Electronic Supplementary Material (ESI) for ChemComm.

Electronic Supplementary Information

Near-Infrared Photoswitching of Cyclodextrin-Guest Complexes Using Lanthanide-Doped $LiYF_4$ Upconversion Nanoparticles

N. Möller,[a] T. Hellwig,[b] L. Stricker,[a] S. Engel,[a] C. Fallnich*[b] and B. J. Ravoo*[a]

Organic Chemistry Institute, Center for Soft Nanoscience and Institute of Applied Physics, Westfälische Wilhelms-Universität Münster, Corrensstrasse 40, 48149 Münster, Germany

fallnich@uni-muenster.de

b.j.ravoo@uni-muenster.de

Table of Content

1. Materials and methods

All chemicals were used as received and without further purification, if not mentioned otherwise and purchased by following companies: *Acros Organics* (*Fischer Scientific GmbH*, Schwerte, Germany), *Aldrich* (*Sigma-Aldrich Chemie GmbH*, Taufkirchen, Germany); *Alfa Aesar* (*Alfa Aesar GmbH & Co KG*, Karlsruhe, Germany), *Fluka* (*Sigma-Aldrich Chemie GmbH*, Taufkirchen, Germany), *Merck* (*Merck KGaA*, Darmstadt, Germany), *TCI, TCI Deutschland GmbH,* Eschborn, Germany. Reactions which were moisture or air sensitive were performed under inert conditions using standard Schlenk-technique and dry solvents. Solvents were dried with standard methods: Toluene Storage over molecular sieves (4 Å), Acetonitrile Storage over molecular sieves (4 Å), DMF Storage over molecular sieves (4 Å). Reactions were monitored by thin layer chromatography on pre-coated aluminium-backed plates (Merck Kieselgel 60 with fluorescent indicator UV_{254}). Flash column chromatography was performed with silica gel (0.040-0.063 mm, Kieselgel 60, Merck). The NMR spectra were recorded on a *AV-300*-spectrometer with 300.1 Hz (^{1}H) or 75.5 Hz (^{13}C) and a *AV-400* spectrometer with 400.1 Hz (^{1}H) or 100.1 Hz (^{13}C) (*Bruker*, Karlsruhe, Germany). All measurements were done in deuterated solvents. The chemical shifts (δ) are reported relative to the residual solvent signals in parts per million (ppm). The measured coupling constants are given in Hertz (Hz). All recorded spectra were analyzed using *MestReNova* 9.0.1 (*Mestrelab Research* S.L., Santiago de Compostela, Spain). The analysis of the nanoparticles was done by using a *Zeiss 200 FE* electron microscope with a *Schottky emitter* and an *energy* Ω *filter*. All measurements were performed at 200 kV. The model of the CCD-camera is the *Gatan USC 4000* with a pixel size of 4096x1024 pixels. The camera has a pixel size of 15x15 μm^2 at 2048x2048 pixels. The electron microscope was produced by CARL ZEISS AG, Oberkochen and the camera by GATAN GMBH, München. For the sample preparation a carbon film on a cupper grid was used. The thickness of the carbon film is around 5-10 nm. The received data was analyzed by the software *ImageJ* (NATIONAL INSTITUTES OF HEALTH (USA), Version 1.39u, Java 1.6.0_02). IR spectra were recorded using a *Varian Type 310* Fourier transformation IR spectrometer. The samples were measured in a solid state and the background was subtracted from every spectrum. The analysis of the spectra was performed using the software *Resolution Pro*. Vibrations were designated according to their intensity as: w = weak, m = medium, s = strong, br = broad. Elemental analyses were conducted using a *Vario EL III* (*ELEMENTAR ANALYSENSYSTEME GmbH*, Hanau, Germany). UV/Vis spectra were recorded with a *JASCO V-650* double-beam spectrophotometer (*JASCO* Labor- und Datentechnik GmbH, Gross-Umstadt) at 25 °C using 1.5 mL low-volume disposable PMMA cuvettes (*BRAND GMBH & CO KG*, Wertheim) for measurements in aqueous medium and 350 µL quarz-glass cuvettes (*100-QS*, 1 mm, *Hellma Analytics*, Müllheim, Germany) for organic solvents. The spectrometer was controlled with Spectra Manager Version 2, Spectra Manager version

2.08.04 [Build 1] (*JASCO* Labor- und Datentechnik GmbH, Gross-Umstadt). The samples were dissolved in a solvent and measured against the same solvent. The data were analyzed using *OriginPro 9.1* (*ORIGINLAB COOPERATION*, Northampton, USA). The used ultrapure water with an electric resistance greater than 18 MΩ was obtained using an *ELGA PurelabTM UHQ II water purification system* (*ELGA LabWater*, High Wycombe, Buckinghamshire, UK).

1.1 Laser experiments

The samples were prepared in 350 µL quarz-glass cuvettes (*100-QS*, 1 mm, *Hellma Analytics*, Müllheim, Germany). Afterwards the samples were illuminated with continuous-wave laser light at a central wavelength of 975.8 nm for different time periods. The laser light was provided by a single-mode fiber coupled GaAs laser diode (3SP Technologies, Model: 2000CHP) with a maximum output power of about 900 mW. The laser light from the single mode fiber was first collimated using an aspheric lens (AL, compare Fig. S1).

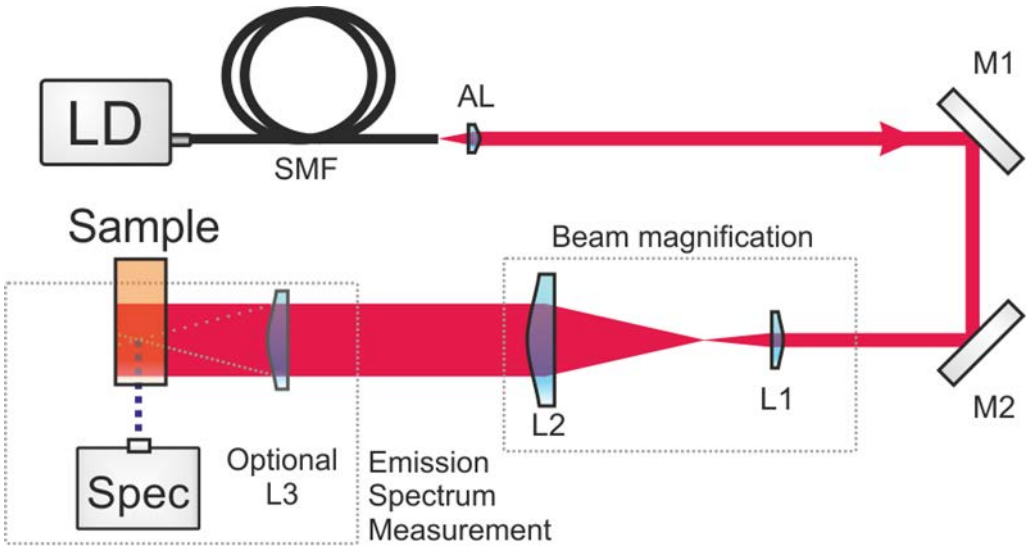


Figure S1: Scheme of the experimental setup for laser light illumination of the samples (LD: laser diode, SMF: single-mode-fiber, AL: aspheric lens, M1-M2: mirrors, L1-L3: spherical lenses, Spec: CCD-based spectrometer).

To achieve a mostly homogenous illumination of the samples its beam diameter was then magnified to a full width at half maximum (FWHM) of about 1.2 cm using a telescope. The effective area of the beam at the sample was, therefore, 3.3 cm^2. Due to loss at the non-perfectly coated lenses in the setup the maximum available power in the sample plane was 720 mW resulting in an illumination intensity of 0.22 W/cm^2. Two mirrors (M1 and M2) were used to adjust the beam position on the glass cuvettes.

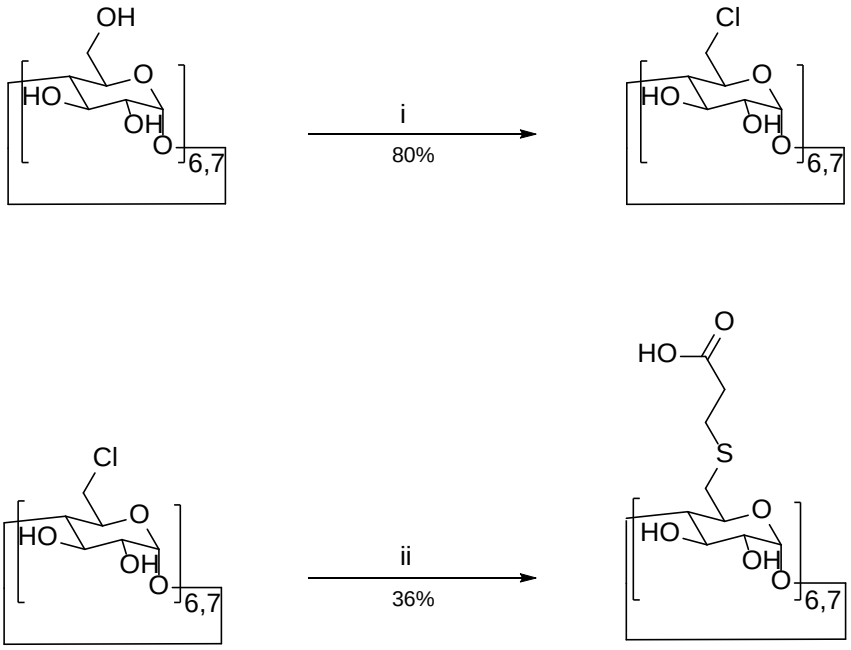
For measurements of the emission spectra of the different samples, the laser light was tightly focused into the sample using an additional lens (L3) with a focal length of 75 mm to achieve

a higher illumination intensity (about 5.1kW/cm^2, effective focal area of 7800 µm^2 with an average power of about 400 mW) and the emitted upconversion fluorescence light was measured at an angle of 90° to the focal plane directly with a CCD based spectrometer (Spec, OceanOptics, Model HR2000+, 200-1100 nm). To account for different upconversion efficiencies and sample concentrations the integration time of the spectrometer was adjusted and the corresponding spectra evaluated on the basis of counts over integration time.

2. Synthesis of the CDA ligands

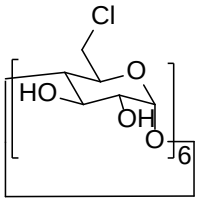
2.1 Synthesis of α- or β-CDA

2.1.1 Synthesis route



Scheme S1: i: For α-CD-Cl: α-CD (1.00 eq.), methanesulfonylchlorid (38.00 eq), DMF, 65 °C, 48 h. For β-CD-Cl: β-CD (1.00 eq.), methanesulfonylchlorid (36.36 eq), DMF, 65 °C, 48 h; **ii**: For α-CDA: α-CD-Cl (1.00 eq.), 3-mercaptopropionic acid (30.00 eq), 60 % NaH (66.00 eq.), DMF, 70 °C, 48 h. For β-CDA: β-CD-Cl (1.00 eq.), 3-mercaptopropionic acid (35.00 eq), 60 % NaH (77.00 eq.), DMF, 70 °C, 48 h.

2.1.2 Synthesis of hexachloro-hexadeoxy-α-cyclodextrin (α-CD-Cl)[1]



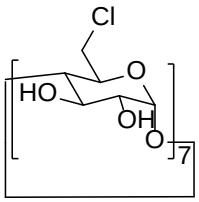
α-CD (4 g, 4.06 mmol, 1 eq.) was solved in 70 mL dry DMF. Then methanesulfonylchloride (12.09 mL, 156.00 mmol, 38 eq.) was added carefully. The solution was heated up to 65 °C and stirred for 2 days. After 2 days it was allowed to cool to room temperature and the solvent was evaporated under reduced pressure. The product was dissolved in methanol and the pH was adjusted to pH 7. The product was precipitated by adding ice water and the solid product was filtered and washed with methanol.

Yield: 80%.

^{1}H-NMR (300 MHz, DMSO-d_6, 298 K): δ = 5.98-5.95 (d, J = 6.5 Hz, 6H), 5.80 (s, 6H), 4.92-4.89 (d, J = 3.2 Hz, 6H), 4.11-3.89 (m, 12H), 3.92-3.71 (m, 12H), 3.46 (t, J = 8.9 Hz, 6H), 3.34 (s, 6H) ppm.

^{13}C-NMR (75 MHz, DMSO-d_6, 298 K): δ = 101.9, 83.7, 72.4, 71.9, 71.15, 45.3 ppm.

2.1.3 Synthesis of hexachloro-hexadeoxy-β-cyclodextrin (β-CD-Cl)[1]



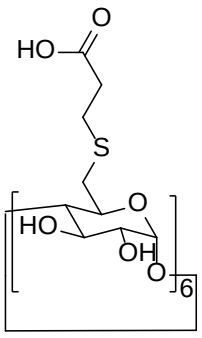
β-CD (14.97 g, 13.2 mmol, 1 eq.) was solved in 250 mL dry DMF. Then methanesulfonylchloride (37.1 mL, 480.00 mmol, 36.36 eq.) was added carefully. The solution was heated up to 65 °C and stirred for 2 days. After 2 days it was allowed to cool to room temperature and the solvent was evaporated under reduced pressure. The product was dissolved in methanol and the pH was adjusted to pH 7. The product was precipitated by adding ice water and the solid product was filtered and washed with methanol.

