Universitat Autònoma de Barcelona

**Departament de Química**

**Facultat de Ciències**

# New Functional Ligands for the Preparation of Photoactive Nanoparticle-Based Materials

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# CHAPTER V

# Summary and conclusions

In this chapter the main results and conclusions are summarized for the two different projects undertaken in this thesis: the study of encapsulation and drug release mechanisms from coordination polymer particles, and the development of a new methodology for controlled covalent quantum dot assembly based on the strain-promoted azide-alkyne cycloaddition reaction.

# V.1. New functional ligands for investigating drug release mechanisms from coordination polymer particles

In the first part of this thesis, new fluorescent model drugs were synthesized to be covalently linked or mechanically encapsulated within Co-based coordination polymer particles. The guest release mechanisms from the resulting materials were then investigated and correlated with the encapsulation method used. (Figure V-1). In this way, physically entrapped model drugs were found to be mainly delivered via fast diffusion processes at physiological conditions, while slow particle degradation was required for the release of chemically-bound guest molecules. This demonstrates that release kinetics from coordination polymer can be finely tuned by proper choice of the encapsulation mechanism, thus allowing the time window of action of the drug delivered to be adjusted to the therapeutic needs. In view of this, a general mathematical model was developed and validated that can be applied to analyze drug release profiles from almost any coordination polymer particle and regardless of the encapsulation mechanism selected.

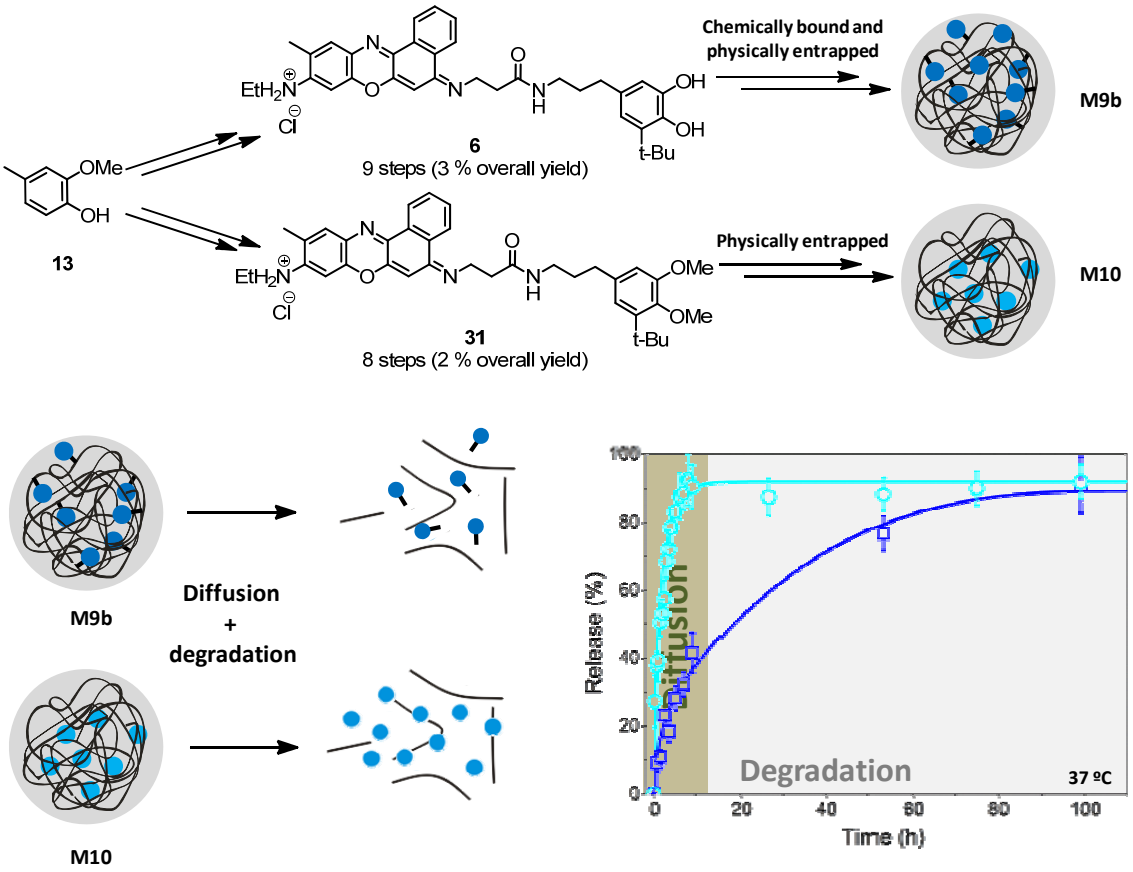



**Figure V-1.** Schematic representation of the studies carried out in Chapter III to investigate diffusion- and degradation-induced guest release from coordination polymer particles.

# V.2. New functional ligands for quantum dot covalent assembly

During the second part of the thesis, the strain-promoted azide-alkyne cycloaddition reaction was explored for the formation of covalently-bonded heteroaggregates of quantum dots. With this aim, different organic ligands bearing reactive azide and cyclooctyne groups were synthesized, characterized and attached to the surface of quantum dots. Upon mixture of azide- and cyclooctyne-functionalized quantum dots, the successful formation of dimers, trimers and more complex structures of these nanocrystals were observed, which displayed in some cases high resonance energy transfer efficiencies (Figure V-2). This result opens up the door to the application of this methodology to the preparation of photonic nanowires of colloidal quantum dots for light harvesting and energy transfer applications on the nanoscale.

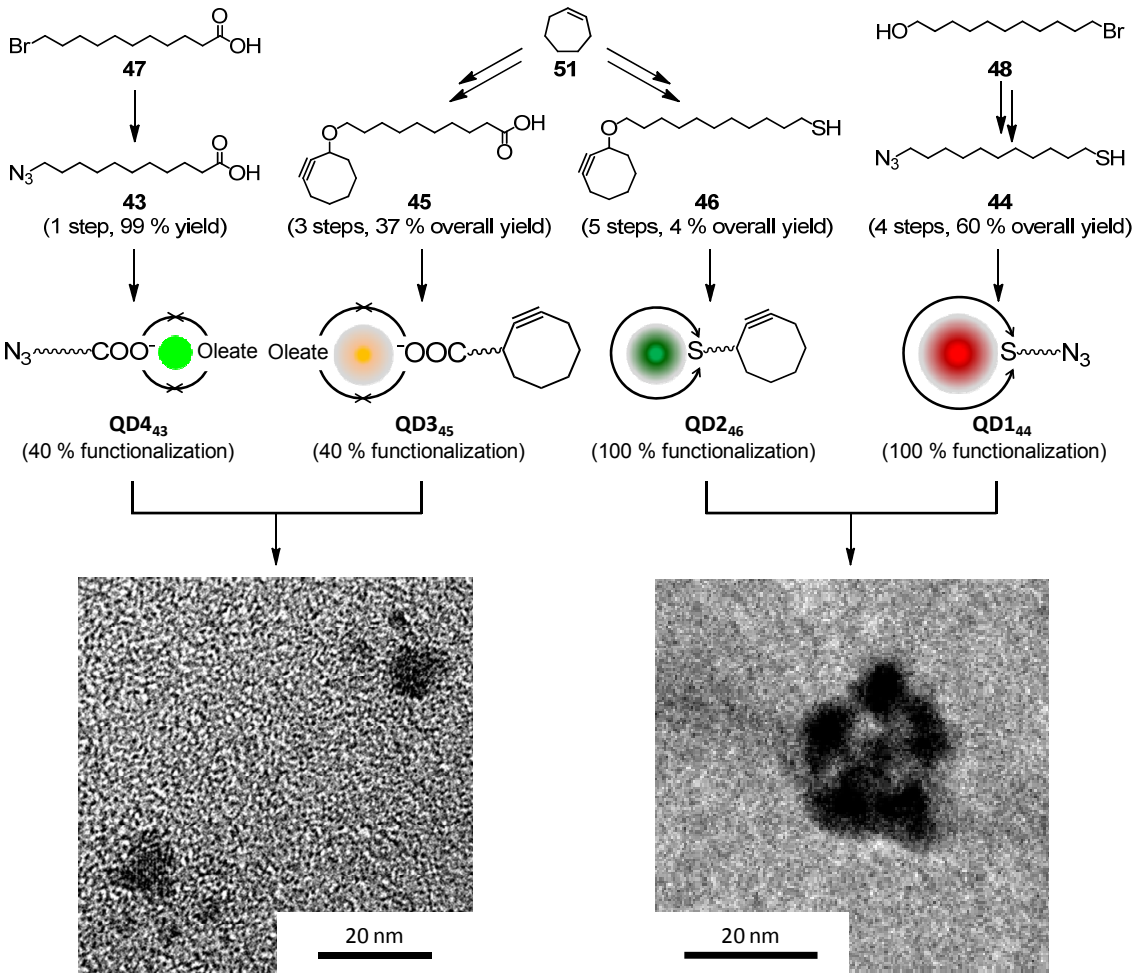



**Figure V-2.** Summary of the studies carried out in Chapter IV to explore strain-promoted azide-alkyne cycloaddition as a new methodology to prepare covalently-bonded heteroaggregates of quantum dots.

# CHAPTER VI

## Experimental Section

# VI.1. GENERAL PROCEDURES

All commercially available reagents were used as received. Anhydrous $CH_2Cl_2$, THF and pentane where used from an automatic drier Innovative technology PureSolv-MD-2. Toluene was dried by distillation over $Na^0$, benzophenone. When needed, reactions were performed avoiding moisture by standard procedures and under Ar atmosphere.

**Nuclear magnetic resonance spectra (NMR)** were registered at the *Servei de Ressonància Magnètica Nuclear* of the *Universitat Autònoma de Barcelona*. $^1$H-NMR, COSY, NOESY, HSQC $^1$H-$^{13}$C and HMBC $^1$H-$^{13}$C spectra were recorded on Bruker DPX250 (250 MHz), Bruker DPX360 (360 MHz) and Bruker AR430 (400 MHz) spectrometers. Characterization of organic QD surface and 1D DOSY experiments were recorded on Bruker AR430 (400 MHz) spectrometer. Proton chemical shifts are reported in ppm ($\delta$) ($CDCl_3$, 7.26 ppm, MeOH-$d_4$, 3.31 ppm and DMSO-$d_6$, 2.50 ppm). $^{13}$C-NMR spectra were recorded with complete proton decoupling on Bruker DPX250 (62.5 MHz), Bruker DPX360 (90 MHz) and Bruker AR430 (100.6 MHz) spectrometers. Carbon chemical shifts are reported in ppm ($CDCl_3$, 77.16 ppm, MeOH-$d_4$, 49.00 ppm and DMSO-$d_6$, 39.52 ppm). All spectra were measured at 298 K.

The abbreviations used to describe signal multiplicities are: s (singlet), br s (broad singlet), d (doublet), br d (broad doublet), t (triplet), q (quartet), $q_t$ (quintet), dd (double doublet), dt (double triplet), m (multiplet), br m (broad multiplet) and *J* (coupling constant).

**Infrared spectra (IR)** were recorded on a Bruker Tensor 27 Spectrophotometer equipped with a Golden Gate Single Refraction Diamond ATR (Attenuated Total Reflectance) accessory at *Servei d'Anàlisi Química* of the *Universitat Autònoma de Barcelona.* Peaks are reported in $cm^{-1}$.

**Electronic absorption spectra (UV-vis)** were recorded on a HP 8453 Spectrophotometer. HPLC or spectroscopy quality solvents were used.

**Excited state lifetime** measurements were carried out with a ns laser flash-photolysis system (LKII, Applied Photophysics) equipped with a Nd:YAG laser (Brilliant, Quantel) as pump source and a photomultiplier tube (PMT, R928, Hamamatsu) coupled to a spectrograph as detector.

**Mass Spectrometry.** High resolution mass spectra (HRMS) were recorded at the *Servei d'Anàlisi Química* of the *Universitat Autònoma de Barcelona* in a Bruker micrOTOFQ spectrometer using ESIMS (QTOF).

**Transmission electron microscopy and High Resolution Transmission electron microscopy.** TEM images were taken at Servei de Microscòpia of the Universitat Autonoma de Barcelona using a HITACHI H-7000 transmission electron microscope (125 kV). HR-TEM images were taken at *Servei de Microscòpia* of the *Universitat Autonoma de Barcelona* using a JEOL JEM-2011 transmission electron microscope (200 kV). A 3 mm copper grid covered with a holey carbon film was immersed in the sample and dried in the air. For spin-coated samples: 100 µL of solution (5 nM) were spin coated onto a 3 mm copper grid covered with a holey carbon film. Gatan DigitalMicrograph for Windows was used for image process and nanoparticle size measurements.

**Chromatography.** All reactions were monitored by analytical thin-layer chromatography (TLC) using silica gel 60 F254 pre-coated aluminium plates (0.25 mm thickness). Development was made using an UV lamp at 254 nm and/or using a $KMnO_4$/KOH aqueous solution. Flash column chromatography was performed using silica gel (230-400 mesh).

**Fluorometry.** Fluorescence emission spectra were measured by means of two different spectrofluorometers: (i) a custom-made spectrofluorometer, where a Nd:YAG (Brillant, Quantel) pulsed laser emitting at 355 nm is used as excitation source and the emitted photons are detected in an Andor ICCD camera coupled to a spectrograph; and (ii) a PerkinElmer LS 55 fluorescence spectrometer. HPLC or spectroscopy quality solvents were used.

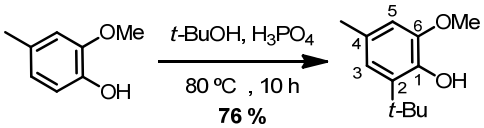
**Excitation Sources.** Different excitation sources were used to characterize PLQY QDs: diode cw lasers at $\lambda_{exc}$ = 473 nm (SDL-BS-300, company), $\lambda_{exc}$ = 532 nm (Z-Laser) and $\lambda_{exc}$ = 594 nm (REO, Inc).

# VI.2. NEW FUNCTIONAL LIGANDS FOR INVESTIGATING DRUG RELEASE MECHANISMS

## VI.2.1. Synthesis of fluorophores of type I

### VI.2.1.1. Synthesis of intermediate 7

#### Synthesis of 2-(*tert*-butyl)-6-methoxy-4-methylphenol, 15



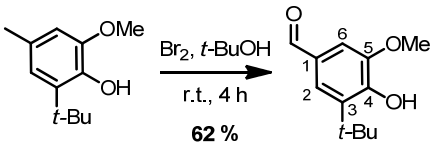

**13** **15**

Compound **15** was synthesized according to ref [1]. tert-buthanol (4 mL) was added to a solution of **13** (4.13 g, 29.9 mmol) in $H_3PO_4$ (9 mL) heated at 80 ºC. After 10 hours, reaction mixture was coold down to room temperatura and wáter was added (8 mL). The aquose layer was extracted twice with EtOAc (16 mL) and once with $CH_2Cl_2$ (16 mL). Combined organic layers were dried with MgSO4 and solvent was removed under reduced pressure. Crude was purified by flash chromatography using hexanes:EtOAc (6:1, v/v) to afford **15** (4.44 g, 76 %) as a colorless oil.

Espectroscopic data of **15**

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 6.73 (d, $J_{3,5}$ = 1.7 Hz, 1H, 1xH-3), 6.63 (d, $J_{5,3}$ = 1.7 Hz, 1H, 1xH-5), 5.86 (s, 1H, -OH), 3.90 (s, 3H: -$OCH_3$), 2.33 (s, 3H: Ph-$CH_3$), 1.46 (s, 9H: -$C(CH_3)_3$).

#### Synthesis of 3-(*tert*-butyl)-4-hydroxy-5-methoxybenzaldehyde, 16



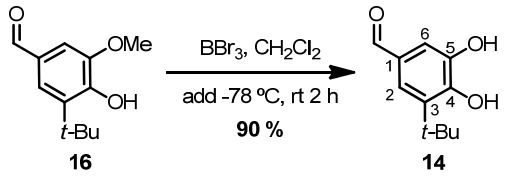

**15** **16**

Compound **16** was synthesized according to ref [1]. To a solution of **15** (4.30 g, 22.1 mmol) in *t*-BuOH (60 mL), was added dropwise molecular bromine (3 mL, 55.8 mmol). Reaction mixture was stirred at room temperature for 4 hours. Next, an aquose solution of sodium hydrogensulfite was added (50 mL, 10 %, v/v) and aquose layer was washed twice with EtOAc (30 mL). Organic extracts were dried with $MgSO_4$ and the solvent was evaporated under vacuum. Residue was purified by flash chromatography using hexanes: EtOAc (4:1, v/v) affording **16** (2.85 g, 62 % yield) as a brownish solid.

