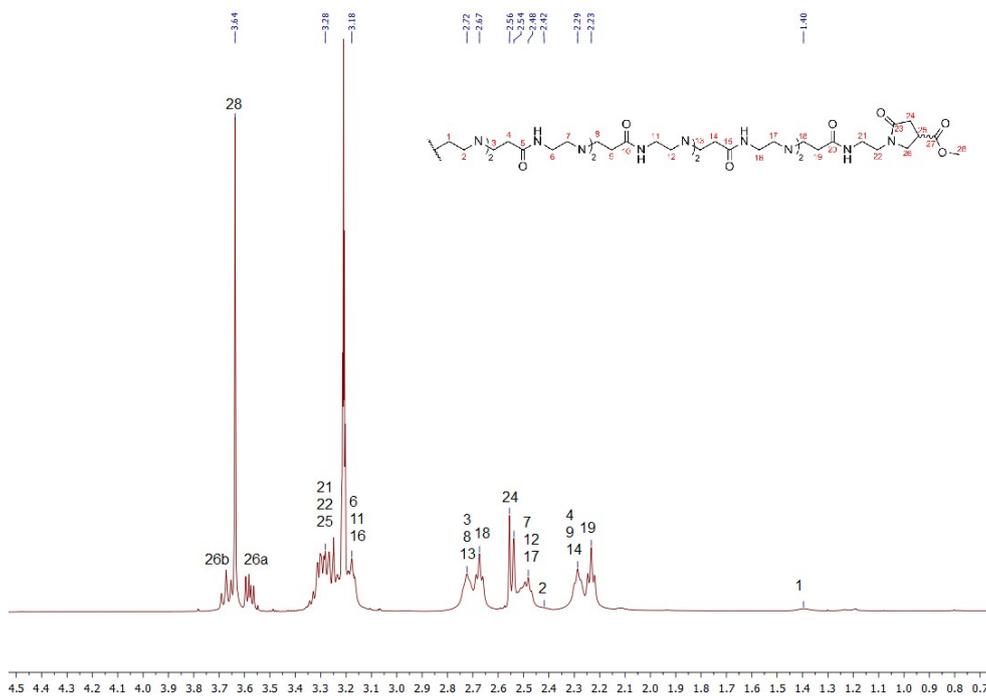


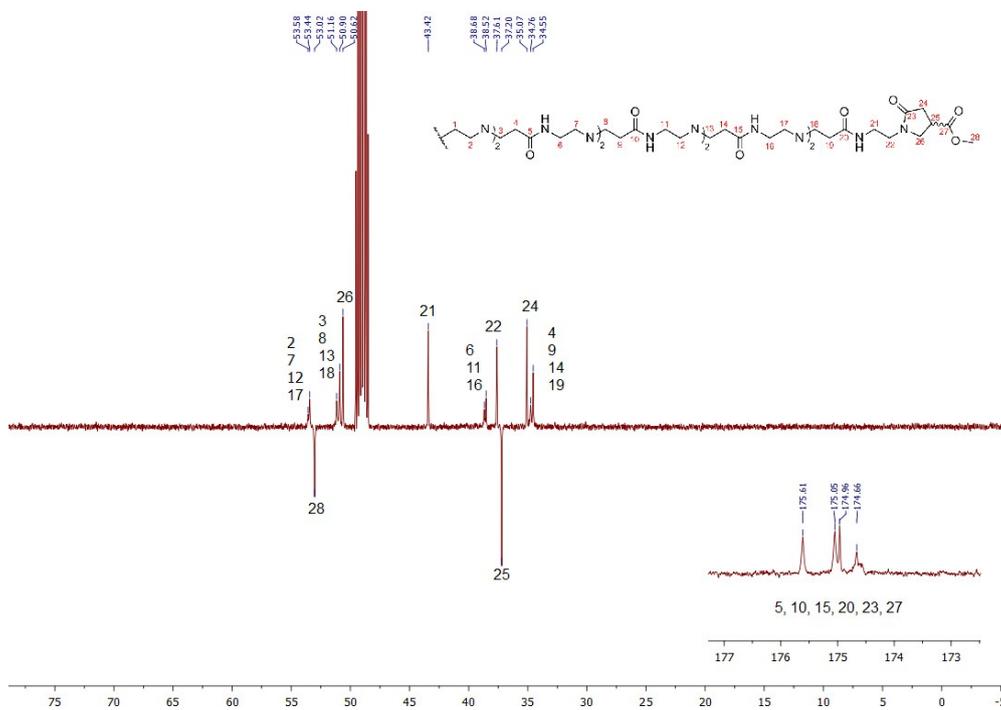
Figure S1 The effective hydrodynamic radii in size average by number is measured by DLS. The standard deviations of 10 individual measurements (each 14 runs) are indicated. G3 is 5.57 nm, G4 is 7.09 nm and G5 7.51 nm.