Yield: 80%.

^{1}H-NMR (300 MHz, DMSO-d_6, 298 K): δ = 6.02-5.89 (d, J = 6.0 Hz, 7H), 4.96 (s, 7H), 4.09-4.06 (d, J = 4.0 Hz, 7H), 3.97-3.72 (m, 14H), 3.71-3.52 (m, 14H), 2.89 (m, 7H), 2.72 (s, 7H) ppm.

^{13}C-NMR (75 MHz, DMSO-d_6, 298 K): δ = 102.1, 83.6, 72.5, 72.0, 71.2, 45.0 ppm.

2.1.4 Synthesis of per-6-deoxy(carboxylpropyl)thio-α-cyclodextrin (α -CDA)[2]



3-mercaptopropionic acid (5.63 mL, 65.1 mmol, 30 eq.) was solved in 90 mL dry DMF. Then 60% NaH (5.74 g, 143.22 mmol, 66 eq.) was added carefully and stirred for 90 min. Subsequently the solution was cooled down to 0 °C and heptachloro-heptadeoxy-α-CD (2.35 g, 2.17 mmol, 1 eq.) was added in one portion. The solution was heated up to 70 °C and stirred for 2 days. After 2 days it was allowed to cool to room temperature and the solvent was evaporated under reduced pressure. The product was then precipitated with a huge amount of iced absolute ethanol, filtered and resolved in as less distilled water as possible. The pH was adjusted to pH 6 and the aqueous solution was dialyzed 3 days (MWCO 1000) by changing the external distilled water from time to time reducing the excess thiol. After 3 days the internal solution was freeze dried and the white solid was washed via soxhlet extraction with cyclohexane to get rid of the mineral oil. The cleaned solid was dissolved in a minimum amount of distilled water, the pH was adjusted to pH 7 by adding a little amount of sodium methoxide and the solution was freeze dried again to afford the desired compound.

Yield: 36%.

^{1}H-NMR (300 MHz, DMSO-d_6, 298 K): δ = 12.37 (bs, 6H), 5.57 (bs, 12H), 4.83 (s, 6H), 3.90-3.74 (m, 12H), 3.48-3.44 (m, 12H), 3.05-3.02 (d, J = 14.5 Hz, 6H), 2.88 (t, J = 6.8 Hz, 6H),

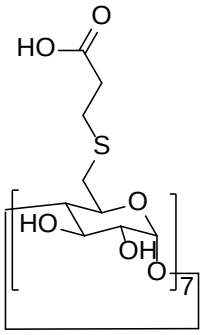
2.77-2.68 (m, 12H), 2.61 (t, *J* = 6.8 Hz, 12H) ppm.

^{13}C-NMR (75 MHz, DMSO-d_6, 298 K): δ = 172.6, 103.7, 84.7, 77.9, 75.8, 68.2, 35.6, 33.0, 27.2 ppm.

MALDI-MS (+; DHB; EtOAc) (m/z): Calculated for $[C_{54}H_{84}O_{36}S_6Na]^+$ = 1523.30; Found = 1523.48.

IR: 3268 (br), 2924 (w), 2828 (w), 1564 (s), 1397 (s), 1353 (s), 1305 (m), 1273 (w), 1146 (s), 1042 (s), 655 (m) cm^{-1}.

2.1.5 Synthesis of per-6-deoxy(carboxylpropyl)thio-β-cyclodextrin (β-CDA)[2]



3-mercaptopropionic acid (3.6 mL, 41.31 mmol, 35 eq.) was solved in 90 mL dry DMF. Then 60% NaH (3.67 g, 91.75 mmol, 77 eq.) was added carefully and stirred for 90 min. Subsequently the solution was cooled down to 0 °C and heptachloro-heptadeoxy-β-CD (1.50 g, 1.19 mmol, 1 eq.) was added in one portion. The solution was heated up to 70 °C and stirred for 2 days. After 2 days it was allowed to cool to room temperature and the solvent was evaporated under reduced pressure. The product was then precipitated with a huge amount of iced absolute ethanol, filtered and resolved in as less distilled water as possible. The pH was adjusted to pH 6 and the aqueous solution was dialyzed 3 days (MWCO 1000) by changing the external distilled water from time to time reducing the excess thiol. After 3 days the internal solution was freeze dried and the white solid was washed via soxhlet extraction with cyclohexane to get rid of the mineral oil. The cleaned solid was dissolved in a minimum amount of distilled water, the pH was adjusted to pH 7 by adding a little amount of sodium methoxide and the solution was freeze dried again to afford the desired compound.

Yield: 36%.

^{1}H-NMR (300 MHz, DMSO-d_6, 298 K): δ = 12.30 (bs, 7H), 5.87 (bs, 14H),4.85 (s, 7H), 3.80-3.56 (m, 14H), 3.41-3.30 (m, 14H, H-7), 3.04-3.01 (d, *J* = 12.7 Hz, 7H), 2.87-2.84 (m, 7H), 2.73-2.58 (m, 14H), 2.48-2.43 (m, 14H) ppm.

^{13}C-NMR (75 MHz, DMSO-d_6, 298 K): δ = 173.2, 102.2, 84.5, 72.6, 72.4, 71.3, 34.8, 33.1, 26.6 ppm.

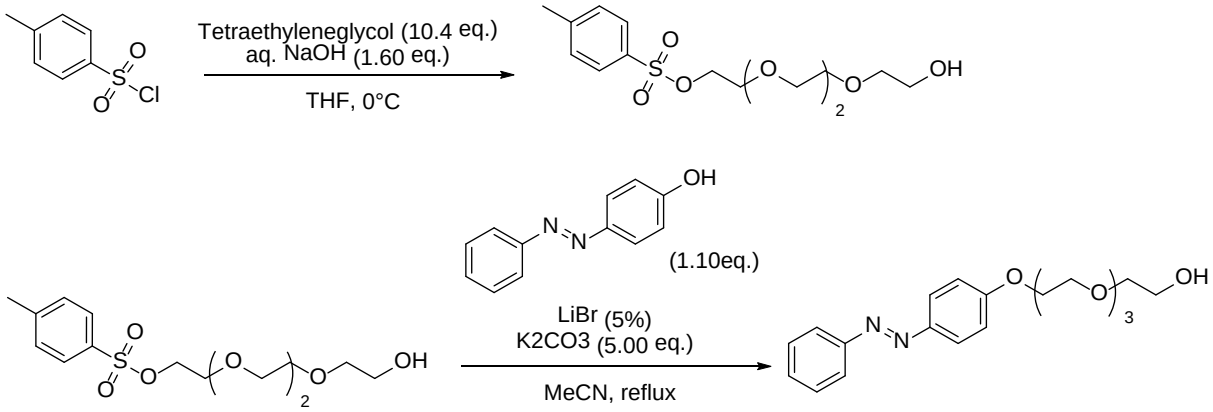
MALDI-MS (+; DHB; EtOAc) (m/z): Calculated for $[C_{63}H_{98}O_{42}S_7Na]^+$ = 1773.35; Found = 1773.37.

IR: 3295 (br), 2920 (w), 1708 (s), 1556 (w), 1405 (m), 1241 (m), 1149 (s), 1038 (s), 655 (w) cm^{-1}.

3. Synthesis of Azo and AAP derivatives

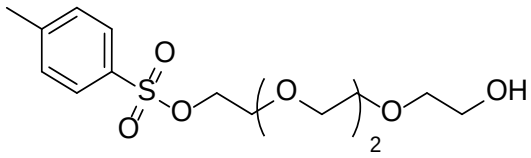
3.1 Synthesis of Azo-TEG

3.1.1 Synthesis route



Scheme S2

3.1.2 Synthesis of 2-(2-(2-hydroxyethoxy)ethoxy)ethyl 4-methylbenzenesulfonate (**Monotosylated TEG**)[3]



Tetraethylene glycol (22.00 g, 113.3 mmol, 10.4 eq.) was mixed with THF (4 mL) and the solution was cooled down to 0 °C. A solution of NaOH (684 mg, 17.1 mmol, 1.60 eq.) in distilled water (4 mL) was added dropwise at the same temperature. A solution of p-toluenesulfonyl chloride (2.08 g, 10.9 mmol, 1.00 eq.) in THF (13 mL) was added dropwise over 40 min and the solution was stirred for 2 h at 0 °C. The solution was poured into ice-water and the layers were separated. The aqueous layer was extracted with DCM (3 x 50 mL) and the combined organic layers were washed with distilled water (2 x 50 mL), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The desired yellowish oily compound was used in the next step without further purification.

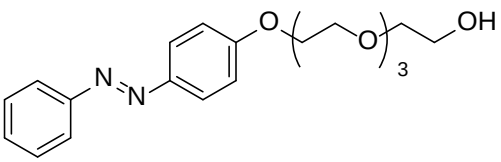
Yield: 91%.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.79 (d, J = 8.33 Hz, 2H), 7.33 (d, J = 8.06 Hz, 2H), 4.15 (t, J = 4.82 Hz, 2H), 3.73-3.55 (m, 14H), 2.43 (s, 3H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.9, 133.0, 129.9, 128.0, 72.5, 70.8, 70.7, 70.5, 70.4, 69.3, 68.8, 61.8, 21.7 ppm.

MS-ESI (m/z): Calculated for $[C_{15}H_{24}O_7SNa]^+$ = 371.1135; Found = 371.1134.

3.1.3 Synthesis (*E*)-2-(2-(2-(2-(4-(phenyldiazenyl)phenoxy)ethoxy)ethoxy)-ethoxy)ethanol (**Azo-TEG**)[4]



2-(2-(2-hydroxyethoxy)ethoxy)ethyl-4-methylbenzene-sulfonate (2.62 g, 7.50 mmol, 1.00 eq.) was dissolved in dry acetonitrile (75 mL, 0.1 M) and K_2CO_3 (5.19 g, 37.5 mmol, 5.00 eq.) and a catalytic amount of LiBr were added. 4-phenylazophenol (1.59 g, 7.90 mmol, 1.10 eq.) dissolved in dry acetonitrile (25 mL, 0.3 M) was added and the solution was refluxed for 2 days under argon. The reaction mixture was cooled down to room temperature and the solvent was removed under reduced pressure. The residue was dissolved in DCM (100 mL), washed with water (1 x 100 mL) and brine (1 x 100 mL). The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. Purification by column chromatography (Dichloromethane/MeOH 95 : 5) gave the desired product as an orange oil.

Yield: 90%.

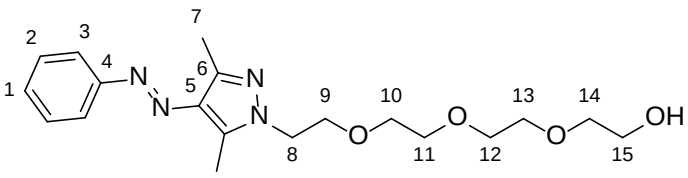
R_f = 0.43. (Dichloromethane/MeOH 95 : 5)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.93-7.85 (m, 4H), 7.53-7.40 (m, 3H), 7.05-7.00 (m, 2H), 4.23-4.20 (m, 2H), 3.91-3.87 (m, 2H), 3.77-3.68 (m, 10H), 3.62-3.59 (m, 2H), 2.49 (bs, 1H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.3, 152.8, 147.1, 130.5, 129.1, 124.8, 122.6, 114.9, 72.6, 70.9, 70.7, 70.7, 70.4, 69.7, 67.8, 61.8 ppm.

MS-ESI (m/z): Calculated for $[C_{20}H_{26}N_2O_5Na]^+$ = 397.1734; Found = 397.1738.

3.2 Synthesis of (E)-2-(2-(2-(2-(3,5-dimethyl-4-(phenyldiazenyl)-1H-pyrazol-1-yl)ethoxy)ethoxy)ethoxy)ethan-1-ol (**AAP-TEG**)



To a stirred solution of AAP (2.51 g, 12.53 mmol, 1 eq.) in 150 mL of dry acetonitrile, containing K_2CO_3 (8.66 g, 62.67 mmol, 5 eq.) and catalytic amounts of LiBr, tosylated tetraethyleneglycole (5.26 g, 15.1 mmol, 1.2 eq.) dissolved in acetonitrile (50 mL) was added and the reaction mixture was refluxed for 3 days under argon. It was then allowed to cool to room temperature and the solvent was removed under reduced

pressure. The residue was dissolved in DCM (120 mL), washed with water (100 mL) and brine (3 × 100 mL). The organic phase was dried over $MgSO_4$ and concentrated. The residue was purified by silica gel column chromatography (DCM → DCM/methanol 95:5) to afford the title compound as a red oil.

Yield: 89%.