Espectroscopic data of **16**

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 9.80 (s, 1H, -CHO), 7.49 (d, $J_{2,6}$ = 3 Hz, 1H, 1xH-2), 7.31 (d, $J_{6,2}$ = 3 Hz, 1H, 1xH-6), 6.58 (br s, 1H, -OH), 3.95 (s, 3H, $-OCH_3$), 1.42 (s,9H, $-C(CH_3)_3$).

## Synthesis of 3-(*tert*-butyl)-4,5-dihydroxybenzaldehyde, 14

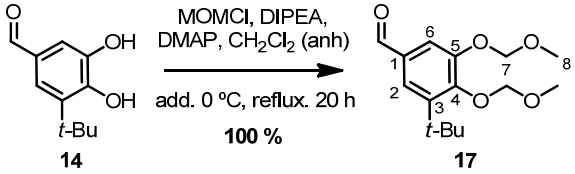



Compound **14** was synthesized according to ref [2]. To a solution of **16** (845 mg, 4 mmol) $CH_2Cl_2$ (30 mL) cooled down at -78 ºC with a $N_2$-acetone bath, boron tribromide (5.5 mL, 32 mmol) was added dropwise. After addition, reaction mixture was stirred at room temperature for 2 hours. Next, reaction mixture was added to water (40 mL). Aquose layer was extracted twice with $CH_2Cl_2$ (30 mL) and combined organic layers were dried with $MgSO_4$ and the solvent was evaporated under vacuum. Residue was purified by flash chromatography using hexanes: EtOAc (4:1, v/v) affording **14** (689 mg, 90 % yield) as a yelowish solid.

Espectroscopic data of **14**

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 9.78 (s, 1H, -CHO), 7.43 (s, 1H, 1xH-2), 7.36(s, 1H, 1xH-6), 6.41 (br s, 1H, -OH), 5.32 (s, 1H, -OH), 1.45 (s, 9H, $-C(CH_3)_3$).

## Synthesis of 3-(*tert*-butyl)-4,5-bis(methoxymethoxy)benzaldehyde, 17

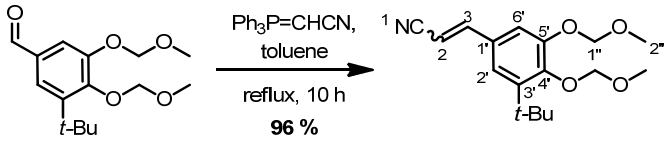



Compound **17** was synthesized according to ref [3] with some modifications. To a solution of **14** (492.4 mg, 2.54 mmol), DIPEA (2.7 mL, 15.5 mmol) and DMAP (30 mg, 0.22 mmol) in dry $CH_2Cl_2$ and cooled down with an ice bath, was added MOMCl (0.65 mL, 8.02 mmol). Reaction mixture was stirred at 55 ºC for 20 hours. Next, reaction mixture was coold down to room temperature and water was added (15 mL). Aquose layer was extracted twice with $CH_2Cl_2$ (30 mL) and combined organic layers were dried with $MgSO_4$ and the solvent was evaporated under vacuum. Residue was purified by flash chromatography using hexanes: EtOAc (4:1, v/v) affording **17** (716.2 mg, 100 % yield) as a yelowish oil.

Espectroscopic data of **17**

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 9.87 (s, 1H, -CHO), 7.55 (s, 2H, 1xH-2, 1xH-6), 5.31 (s, 2H, 2xH-7), 5.23 (s, 2H, 2xH-7'), 3.66 (s, 3H, 3xH-8), 3.52 (s, 3H, 3xH-8'), 1.45 (s, 9H, -C($CH_3$)$_3$). **$^{13}$C RMN** (100 MHz, $CDCl_3$): $\delta$ 191.5 (-CHO), 151.9 (C-4), 150.4 (C-5), 144.0 (C-3), 131.5 (C-1), 123.8 (C-2), 114.5 (C-6), 99.4 (C-7), 95.4 (C-7'), 57.9 (C-8), 56.6 (C-8'), 35.4 (-**C**($CH_3$)$_3$), 30.3 (-C(**C**$H_3$)$_3$). **IR (ATR)** 3009, 2953, 2905, 1690, 1578, 1153, 924. **HR-MS** (ESI+) calcd. for [$C_{15}H_{22}O_5$+Na]: 305.1359; found: 305.1356 ([M+Na]$^+$, 100).

## Synthesis of (*E*)- and (*Z*)-3-(3-(tert-butyl)-4,5-bis(methoxymethoxy)phenyl)-acrylonitrile, (*E*)- and (*Z*)-18

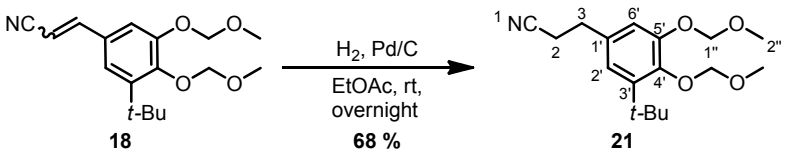



To a solution of **17** (1.59 g, 5.53 mmol) in toluene (45 mL), was added 2-(triphenylphosphoranylidene)acetonitrile (2.07 g, 6.87 mmol). Reaction mixture was warmed up at 130 ºC for 10 hours. Next, reaction mixture was cooled down at room temperature and solvent was evaporated. Crude was purified by flash chromatography using hexanes: EtOAc (6:1, v/v) to afford a mixture of **(*E*)-** and **(*Z*)-18** (1.62 g, 96 % yield) as a brownish oil, with a diastereomeric ratio of 2.3:1, respectively.

Espectroscopic data of **(*E*)-** and **(*Z*)-18**

**1H RMN** (400 MHz, $CDCl_3$): $\delta$ 7.57 (d, $J_{6',2'}$ = 12.0 Hz, 1H, 1x(*Z*)-H-6'), 7.47 (d, $J_{2',6'}$ = 2.2 Hz, 1H, 1x(*Z*)-H-2'), 7.32 (d, $J_{3,2}$ = 16.6 Hz, 1H, 1x(*E*)-H-3), 7.16 (d, $J_{6',2'}$ = 2.2 Hz, 1H, 1x(*E*)-H-6'), 7.06 (d, $J_{2',6'}$ = 2.2 Hz, 1H, 1x(*E*)-H-2'), 7.03 (d, $J_{3,2}$ = 2.2 Hz, 1H, 1x(*Z*)-H-3), 5.75 (d, $J_{2,3}$ = 16.6 Hz, 1H, 1x(*E*)-H-2), 5.34 (d, $J_{2,3}$ = 12.0 Hz, 1H, 1x(*Z*)-H-2), 5.26 (s, 2H, 2x(*Z*)- H-1''), 5.24 (s, 2H, 2x(*E*)-H-1''), 5.21 (s, 2H, 2x(*Z*)-H-1''), 5.19 (s, 2H, 2x(*E*)-H-1''), 3.66 (s, 3H, 3x(*Z*)- H-2''), 3.65 (s, 3H, 3x(*E*)-H-2''), 3.53 (s, 3H, 3x(*Z*)- H-2''), 3.51 (s, 3H, 3x(*E*)-H-2''), 1.43 (s, 9H, (*Z*)-C($CH_3$)$_3$). 1.41 (s, 9H: (*E*)-C($CH_3$)$_3$). **13C RMN** (100 MHz, $CDCl_3$): $\delta$ 150.7 ((*E*)-C-3), 150.5 ((*E*)-C-5'), 150.0 ((*E*)-C-4'), 148.9 ((*Z*)-C-5'), 148.7 ((*Z*)-C-3), 148.6 ((*Z*)-C-4'), 143.9 ((*E*)-C-3'), 143.8 ((*Z*)-C-3'), 128.6 ((*Z*)-C-1'), 128.5 ((*E*)-C-1'), 122.5 ((*Z*)-C-2'), 121.0 ((*E*)-C-2'), 118.6 ((*E*)-C-1), 117.9 ((*Z*)-C-1), 115.0 ((*Z*)-C-6'), 112.5 ((*E*)-C-6'), 99.3 ((*E*)-C-1''), 95.5 ((*E*)-C-2), 94.8 ((*Z*)-C-1''), 93.4 ((*Z*)-C-2), 57.9 ((*E*)-C-2'',), 56.6 ((*Z*)-C-2''), 35.5 ((*Z*)-**C**($CH_3$)$_3$), 35.3 ((*E*)-**C**($CH_3$)$_3$), 30.4((*Z*)-C(**C**$H_3$)$_3$), 30.3(-C(**C**$H_3$)$_3$). **IR (ATR)** 3010, 2964, 2213, 1615, 1429. **HR-MS** (ESI+) calcd. for [$C_{18}H_{23}NO_4$+Na]: 328.1519; found: 328.1519.

## Synthesis of 3-(3-(tert-butyl)-4,5-bis(methoxymethoxy)phenyl)propanenitrile, 21

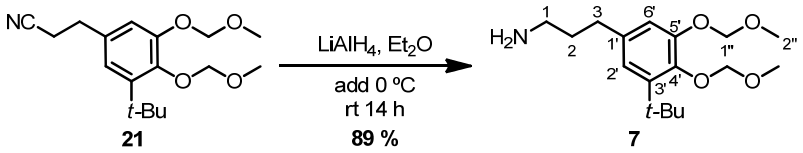



To a solution of (*E*)- and (*Z*)-**18** (1.442 g, 4.8 mmol) and 10% Pd/C (5:1, substrate/catalyst) in ethyl acetate (16 mL) was stirred at room temperature under hydrogen atmosphere for 24 h. Next, Pd/C was filtered off through a celite bed and the solvent was removed in vacuo to afford **21** (1.003 g, 68 %) as a brown oil.

Espectroscopic data of **21**

**$^1$H RMN** (400 MHz, $CDCl_3$): $\delta$ 6.90 (d, $J_{6',2'}$ = 2.1 Hz, 1H, 1xH-6'), 6.84 (d, $J_{2',6'}$ = 2.1 Hz, 1H, 1xH-2'), 5.18 (s, 2H, 2xH-1''), 5.16 (s, 2H, 2xH-1''), 3.64 (s, 3H, 3xH-2''), 3.51 (s, 3H, 3xH-2''), 2.88 (t, $J_{3,2}$ = 7.4 Hz, 2H, 2xH-3), 2.58 (t, $J_{2,3}$ = 7.4 Hz, 2H, 2xH-2), 1.41 (s, 9H, -C($CH_3$)$_3$). **$^{13}$C RMN** (100 MHz, $CDCl_3$): $\delta$ 150.6 (C-5'), 145.0 (C-3'), 143.9 (C-4'), 133.0 (C-1'), 120.6 (C-2'), 119.2 (C-1), 114.7 (C-6'), 99.1 (C-1''), 95.6 (C-1''), 57.6 (C-2''), 56.4 (C-2''), 35.3 (C-3), 31.7 (-**C**($CH_3$)$_3$), 30.6 (-C(**C**$H_3$)$_3$), 19.6 (C-2). **IR (ATR)** 3016, 2952, 2904, 2245, 1725, 1475. **HR-MS** (ESI+) calcd. for [$C_{17}H_{25}NO_4$+Na]: 330.1676; found: 330.1675.

## Synthesis of 3-(3-(tert-butyl)-4,5-bis(methoxymethoxy)phenyl)propanamine, 7




To a suspension of $LiAlH_4$ (298 mg, 7.9 mmol) in anhydrous $Et_2O$ (2 mL) cooled down in a water bath, a solution of **21** (695 mg, 2.2 mmol) in anhydrous $Et_2O$ (2 mL) was added dropwise. Next, the reaction mixture was stirred at room temperature for 14h under inert atmosphere. The reaction mixture was cooled down to 0 ºC and quenched with NaOH 1M (15 mL). The resulting aqueous layer was extracted with $Et_2O$ (15 mL) and $CHCl_3$ (15 mL). The combined organic extracts were dried with $MgSO_4$ and the solvent removed in vacuo to afford **7** (627 mg, 89 %) as a yellowish oil. This product was used without further purification.

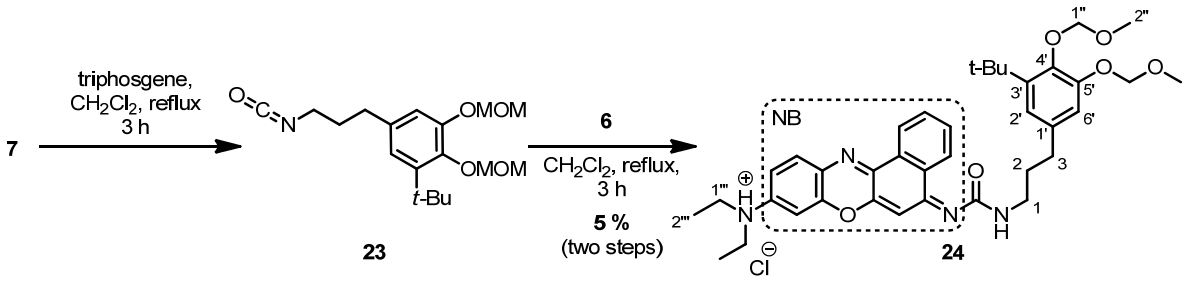
Espectroscopic data of **7**

**$^1$H RMN** (400 MHz, $CDCl_3$): $\delta$ 6.85 (d, $J_{6',2'}$ = 2.0 Hz, 1H, 1xH-6'), 6.80 (d, $J_{2',6'}$ = 2.0 Hz, 1H, 1xH-2'), 5.17 (s, 2H, 2xH-1''), 5.16 (s, 2H, 2xH-1''), 3.64 (s, 3H, 3xH-2''), 3.50 (s, 3H, 3xH-2''), 2.73 (t, $J_{1,2}$ = 7.6 Hz, 2H, 2xH-1), 2.58 (t, $J_{3,2}$ = 7.6 Hz, 2H, 2xH-3), 1.74 ($q_t$, $J_{2,1}$ = $J_{2,3}$ = 7.6 Hz, 2H, 2xH-2), 1.40 (s, 9H, -C($CH_3$)$_3$). **$^{13}$C RMN** (100.6 MHz, $CDCl_3$): δ 150.2 (C-5'), 143.9 (C-4'), 143.3 (C-3'), 137.2 (C-1'), 120.6 (C-2'), 114.7 (C-6'), 99.1 (C-1''), 95.5 (C-1''), 57.6 (C-2''), 56.4 (C-2''), 42.1 (C-1), 35.7 (C-

2), 35.2 (-**C**($CH_3$)$_3$), 33.4 (C-3), 30.7 (-C(**C**$H_3$)$_3$). **IR (ATR)** 3362, 3302, 3005, 2949, 2904, 1578, 1431. **HR-MS** (ESI+) calcd. for [$C_{17}H_{29}NO_4$+Na]: 334.1989; found: 334.1979.

## VI.2.1.2. Synthesis of ligand 4

### Synthesis of 5-(((3-(3-(tert-butyl)-4,5-bis(methoxymethoxy)phenyl)propyl) carbamoyl)imino)-N,N-diethyl-5H-benzo[a]phenoxazin-9-aminium chloride, 24

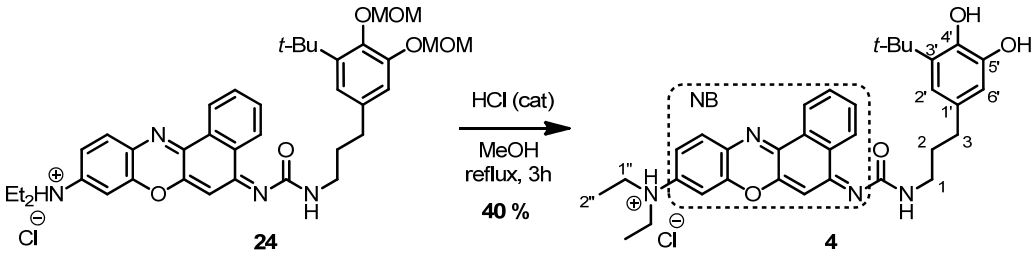



To a solution of **7** (104 mg, 0.33 mmol) and $NEt_3$ (150 μL, 1.1 mmol) in dry $CH_2Cl_2$ (2 mL), a solution of triphosgene (38 mg, 0.12 mmol) in dry $CH_2Cl_2$ (2 mL) was added dropwise. Reaction mixture was heated at 55 ºC for 3 hours. Next, a solution of the neutral form of the commercial nile blue A (101 mg, 0.32 mmol) in dry $CH_2Cl_2$ (10 mL) was added to the reaction mixture and stirred at 55 ºC for 3 hours after which solvent was removed in vacuo. Residue was purified by successive preparative TLCs using $CHCl_3$:EtOH:$NEt_3$ (98:2:1) to afford **24** (12 mg, 5 % yield) as a blue solid.