5. Dendrimer characterization

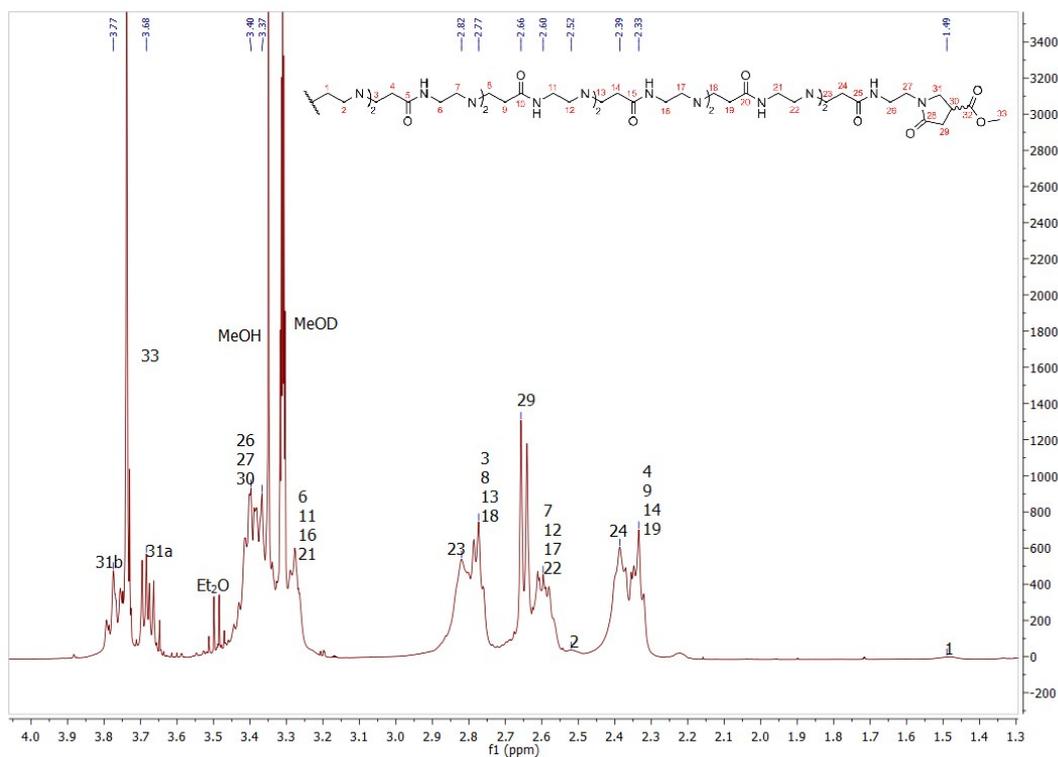
¹H-NMR G3-Pyrrolidone:



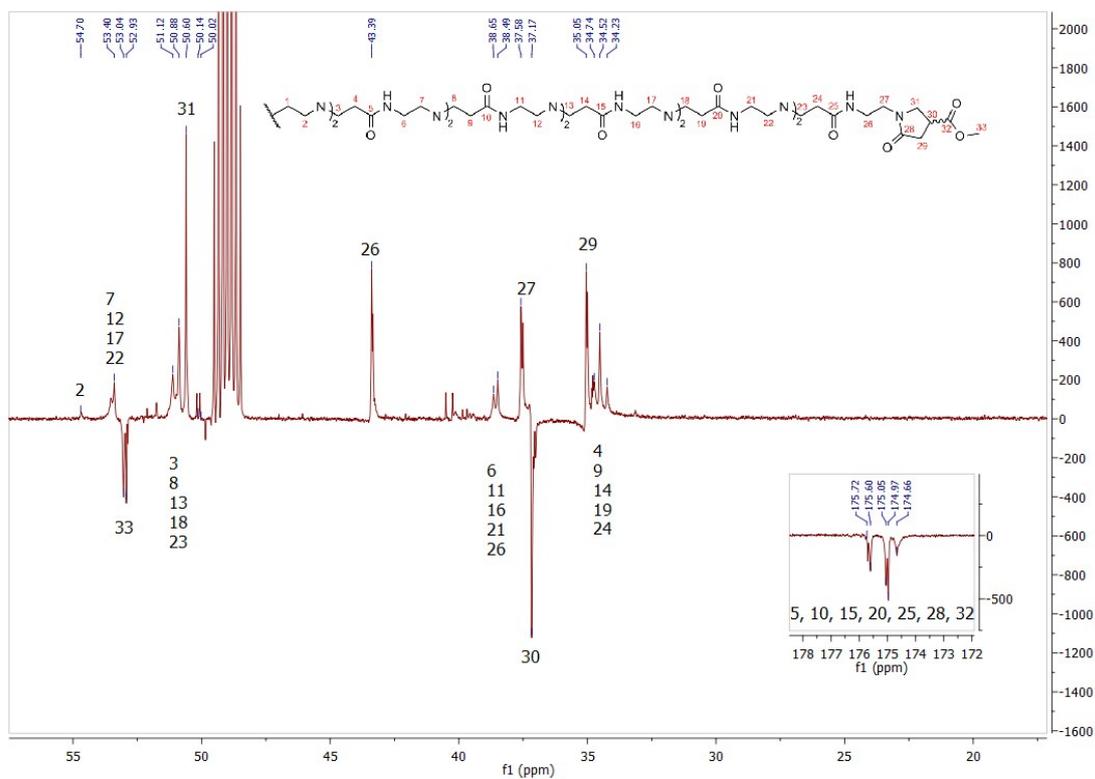
¹³C-NMR G3-Pyrrolidone:



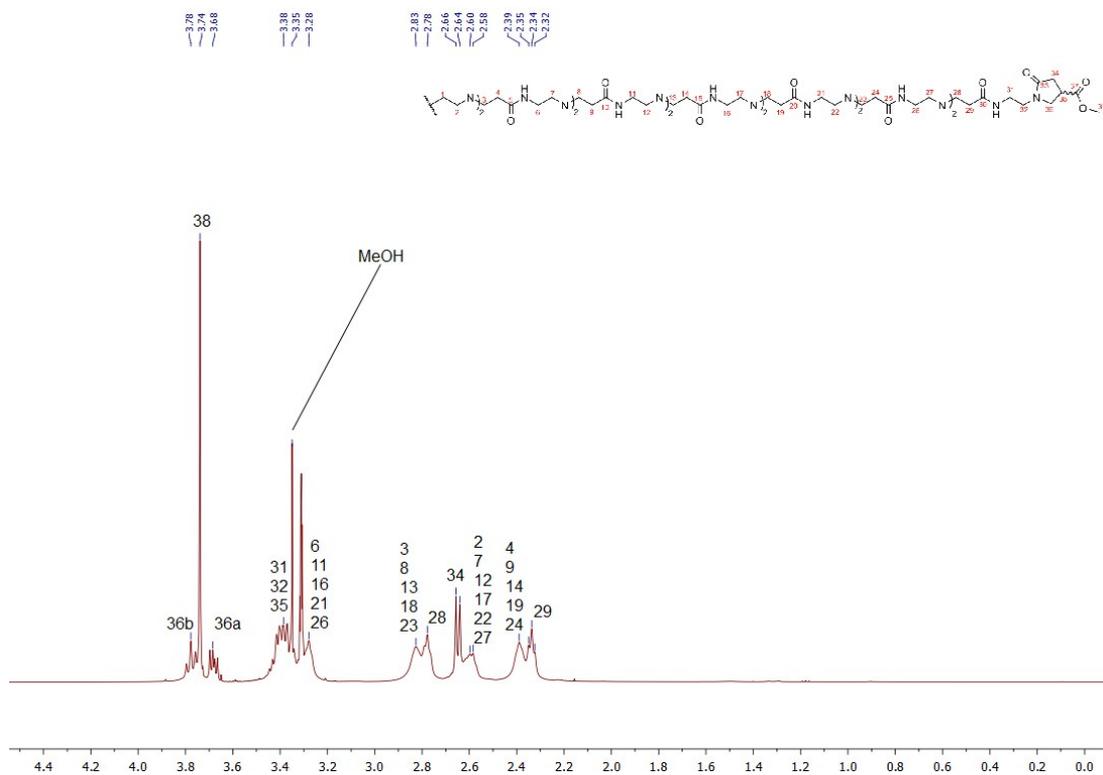
¹H-NMR G4-Pyrrolidone:



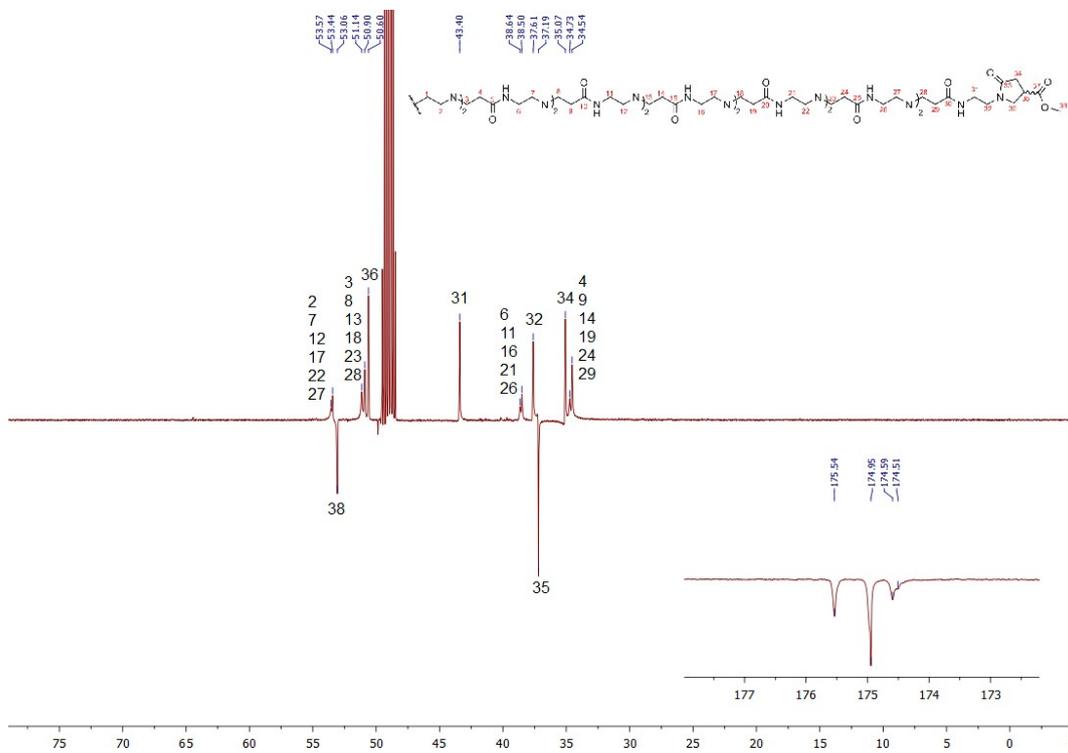
¹³C-NMR G4-Pyrrolidone:



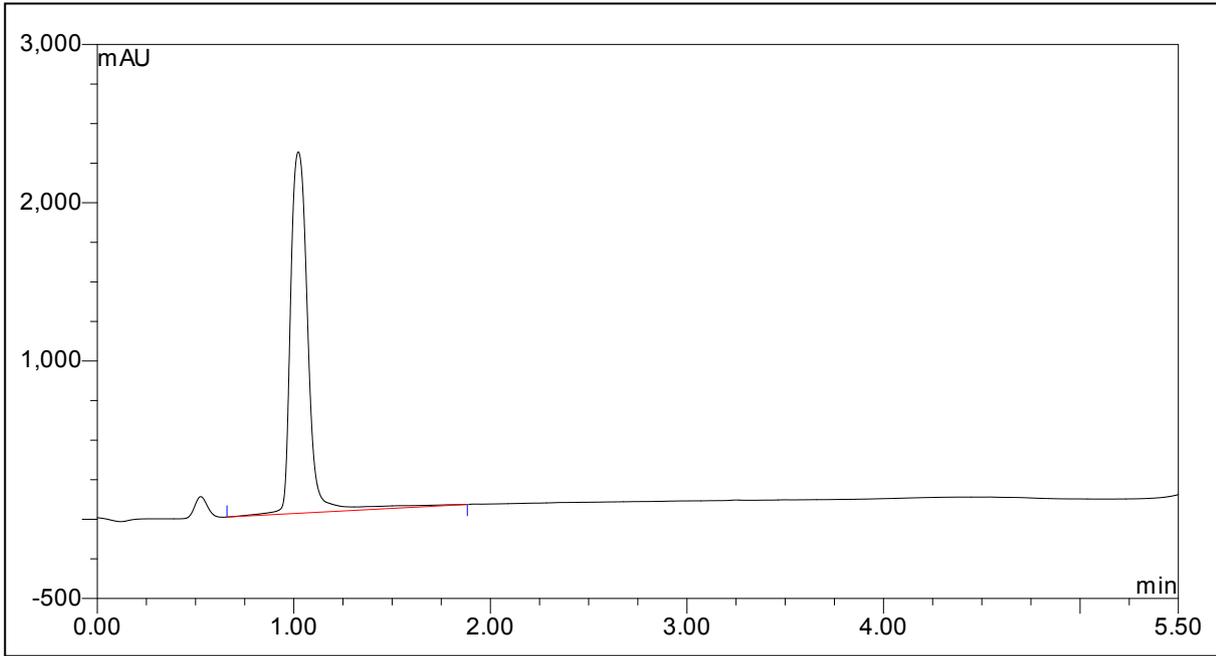
¹H-NMR G5-Pyrrolidone:



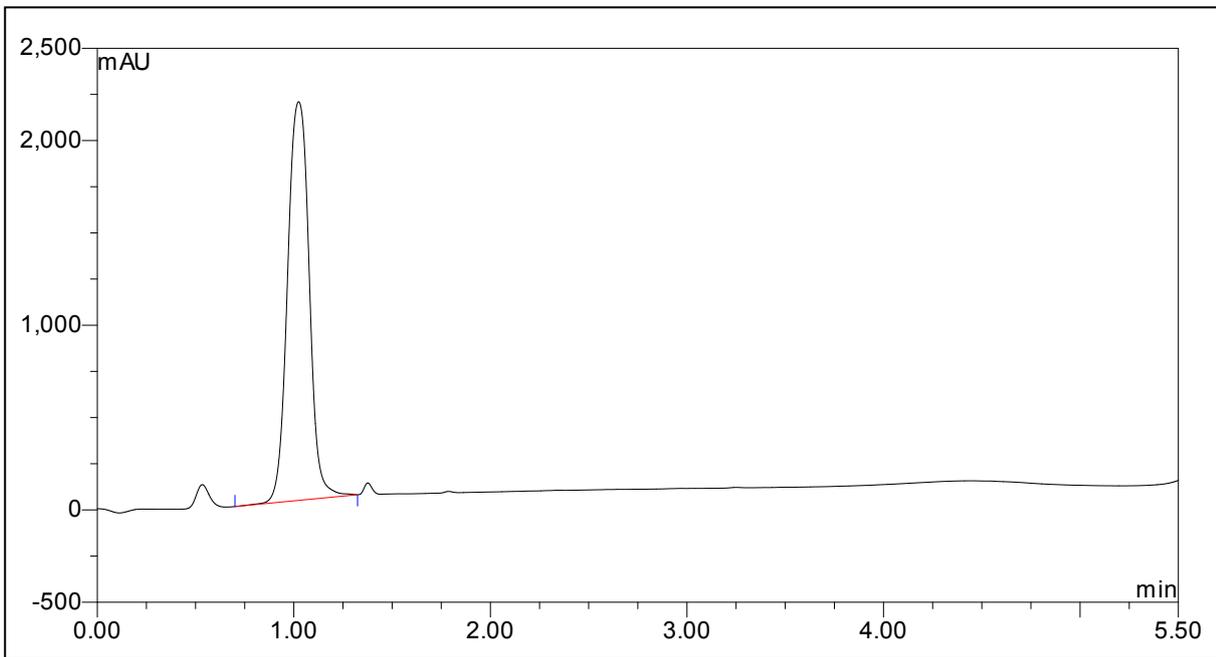
¹³C-NMR G5-Pyrrolidone:



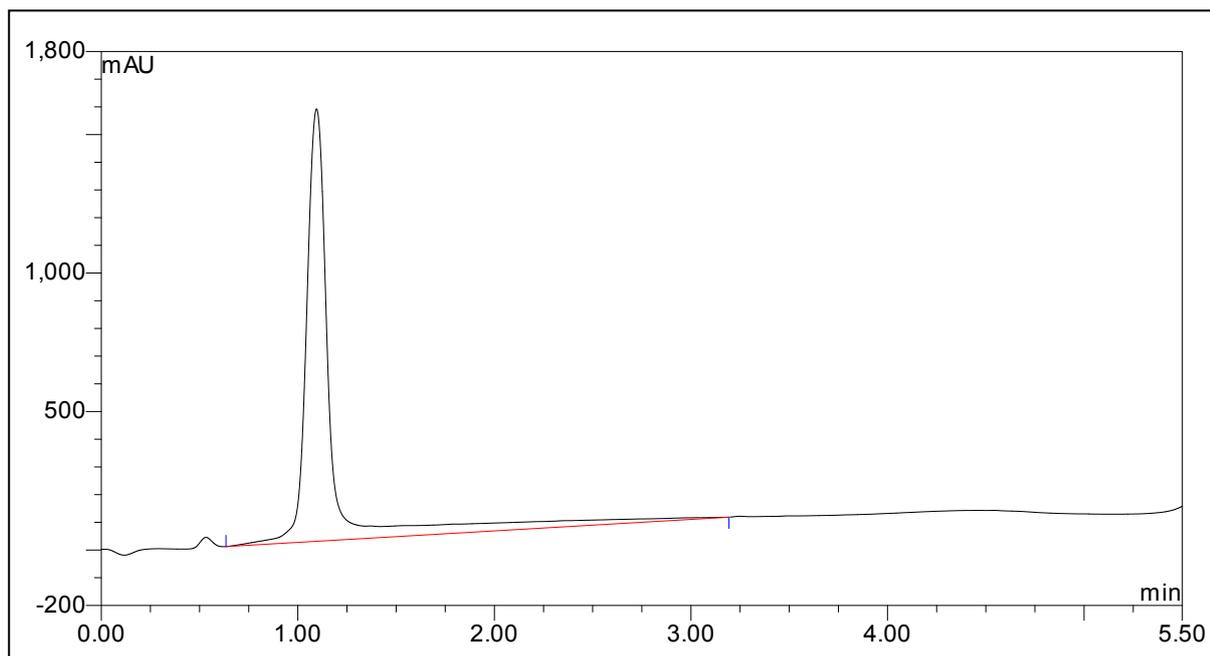
HPLC of G3-Pyr₃₂:



HPLC of G4-Pyr₆₄:



HPLC of G5-Pyr₁₂₈:



ICP-MS:

Four different dendrimer encapsulated CoCu-nanoparticles were prepared with Cu:Co ratios 1:1; 2:1; 3:1 and 4:1. After centrifugation, a sample of the top layer were carefully removed and destroyed by reaction with 1 mL 62 % HNO₃ overnight to give solutions containing the released cobalt(II) and copper(II), which were analyzed by ICP-MS.

Found Co (µg/L)	Found2 Cu (µg/L)	µM Co	µM Cu	Measured molar ratio Cu:Co	Calculated molar ratio Cu:Co
574400	506900	9746.629378	7976.898625	1.0 : 0.9	1.0 : 1.0
347300	639500	5893.11348	10063.57599	1.8 : 1.0	2.0 : 1.0
219400	587900	3722.859481	9251.565795	2.7 : 1.0	3.0 : 1.0
186600	678500	3166.297079	10677.30463	3.6 : 1.0	4.0 : 1.0

The ratios measured by ICP-MS correspond reasonable to the theoretical values making a method for obtaining the relative ratios between the metals.

Literature

- [1] Fréchet, J. M. J.; Tomalia, D. A. *Dendrimers and other Dendritic Compounds*; John Wiley & Sons: Chichester, U.K., 2001.
- [2] Ciolkowski, M.; Petersen, J. F.; Ficker, M.; Janaszewska, A.; Christensen, J. B.; Klajnert, B.; Bryszewska, M. Surface modification of PAMAM dendrimer improves its biocompatibility. *Nanomedicine* **2012**, *8*, 815-817.
- [3] Tomalia, D. A.; Swanson, D.R.; Huang, B.; *inventors: Dendritic Nanotechnologies Ltd. (US)*, Tomalia, D. A.; Swanson, D.R.; Huang, B. assignees. *Heterocycle functionalized dendritic polymers. World Patent WO 2004/069878*. 19 August **2004**.