R_f = 0.36 (DCM/methanol 95:5)

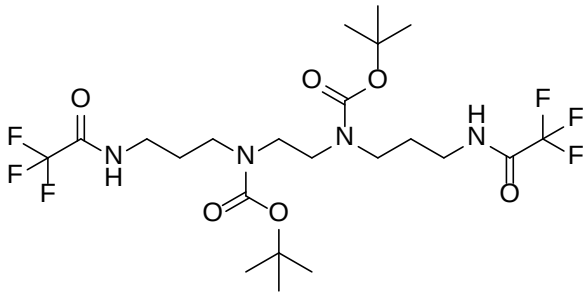
^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.83 – 7.72 (m, 2H, 3,3'-H), 7.46 (dd, *J* = 8.4, 6.9 Hz, 2H, 2, 2'-H), 7.41 – 7.34 (m, 1H, 1-H), 4.24 (t, *J* = 5.4 Hz, 2H, 8-H), 3.88 (t, *J* = 5.4 Hz, 2H, 9-H), 3.73 – 3.65 (m, 2H, 15-H), 3.65 – 3.46 (m, 11H, 10-, 11-, 12-, 13-,14-H, -OH), 2.63 (s, 3H, 7,7'-H), 2.51 (s, 3H, 7, 7'-H) ppm.

^{13}C-NMR (101 MHz, $CDCl_3$) δ = 153.7 (C-4), 142.5 (C-9), 140.7 (C-6,-6'), 135.0 (C-1), 129.5, 129.0 (C-2,2'), 121.90 (C-3'), 72.6, 70.8, 70.7, 70.6, 70.4, 69.9 (C-9, -10, -11, -12, -13, -14), 61.8 (C-15), 49.2 (C-8), 14.1, 10.0 (C-7, -7') ppm.

HRMS: calculated for $[C_{19}H_{28}N_4O_4Na]^+$: 399.2003, found: 399.1999.

3.3 Synthesis of Azo-Linker

3.3.1 Synthesis of di-tert-butylethane-1,2-diylbis((3-(2,2,2)trifluoroacetamido)-propyl)carbamate) (**I-1**)[5]



N,N-(ethane-1,2-diyl)bis(propane-1,3-diamine) (3.49 g, 20.0 mmol, 1.0 eq.) was dissolved in 35 mL of DCM and a solution of ethyl trifluoroacetate (5.97 g, 42.0 mmol, 2.1 eq.) in 5 mL DCM was added dropwise at 0 °C over 30 minutes. After further stirring at 0 °C for 30 minutes, the solution was warmed up to room temperature and stirred at this temperature for 60 minutes. Subsequently triethylamine (7.21 mL, 52.0 mmol, 2.6 eq.) was added to the reaction mixture, followed by a dropwise addition of di-*tert*-butyl dicarbonat (11.4 g, 52.0 mmol, 2.6 eq.) dissolved in 5 mL of DCM. The solution was stirred overnight at room temperature. The received reaction mixture was then extracted twice with saturated $NaHCO_3$ (2 × 60 mL) and brine (2 × 60 mL). The organic phases were combined, dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was purified by recrystallization in DCM/Hexane, affording the title compound.

Yield: 79%.

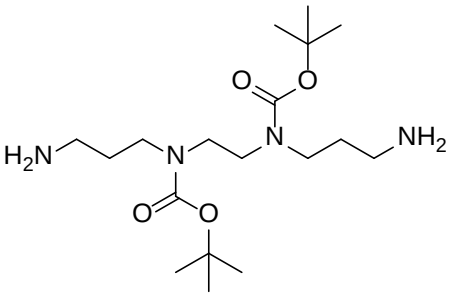
^{1}H-NMR (300 MHz, $CDCl_3$, 298 K): δ = 8.12 (br s, 2H), 3.32-3.26 (m, 12H), 1.73-1.67 (m, 4H), 1.46 (s, 18H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$, 298 K): δ = 157.7, 157.2, 156.8, 45.2, 43.6, 35.9, 28.5, 27.1 ppm.

^{19}F-NMR (282 MHz, $CDCl_3$, 298 K): δ = -76.16 (s, 6F) ppm.

ESI-HRMS (m/z): Calculated for $[C_{22}H_{36}N_4O_6F_6Na]^+$ = 589.2431; Found = 589.2414.

3.3.2 Synthesis of di-tert-butylethane-1,2-diylbis((3-aminopropyl)carbamate) (**I-2**)[5]



To a solution of **I-1** (8.6 g, 15.17 mmol, 1.0 eq.) in 60 mL EtOH an aqueous solution of 36.4 mL NaOH (20.0 wt%, 227.55 mmol, 15.0 eq.) was added and the reaction mixture was stirred overnight at room temperature. Subsequently the solution was extracted twice with DCM (2 × 70 mL). The combined organic phases were dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was purified by silica gel column chromatography (DCM/MeOH/NH_4OH 80:18:2) to afford the desired title compound.

Yield: 91%.

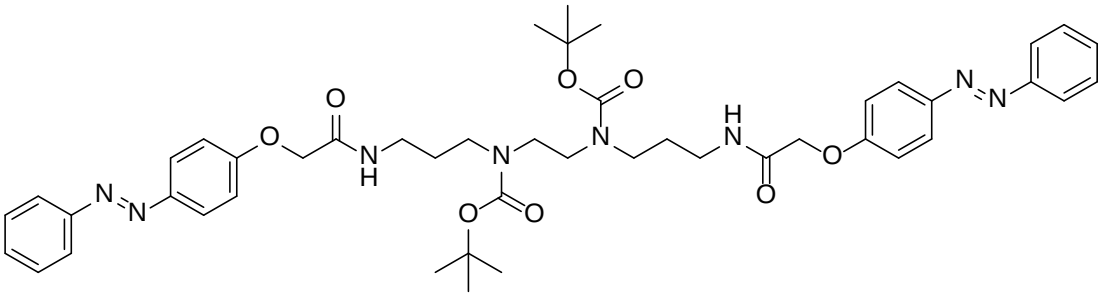
R_f = 0.15. (DCM/MeOH/NH_4OH 80 : 18 : 2).

^{1}H-NMR (300 MHz, $CDCl_3$, 298 K): δ = 3.30-3.23 (m, 8H), 2.69-2.65 (t, J = 6.75 Hz, 4H), 1.94 (s, 4H), 1.67-1.61 (m, 4H), 1.43 (s, 18H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$, 298 K): δ = 156.7, 79.9, 45.5, 44.5, 39.0, 31.6, 28.6 ppm.

ESI-HRMS (m/z): Calculated for $[C_{18}H_{38}N_4O_4H]^+$ = 375.2966; Found = 375.2977.

3.3.3 Synthesis of di-tert-butylethane-1,2-diylbis((3-(2-(4-((E)-phenyldiazenyl)phenoxy)acetamido) propyl)carbamate) (**I-3**)



To a stirred solution of **I-2** (105 mg, 0.28 mmol, 1.0 eq.) in 3 mL dry DMF a solution of perfluorophenyl (E)-2-(4-(phenyldiazenyl)phenoxy)acetate (114 mg, 0.34 mmol, 1.2 eq.) in 7 mL dry DMF was added dropwise. Subsequently DIPEA (48.8 µL, 0.28 mmol) was added and the reaction mixture was stirred at room temperature for 48 h. The crude product was purified by silica gel column chromatography (DCM/MeOH 96:4) to afford the desired title compound.

Yield: 71%.

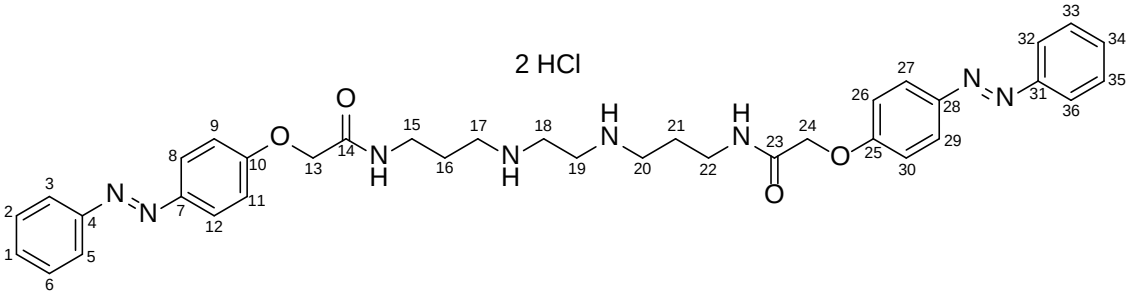
$\mathbf{R_f}$ = 0.26. (DCM/MeOH 96 : 4).

^{1}H-NMR (300 MHz, $CDCl_3$, 298 K): δ = 7.96-7.85 (m, 8H), 7.53-7.41 (m, 6H), 7.11-7.08 (m, 4H), 4.58 (s, 4H), 3.30-3.23 (m, 12 H),1.72-1.65 (m, 4H), 1.44 (s, 18H) ppm.

^{13}C-NMR (75 MHz, $CDCl_3$, 298 K): δ = 168.4, 163.1, 159.7, 152.8, 147.9, 130.8, 129.2, 124.9, 122.8, 115.2, 80.7, 67.4, 36.9, 31.8, 28.5 ppm.

ESI-HRMS (m/z): Calculated for $[C_{46}H_{58}N_8O_8Na]^+$ = 873.4270; Found = 873.4247.

3.3.4 Synthesis of *N,N'*-((ethane-1,2-diylbis(azanediyl))bis(propane-3,1-diyl))bis(2-(4-((E)-phenyldi-azenyl)diazenyl)phenoxy)acetamide)



To a solution of **I-3** (140 mg, 0.16 mmol, 1.0 eq.) in 100 mL MeOH 2 mL acetyl chloride (28.00 mmol, 175 eq.) was added at 0 °C. The reaction mixture was first stirred for 5 h at the same temperature and then further 24 h at room temperature. The product was separated from the solvent by filtration.

Yield: 50%.

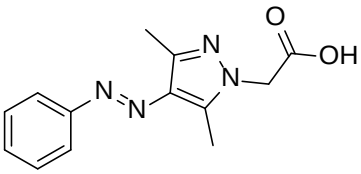
^{1}H-NMR (300 MHz, DMSO-d_6, 298 K): δ = 9.24 (bs, 4H, NH) 7.90-7.88 (m, 4H, H-8, H-12, H-27, H-29), 7.83-7.82 (m, 4H, H-3, H-5, H-32, H-36), 7.57-7.50 (m, 6H, H-1, H-2, H-6, H-33, H-34, H-35), 7.17-7.15 (m, 4H, H-9, H-11, H-26, H-30), 4.61 (s, 4H, H-13, H-24), 3.25-3.23 (m, 8 H, H-15, H-17, H-20, H-22), 2.95 (t, 4H, J = 7.45 Hz, H-18, H-19), 1.85-1.80 (m, 4H, H-16, H-21) ppm.

^{13}C-NMR (75 MHz, DMSO-d_6, 298 K): δ = 167.7 (C_q (C-14, C-23), 160.3 (C_q (C-10, C-25), 152.0 (C_q (C-4, C-31), 146.6 (C_q (C-7, C.28), 131.0 (CH (C-1, C-34), 129.5 (CH (C-2, C-6, C-33, C-35), 124.5 (CH (C-8, C-12, C-27, C-29), 122.3 (CH (C-3, C-5, C-32, C-36), 115.5 (CH (C-9, C-11, C-26, C-30), 67.1 (CH_2 (C-13,C-24), 44.9 (CH_2 (C-18, C-19), 43.0 (CH_2 (C-16, C-21), 35.5 (CH_2 (C-15, C-17, C-20, C-22) ppm.

ESI-HRMS (m/z): Calculated for $[C_{36}H_{42}N_8O_4H]^+$ = 651.3402; Found = 651.3395.

3.4 Synthesis of AAP-linker

3.4 1 Synthesis of (E)-2-(3,5-dimethyl-4-(phenyldiazenyl)-1*H*-pyrazol-1-yl)acetic acid (**II-1**)[6]



The arylazopyrazole methylester (3.59 g, 13.17 mmol, 1 eq.) was dissolved in THF/water (120 mL, 4:1) and LiOH (473 mg, 19.76 mmol, 1.5 eq.) was added. The solution was stirred overnight at rt. After removing THF under reduced pressure, the aqueous phase was extracted with EtOAc (20 mL) and the organic layer was discarded. The aqueous phase was acidified with HCl (pH = 1-2) and was extracted again with EtOAc (3 × 50 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$ and concentrated under reduced pressure yielding the corresponding carboxylic acids.

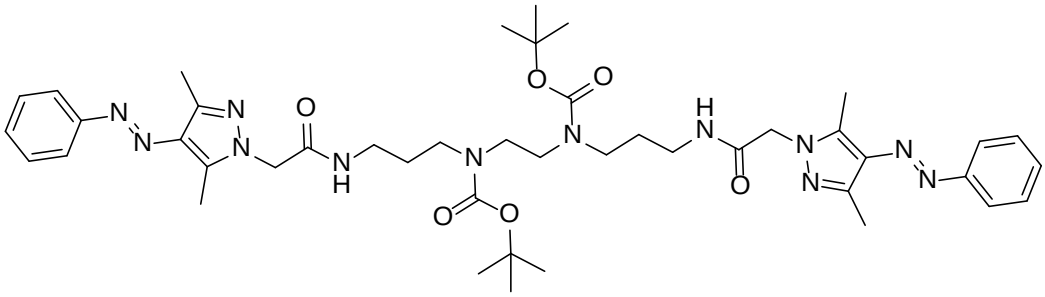
Yield: 89%.