Espectroscopic data of **24**

**$^1$H RMN** (400 MHz, $CDCl_3$): $\delta$ 8.65 – 6.86 and 6.65 – 6.35 (8H, NB), 6.85 – 6.78 (s, 2H 1xH-2', 1xH-6'), 5.34 (m, 1H, -NH- urea), 5.16 (s, 4H, 4xH-1''), 3.64 (s, 3H, 3xH-2''), 3.51 (s, 3H, 3xH-2''), 3.43 (q, $J_{1''',2'''}$ = 7.1 Hz, 4H, 4xH-1'''), 3.21 (t, $J_{1,2}$ = 7.4 Hz, 2H, 2xH-1), 2.66 (t, $J_{3,2}$ = 7.6 Hz, 2H, 2xH-3), 1.93 (t, $J_{2,1}$ = $J_{2,3}$ = 7.6 Hz, 2H, 2xH-2), 1.41 (s, 9H, -C($CH_3$)$_3$), 1.24 (t, $J_{2''',1'''}$ = 7.1 Hz, 6H, 6xH-2'''). **HR-MS** (ESI+) calcd. for [$C_{38}H_{46}N_4O_6$+D]: 656.347; found: 656.412.

**Synthesis of 5-(((3-(3-(tert-butyl)-4,5-dihydroxyphenyl)propyl)carbamoyl) imino)-N,N-diethyl-5H-benzo[a]phenoxazin-9-aminium chloride, 4**



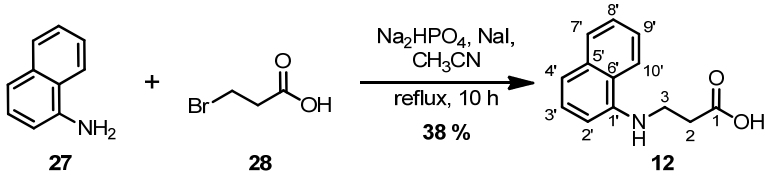

To a solution of **24** (10.4 mg , 14 μmol) in methanol (1 mL), was added hydrogen chloride (2 drops, 37 %). Reaction mixture was heated at 80 ºC for 3 hours. Next, reaction crude was cooled down at room temperature, and solvent evaporated. Residue was purified by preparative TLC using $CHCl_3$:EtOH:$NEt_3$ (98:2:1) to afford **4** (3.3 mg, 40 % yield) as a blue solid.

Espectroscopic data of **4**

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 8.68 – 7.53 and 6.78 – 6.38 (8H, NB), 6.86 (s, 2H, 1xH2', 1xH-6'), 5.39 (s, 1H, -NH- urea), 3.44 (q, $J_{1'',2''}$ = 4.1 Hz, 4H, 4xH-1''), 3.28 – 3.11 (m, 2H, 2xH-1), 2.72 – 2.61 (m, 2H, 2xH-3), 2.05 – 1.83 (m, 2H, 2xH-2), 1.41 (s, 9H, -C($CH_3$)$_3$), 1.33 – 1.20 (m, 6H, 6xH-2''). **HR-MS** (ESI+) calcd. for [$C_{34}H_{39}ClN_4O_4$+Na]: 625.2587; found: 625.4370

## VI.2.1.3. Synthesis of ligand 5

**Synthesis of 3-(naphthalen-1-ylamino)propanoic acid, 12**

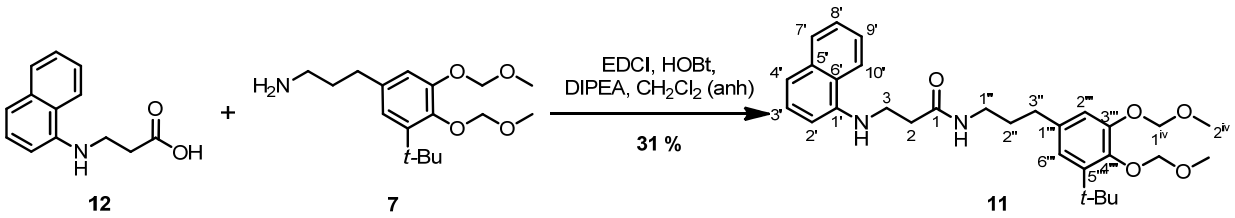



Compound **12** was synthesized according to ref [4] with some modifications. To a solution of naphthylamine (1.09 g, 7.6 mmol), $Na_2HPO_4$ (1.20 g, 8.4 mmol) and NaI (393.5 mg, 2.8 mmol) in anhydrous acetonitrile (30 mL) was added dropwise a solution of 3-bromopropanoic acid (1.29 g, 8.4 mmol) in anhydrous acetonitrile (20 mL). Mixture was heated under reflux 10 h. After this time, water was added (40 mL) and aquose layer was extracted three times with EtOAc (30 mL). Combined organic layers were dried with MgSO4, filtered off and solvent was evaporated in vacuum. Crude was purified by flash chromatography using hexanes and ethyl acetate (1:1, v/v) to afford **12** (622.8 mg, 38 %) as a white solid.

Espectroscopic data of **12**

**$^1$H RMN** (400 MHz, MeOD-$d_4$): $\delta$ 8.10 (d, 1H, $J_{7',8'}$ = 12.5 Hz, 1xH-7'), 7.75 (d, 1H, $J_{10'9'}$ = 12.5, 1xH-10'), 7.47 – 7.35 (m, 2H, 1xH-8', 1xH-9'), 7.34 – 7.25 (t, $J_{3',2'}$ = $J_{3',4'}$ = 8.2 Hz, 1H, 1xH-3'), 7.13 (d, 1H, $J_{4',3'}$ = 8.2 Hz, 1xH-4'), 6.57 – 6.51 (d, 1H, $J_{2',3'}$ = 8.2 Hz, 1xH-2'), 3.46 (t, 2H, $J_{3,2}$ = 7.0 Hz, 2xH-3), 2.67 (t, 2H, $J_{2,3}$ = 7.0 Hz, 2xH-2).

## Synthesis of N-(3-(3-(tert-butyl)-4,5-bis(methoxymethoxy)phenyl)propyl)-3-(naphthalen-1-yl-amino)propanamide, 11



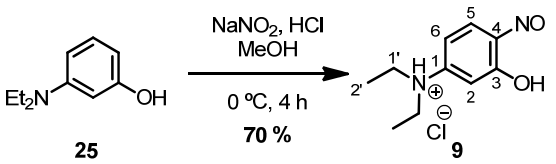

**12** **7** **11**

To a solution of 3-(naphthalen-1-ylamino)propanoic acid (646 mg, 3 mmol), HOBt (589 mg, 4.3 mmol), EDCI (760 mg, 3.9 mmol) and DIPEA (1.6 mL, 9.1 mmol) in 20 mL of anhydrous $CH_2Cl_2$, a solution of **7** (956 mg, 3 mmol) in 10 mL of anhydrous $CH_2Cl_2$ was added. The reaction mixture was stirred at room temperature for 17h. Then, it was washed twice with a solution of saturated $NaHCO_3$ (10 mL) and once with a solution of saturated NaCl (10 mL). The organic layer was dried with $MgSO_4$ and solvent was evaporated under vacuum. Crude was purified by flash chromatography using hexanes and ethyl acetate (1:1, v/v) to afford **11** (482 mg, 31 %) as a brown oil.

Espectroscopic data of **11**

**$^1$H RMN** (400 MHz, $CDCl_3$): $\delta$ 7.81 (d, $J_{7',8'}$ = 8.1 Hz, 1H, 1xH-7'), 7.74 (d, $J_{10',9'}$ = 7.6 Hz, 1H, 1xH-10'), 7.38 – 7.23 (m, 4H, 1xH-3', 1xH-4', 1xH-8', 1xH-9'), 6.79 (d, $J_{2''',6'''}$ = $J_{6''',2'''}$ = 1.9 Hz, 2H, 1xH-2''', 1xH-6'''), 6.58 (d, $J_{2',3'}$ = 1.9 Hz, 1H, 1xH-2'), 6.04 (s, 1H, -NH- amide), 5.16 (s, 2H, 2xH1$^{iv}$), 5.11 (s, 2H, 2xH1$^{iv}$), 3.63 (s, 3H, 3xH2$^{iv}$), 3.54 (t, $J_{3,2}$ = 6.02 Hz, 2H, 2xH-3), 3.46 (s, 3H, 3xH2$^{iv}$), 3.24 (q, $J_{1'',2''}$ = 7.6 Hz, 2H, 2xH-1''), 2.50 (m, 4H, 2xH-2, 2xH-3''), 1.73 ($q_t$, $J$ = 7.6 Hz, 2H, 2xH-2''), 1.39 (s, 9H, -C($CH_3$)$_3$). **$^{13}$C RMN** (100 MHz, $CDCl_3$): $\delta$ 171.9 (C-1), 150.1 (C-5'''), 143.4 (C-5'), 143.1 (C-4'''), 136.23 (C-1'''), 134.4 (C-6' and C-3'''), 128.6 (C-10'), 126.5, 125.9, 124.9 and 117.8 (C -3', C -4', C -8', C-9'), 123.9 (C-1'), 117.8 and 114.5 (C-2''', C-6'''), 120.4 (C-7'), 104.5 (C-2'), 99.0 (C-1$^{iv}$), 95.4 (C-1$^{iv}$), 57.6 (C-2$^{iv}$), 56.4 (C-2$^{iv}$), 40.4 (C-3), 39.3 (C-1''), 35.3 and 35.2 (C-2, C-3''), 33.3 (-**C**($CH_3$)$_3$), 31.2 (C-2''), 30.7 (-C(**C**$H_3$)$_3$). **IR (ATR)** 3304.4, 2949.4, 1638.2, 1580.4, 1526.7, 1199.4, 1035.5, 961.9. **HR-MS** (ESI+) calcd. for [$C_{30}H_{40}N_2NaO_5$+Na]: 531.2829; found: 531.2834.

## Synthesis of N,N-diethyl-3-hydroxy-4-nitrosobenzenaminium chloride, 9

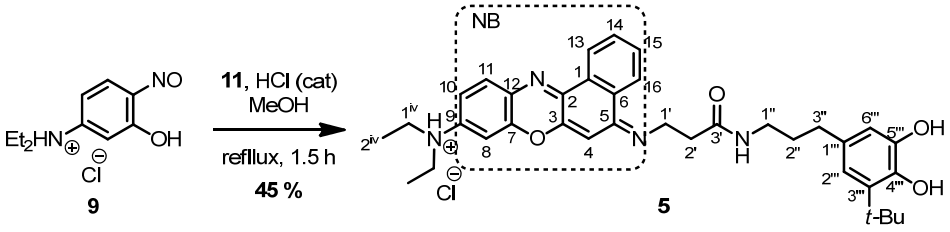



Compound **9** was synthesized according to ref [5]. To a solution of **25** (5,85 g, 35.4 mmol) in HCl (20 mL, 12 %) cooled down with an ice bath, a solution of sodium nitrite (2.55 g, 36.9 mmol) in water (13 mL) was added dropwise. Reaction mixture was stirred at 0-5 ºC for 2 hours. Next, solid obtained was filtered off and recrystallized with ethanol affording **9** (5.02 g, 70 % yield) as a brown and crystalline solid.

Espectroscopic data of **9**

**$^1$H RMN** (360 MHz, DMSO-$d_6$) $\delta$ 7.30 (d, $J_{5,6}$ = 9.9 Hz, 1H, 1xH-5), 6.88 (d, $J_{6,5}$ = 10.0 Hz, 1H, 1xH-6), 5.72 (s, 1H, 1xH-2), 3.05 (q, $J_{1',2'}$ = 7.3 Hz, 4H, 4xH-1'), 1.19 (t, $J_{2',1'}$ = 7.2 Hz, 6H, 6xH-2').

## Synthesis of 5-((3-((3-(3-(tert-butyl)-4,5-dihydroxyphenyl)propyl)amino)-3-oxopropyl)imino)-N,N-diethyl-5H-benzo[a]phenoxazin-9-aminium chloride, 5




To a solution of **9** (10.6 mg, 0.05 mmol) in 0.2 mL of MeOH cooled down in a water bath and under inert atmosphere, a solution of **11** (28.2 mg, 0.06 mmol) in 0.2 mL of degassed MeOH and a 2 droplets of HCl 35 % were added. This mixture was heated under reflux for 1.5 h. Then it was cold down to room temperature and $CH_2Cl_2$ (1 mL) and a mixture of saturated NaCl (1 mL) and 3 droplets of HCl 35 % were added. The resulting organic layer was washed twice with saturated $NaHCO_3$ (2 mL) and once with saturated NaCl (2 mL). Next, it was dried with $MgSO_4$ and solvent was removed in vacuo. Crude was purified by flash chromatography using $CH_2Cl_2$ and MeOH (10:1, v/v) to afford **5** (14.2 mg, 45 %) as a bluish-violet solid.

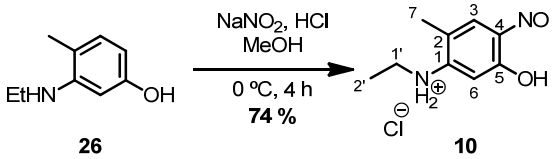
Espectroscopic data of **5**

**$^1$H RMN** (360 MHz, MeOD-$d_4$): $\delta$ 8.75 (d, $J_{13,14}$ = 7.9 Hz, 1H, 1xH-13), 8.25 (br s, 1H, 1xH-16), 7.83 (t, $J_{14,13}$ = 7.4 Hz, 1H, 1xH-14), 7.75 (m, 2H, 1xH-15, 1xH11), 7.24 (d, $J_{10,11}$ = 9.2 Hz, 1H, 1xH-10), 6.95, (br s, 1H, 1xH-4), 6.82 (s, 1H, 1xH-8), 6.43 (s, 1H, 1xH-2''), 6.41 (s, 1H, 1xH-6''), 3.98 (s, 2H, 2xH-1'), 3.78 – 3.62 (m, 4H, 4xH-1$^{iv}$), 3.20 (t, $J_{1'',2''}$ = 9.5 Hz, 2H, 2xH-1''), 2.78 (br s, 2H, 2xH-2'), 2.36 (t, $J_{3'',2''}$ = 7.1 Hz, 2H, 2xH-3''), 1.69 (m, 2H, 2xH-2''), 1.36 (m, 6H, 6xH-2$^{iv}$), 1.32 (s, 9H, -

$C(CH_3)_3$). **$^{13}$C RMN** (90 MHz, MeOD-$d_4$): $\delta$ 171.4 (C-3'), 157.5, 154.4, 151.5, 148.2, 144.3, 144.3, 141.9, 135.4, 133.1, 132.8, 131.4, 131.0, 130.5, 129.4, 124.1, 123.2, 122.4, 115.6, 95.5 and 93.1, (NB, C-1''', C-3''', C-4''', C-5'''), 116.9 and 112.1 (C-2''', C-6'''), 47.7(C-1'), 42.1 (C-1$^{iv}$), 40.32 (C-2'), 35.7 (-**C**$(CH_3)_3$), 35.4 (C-1''), 33.9 (C-2''), 33.5 (C-3''), 30.2 (-C(**C**$H_3)_3$), 13.1 (C-2$^{iv}$),. **IR (ATR)** 3364.1, 2953.5, 1640.3, 1587.8. **HR-MS** (ESI+) calcd. for [C36H43N4O4+H]: 595.3279; found: 595.3289.

## VI.2.1.4. Synthesis of ligand 6

### Synthesis of N-ethyl-5-hydroxy-2-methyl-4-nitrosobenzenaminium chloride, 10



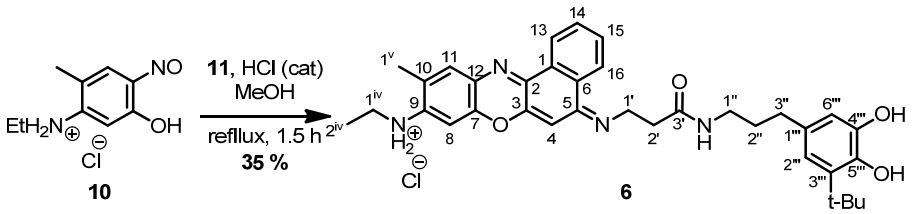

**26** **10**

Compound **10** was synthesized according to ref [5]. To a solution of **26** (1.503 g, 9.9 mmol) in HCl (10 mL, 12 %) cooled down with an ice bath, a solution of sodium nitrite (780 mg, 11.4 mmol) in water (4 mL) was added dropwise. Reaction mixture was stirred at 0-5 ºC for 2 hours. Next, solid obtained was filtered off and recrystallized with ethanol to afford **10** (1.587 g, 74 % yield) as a brown and crystalline solid.

Espectroscopic data of **10**

**$^1$H NMR** (250 MHz, DMSO-$d_6$) $\delta$ 8.00 (br s, 1H, -OH), 6.91 (d, $J_{3,6}$ = 1.2 Hz, 1H, 1xH-3), 5.60 (s, 1H, 1xH-6), 3.42 – 3.21 (m, 5H, 2xH-1', 3xH-7), 1.17 (t, $J$ = 9.6 Hz, 3H, 3xH-2').

### Synthesis of 5-((3-((3-(3-(tert-butyl)-4,5-dihydroxyphenyl)propyl)amino)-3-oxopropyl)imino)-N-ethyl-10-methyl-5H-benzo[a]phenoxazin-9-aminium chloride, 6




**10** **6**

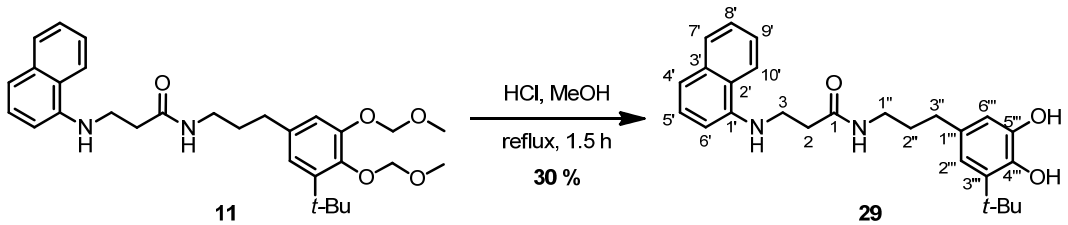
To a solution of **10** (38.8 mg, 0.21 mmol) in 1 mL of MeOH cooled down in a water bath and under inert atmosphere, a solution of **11** (98.2 mg, 0.19 mmol) in 1 mL of degassed MeOH and a 3 droplets of HCl 35 % were added. This mixture was heated under reflux for 1.5 h. Then it was cold down to room temperature and $CH_2Cl_2$ (5 mL) and a mixture of saturated NaCl (2 mL) and 3 droplets of HCl 35 % were added. The resulting organic layer was washed twice with saturated $NaHCO_3$ (3 mL) and once with saturated NaCl (3 mL). Next, it was dried with $MgSO_4$ and solvent

was removed in vacuo. Crude was purified by flash chromatography using $CH_2Cl_2$ and MeOH (10:1, v/v) to afford **6** (41 mg, 35 %) as a bluish-violet solid.

Espectroscopic data of **6**

**$^1$H NMR** (400 MHz, MeOD-$d_4$) $\delta$ 8.73 (d, $J_{16,15}$ = 8.1 Hz, 1H, 1xH-16), 8.22 (d, $J_{13,14}$ = 8.3 Hz, 1H, 1xH-13), 7.82 (t, $J_{15,16}$ = $J_{15,14}$ = 7.5 Hz, 1H, 1xH-15), 7.71 (t, $J_{14,13}$ = $J_{14,15}$ = 7.1 Hz, 1H, 1xH-14), 7.51 (s, 1H, 1xH-11), 6.90 (s, 1H, 1xH-4), 6.71 (s, 1H, 1xH-8), 6.40 (d, $J_{2''',6'''}$ = 2.0 Hz, 1H, 1xH-2'''), 6.37 (d, $J_{6''',2'''}$ = 2.0 Hz, 1H, 1xH-6'''), 3.95 (t, $J_{1',2'}$ = 6.2 Hz, 2H, 2xH-1'), 3.49 (q, $J_{1^{iv},2^{iv}}$ = 7.2 Hz, 1xH-1$^{iv}$), 3.20 (m, 2H, 2xH-1''), 2.75 (t, $J_{2',1'}$ = 6.2 Hz, 2H, 2xH-2'), 2.38 – 2.32 (m, 2H, 2xH-3''), 2.30 (s, 3H, 3xH-1$^{v}$), 1.67 ($q_t$, $J$ = 7.2 Hz, 2H, 2xH-2''), 1.44 – 1.34 (m, 3H, 3xH-2$^{iv}$), 1.34 – 1.27 (m, 9H, -C($CH_3$)$_3$). **$^{13}$C NMR** (101 MHz, MeOD-$d_4$) $\delta$ 172.9 (C-3'), 158.2, 156. 9, 152.5, 149.3, 145.7, 143.3, 136.8, 133.9, 132.9, 132.4, 132.4, 132.3 and 123.6 (C-1, C-2, C-3, C-5, C-6, C-7, C-9, C-10, C-12, C-1''', C-3''', C-4''' and C-5'''), 132.6 (C-4), 130.7 (C-15), 129.0 (C-14), 125.5 (C-13), 124.5 (C-16), 118.3 (C-2'''), 113.5 (C-6''', 94.5 (C-11), 94.1 (C-8), 41.9 (C-1'), 40.3 (C-2''), 39.8 (-**C**($CH_3$)$_3$), 35.8 (C-1''), 35.4 (C-1$^{iv}$), 34.0 (C-2'), 32.5 (C-3''), 30.1 (-C(**C**$H_3$)$_3$), 17.8 (C-1$^{v}$), 14.2 (C-2$^{iv}$). **IR (ATR)** 3213.7, 3076.2, 2921.8, 2852.5, 1640.1, 1587.6, 1540.9, 1433.8, 1307.7, 1160.8. **HR-MS** (ESI+) calcd. for [$C_{35}H_{41}N_4O_4^+$]: 581.3122; found: 581.3124.

## Synthesis of N-(3-(3-(tert-butyl)-4,5-dihydroxyphenyl)propyl)-3-(naphthalen-1-ylamino)-propanamide, 29




This compound was obtained as byproduct of compounds **5** and **6**. From the reaction crude of a mixture of **6** and **29**, it was isolated by flash chromatography using $CH_2Cl_2$ and MeOH (10:1, v/v) to afford **29** (23.9 mg, 30 % yield) as a yellowish oil.

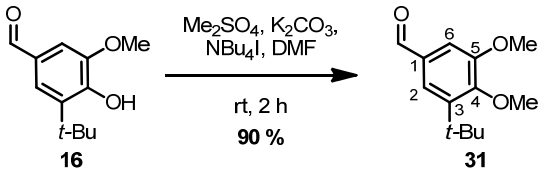
Espectroscopic data of **29**

**$^1$H NMR** (360 MHz, MeOD-$d_4$) $\delta$ 8.33 (m, 1H, 1xH-7'), 8.13 (s, 1H, 1xH-10'), 7.98 (s, 1H, 1xH-4'), 7.87 – 7.41 (m, 4H, 1xH-5', 1xH-6', 1xH-8' and 1xH-9'), 6.56 (s, 1H, 1xH-2'''), 6.52 (s, 1H, 1xH-6'''), 4.89 (s, 1H, -NH- amide), 3.68 (m, 2H, 2xH-3), 3.18 (m, 2H, 2xH-1''), 2.88 (m, 2H, 2xH-2), 2.45 (m, 2H, 2xH-3'''), 1.74 (m, 2H, 2xH-2''), 1.32 (s, 9H, -C($CH_3$)$_3$). **$^{13}$C NMR** (101 MHz, MeOD-$d_4$) $\delta$ 174.7 (C-1), 145.7 (C-4'''), 143.3 (C-1''' and C-6'), 136.9 (C-3''), 134.3 (C-5'), 132.7 (C-3'''), 128.7, 126.8, 126.5, 126.0, 125.8, 125.6, 125.3, 122.2 (C-1', C-3', C-4', C-7' C-8', C-9', C-10' and C-5'''), 118.5, 113.6 (C-2''' and C-6'''), 105.44 (C-2'), 41.7 (C-3), 40.1 (C-1''), 36.4 (C-2), 35.8 (-**C**($CH_3$)$_3$), 34.0 (C-

3''), 32.4 (C-2''), 30.72, 30.1 (-C(**C**$H_3$)$_3$). **IR (ATR)** 3304.4, 2949.3, 1720.0, 1638.2, 1477.5. **HR-MS** (ESI+) calcd. for [$C_{26}H_{32}N_2O_3$+Na]: 443.3248; found: 443.3241.

# VI.2.2. Synthesis of fluorophore of type II, ligand 30

### Synthesis of 3-(tert-butyl)-4,5-dimethoxybenzaldehyde, 31

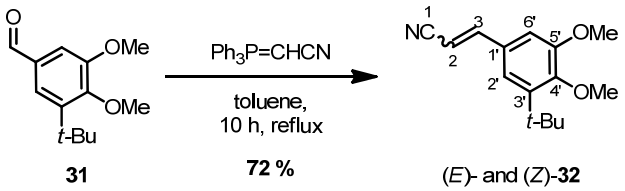



Compound **31** was synthesized according to ref [2] with some modifications. To a solution of **16** (3.5 g, 16.8 mmol) in DMF (100 mL), $K_2CO_3$ (6.95 g, 50.4 mmol) and *N*,*N*,*N*-tributyl-1-butanaminium iodide (270 mg, 0.73 mmol) were added. The reaction mixture was stirred for 2 h at room temperature. After this time, $Me_2SO_4$ (3.2 mL, 33.6 mmol) was added dropwise and the mixture was allowed to react for 16 h. The resulting mixture was treated with water (100 mL) and the aqueous layer was extracted four times with EtOAc (50 mL). The organic extracts were dried with $MgSO_4$ and the solvent evaporated under vacuum to afford **31** (3.36 g, 90 %) as a dark green oil.

Espectroscopic data of **31**

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 8.01 (s, 1H, -CHO), 7.45 (d, $J_{2,6}$ = 1.9 Hz, 1H, 1xH-2), 7.35 (d, $J_{6,2}$ = 1.9 Hz, 1H, 1xH-6), 3.95 (s, 3H, -OMe), 3.91 (m, 3H, -OMe), 1.40 (s, 9H, -C($CH_3$)$_3$).

### Synthesis of (*E*)- and (*Z*)-3-(3-(tert-butyl)-4,5-dimethoxyphenyl)acrylonitrile, (*E*)- and (*Z*)-32

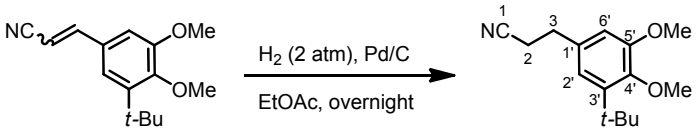



To a solution of **31** (3.12 g, 14.0 mmol) in toluene (100 mL), was added 2-(triphenylphosphoranylidene)acetonitrile (5.01 g, 16.6 mmol). Reaction mixture was warmed up at 130 ºC for 10 hours. Next, reaction mixture was cooled down at room temperature and solvent was evaporated. Crude was purified by flash chromatography using hexanes: EtOAc (6:1, v/v) to afford a mixture of (*E*)- and (*Z*)-**32** (2.61 g, 72 % yield) as a brownish oil, with a diastereomeric ratio of 4.8:1, respectively.

Espectroscopic data of **(*E*)-** and **(*Z*)-32**

**1H RMN** (400 MHz, $CDCl_3$): $\delta$ 7.53 (d, $J_{6',2'}$ = 2.2 Hz, 1H, 1x(*Z*)-H-6'), 7.33 (d, $J_{3,2}$ = 16.6 Hz, 1H, 1x(*E*)-H-3), 7.23 (d, $J_{2',6'}$ = 2.1 Hz, 1H, 1x(*Z*)-H-2'), 7.05 (d, $J_{3,2}$ = 12.2 Hz, 1H, 1x(*Z*)-H-3), 7.00 (d, $J_{6',2'}$ = 2.1 Hz, 1H, 1x(*E*)-H-6'), 6.88 (d, $J_{2',6'}$ = 2.1 Hz, 1H, 1x(*E*)-H-2'), 5.75 (d, $J_{2,3}$ = 16.6 Hz, 1H, 1x(*E*)-H-2), 5.33 (d, $J_{2,3}$ = 12.0 Hz, 1H, 1x(*Z*)-H-2), 3.93 (s, 3H, 3x(*Z*)-OMe), 3.92 (s, 3H, 3x(*Z*)-OMe), 3.90 (s, 3H, 3x(*E*)-OMe), 3.88 (s, 3H, 3x(*E*)-OMe), 1.39 (s, 9H, s, 3H, (*Z*)-C($CH_3$)$_3$), 1.38 (s, 9H, (*E*)-C($CH_3$)$_3$). **$^{13}$C NMR** (101 MHz, $CDCl_3$) $\delta$ 153.7 ((*E*)-C-4'), 153.4 ((*Z*)-C-4'), 151.7 ((*Z*)-C-3'), 151.2 ((*E*)-C-3'), 151.0 ((*E*)-C-2), 149.2 ((*Z*)-C-3), 144.1 ((*E*)-C-5'), 143.7 ((*Z*)-C-5'), 128.5 ((*Z*)-C-1'), 128.4 ((*E*)-C-1'), 122.0 ((*Z*)-C-2'), 119.9 ((*E*)-C-2'), 118.8 ((*Z*)-C-1), 118.8 ((*E*)-C-1), 110.2 ((*Z*)-C-6'), 108.6 ((*E*)-C-6'), 94.5 ((*E*)-C-3), 92.9 ((*Z*)-C-2), 60.7, 60.7, 56.0 and 56.0 ((*Z*)- and (*E*)- OMe), 35.3 ((*Z*)-**C**($CH_3$)$_3$), 35.3 ((*E*)-**C**($CH_3$)$_3$), 30.4 ((*Z*)-C(**C**$H_3$)$_3$), 30.4 ((*E*)-C(**C**$H_3$)$_3$). **IR (ATR)** 2952.0, 2213.3, 1615.6, 1571.5, 1415.0, 1142.9, 1067.0, 1023.7. **HR-MS** (ESI+) calcd. for [$C_{15}H_{19}NO_2$+Na]: 268.1309; found: 268.1308.

## Synthesis of 3-(3-(tert-butyl)-4,5-dimethoxyphenyl)propanenitrile, 33



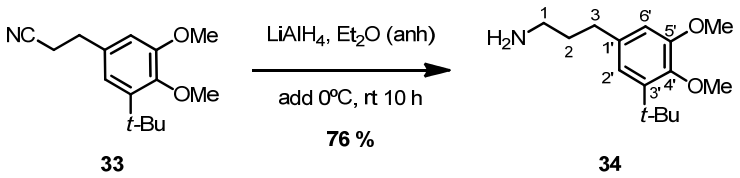

(*E*)- and (*Z*)-**32** **33**

To a solution of (*E*)- and (*Z*)-**32** (3.42 g, 10.2 mmol) and 10% Pd/C (5:1, substrate/catalyst) in ethyl acetate (40 mL) was stirred at room temperature under hydrogen atmosphere for 24 h. Next, Pd/C was filtered off through a celite bed and the solvent was removed in vacuo. The residue was purified by flash chromatography using hexanes and ethyl acetate (4:1, v/v) to afford **33** (1.69 g, 67 %) as a brown oil.

Espectroscopic data of **33**

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 6.74 (d, $J_{2',6'}$ = 2.1 Hz, 1H, 1xH-2'), 6.69 (d, $J_{6',2'}$ = 2.1 Hz, 1H, 1xH-6'), 3.86 (s, 6H, 2x-OMe), 2.90 (t, $J_{3,2}$ = 7.4 Hz, 2H, 2xH-3), 2.60 (d, $J_{2,3}$ = 7.4 Hz, 2H, 2xH-2), 1.37 (s, 9H, -C($CH_3$)$_3$). **$^{13}$C NMR** (63 MHz, $CDCl_3$) $\delta$ 153.7 (C-4'), 148.0 (C-5'), 144.0 (C-3'), 133.0 (C-1), 119.7 (C-1'), 119.0 (C-6'), 111.0 (C-2'), 60.8 (-OMe), 55.8 (-OMe), 35.9 (-**C**($CH_3$)$_3$), 32.2 (C-3), 31.0 (-C(**C**$H_3$)$_3$), 19.7 (C-2). **IR (ATR)** 2951.4, 2866.4, 2831.8, 2245.0, 1688.2, 1580.1, 1421.9, 1346.7. **HR-MS** (ESI+) calcd. for [$C_{15}H_{21}NaNO_2$+Na]: 270.1465; found: 270.1465.