^{1}H-NMR (300 MHz, DMSO-d_6) δ = 13.25 (s, 1H), 7.77 – 7.68 (m, 2H), 7.57 – 7.46 (m, 2H), 7.45 – 7.34 (m, 1H), 4.94 (s, 2H), 2.50 (s, 3H), 2.36 (s, 3H) ppm.

^{13}C-NMR (75 MHz, DMSO-d_6) δ = 169.2, 153.0, 140.9, 140.8, 134.6, 129.6, 129.2, 121.5, 119.8, 86.9, 50.5, 13.9, 9.5, 9.4 ppm.

ESI-HRMS (m/z): Calculated for $[C_{13}H_{13}N_4O_2]^-$ = 257.1044; Found = 257.1055.

3.4 2 Synthesis of di-tert-butyl ethane-1,2-diylbis((3-(2-(3,5-dimethyl-4-((E)-phenyldiazenyl)-1*H*-pyrazol-1-yl)acetamido)propyl)carbamate) (**II-2**)[6]



To a solution of **II-1** (310 mg, 1.2 mmol, 2.5 eq.) in DMF (15 mL) EDCl (276 mg, 1.44 mmol, 3 eq.) and HOBt (195 mg, 1.44 mmol, 3 eq.) were added and it was stirred for 30 minutes. Afterwards di-Boc-protected polyamineS3 (180 mg, 0.48 mmol, 1 eq.) in a minimum amount of DMF and N-methylmorpholine (0.16 mL, 1.44 mmol, 3 eq.) and the solution was stirred overnight. After removing the solvent in vacuo the compound was purified by column chromatography (DCM/MeOH 96:4).

Yield: 97%.

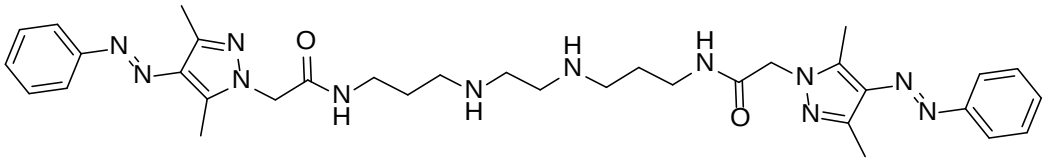
R_f = 0.38. (DCM/MeOH 96 : 4).

^{1}H-NMR (400 MHz, $CDCl_3$) δ = 7.79 – 7.73 (m, 4H), 7.45 (t, *J* = 7.6 Hz, 4H), 7.37 (t, *J* = 7.2 Hz, 2H), 4.73 (s, 4H), 3.23 – 3.07 (m, 16H), 2.57 (s, 6H), 2.50 (s, 6H), 1.57 (s, 4H), 1.31 (m, 18H) ppm.

^{13}C-NMR (101 MHz, $CDCl_3$) δ = 166.9, 162.6, 153.6, 144.1, 129.6, 129.0, 121.9, 80.4, 52.6, 44.8, 43.4, 36.6, 35.5, 31.6, 28.2, 27.5, 14.2, 9.9 ppm.

ESI-HRMS (m/z): Calculated for $[C_{44}H_{62}N_{12}O_6Na]^+$ = 877.4807; Found = 877.4774.

3.4 3 Synthesis of N,N'-((ethane-1,2-diylbis(azanediyl))bis(propane-3,1-diyl))bis(2-(3,5-dimethyl-4-((E)-phenyldiazenyl)-1H-pyrazol-1-yl)acetamide)[6]



The Boc-protected **II-2** (410 mg, 0.47 mmol, 1 eq.) was dissolved in MeOH and acetylechloride (1 mL) was added at 0 °C. After one hour the ice-bath was removed and stirring was continued overnight. After evaporation of the solvent the residue was dissolved in water and freeze-dried.

Yield: 89%.

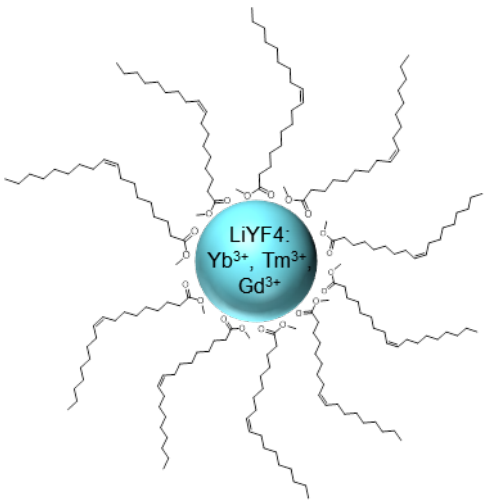
^{1}H-NMR (400 MHz, DMSO-d_6) δ = 9.45 (s, 4H), 7.74 – 7.60 (m, 4H), 7.46 (t, *J* = 7.6 Hz, 4H), 7.40 – 7.31 (m, 2H), 4.75 (s, 4H), 3.24 (s, 4H), 3.15 (q, J = 6.6 Hz, 4H), 2.93 (s, 4H), 2.48 (s, 6H), 2.32 (s, 6H), 1.78 (p, *J* = 7.0 Hz, 4H) ppm.

^{13}C-NMR (101 MHz, DMSO-d_6) δ = 166.40, 152.98, 141.12, 140.85, 134.51, 129.53, 129.19, 121.39, 62.79, 51.55, 44.74, 42.87, 36.01, 34.10, 25.80, 13.91, 9.61 ppm.

ESI-HRMS (m/z): Calculated for $[C_{34}H_{46}N_{12}O_2H]^+$ = 655.39395; Found = 655.39479.

4. Synthesis of upconversion nanoparticles – $LiYF_4:Yb^{3+},Tm^{3+},Gd^{3+}$

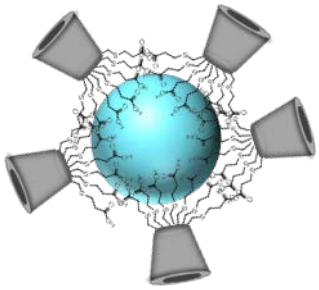
4.1 Modified synthesis of methyl oleate (MO) stabilized $LiYF_4:Yb^{3+},Tm^{3+},Gd^{3+}$ [7]



Stoichiometric quantities of Y_2O_3 (83 mol%, 1.0375 mmol, 0.2343 g), Yb_2O_3 (15 mol%, 0.1875 mmol, 0.0739 g), Tm_2O_3 (0.5 mol%, 0.0063 mmol, 0.0024 g) and Gd_2O_3 (1.5 mol%, 0.0188 mmol, 0.0068 g) were dissolved in 10 mL of 50 % aqueous trifluoroacetic acid at 80 °C under reflux and constant argon flow. Once the solution was clear it was allowed to cool down to 60 °C and to evaporate the solvent. The received white solid was mixed with lithium trifluoroacetate (2.5 mmol, 0.2999 g, 1 eq.). After the addition of 20 mL 1-octadecene and 20 mL methyl oleate the solution was heated to 110 °C under vacuum for 30 minutes to remove residual water and oxygen. Meanwhile the reaction flask was purged with argon gas for a few times. Subsequently the solution was heated to 330 °C at a rate of 5 °C/min under a constant argon flow and was held at the final temperature for 1 h. Around 270 °C little explosions were observed indicating the decomposition step. After 1 h the solution was cooled to 70 °C and the particles were precipitated with absolute ethanol. The nanoparticles were isolated via centrifuge (3000 rpm, 5 min), washed once with absolute ethanol and isolated again via centrifuge (3000 rpm, 2.5 min). The resulting nanocrystals were redispersed and stored in toluene. The redispersion was more successful by using not dried nanoparticles (‘muddy’ state) after centrifuge and by adding two drops of oleic acid.

TEM: Particle diameter: ca. 41.0 ± 7.1 nm (150 measured $LiYF_4$ UCNPs)

4.2 Ligand exchange reaction of methyl oleate (MO) to α- or β-CDA stabilized $LiYF_4:Yb^{3+},Tm^{3+},Gd^{3+}$



20 mg of dried methyl oleate capped UCNPs and 30 mg of α-CDA (0.020 mmol) or β-CDA (0.018 mmol) were mixed in 10 mL ultra pure water and sonicated for 20 minutes. Subsequently the dispersion was extracted with diethyl ether to remove the methyl oleate, which absence was monitored by measuring mass

spectrometry. The dirspersion was centrifuged (1000 rpm, 10 minutes), redispersed in ultra pure water and sonicated for 10 minutes.

Characterization for α-CDA@UCNPs:

TEM: Particle diameter: ca. 39.6 ± 7.0 nm (204 measured $LiYF_4$ UCNPs)

IR: 3269 (br), 2923 (w), 2828 (w), 1565 (s), 1397 (s), 1357 (s), 1305 (m), 1273 (w), 1150 (s), 1042 (s), 651 (m) cm^{-1}.

Characterization for β-CDA@UCNPs:

TEM: Particle diameter: ca. 41.0 ± 7.5 nm (154 measured $LiYF_4$ UCNPs)

IR: 3295 (br), 2920 (w), 2812 (w), 1576 (s), 1405 (m), 1156 (s), 1038 (s), 655 (w) cm^{-1}.

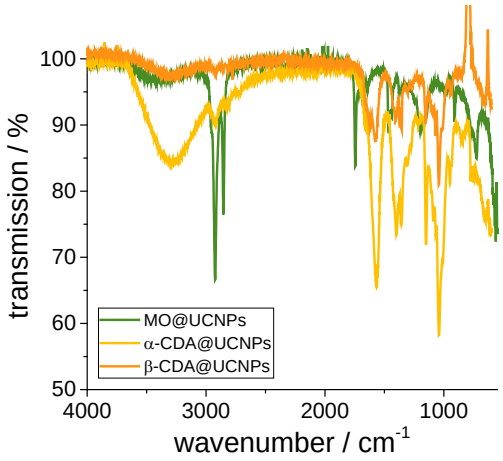


Figure S2 IR spectra for UCNP coated with MO, α-CDA and β-CDA.

5. Analysis

5.1 UV/Vis Spectra of AAP-TEG

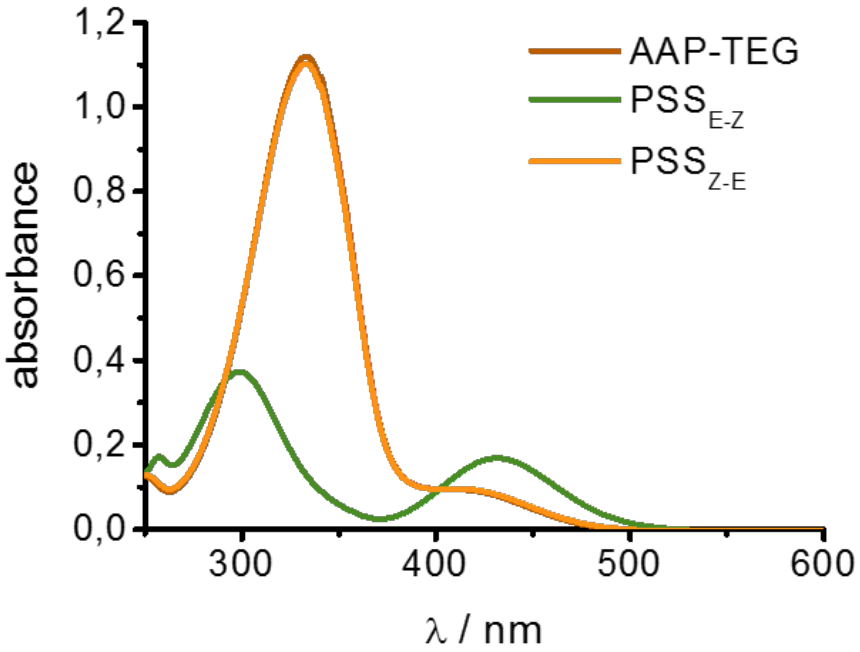


Figure S3: UV/Vis spectra of the AAP-TEG (35 µM) and its photostationary states (PSS).

5.2 TEM of MO@ $LiYF_4:Yb^{3+},Tm^{3+},Gd^{3+}$

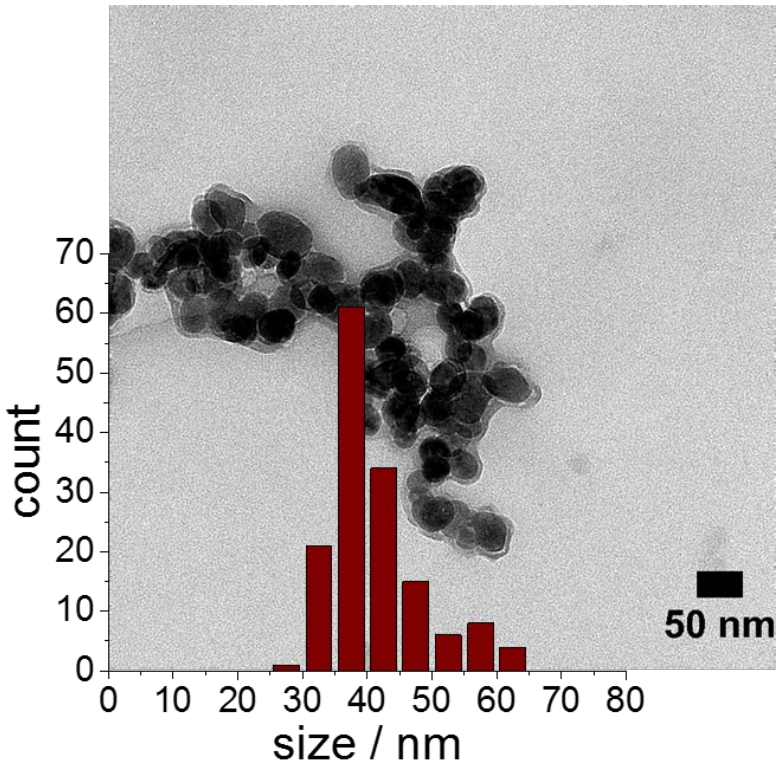


Figure S4: TEM image of the MO@$LiYF_4:Yb^{3+},Tm^{3+},Gd^{3+}$ (particle diameter: 41.0±7.1 nm).

5.3 TEM of nanoparticle aggregates

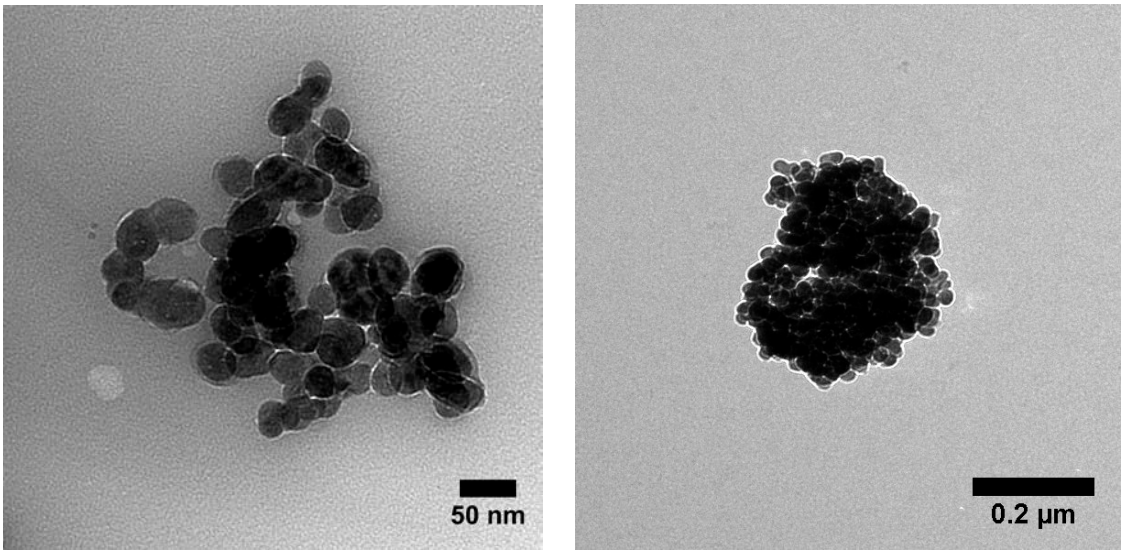


Figure S5: Aggregation experiment of α-CDA@UCNPs (0.085 mg/mL) with the Azo-linker (80 µM) monitored via TEM measurements (right image; aggregate diameter around 0.4 µm) compared to of α-CDA@UCNPs (left image).

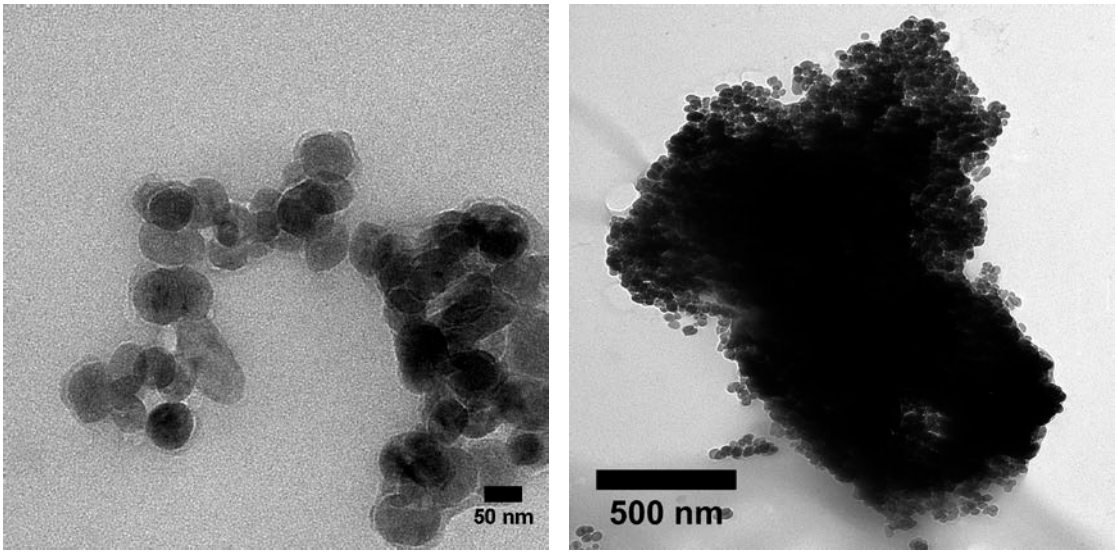


Figure S6: Aggregation experiment of β-CDA@UCNPs (0.085 mg/mL) with the AAP-linker (80 µM) monitored via TEM measurements (right image; aggregate diameter around 1.2 µm).

5.4 ^{1}H-NMR spectra

5.4.1 MO@ $LiYF_4$:Yb^{3+},Tm^{3+}, Gd^{3+} compared to MO

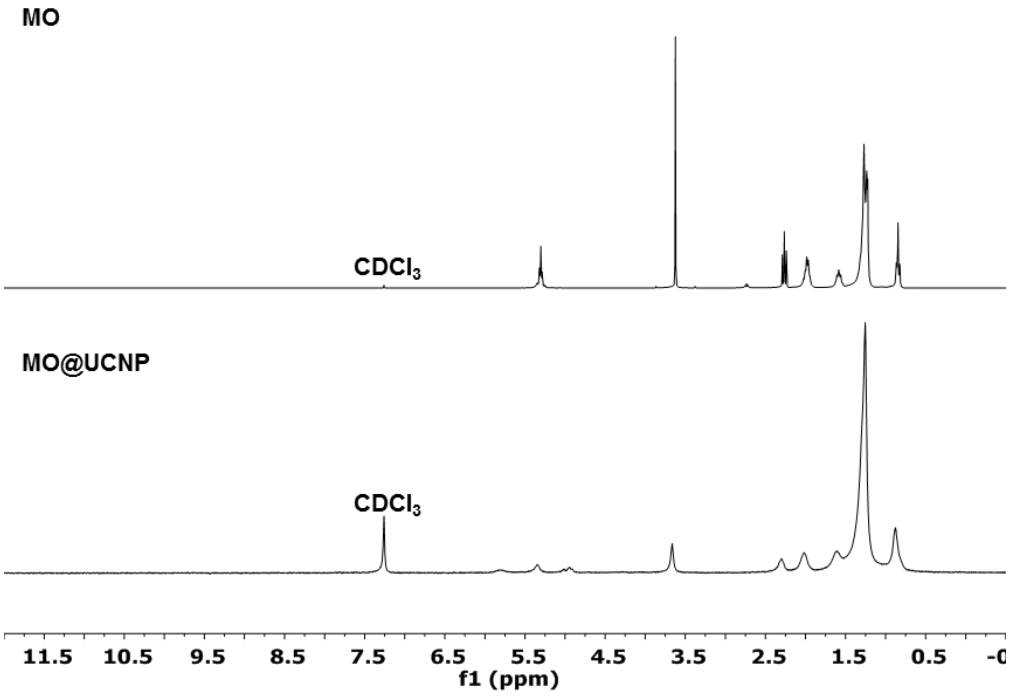


Figure S7

Broader signals in the MO@UCNPs spectra were observed due to the limited rotational freedom when the MO binds to the surface of the nanoparticles compared to the free MO.

5.5 XRD spectra of CDA@UCNPs

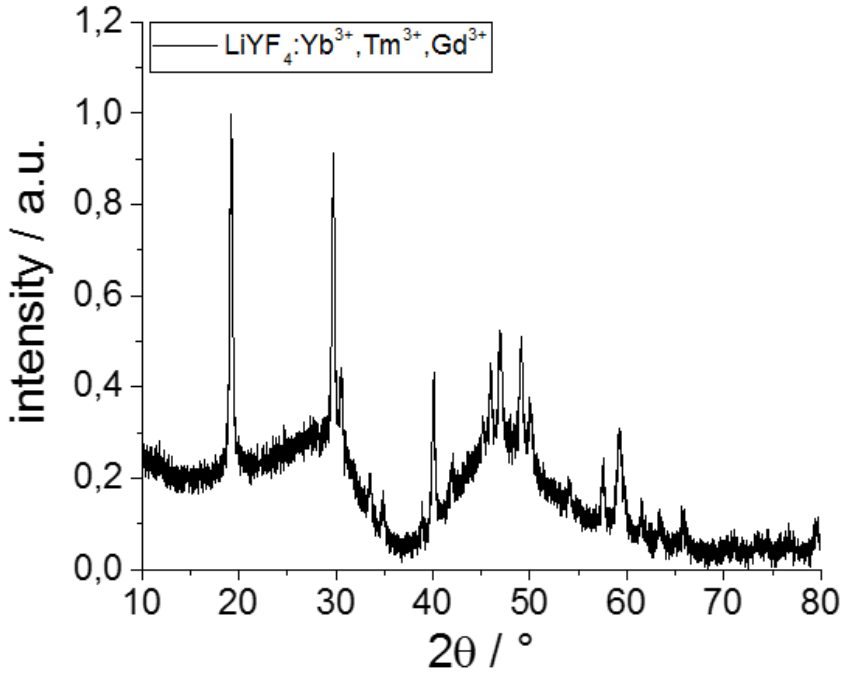


Figure S8: XRD-spectra of $LiYF_4:Yb^{3+},Tm^{3+},Gd^{3+}$ showing the characteristic 2θ signals of the tetragonal Scheelite structure of $Ca[WO_4]$.[8]

5.6 Emission spectra of CDA@UCNPs and MO@UCNPs

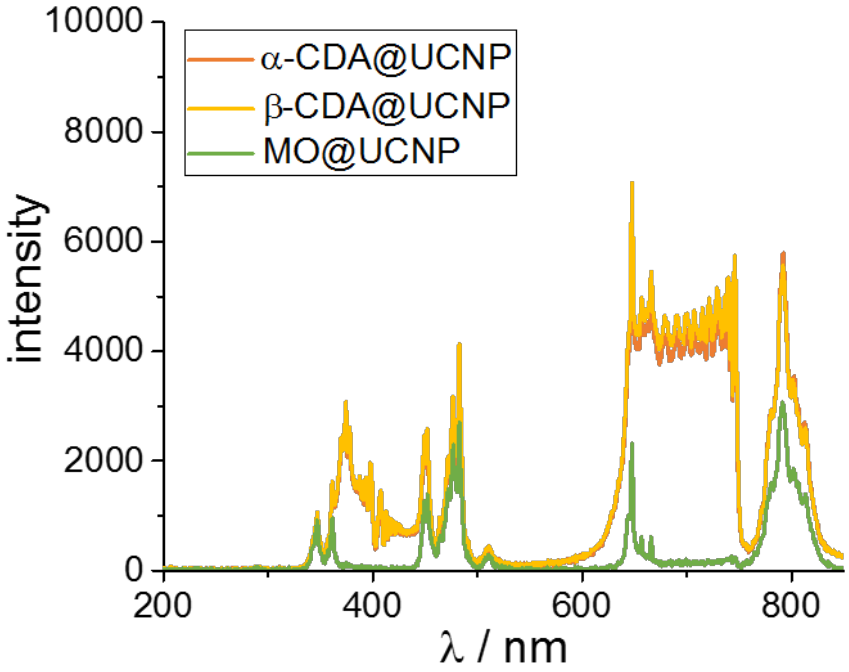


Figure S9: Emission spectra of α- (orange) and β-CDA@UCNPs (yellow) compared to the emission spectra of MO@UCNPs (green). Laser intensity was about 5.1 kW/cm².