## Synthesis of 3-(3-(tert-butyl)-4,5-dimethoxyphenyl)propanamine, 34



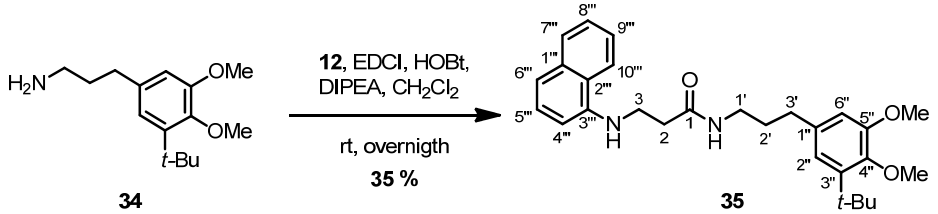

**33** **34**

To a suspension of $LiAlH_4$ (386.0 mg, 10.2 mmol) in anhydrous $Et_2O$ (5 mL) cooled down in a water bath, a solution of **33** (430 mg, 1.7 mmol) in anhydrous $Et_2O$ (5 mL) was added dropwise. Next, the reaction mixture was stirred at room temperature for 14h under inert atmosphere. The reaction mixture was cooled down to 0 ºC and quenched with NaOH 1M (30 mL). The resulting aqueous layer was extracted with $Et_2O$ (30 mL) and $CHCl_3$ (30 mL). The combined organic extracts were dried with $MgSO_4$ and the solvent removed in vacuo to afford **34** (324.7 mg, 76 %) as a yellowish oil. This product was used without further purification.

Espectroscopic data of **34**

**$^1$H RMN** (250 MHz, MeOD-$d_4$): $\delta$ 6.74 (d, $J_{2',6'} = J_{6',2'}$ = 2.0 Hz, 2H, 1xH-2', 1xH-6'), 3.82 (s, 3H, -OMe), 3.80 (s, 3H, -OMe), 2.69 (t, $J_{1,2}$ = 7.24 Hz, 2H, 2xH-1), 2.58 (t, $J_{3,2}$ = 7.50, 2H, 2xH-3), 1.79 (dt, $J_{2,3}$ = 7.50 Hz, $J_{2,1}$ = 7.24 Hz, 2H, 2xH-2), 1.34 (s, 9H, -C($CH_3$)$_3$). **$^{13}$C RMN** (60 MHz, MeOD-$d_4$): δ 153.5 (C-4'), 146.9 (C-5'), 142.7 (C-3'), 136.8 (C-1'), 118.7 (C-2'), 111.3 (C-6'), 59.8 (-OMe), 55.9 (-OMe), 40.8 (C-1), 34.8 (-**C**($CH_3$)$_3$), 33.9 (C-2), 33.3 (C-3), 30.2 (-C(**C**$H_3$)$_3$). **IR (ATR)** 3452.3, 2936.2, 1578.1, 1421.9, 1321.1, 1262.1. **HR-MS** (ESI+) calcd. for [$C_{15}H_{25}NO_2$+Na]: 252.1958; found: 252.1963.

## Synthesis of N-(3-(3-(tert-butyl)-4,5-dimethoxyphenyl)propyl)-3-(naphthalen-1-ylamino)-propanamide, 35



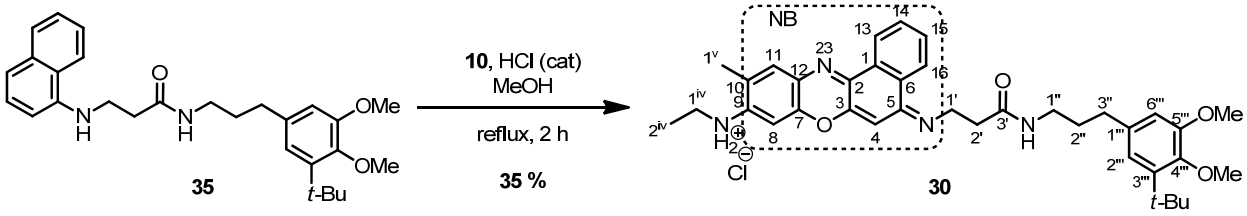

**34** **35**

To a solution of **12** (146.4 mg, 0.68 mmol), HOBt (109.6 mg, 0.80 mmol), EDCI (161.4 mg, 0.84 mmol) and DIPEA (0.4 mL, 2.3 mmol) in 3 mL of anhydrous $CH_2Cl_2$, a solution of **34** (172.0 mg, 0.68 mmol) in 2 mL of anhydrous $CH_2Cl_2$ was added. The reaction mixture was stirred at room temperature for 15h. Then, it was washed twice with a solution of saturated $NaHCO_3$ (5 mL) and once with a solution of saturated NaCl (5 mL). The organic layer was dried with $MgSO_4$ and solvent was evaporated under vacuum. Crude was purified by flash chromatography using hexanes and ethyl acetate (1:1, v/v) to afford **35** (106.7 mg, 35 %) as a brown oil.

Espectroscopic data of **35**

**$^1$H NMR** (360 MHz, MeOD-$d_4$) $\delta$ 7.93 (d, $J_{7''',8'''}$ = 8.1 Hz, 1H, 1xH-7'''), 7.69 (d, $J_{10''',9'''}$ = 7.9 Hz, 1H, 1xH-10'''), 7.41 – 7.23 (m, 3H, 1xH-5''', 1xH-8''', 1xH-9'''), 7.14 (d, $J_{6''',5'''}$ = 8.2 Hz, 1H, 1xH-6'''), 6.65 (s, 1H, 1xH-4'''), 6.60 (s, 2H, 1xH-2'', 1xH-6''), 3.76 (s, 3H, -OMe), 3.69 (s, 3H, -OMe), 3.54 (t, $J_{3,2}$ = 6.6 Hz, 2H, 2xH-3), 3.17 (t, $J_{1',2'}$ = 7.0 Hz, 2H, 2xH-1'), 2.59 (t, $J_{2,3}$ = 6.6 Hz, 2H, 2xH-2), 2.53 – 2.45 (m, 2H, 2xH-3'), 1.79 – 1.65 (m, 2H, 2xH-2'), 1.31 (s, 9H, -C($CH_3$)$_3$). **$^{13}$C NMR** (90 MHz, MeOD-$d_4$) $\delta$ 174.6 (C-1), 154.3, 147.7, 144.7, 143.5, 137.6, 135.8, 129.3, 127.6, 126.6, 125.4, 125.1, 121.7, 119.5, 118.1 (naphthyl, C-1'', C-3'', C-4'' and C-5''), 112.1, 105.1 (C-2'', C-6''), 60.7 (-OMe), 56.1 (-OMe), 41.6 (C-3), 40.6 (C-1'), 40.0 (C-2), 36.4 (-**C**($CH_3$)$_3$), 35.8 (C-3'), 34.2 (C-2'), 32.26 (-C(**C**$H_3$)$_3$). **IR (ATR)** 2919.5, 2478.6, 2065.58, 1627.1, 1577.7, 1450.4, 1420.8, 1143.8, 1067.9. **HR-MS** (ESI+) calcd. for [$C_{28}H_{36}N_2O_3$+Na]: 449.2799; found: 449.2804.

## Synthesis of 5-((3-((3-(3-(tert-butyl)-4,5-dimethoxyphenyl)propyl)amino)-3-oxopropyl)imino)-N-ethyl-10-methyl-5H-benzo[a]phenoxazin-9-aminium chloride, 30




To a solution of **10** (58.5 mg, 0.25 mmol) in 1 mL of MeOH cooled down in a water bath and under inert atmosphere, a solution of **34** (112.0 mg, 0.25 mmol) in 1 mL of degassed MeOH and a 3 droplets of HCl 35 % were added. This mixture was heated under reflux for 1.5 h. Then it was cold down to room temperature and $CH_2Cl_2$ (5 mL) and a mixture of saturated NaCl (2 mL) and 3 droplets of HCl 35 % were added. The resulting organic layer was washed twice with saturated $NaHCO_3$ (3 mL) and once with saturated NaCl (3 mL). Next, it was dried with $MgSO_4$ and solvent was removed in vacuo. Crude was purified by flash chromatography using $CH_2Cl_2$ and MeOH (10:1, v/v) to afford **30** (58.9 mg, 35 %) as a bluish-violet solid.

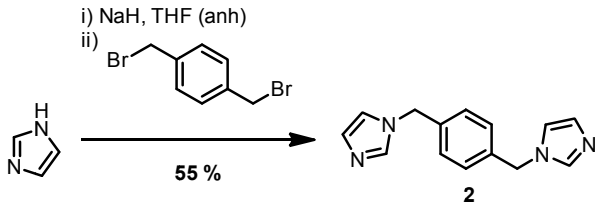
Espectroscopic data of **30**

**$^1$H NMR** (250 MHz, MeOD-$d_4$) $\delta$ 8.72 (d, $J_{16,15}$ = 8.1 Hz, 1H, 1xH-16), 8.22 (d, $J_{13,14}$ = 8.1 Hz, 1H, 1xH-13), 7.83 (t, $J_{15,14}$ = 7.6 Hz, 1H, 1xH-15), 7.72 (t, $J_{14,15}$ = 7.7 Hz, 1H, 1xH-14), 7.50 (s, 1H, 1xH-11), 6.93 (s, 1H, 1xH-4), 6.72 (s, 1H, 1xH-8), 6.54 (s, 1H, 1xH-2'''), 6.51 (s, 1H, 1xH-6'''), 3.99 (t, $J_{1',2'}$ = 5.9 Hz, 2H, 2xH-1'), 3.76 (s, 3H, -OMe), 3.72 (s, 3H, -OMe), 3.51 (q, $J_{1^{iv},2^{iv}}$ = 7.1 Hz, 2H, 2xH-1$^{iv}$), 3.25 (t, $J_{1'',2''}$ = 6.8 Hz, 2H, 2xH-1''), 2.79 (d, $J_{1',2'}$ = 6.2 Hz, 2H, 2xH2'), 2.48 – 2.34 (m, 2H, 2xH.3''), 2.30 (s, 3H, 3xH-1$^{v}$), 1.77 – 1.62 (m, 2H, 2xH.2''), 1.39 (s, 3H, 2xH-2$^{iv}$), 1.34 – 1.25 (m, 9H, -C($CH_3$)$_3$). **$^{13}$C NMR** (63 MHz, MeOD-$d_4$) $\delta$ 173.0 (C-3'), 158.2, 156.8, 154.3, 152.5, 149.2, 147.85, 143.6, 137.4, 133.9, 132.9, 132.6, 132.3, 130.7, 129.0, 125.5, 124.5, 119.4 and 114.68 (NB, C-1''',

C-3''', C-4''', C-5'''), 123.6 and 112.1 (C-2''' and C-6'''), 94.5 (-OMe), 94.2 (-OMe), 41.9 (C-1'), 40.2 (C-1$^{iv}$), 39.8 (C-1''), 35.9 (C-2'), 34.9 (-**C**$(CH_3)_3$), 34.2 (C-3''), 32.4 (C-2''), 31.0 (-C(**C**$H_3)_3$), 23.7 (C-1$^{v}$), 14.43 (C-2$^{iv}$).**IR (ATR)** 2920.8, 2851.6, 1640.4, 1588.12, 1541.4, 1451.0, 1310.0, 1160.9, 1133.6, 1006.6. **HR-MS** (ESI+) calcd. for [$C_{37}H_{44}N_4O_4$+Na]: 609.3435; found: 609.3435.

# VI.2.3. Synthesis of coordination polymer particles

### Synthesis of 1,4-bis((1H-imidazol-1-yl)methyl)benzene, 2

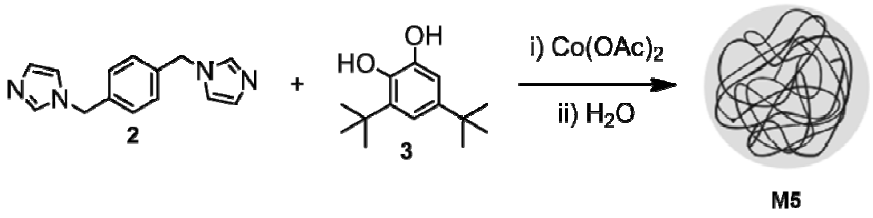



Compound **2** was synthesized according to ref [6]. Sodium hydride (2.13 g, 53.3 mmol, 60% suspension in mineral oil) was washed with dry THF (15 mL) under argon atmosphere. Fresh dry THF (35 mL) was added, followed by slow addition of a solution of imidazole (3.11 g, 45.7 mmol) in dry THF (25 mL). The reaction mixture was stirred for 30 min. Next, $\alpha,\alpha$'-Dibromo-p-xylene (5.53 g, 20.9 mmol) in dry THF (25 mL) was added to the resulting suspension. Reaction mixture was then heated at 50 ºC for 4 h and, after cooling down, treated with ice-cold water (30 mL) and stirred for 20 min. The organic phase was extracted three times with chloroform (50 mL), and the combined organic layers were dried with $MgSO_4$. The solvent was removed under reduced pressure, and the residue was recrystallized twice from ethyl acetate to afford **2** (2.74 g, 55 % yield).

Espectroscopic data of **2**

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 7.52 (s, 2H, 2xH-1''), 7.13 (s, 4H, 2xH-2'', 2xH-3''), 7.07 (m, 2H, 2xH-2), 6.88 (m, 2H, 2xH-3), 5.10 (s, 4H, 4xH-1').

## VI.2.3.1. Synthesis of M5



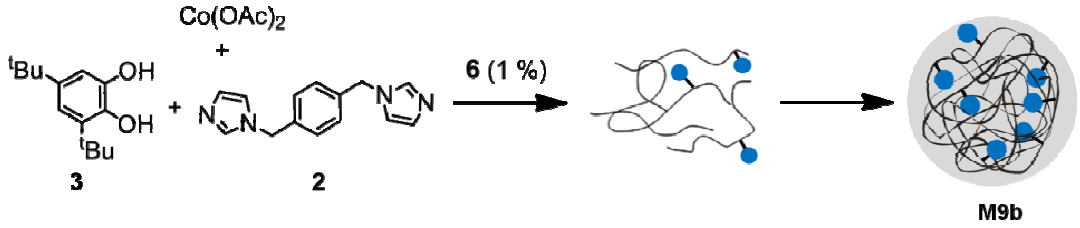

To a solution of di-*tert*-buthylcathecol (107.2 mg, 0.48 mmol) and 1,4-bis(imidazol-1-ylmethyl)benzene (59.6 mg, 0.25 mmol) in EtOH (5 mL), 1 mL of an aqueous solution of $Co(CH_3COO)_2{\cdot}4H_2O$ (61.7 mg, 0.24 mmol) was added dropwise. The mixture was stirred for 10 min

and then the formation of nanoparticles was induced by fast addition of 25 mL of miliQ $H_2O$. Ligand excess was removed by centrifugation and the nanoparticles were washed three times with $H_2O$.

Espectroscopic data of **M5**

**EA** (%) Calcd. for [$C_{32}H_{48}O_4CoN_2$]: C 68.36, N 7.59, H 7.39; found: C 68.02, N 7.63, H 7.46. **IR (ATR)** 2951.1, 1421.2, 1304.9, 1231.6.

## VI.2.3.2. Synthesis of M9b

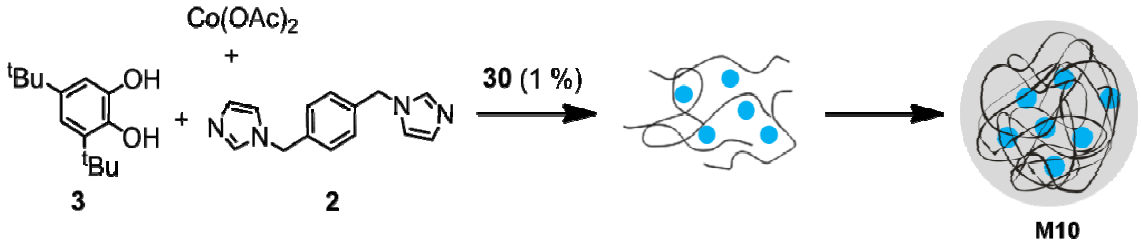



To a solution of **6** (5.5 mg, 9.5 µmol), di-*tert*-buthylcathecol (211.5 mg, 0.95 mmol) and 1,4-bis(imidazol-1-ylmethyl)benzene (117.3 mg, 0.49 mmol) in EtOH (20 mL), 4 mL of an aqueous solution of $Co(CH_3COO)_2{\cdot}4H_2O$ (121.4 mg, 0.49 mmol) were added dropwise. The mixture was stirred for 10 min and then the formation of nanoparticles was induced by fast addition of 100 mL of miliQ $H_2O$. Ligand excess was removed by centrifugation and the nanoparticles were washed with a mixture of EtOH:$H_2O$ (v/v 1:5) until no red fluorescence was observed from the supernatant solution.

Espectroscopic data of **M9b**

**EA** (%) Calcd. for [$C_{28.5}H_{34.5}O_2CoN_{4.1}$]: C 65.05, N 10.91, H 6.61; found: C 66.02, N 9.85, H 6.36. **IR (ATR)** 2963.7, 1664.6, 1599.4, 1512.8, 1423.0, 1357.7.