5.7 Aggregation of CDA@UCNPs

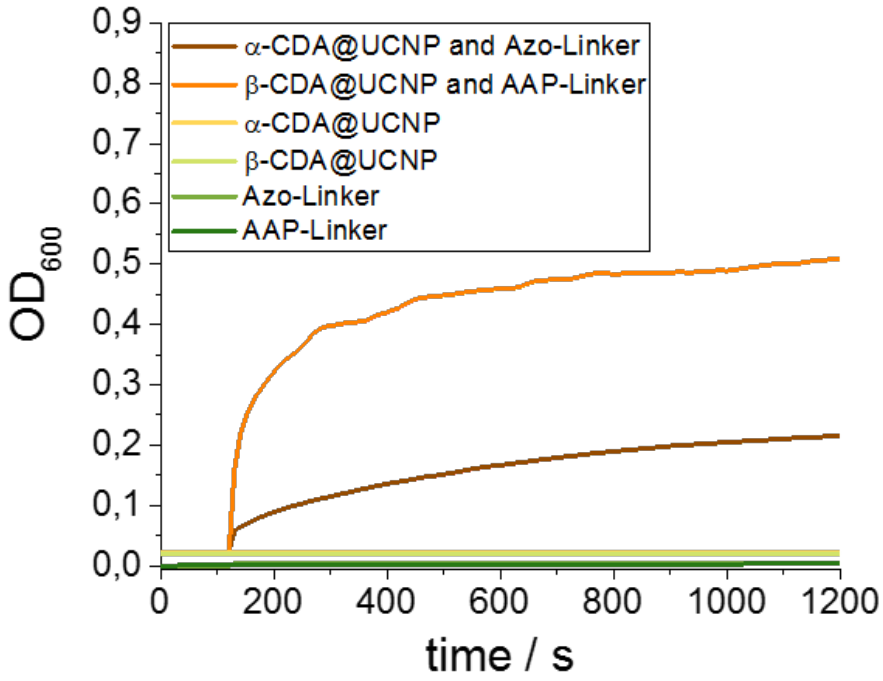


Figure S10: Spectra of the measured OD_{600} during the aggregation experiment. Only in case of the combination of CDA@UCNPs and linker an aggregation could be observed. All samples were prepared in ultra pure water. For each measurements - also for the blind measurements with only the linker in absence of the nanoparticles - the linker was added after an equilibration time of 120 seconds. The concentration of the UCNPs was 0.085 mg/mL. For the Azo- and AAP-Spermine-Linker the concentration was 80 µM. For both only the particles or only the linker in water no agglomeration could be observed.

Comment MeOH pur

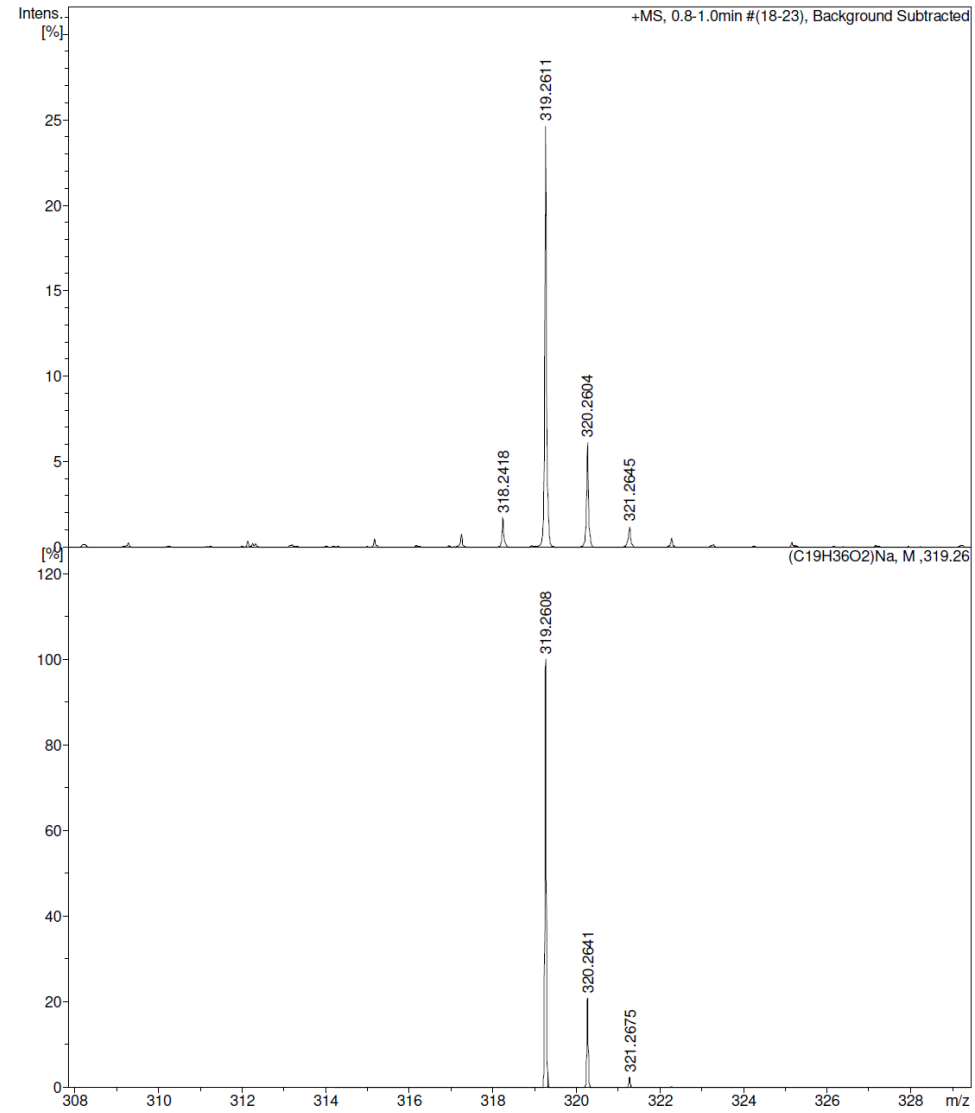


Figure S11 Mass analysis of the Et_2O phase after the extraction to control the successful exchange of the methyloleate by the CDA. Only the methyloleate was found in the mass spectra.

5.8 Control experiment: UV/Vis-Spectra of Azo-TEG or AAP-TEG and α- or β-CDA@$LiYF_4$ without irradiation

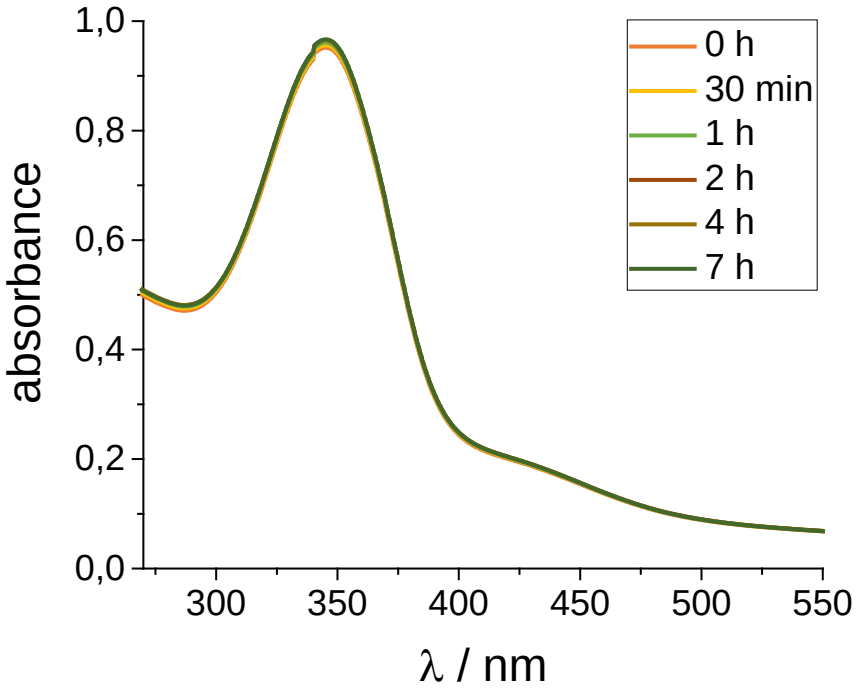


Figure S12: UV/Vis spectra of 0.91 mM Azo-TEG in 2 mg/mL α-CDA@UCNPs without irradiation at 980 nm.

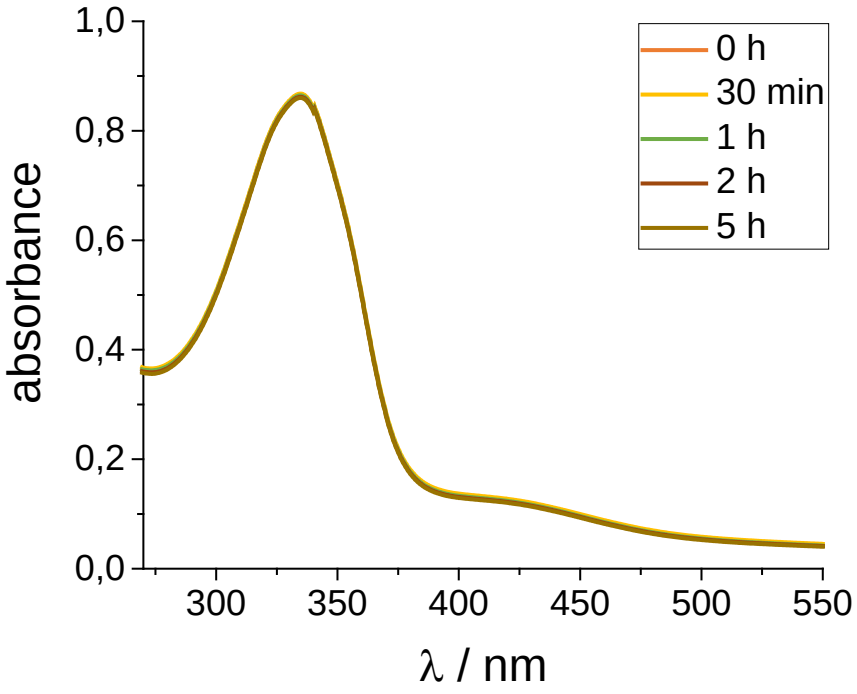


Figure S13: UV/Vis spectra of 0.91 mM AAP-TEG in 2 mg/mL β-CDA@UCNPs without irradiation at 980 nm.

5.9 Control experiment: UV/Vis-Spectra of Azo-TEG or AAP-TEG irradiated without UCNPs

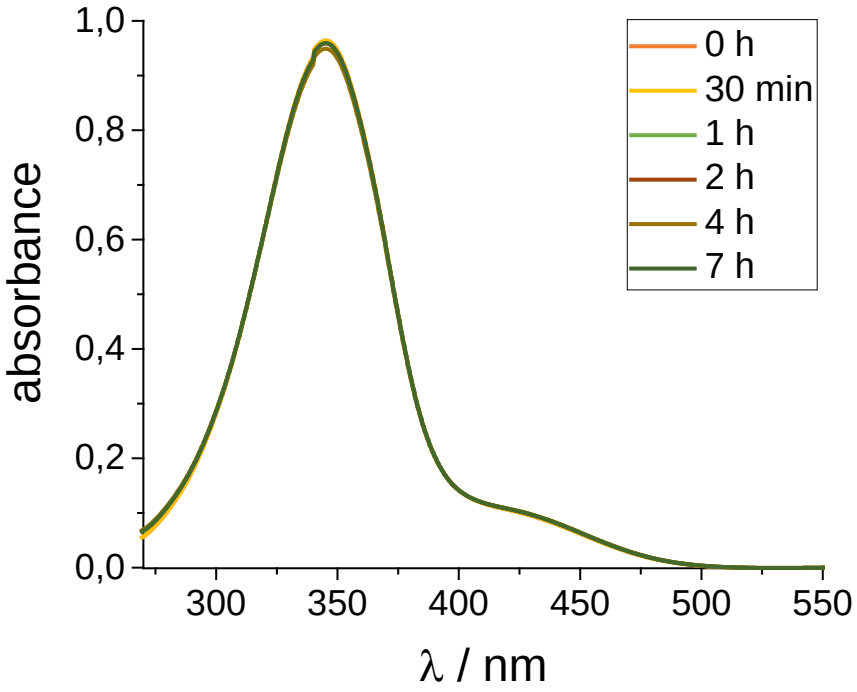


Figure S14: UV/Vis spectra of 0.91 mM Azo-TEG in ultra pure water irradiated at 980 nm without α-CDA@UCNPs.

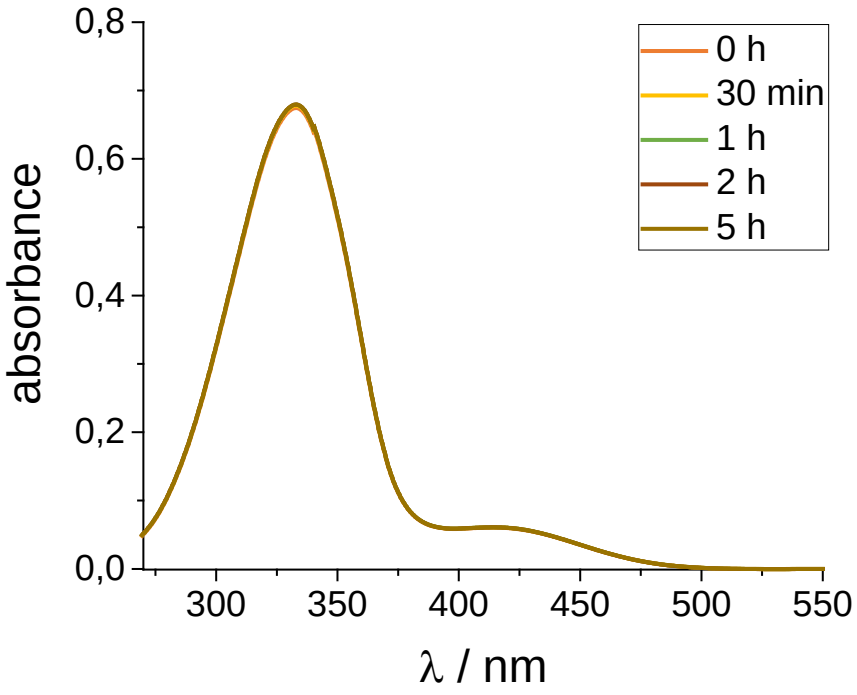


Figure S15: UV/Vis spectra of 0.91 mM AAP-TEG in ultra pure water irradiated at 980 nm without β-CDA@UCNPs.

5.10 Determination of the photostationary state of Azo and AAP in a α- or β-CDA@$LiYF_4$ dispersion after irradiation

Azo:

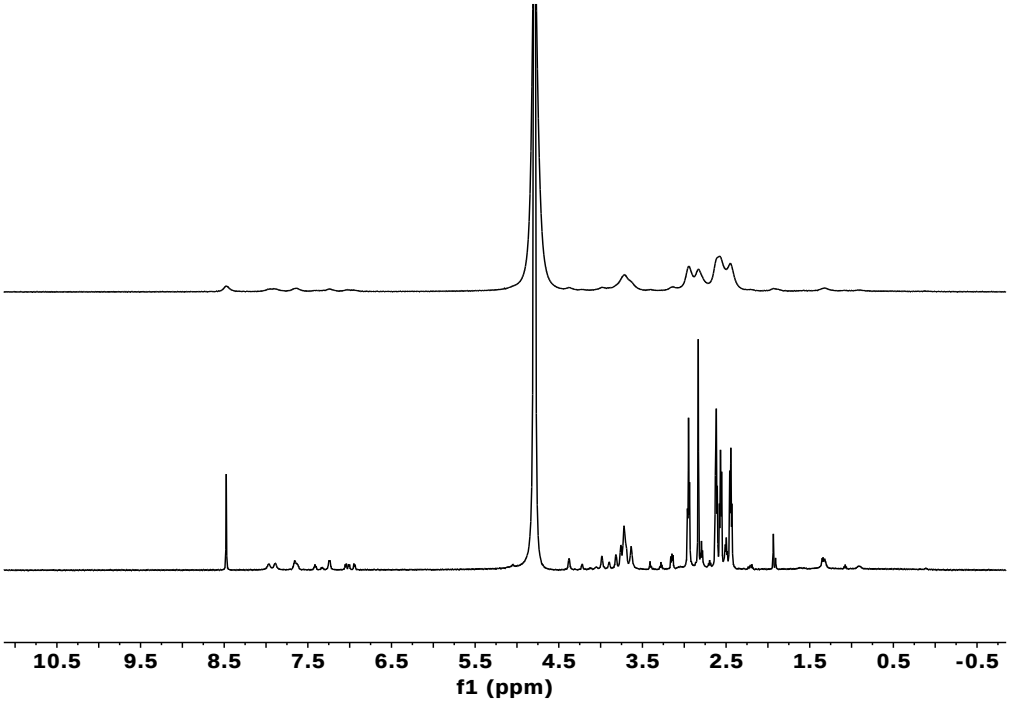


Figure S16: Azobenzene in a α-CDA@$LiYF_4$ dispersion in D_2O before irradiation (top) and after irradiation at 980 nm (bottom).

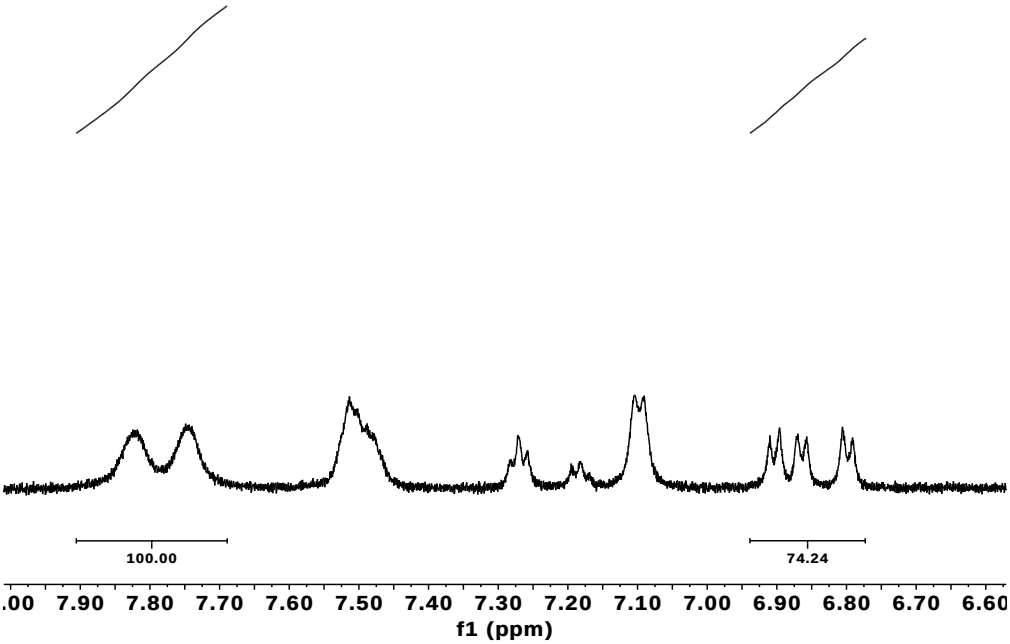


Figure S17: Azobenzene in a α-CDA@$LiYF_4$ dispersion in D_2O after irradiation at 980 nm – magnification and integration (7.80 ppm trans-isomer and 6.90 ppm cis-isomer).

Before irradiation: 80% trans and 20% cis (see ref [4]).

After irradiation at 980 nm: Photostationary state of about 57% trans and 43% cis.

Moreover, after irradiation at 980 nm, the peaks gets sharper and more discrete indicating that the cis isomer is no longer close to the particle because it does not bind in the CDA cavity anymore.

AAP:

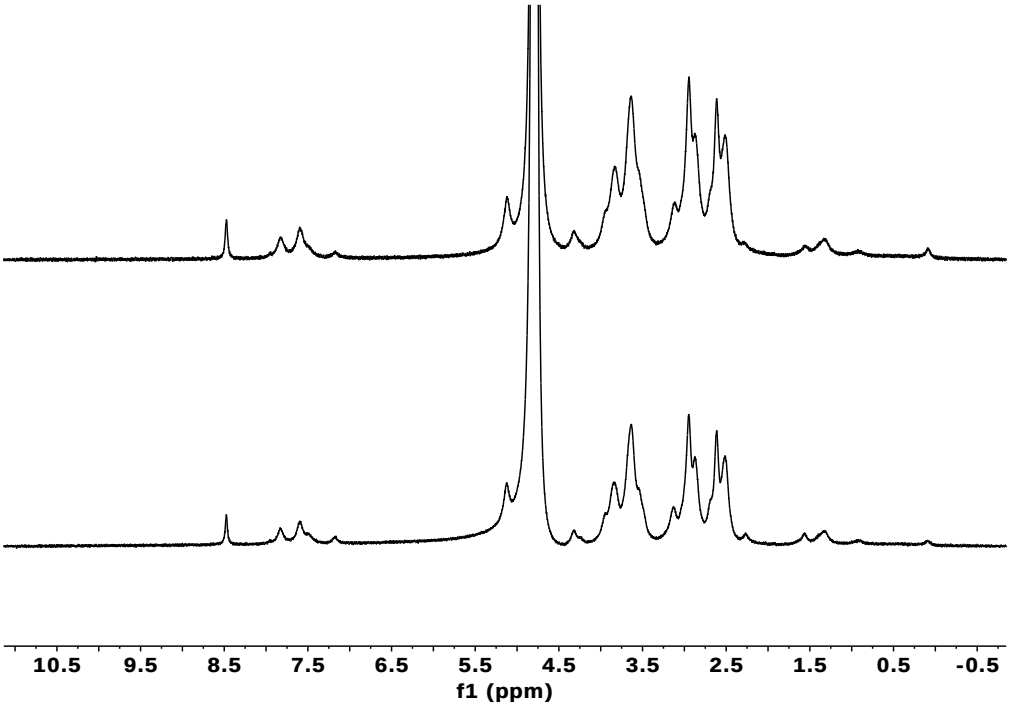


Figure S18: AAP in a β-CDA@$LiYF_4$ dispersion in D_2O before irradiation at 980 nm (top) and after irradiation (bottom).

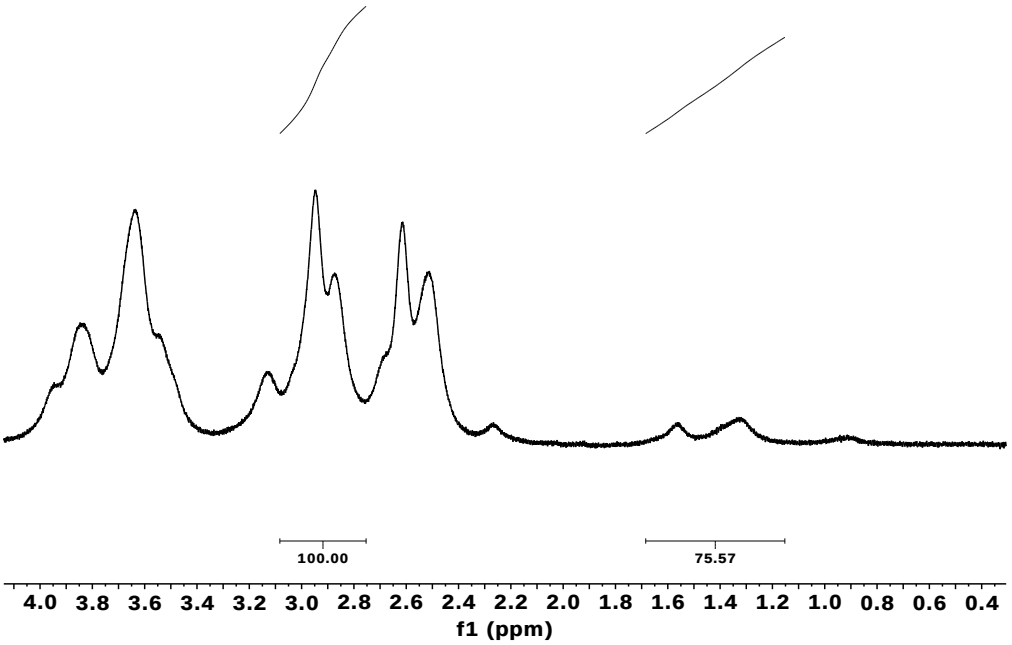


Figure S19: AAP in a β-CDA@$LiYF_4$ dispersion in D_2O after irradiation at 980 nm – magnification and integration (2.90 ppm trans-isomer and 1.40 ppm cis-isomer).