## VI.2.3.3. Synthesis of M10




To a solution of **30** (3.1 mg, 5.1 µmol), di-*tert*-buthylcathecol (120 mg, 0.53 mmol) and 1,4-bis(imidazol-1-ylmethyl)benzene (65 mg, 0.27 mmol) in EtOH (10 mL), 2 mL of an aqueous solution of $Co(CH_3COO)_2{\cdot}4H_2O$ (68.9 mg, 0.28 mmol) were added dropwise. The mixture was stirred for 10 min and then the formation of the nanoparticles was induced by fast addition of 50 mL of miliQ $H_2O$. Ligand excess was removed by centrifugation and the nanoparticles were washed with a mixture of EtOH:$H_2O$ (v/v 1:5) until no red fluorescence was observed from the supernatant solution.

Espectroscopic data of **M10**

**EA** (%) Calcd. for [$C_{28.2}H_{34.2}O_2CoN_{4.1}$]: C 65.02, N 10.95, H 6.60; found: C 64.86, N 9.99, H 6.74. **IR (ATR)** 2952.0, 1662.8, 1588.2, 1510.6, 1454.1, 1421.3.

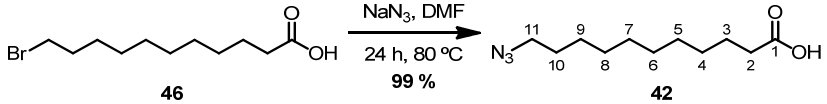
## VI.2.4. Guest release experiments

A dialysis bag (cut-off molecular weight: 3500) containing **M9b** or **M10** (c ~ 3 mg/mL) dispersed in phosphate buffered saline solution (PBS; pH = 7.4) was placed in 150 mL of PBS (pH = 7.4; dialysate) at 37 ºC under light stirring. To determine the increase of **6** or **30** concentration diffused through the dialysis bag, 0.5 mL of external PBS solution were taken from the dialysate at prefixed times and diluted in 2 mL of MeOH, and each aliquot was analyzed by fluorescence spectroscopy. The solid material remaining in the dialysis bag after 100 hours was dissolved in methanol and characterised by absorption spectroscopy.

# VI.3. NEW FUNCTIONAL LIGANDS FOR QUANTUM DOT ASSEMBLY

## VI.3.1. Synthesis of stabilizers

### VI.3.1.1. Synthesis of 11-azidoundecanoic acid, 42




**46** **42**

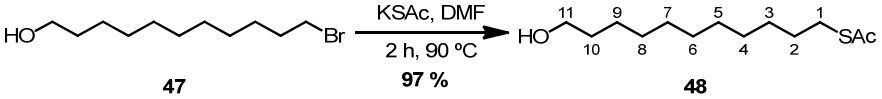
Compound **42** was synthesized according to ref [7] with some modifications. To a solution of 11-bromoundecanoic acid (5.04 g, 19.00 mmol) in dry DMF (30 mL), sodium azide (4.93 g, 75.83 mmol) was added. The reaction mixture was stirred at 25 ºC for 18 hours, after which water (30 mL) and diethyl ether (20 mL) were added and the aqueous layer was extracted three times with $Et_2O$ (30 mL). The organic extracts were dried with $MgSO_4$ and the solvent evaporated under vacuum to afford **42** as a pale orange oil (4.30 g, 18.92 mmol, 99 % yield).

Espectroscopic data of **42**

**$^1$H NMR** ($CDCl_3$, 250 MHz) $\delta$ 3.24 (t, $J_{10,11}$ = 6.9 Hz, 2H, 2xH-11), 2.34 (t, $J_{2,3}$ = 6.9 Hz, 2H, 2xH-2), 1.65-1.56 (m, 4H, 2xH-3, 2xH-10), 1.29 (m, 12H, 2xH-(4-9)).

## VI.3.1.2. Synthesis of 11-azidoundecanthiol, 43

### Synthesis of 11-hydroxyundecyl ethanethioate, 48



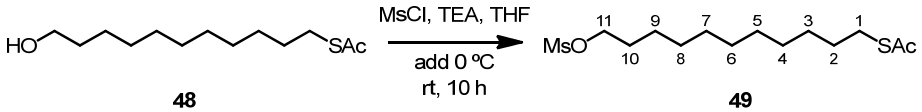

47 48

Compound **48** was synthesized according to ref [8] with some modifications. To a solution of **47** (2.00 g, 7.96 mmol) in DMF (40 mL), a solution of potassium thioacetate (2.20 g, 19.3 mmol) in DMF (40 mL) was added. The reaction mixture was heated at 90 ºC for 20 h. After this time, mixture was cooled to room temperature and water was added. The aqueous layer was extracted four times with $Et_2O$ (50 mL). The organic extracts were washed three times with water (30 mL), dried with $MgSO_4$ and the solvent was evaporated under vacuum to afford **48** as a yellowish oil (1.90 g, 7.71 mmol, 97 % yield).

Espectroscopic data of **48**

**$^1$H NMR** ($CDCl_3$, 250 MHz) $\delta$ 3.64 (t, $J_{10,11}$ = 6.5 Hz, 2H, 2xH-11), 2.85 (t, $J_{1,2}$ = 7.2 Hz, 2H, 2xH-1), 2.32 (s, 3H, -SAc), 1.67-1.44 (m, 4H, 2xH-2, 2xH-10), 1.27 (m, 14H, 2xH-3, 2xH-4, 2xH-5, 2xH-6, 2xH-7, 2xH-8, 2xH-9).

### Synthesis of 11-((methylsulfonyl)oxy)undecyl ethanethioate, 49



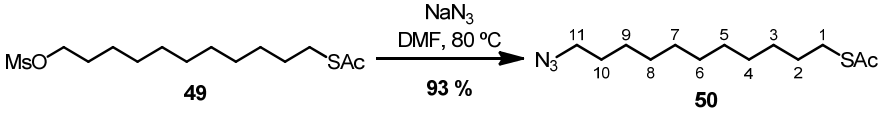

48 49

To a mixture of **48** (2.00 g, 8.12 mmol) and methanesulfonyl chloride (1.4 mL, 22.5 mmol) in dry THF (50 mL) cooled down in a water-ice bath, a solution of triethylamine (5.1 mL, 36.8 mmol) in dry THF (5 mL) was added dropwise. Next, the reaction was allowed to proceed at room temperature for 10 hours. After this time, 35 mL of ice-cold water was added, and the aqueous layer was extracted with $Et_2O$ (2 x 35 mL). The combined organic layers were washed once with 1M HCl (20 mL), $H_2O$ (20 mL), $NaHCO_3$ (20 mL) and $H_2O$ (20 mL), dried with $MgSO_4$ and the solvent was removed under reduced pressure to afford **49** as a colorless oil (2.60 g, 8.01 mmol, 98 % yield).

Espectroscopic data of **49**

**$^1$H NMR** ($CDCl_3$, 400MHz) $\delta$ 4.21 (t, $J_{10,11}$ = 6.5 Hz, 2H, 2xH-11), 3.00 (s, 3H, -OMs), 2.85 (t, $J_{1,2}$ = 7.3 Hz, 2H, 2xH-1), 2.31 (s, 3H, -SAc), 1.85-1.65 (m, 2H, 2xH-10), 1.65-1.46 (m, 2H, 2xH-2), 1.22-1.42 (m, 14H, 2xH-3, 2xH-4, 2xH-5, 2xH-6, 2xH-7, 2xH-8, 2xH-9). **$^{13}$C NMR** (101 MHz, $CDCl_3$) $\delta$ 196.2 (thioacetate), 70.3 (C-1), 37.5 (C-11), 30.8 (-OMs), 29.6 (-Ac), 29.2 - 25.5 (-OMs, C-(2-10)).

## Synthesis of 11-azidoundecyl ethanethioate, 50

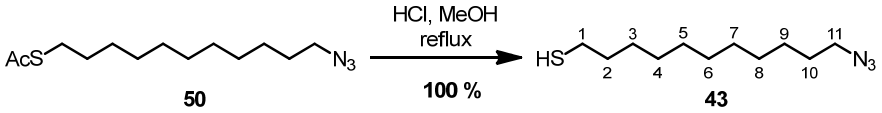



To a solution of **49** (2.60 g, 8.01 mmol) in dry DMF (80 mL), sodium azide (825 mg, 12.7 mmol) was added. The reaction mixture was stirred at 80 ºC for 24 hours. After cooling down, water (100 mL) and diethyl ether (50 mL) were added and the aqueous layer was extracted three times with $Et_2O$ (50 mL). The organic extracts were dried with $MgSO_4$ and the solvent evaporated under vacuum to afford **50** as a yelowish oil (2.02 g, 7.44 mmol, 93 % yield).

Espectroscopic data of **50**, ref [9]

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 3.25 (t, $J_{10,11}$ = 6.9 Hz, 2H, 2xH-11), 2.86 (t, $J_{1,2}$ = 7.3 Hz, 2H, 2xH-1), 2.32 (s, 3H, SAc), 1.74 – 1.45 (m, 4H, 2xH-2, 2xH-10), 1.27 (s, 14H, 2xH-3, 2xH-4, 2xH-5, 2xH-6, 2xH-7, 2xH-8, 2xH-9).

## Synthesis of 11-azidoundecanethiol, 43



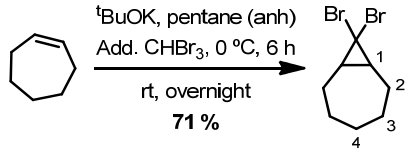

To a solution of **50** (2.02 g, 7.44 mmol) in MeOH (80 mL), HCl (6 mL, 72.5 mmol) was added dropwise. The reaction mixture was heated under reflux for 10 h, after which the mixture was cooled down at rt. $H_2O$ (100 mL) and diethyl ether (50 mL) were added and the aqueous layer was extracted three times with $Et_2O$ (50 mL). The combined organic layers were dried with $MgSO_4$ and the solvent evaporated under vacuum to afford **43** as a yellowish oil (1.70 g, 7.44 mmol, 100 % yield).

Espectroscopic data of **43**

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 3.25 (t, $J_{10,11}$ = 6.9 Hz, 2H, 2xH-11), 2.52 (q, $J_{1,2}$ = 7.4 Hz, 2H, 2xH-1), 1.73 – 1.49 (m, 4H, 2xH-2, 2xH-10), 1.46 – 1.16 (m, 14H, 2xH-3, 2xH-4, 2xH-5, 2xH-6, 2xH-7, 2xH-8, 2xH-9).

# VI.3.1.3. Synthesis of 10-(cyclooct-2-ynyloxy)decanoic acid, 44

## Synthesis of 8,8-dibromobicyclo[5.1.0]octane, 52



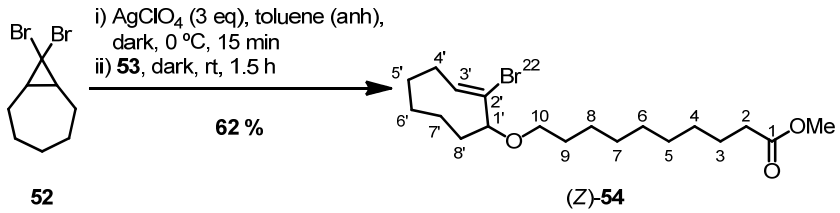

51 52

This compound was synthesized accordingly to ref [10]. To a suspension of cycloheptene (1.98 g, 19.97 mmol) and potassium tert-butoxide (2.58 g, 21.84 mmol) in dry pentane (50 mL) cooled down in a water-ice bath, a solution of bromoform (1.75 mL, 20.01 mmol) in dry pentane (50 mL) was added dropwise over 6 h. Next, the reaction was allowed to proceed at room temperature for 15 h, after which water (200 mL) was added. After neutralization with HCl (10 %, v/v), aquose layer was extracted three times with pentane (100 mL). The combined organic layers were dried with $MgSO_4$ and the solvent evaporated under vacuum to afford **52** as a colorless oil (3.74 g, 13.97 mmol, 71 % yield).

Espectroscopic data of **52**

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 2.40 – 2.13 (m, 2H, 2xH-1), 2.00 – 1.60 (m, 4H, 4xH-2), 1.37 (q, $J_{4,3}$ = 11.9 Hz, 2H, 2xH-4), 1.26 – 1.03 (m, 4H, 4xH-3).

## Synthesis of (*Z*)-methyl 10-((2-bromocyclooct-2-enyl)oxy)decanoate, (*Z*)-54




52 (*Z*)-**54**

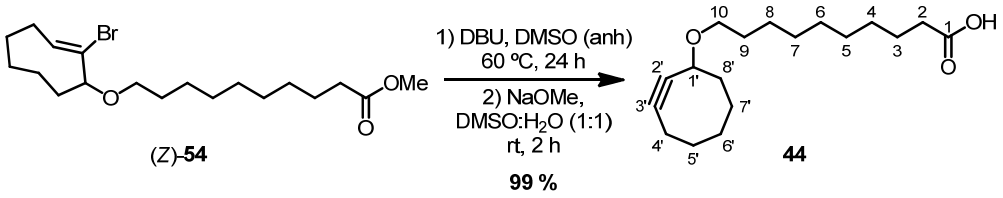
Compound **54** was synthesized according to ref [10] with some modifications. To a solution of **51** (119.1 mg, 0.46 mmol) in dry toluene (5 mL) wrapped and cooled down in a water-ice bath, $AgClO_4$ (290.5 mg, 1.40 mmol) was added and stirred for 15 min at 0 ºC. Next, methyl 10-hydroxydecanoate (**53**, 971.1 mg, 4.8 mmol) was added. Mixture was stirred at rt under argon atmosphere for 1.5 h, after which, mixture was filtered off through a celite bed and solvent was evaporated under high vacuum in darkness. Residue was purified by flash chromatography using hexanes:AcOEt (8:1 to 4:1, v/v), affording (*Z*)-**54** (106.2 mg, 62 % yeld) as a colorless oil.

Espectroscopic data of (*Z*)-**54**

**$^1$H NMR** (360 MHz, $CDCl_3$) $\delta$ 6.15 (dd, $J_{3',4'a}$ = 11.7 Hz, $J_{3',4'b}$ = 4.1 Hz, 1H, 1xH-3'), 3.81 (dd, $J_{1',8'a}$ = 10.0 Hz, $J_{1',8'b}$ = 5.0 Hz, 1H, 1xH-1'), 3.64 (s, 3H, COOMe), 3.48 (dt, $J_{gem}$ = 16.0 Hz, $J_{10a,\ 9}$ = 6.7 Hz,

1H, 1xH-10), 3.24 (dt, $J_{gem}$ = 9.0 Hz, $J_{10b,\ 9}$ = 6.6 Hz, 1H, 1xH-10), 2.72 (qd, $J_{4'a,3'}$ = 11.7 Hz, $J_{4'a,5'}$ = 5.4 Hz, 1H, 1xH-4'), 2.32 – 2.18 (m, 3H, 1xH-4', 2xH-2), 2.07 – 1.75 (m, 4H, 1xH-6', 1xH-7', 2xH-8'), 1.75 – 1.65 (m, 1H, 1xH-6'), 1.60 (m, 4H, 2xH-3, 2xH-9), 1.46 (dd, *J* = 12.7, 5.0 Hz, 1H, 1xH-5'), 1.39 – 1.21 (m, 11H, 2xH-4, 2xH-5, 2xH-6, 2xH-7, 2xH-8, 1xH-5'), 0.92 – 0.71 (m, 1H, 1xH-7').

### Synthesis of 10-(cyclooct-2-ynyloxy)decanoic acid, 44



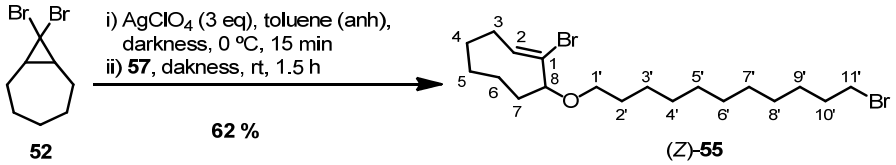

This compound was synthesized according to ref [10] with some modifications. A solution of (*Z*)-**54** (100 mg, 0.27 mmol) in DMSO (2 mL) was heated at 60 ºC and DBU (400 μL) was added. The reaction mixture was stirred at 60 ºC for 24 h. After this time, reaction crude was cooled down and water (0.6 mL) and NaOMe (79 mg, 1.46 mmol) were added. Mixture was stirred at rt for 2 h. Next, HCl (1 M) was added till pH = 1 followed by addition of EtOAc (5 mL). Aquose layer was extracted four times with EtOAc (5 mL). Combined organic layers were dried with $MgSO_4$ and the solvent evaporated under vacuum to afford **44** as a colorless oil (78.7 mg, 0.26 mmol, 99 % yield).

Espectroscopic data of **44**

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 4.14 (qt, $J_{1',8'}$ = 5.1, $J_{1',7'}$ = 2.1 Hz, 1H, 1xH-1'), 3.53 (dt, $J_{10a,10b}$ = 9.2, $J_{10a,9}$ = 6.8 Hz, 1H, 1xH-10), 3.27 (dt, $J_{10b,10a}$ = 9.2, $J_{10b,9}$ = 6.8 Hz, 1H, 1xH-10), 2.32 (t, $J_{2,3}$ = 5.1 Hz, 2H, 2xH-2), 2.27 – 2.12 (m, 2H, 2xH-4'), 2.12 – 2.03 (m, 1H, 1xH-8'), 2.03 – 1.72 (m, 4H, 1xH-5', 1xH6', 1xH-7', 1xH-8'), 1.72 – 1.46 (m, 5H, 2xH-3, 2xH-9, 1xH5'), 1.42 (m, 1H, 1xH-6'), 1.40 – 1.16 (m, 10H, 2xH-4, 2xH-5, 2xH-6, 2xH-7, 2xH-8), 0.93 – 0.77 (m, 1H, 1xH-7').

## VI.3.1.4. Synthesis of 11-(cyclooct-2-ynyloxy) undecanethiol, 45

### Synthesis of (*Z*)-1-bromo-8-((11-bromoundecyl)oxy)cyclooctene, (*Z*)-55



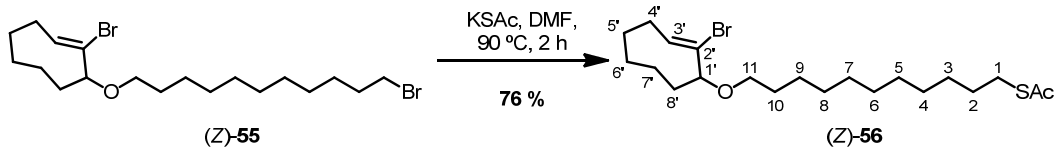

To a solution of **52** (667.3 mg, 2.49 mmol) in dry toluene (5 mL) wrapped and cooled down in a water-ice bath, $AgClO_4$ (1.55 g, 7.47 mmol) was added and stirred for 15 min at 0 ºC. Next, 11-bromoundecanol (**57**, 4.73 g, 18.8 mmol) was added. Mixture was stirred at rt under argon atmosphere for 1.5 h, after which, mixture was filtered off through a celite bed and solvent was

evaporated under high vacuum in darkness. Residue was purified by flash chromatography using hexanes:$Et_2O$ (30:1, v/v), affording (*Z*)-**55** (683 mg, 62 % yield) as a colorless oil.

Espectroscopic data of (*Z*)-**55**

**$^1$H NMR** (360 MHz, $CDCl_3$) $\delta$ 6.16 (dd, $J_{2,3a}$ = 11.7 Hz, $J_{2,3b}$ = 4.1 Hz, 1H, 1xH-2), 3.83 (dd, $J_{8,7a}$ = 10.0 Hz, $J_{8,7b}$ = 5.1 Hz, 1H, 1xH-8), 3.50 (dt, $J_{gem}$ = 9.1, $J_{1',2'}$ = 6.9 Hz, 1H, 1xH-1'), 3.39 (t, $J_{11',10'}$ = 6.5 Hz, 2H, 2xH11'), 3.25 (dt, $J_{gem}$ = 9.1, $J_{1',2'}$ = 6.9 Hz, 1H, 1xH-1'), 2.74 (qd, $J_{3,2}$ = 11.9 Hz, $J_{gem}$ = 5.5 Hz, 1H, 1xH-3), 2.26 (m, 1H, 1xH-3), 2.10 – 1.76 (m, 6H, 1xH-4, 2xH-5, 1xH-6, 2xH-7), 1.76 – 1.53 (m, 5H, 1xH-4, 2xH-2', 2xH-10'), 1.53 – 1.10 (m, 14H, 2xH-3', 2xH-4', 2xH-5', 2xH-6', 2xH-7', 2xH-8', 2xH-9'), 0.81 (m, 1H, 1xH-6). **$^{13}$C NMR** ($CDCl_3$, 91 MHz) $\delta$ 134.0 (C-1), 131.1 (C-2), 85.1 (C-8), 69.1 (C-1'), 39.8 (C-7), 36.6 (C-3), 34.2 (C-11'), 33.4 (C-4), 33.0 (C-5), 29.8 - 26.5 (C-2', C-3', C-4', C-5', C-6', C-7', C-8', C-9', C-10'), 26.4 (C-6). **IR (ATR) cm$^{-1}$** 3005.7, 2929.8, 2854.0, 1452.2, 1127.0. **HR-MS** (ESI+) calcd. for [$C_{19}H_{34}Br_2O$+Na]: 459.0869; found: 459.0870.

## Synthesis of (*Z*)-(11-((2-bromocyclooct-2-enyl)oxy)undecyl) ethanethioate, (*Z*)-56



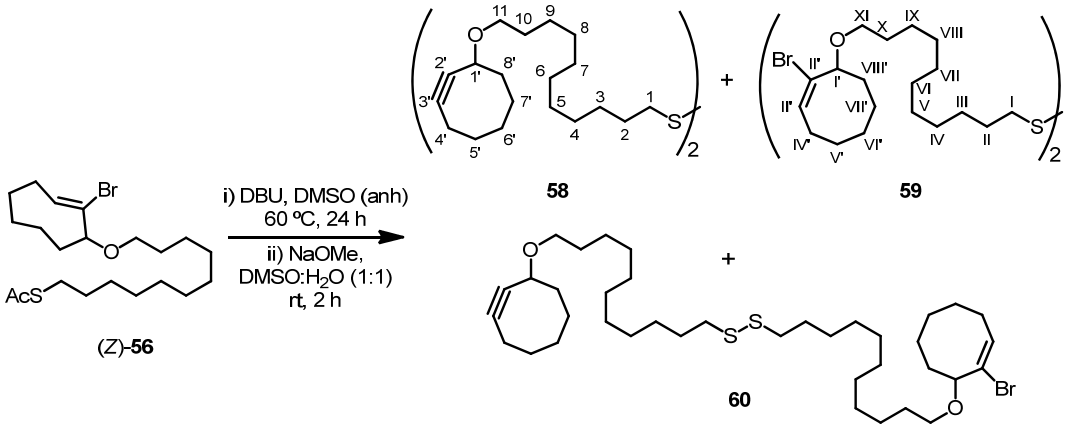

(*Z*)-**55** (*Z*)-**56**

To a solution of (*Z*)-**55** (151.8 mg, 0.35 mmol) in DMF (1 mL) wrapped and heated at 90 ºC, a solution of KSAc (47.9 mg, 0.42 mmol) was added. The reaction mixture was stirred at 90 ºC for 2 h. After cooling down at rt, water (2 mL) and $Et_2O$ were added. Aquose layer was extracted twice with $Et_2O$. Combined organic layers were dried with $MgSO_4$ and the solvent evaporated under vacuum. Residue was purified by flash chromatography using hexanes: $Et_2O$ (10:1, v/v), affording (*Z*)-**56** (106.2 mg, 76 % yield) as a brown oil.

Espectroscopic data of (*Z*)-**56**

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 6.17 (dd, $J_{3',4'a}$ = 11.7 Hz, $J_{3',4'b}$ = 4.1 Hz, 1H, 1xH-3'), 3.83 (dd, $J_{1',8'a}$ = 9.7 Hz, $J_{1',8'b}$ = 5.2 Hz, 1H, 1xH-1'), 3.51 (dt, $J_{gem}$ = 9.1, $J_{1',2'}$ = 6.9 Hz, 1H, 1xH-11), 3.25 (dt, $J_{gem}$ = 9.1, $J_{1',2'}$ = 6.9 Hz, 1H, 1xH-11), 2.86 (t, $J_{1,2}$ = 7.3 Hz, 2H, 2xH-1), 2.73 (qd, $J_{4'a,3'}$ = 11.9 Hz, $J_{gem}$ = 5.5 Hz, 1H, 1xH-4'), 2.39 – 2.21 (m, 4H, 1xH-4', SAc), 2.12 – 1.79 (m, 5H, 1xH-5', 1xH-6', 1xH-7', 2xH-8'), 1.79 – 1.49 (m, 5H, 1xH-6', 2xH-2, 2xH-10), 1.49 – 1.43 (m, 1H, 1xH-5'), 1.43 – 1.12 (m, 14H, 2xH-3, 2xH-4, 2xH-5, 2xH-6, 2xH-7, 2xH-8, 2xH-9), 0.92 – 0.69 (m, 1H, 1xH-7'). **$^{13}$C NMR** (91 MHz, $CDCl_3$) $\delta$ 196.2 (thiocarboxyl), 134.0 (C-2'), 131.1 (C-3'), 85.11 (C-1'), 69.1 (C-11), 39.8 (C-8'), 36.6 (C-5'), 33.4 (C-4'), 30.8 - 29.6 and 29.6 – 29.2 (C-3, C-4, C-5, C-6, C-7, C-8, C-9, C-10), 29.6 (SAc), 29.0 (C-1), 28.3 (C-7'), 26.5 (C-6'), 26.4 (C-2). **IR (ATR)** 3005.7, 2958.0, 2850.5, 1697.0, 1129.4, 1088.8. **HR-MS** (ESI+) calcd. for [$C_{21}H_{37}BrO_2S$+Na]: 455.1590; found: 455.1597.

## Synthesis of 1,2-bis(11-(cyclooct-2-ynyloxy)undecyl)disulfane, 58




To a solution of (*Z*)-**56** (179 mg, 0.41 mmol) in DMSO (4 mL) wrapped and heated at 60 ºC, DBU (400 μL) was added. The reaction mixture was stirred at 60 ºC for 24 h. After this time, reaction crude was cooled down and water (2 mL) and NaOMe (34.2 mg, 0.63 mmol) were added. Mixture was stirred at rt for 20 h. Next, HCl (1 M) was added till pH = 1 followed by addition of $Et_2O$ (5 mL). Aquose layer was extracted four times with $Et_2O$ (5 mL). organic extracts were dried with $MgSO_4$ and the solvent evaporated under vacuum. Residue was purified by successive flash chromatographies using hexanes:$Et_2O$ (10:1, v/v), hexanes:$Et_2O$ (30:1, v/v), and hexanes to afford a mixture of **58**, **59** and **60** (130 mg) as a yellowish oil with a cyclooctyne:cyclooctene moietes ratio of 5.8:1, respectively. For characterization of **58** a small pure fraction was obtained (5 mg). None fraction was pure enough for characterization of **59**, even though some characteristic signals form $^1$H NMR were identified from the mixture of **59** and **60**.

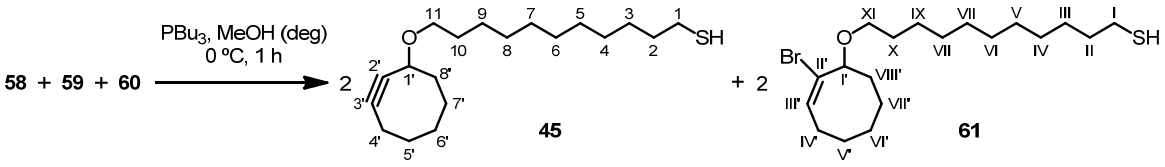
Espectroscopic data of **58**

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 4.21 – 4.08 (m, 1H, 1xH1'), 3.54 (dt, $J_{gem}$ = 9.2, $J_{11,10}$ = 6.8 Hz, 1H, 1xH-11), 3.29 (dt, $J_{gem}$ = 9.2, $J_{11,10}$ = 6.8 Hz, 1H, 1xH-11), 2.68 (t, $J_{1,2}$ = 9.2 Hz, 2H, 2xH-1), 2.35 – 2.04 (m, 3H, 2x-H4', 1xH-8'), 2.04 – 1.74 (m, 7H, 2xH-5', 2xH-6', 2xH-7', 1xH-8'), 1.74 – 1.48 (m, 4H, 2xH-2, 2xH-10), 1.48 – 1.13 (m, 14H, 2xH-3, 2xH-4, 2xH-5, 2xH-6, 2xH-7, 2xH-8, 2xH-9). **$^{13}$C NMR** (63 MHz, $CDCl_3$) $\delta$ 98.6 (C-3'), 92.5 (C-2'), 71.5 (C-1'), 68.7 (C-11), 41.9 (C-8'), 38.4 (C-1), 33.5 (C-7'), 33.5 (C-6'), 29.0 - 27.7 and 25.3 (C-2, C-3, C-4, C-5, C-6, C-7, C-8, C-9, C-10), 25.6 (C-5'), 20.9 (C-4'). **IR (ATR)** 3198.4, 2918.9, 2849.8, 1544.4. **HR-MS** (ESI+) calcd. for [$C_{38}H_{66}O_2S_2$+Na]: 641.4569; found: 441.4573.

Espectroscopic data of the mixture of **59** and **60**

**$^1$H NMR** (250 MHz, $CDCl_3$) $\delta$ 6.29 (t, $J_{3',4'}$ = 8.65 Hz, 1H, 1xH-III'), 4.30 (t, $J_{1',8'}$ = 6.67 Hz, 1H, 1xH-I'), 3.53 (dt, $J_{gem}$ = 8.99 Hz, $J_{11,10}$ = 6.87 Hz, 1H, 1xH-XI), 3.25 (dt, $J_{gem}$ = 8.99 Hz, $J_{11,10}$ = 6.87 Hz, 1H, 1xH-XI). Other signals overlap with signals of **60**.

## Synthesis of 11-(cyclooct-2-yn-1-yloxy)undecanethiol, 45



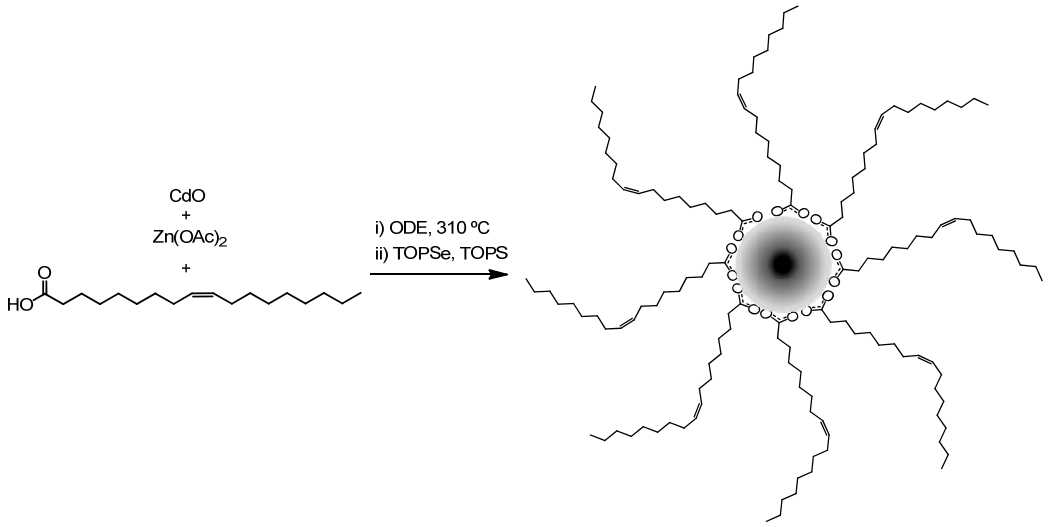

To a solution of mixture **58**, **59** and **60** (115 mg, 0.19 mmol of cyclooctyne units) in degassed MeOH (1 mL) wrapped and cooled down in a water-ice bath, tributylphospine (100 μL, 0.4 mmol) was added. The reaction mixture was stirred at 0 ºC for 1 h. After this time, ice (0.1 g) and $Et_2O$ (2 mL) were added. Aquose layer was extracted three times with $Et_2O$ (2 mL). Organic extracts were dried with $MgSO_4$ and the solvent evaporated under vacuum to afford a mixture of **45** (51.9 mg, 0.17 mmol, 45 % yield) and **61** (38.3 mg, 0.097 mmol, 25 % yield), according the $^1H$ NMR of the mixture, as a yellowish oil with a ratio 1.37:1, respectively.

Espectroscopic data of the mixture **45** and **61**

**$^1H$ NMR** (250 MHz, $CDCl_3$) $\delta$ 6.32 (t, $J_{III',IV'}$ = 8.8 Hz, 1H, 1xH-III'), 4.33 (t, $J_{I',VII'}$ = 8.8 Hz, 1H, 1xH-VIII'), 4.17 (m, 1H, 1xH-1'), 3.65 – 3.45 (m, 2H, 1xH-11, 1xH-XI), 3.40 – 3.20 (m, 2H, 1xH-11, 1xH-XI), 2.58 – 2.45 (m, 4H, 2xH-1, 2xH-I), 2.30 – 2.16 (m, 6H, cyc), 2.06 – 1.82 (m, 14H, cyc), 1.82 – 1.59 (m, 8H, 2xH-2, 2xH-10, 2xH-II, 2xH-X), 1.49 – 1.12 (m, 28H, 14xH-(3-9), 14xH-(III-IX)).