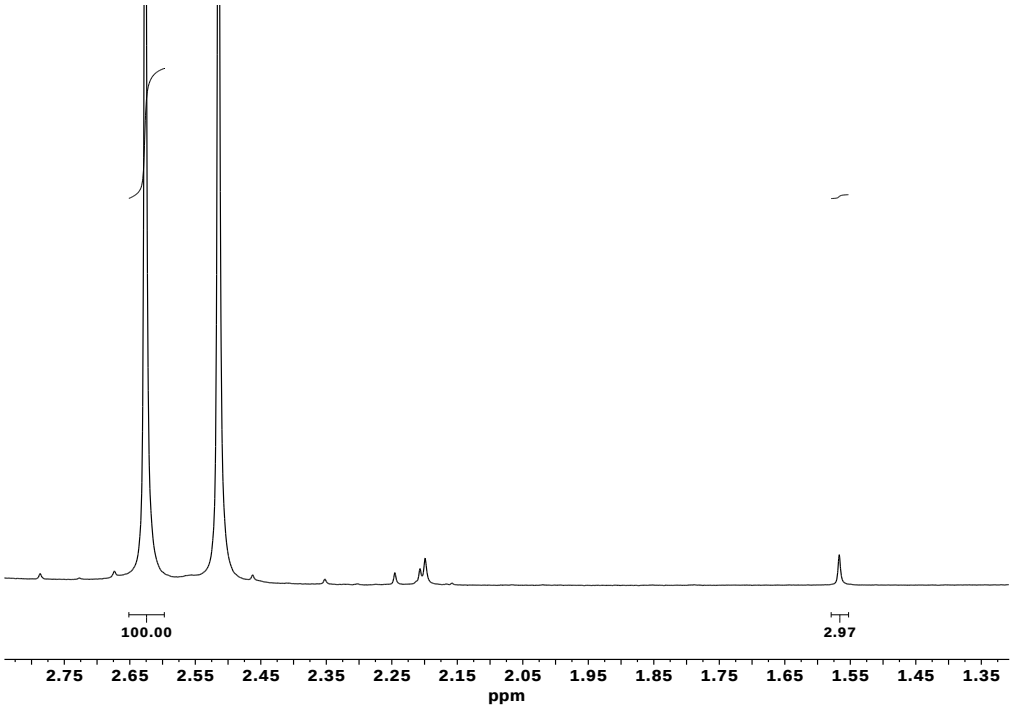


Figure S20: Free AAP in $CDCl_3$ before irradiation – magnification and integration.

Before irradiation: 97% trans 3% cis (see ref [6])

After irradiation at 980 nm: Photostationary state of about 57% trans and 43% cis, which is the same result as for the azobenzene.

6. Spectra

(E)-2-(2-(2-(2-(3,5-dimethyl-4-(phenyldiazenyl)-1H-pyrazol-1-yl)ethoxy)ethoxy)ethoxy)ethan-1-ol **(AAP-TEG)**

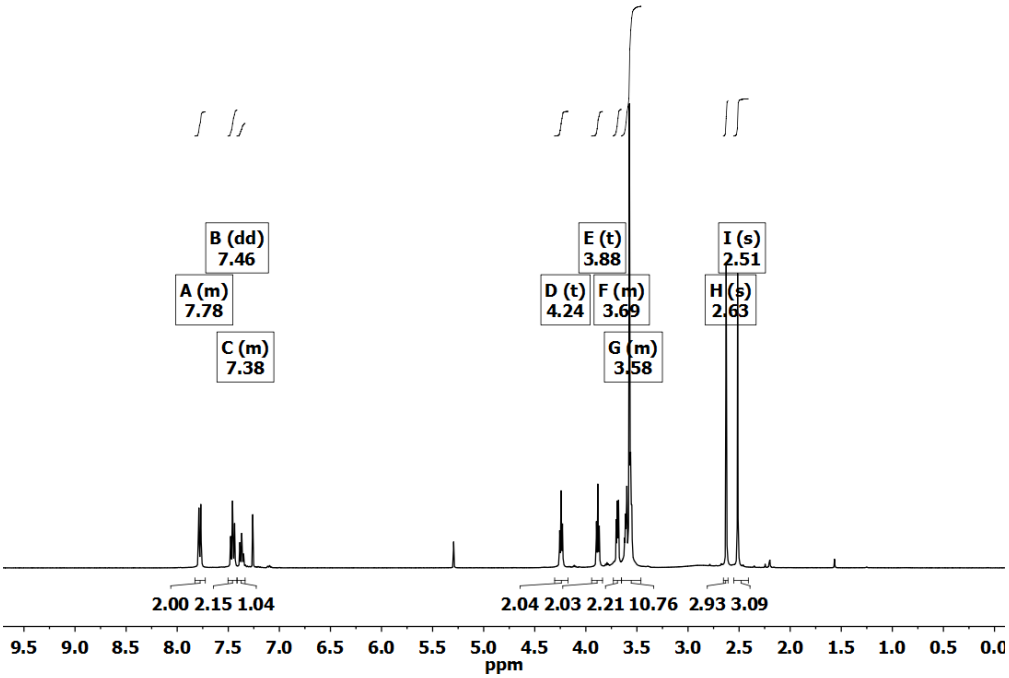


Figure S21: ^{1}H-NMR of AAP-TEG.

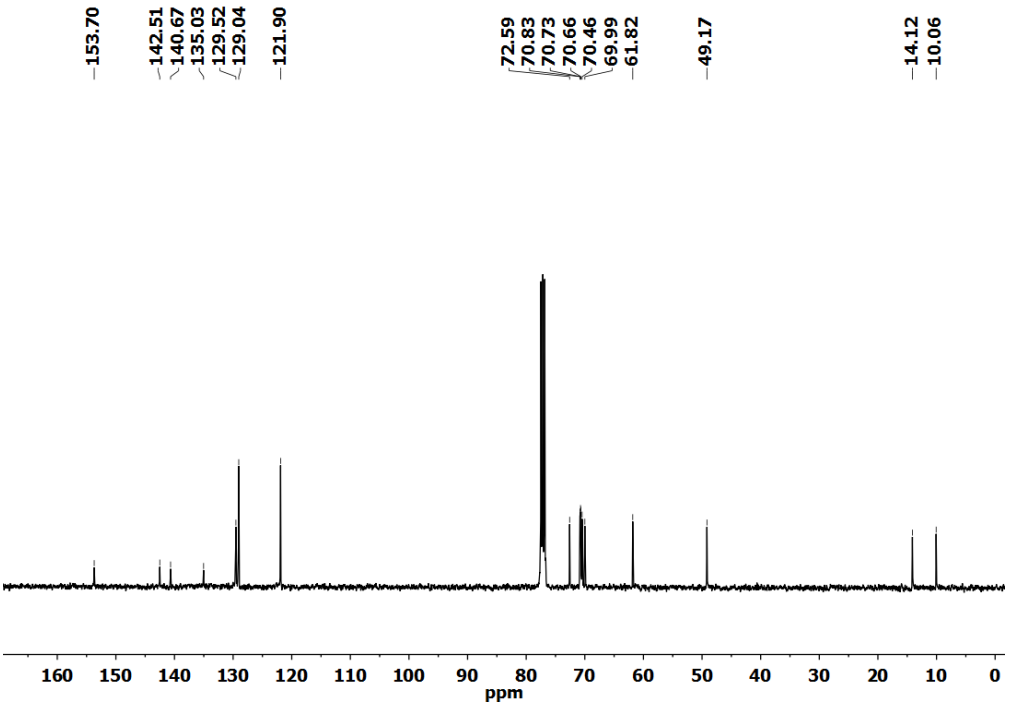


Figure S22: ^{13}C-NMR of AAP-TEG.

N,N'-((ethane-1,2-diylbis(azanediyl))bis(propane-3,1-diyl))bís(2-(4-((E)-phenyldiazenyl)diazenyl)phenoxy)acetamide) (**Azo-linker**)

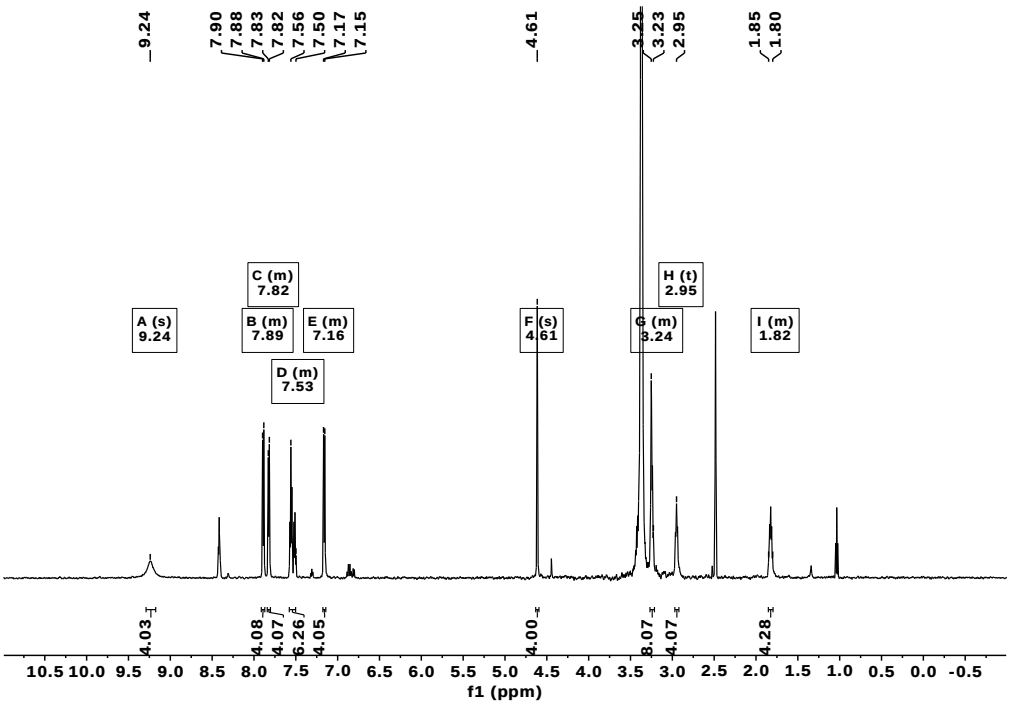


Figure S23: [1]H-NMR of Azo-linker.

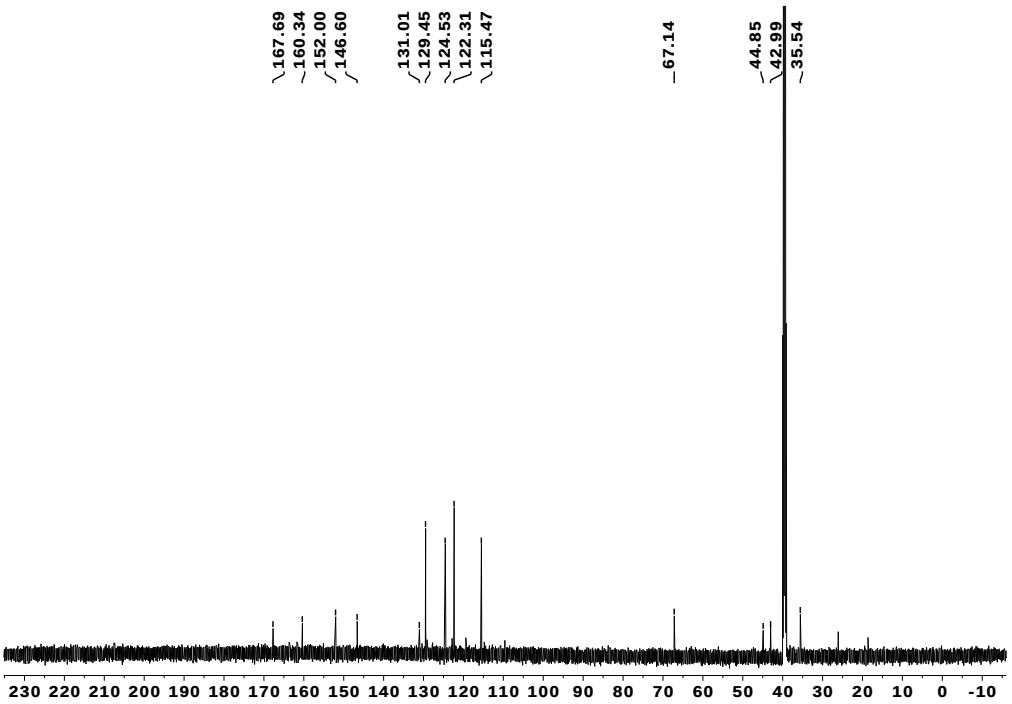


Figure S24: [13]C-NMR of Azo-linker.

7. References

[1] F. Guillo, B. Hamelin, I.Jullien, J. Cancelli, J.-M. Lehn, L. De Robertis, H.Driguez, *Bull. Soc. Chim. Fr.* **1995**, *132*, 857.

[2] J. M. Adam, D. J. Bennett, A. Bom, J. K. Clark, H. Feilden, E. J. Hutchinson, R. Palin, A. Prosser, D. C. Rees, G. M. Rosair, D. Stevenson, G. J. Tarver, M. Q. Zhang, J. Med. Chem. **2002**, *45*, 1806.

[3] K. Kishimoto, T. Suzawa, T. Yokota, T. Mukai, H. Ohno, T. Kato, *J. Am. Chem. Soc.* **2005**, *127*, 15618.

[4] S. K. Nalluri, J. Voskuhl, J. B. Bultema, E. J. Boekema, B. J. Ravoo, *Angew. Chem. Int. Ed.* **2011**, *50*, 9747.

[5] A. Samanta, B. J. Ravoo, *Chem. Eur. J.* **2014**, *20*, 4966.

[6] L. Stricker, E.-C. Fritz, M. Peterlechner, N. L. Doltsinis, B. J. Ravoo, *J. Am. Chem. Soc.*, **2016**, *138*, 4547.

[7] B. Meesaragandla, V. N. Adusumalli, V. Mahalingam, *Langmuir* **2015**, *31*, 5521.

[8] A. Grzechnik, K. Syassen, I. Loa, M. Hanfland, J. Y. Gesland, *Phys. Rev. B* **2002**, *65*, 104102.