# VI.3.2. Synthesis of quantum dots and ligand exchange

## VI.3.2.1. Synthesis of core/shell quantum dots




### General procedure

CdSe/ZnS QDs were synthesized accordingly to ref [11]. To a three necked bottom flask equipped with a reflux condenser, a thermometer and under $N_2$ atmosphere, containing a solution of CdO, Zn(OAc) and oleic acid (5.5 mL, 17.4 mmol) in octadecene (20 mL) heated at 310 ºC, a solution of Se and S in trioctylphosphine (3 mL) was added. Reaction mixture was allowed to stir at 310 ºC for convenient time, after which was cooled down with an ice bath. Reaction crude was dissolved in $CHCl_3$ (20 mL) and QDs were precipitated by addition of acetone (60 mL). The corresponding suspension was centrifuged (6000 rpm for 15 min) and QDs were washed with $CHCl_3$:MeOH (1:3, v/v) until no free OA was detected by $^1$H NMR.

### Synthesis of $QD1_{OA}$

CdO (52.2 mg, 0.4 mmol), $Zn(OAc)_2$ (805.1 mg, 4.39 mmol), Se (31.9 mg, 0.40 mmol), S (127 mg, 3.96 mmol). Reaction time: 10 min.

Espectroscopic data of **$QD1_{OA}$**

**1D DOSY NMR** (400 MHz, $CDCl_3$) $\delta$ 5.37 (m, 2H, 1xH-9, 1xH-10), 2.04 (m, 4H, 2xH-8, 2xH-11), 1.29 (s, 2x(H-3-7), 2xH-(12-17)) 0.91 (m, 3H, 2xH-18). **IR (ATR)** 2918.1, 2849.7, 1541.6, 1428.5. $\lambda_{Abs}$ = 609 nm, $\lambda_{em,max}$ = 623 nm. **PLQY** = 0.25. **TEM**: $\varnothing$ = (9.54 ± 1.31) nm. **EA (ICP)**: 9.4 % Cd, 5.0 % Se, 24.8 % Zn, 11.4 % S.

### Synthesis of $QD2_{OA}$

CdO (52.6 mg, 0.41 mmol), $Zn(OAc)_2$ (800.5 mg, 4.36 mmol), Se (4.8 mg, 0.006 mmol), S (128.8 mg, 4.02 mmol). Reaction time: 10 s.

Espectroscopic data of **$QD2_{OA}$**

**1D DOSY NMR** (400 MHz, $CDCl_3$) $\delta$ 5.37 (m, 2H, 1xH-9, 1xH-10), 2.04 (m, 4H, 2xH-8, 2xH-11), 1.29 (s, 2x(H-3-7), 2xH-(12-17)) 0.91 (m, 3H, 2xH-18). **IR (ATR)** 2920.2, 2850.4, 1534.5, 1453.2. $\lambda_{Abs}$ = 540 nm, $\lambda_{em,max}$ = 550 nm. **PLQY** = 0.26. **TEM**: $\varnothing$ = (6.32 ± 0.91) nm. **EA (ICP)**: 44.3 % Cd, 1.6 % Se, 5.8 % Zn, 13.3 % S.

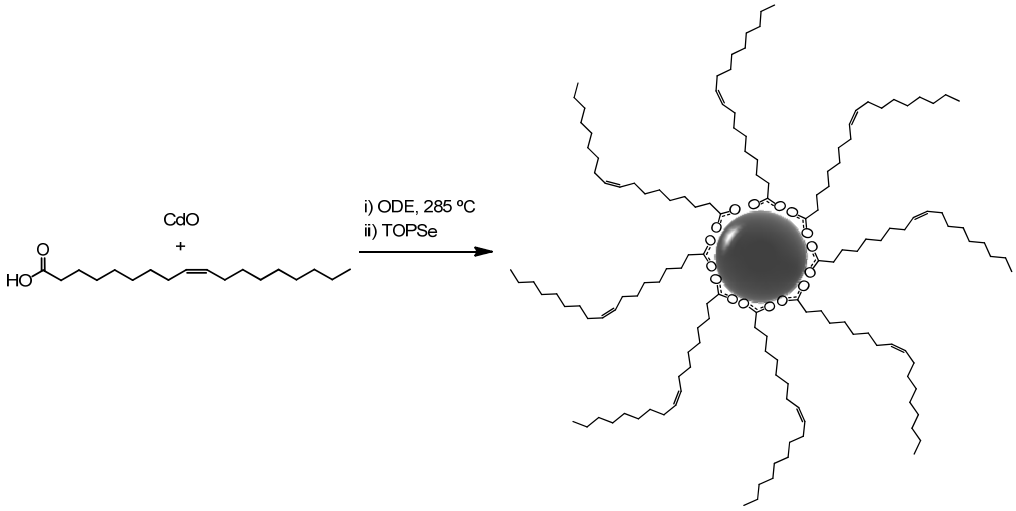
### Synthesis of $QD3_{OA}$

CdO (51.3 mg, 0.40 mmol), $Zn(OAc)_2$ (814.6 mg, 4.44 mmol), Se (15.9 mg, 0.021 mmol), S (126.4 mg, 3.94 mmol). Reaction time: 10 s.

Espectroscopic data of **$QD3_{OA}$**

**1D DOSY NMR** (400 MHz, $CDCl_3$) $\delta$ 5.37 (m, 2H, 1xH-9, 1xH-10), 2.04 (m, 4H, 2xH-8, 2xH-11), 1.29 (s, 2x(H-3-7), 2xH-(12-17)) 0.91 (m, 3H, 2xH-18). **IR (ATR)** 2919.2, 2850.8, 1533.5, 1458.1. $\lambda_{Abs}$ = 571 nm, $\lambda_{em,max}$ = 593 nm. **PLQY** = 0.26. **TEM**: $\varnothing$ = (6.10 ± 0.66) nm. **EA (ICP)**: 12.2 % Cd, 6.2 % Se, 30.5 % Zn, 14.4 % S.

## VI.3.2.2. Synthesis of core quantum dots, $QD4_{OA}$



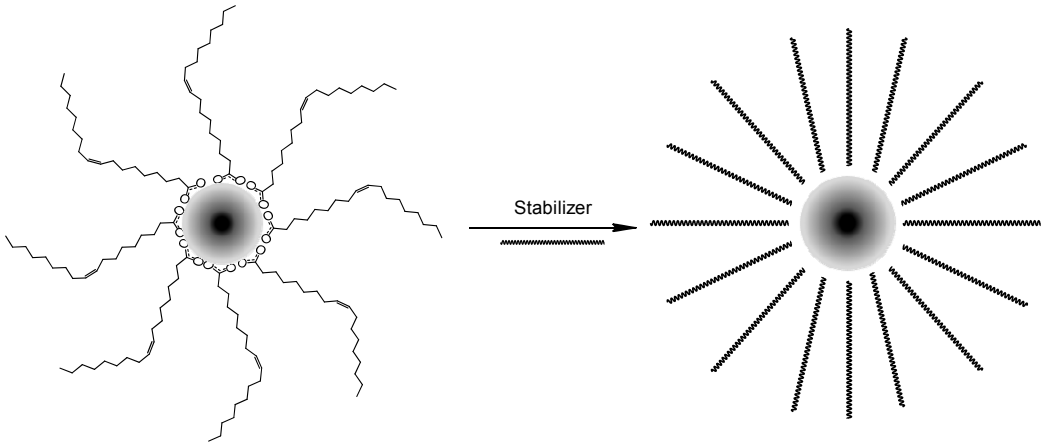

CdSe QDs were synthesized accordingly to ref [12]. To a three necked bottom flask equipped with a reflux condenser, a thermometer and under $N_2$ atmosphere, containing a solution of CdO (128 mg, 1 mmol), oleic acid (2.6 mL, 8.3 mmol) in octadecene (35 mL) heated at 285 ºC, a solution of Se (88.7 mg, 1.12 mmol) in octadecene (9 mL) was added. Reaction mixture was allowed to stir at 285 ºC for 20 seconds, after which was cooled down with an ice bath. Reaction crude was dissolved in $CHCl_3$ (20 mL) and QDs were precipitated by addition of acetone (60 mL).

The corresponding suspension was centrifuged (6000 rpm for 15 min) and QDs were washed with $CHCl_3$:acetone (1:3, v/v) until no free OA was detected by $^1H$ NMR.

Espectroscopic data of **$QD4_{OA}$**

**1D DOSY NMR** (400 MHz, $CDCl_3$) $\delta$ 5.37 (m, 2H, 1xH-9, 1xH-10), 2.04 (m, 4H, 2xH-8, 2xH-11), 1.29 (s, 2x(H-3-7), 2xH-(12-17)) 0.91 (m, 3H, 2xH-18). **IR (ATR)** 2918.7, 2878.2, 1539.5, 1458.3. $\lambda_{Abs}$ = 525 nm, $\lambda_{em,max}$ = 532 nm. **PLQY** = 0.09. **TEM**: $\varnothing$ = (2.48 ± 0.32) nm. **EA (ICP)**: 20.0 % Cd, 9.9 % Se.

## VI.3.2.3. Ligand exchange




### General procedure for ligand exchange

To a suspension of suspension of QD (1mM) in $CHCl_3$ (2 mL), a solution of the corresponded stabilizer in $CHCl_3$ (1 mL) was added. Mixture was stirred at rt for 2 h. Next, addition of MeOH (9 mL) induced quantum dot precipitation. Ligand excess was removed by centrifugation, QDs were redispersed in $CHCl_3$ and washed once with a mixture of $CHCl_3$:MeOH (4 mL, 1:3, v/v).

### Synthesis of $QD1_{43}$

Stabilizer **43**. Concentration = 25 mM. Ligand exchanged: 95 %.

Espectroscopic data of **$QD1_{43}$**

**1D DOSY NMR** (400 MHz, $CDCl_3$) $\delta$ 5.37 (m, OA), 3.25 (m, H-11), 2.04 (m, OA), 1.49 (m, H-2, H-10), 1.29 (s, H-(3-10), OA). **IR (ATR)** 2919.5, 2850.2, 2092.5, 1552.9, 1456.9. $\lambda_{Abs}$ = 609 nm, $\lambda_{em,max}$ = 623 nm. **PLQY** = 0.33. **TEM**: $\varnothing$ = (9.51 ± 1.45) nm.

### Synthesis of $QD2_{45}$

Stabilizer **45**. Concentration = 25 mM. Ligand exchanged: 100 %.

Espectroscopic data of **$QD2_{45}$**

**1D DOSY NMR** (400 MHz, $CDCl_3$) $\delta$ 6.32 (m, alkene), 4.33 (m, alkene), 4.17 (m, H-1'), 3.65 – 3.20 (m, H-10, alkene), 1.49 – 0.87 (m, H-(4'-8'), H-(2-9), alkene).**IR (ATR)** 2920.4, 2850.8, 1727.07, 1546.7, 1454.9. $\lambda_{Abs}$ = 542 nm, $\lambda_{em,max}$ = 551 nm. **PLQY** = 0.25. **TEM**: $\varnothing$ = (5.21 ± 0.81) nm.

### Synthesis of $QD3_{44}$

Stabilizer **44**. Concentration = 10 mM. Ligand exchanged: 45 %.

Espectroscopic data of **$QD3_{44}$**

**1D DOSY NMR** (400 MHz, $CDCl_3$) $\delta$ 5.37 (m, OA), 3.24 (m, H-11), 2.04 (m, OA), 1.60 (m, H-3, H-10), 1.29 (s, H-(4-9), OA). $\lambda_{Abs}$ = 571 nm, **IR (ATR)** 2977.7, 1928.20, 2095.4, 1528.4, 1424.4. $\lambda_{em,max}$ = 598 nm. **PLQY** = 0.40. **TEM**: $\varnothing$ = (6.12 ± 0.72) nm.

### Synthesis of $QD4_{42}$

Stabilizer **42**. Concentration = 10 mM. Ligand exchanged: 34 %.

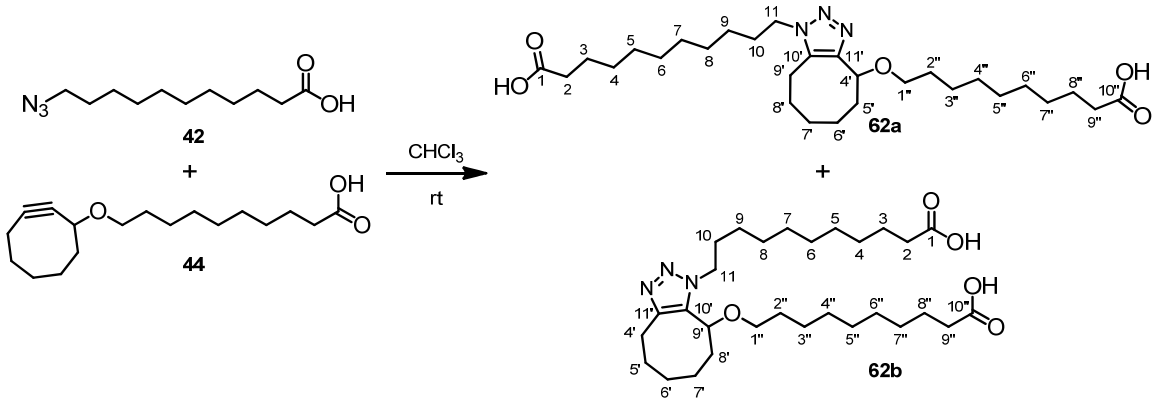
Espectroscopic data of **$QD4_{42}$**

**1D DOSY NMR** (400 MHz, $CDCl_3$) $\delta$ 5.37 (m, OA), 4.14 (m, H-1'), 3.65 – 3.20 (m, H-10), 1.49 – 0.87 (m, H-(4'-8'), H-(2-9), OA). **IR (ATR)** 2920.4, 2850.8, 1546.7, 1454.9. $\lambda_{Abs}$ = 523 nm, $\lambda_{em,max}$ = 531 nm. **PLQY** = 0.13. **TEM**: $\varnothing$ = (2.48 ± 0.15) nm.

# VI.3.3. Formation of Aggregates of quantum dots

## VI.3.3.1. Free quantum dot SPAAC

### Synthesis of 11-(4-((9-carboxynonyl)oxy)-4,5,6,7,8,9-hexahydro-1H-cycloocta[d][1,2,3]triazolyl)undecanoic acid and 11-(9-((9-carboxynonyl)oxy)-4,5,6,7,8,9-hexahydro-1H-cycloocta[d][1,2,3]triazol-1-yl)undecanoic acid, 62a and 62b



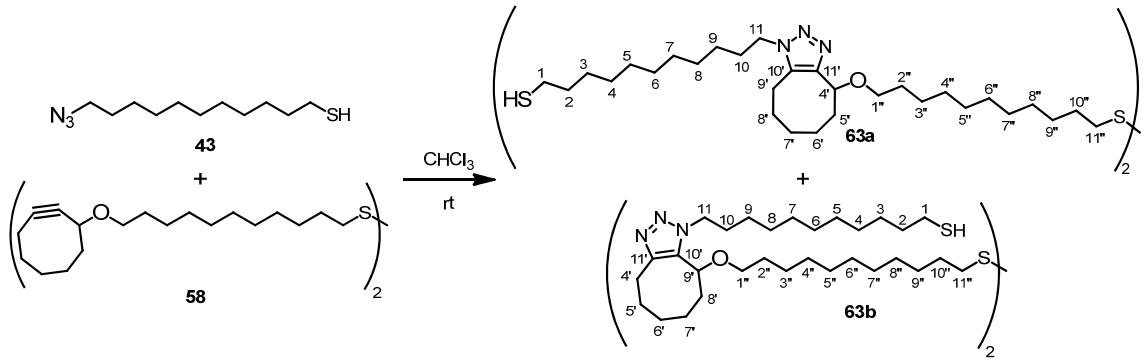

To a solution of **44** (29.1 mg, 0.09 mmol) in $CHCl_3$ (50 μL), a solution of **42** (20.9 mg, 0.1 mmol) in $CHCl_3$ (50 μL) was added. Reaction mixture was stirred at rt for 3.5 h and solvent was evaporated under vacuum to afford a mixture of **62a** and **62b** (46.9 mg, 0.09 mmol, 100 % yield) with a ratio of 1.2:1, respectively.

Espectroscopic data of mixture **62a** and **62b**

**$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 4.83 (dd, $J_{4';5'a}$ = 5.3 Hz, $J_{4';5'b}$ = 3.6 Hz, 1H, 1xH-4'(**62a**)), 4.64 (dd, $J_{9';8'a}$ = 8.9 Hz, $J_{9';8'b}$ = 3.5 Hz, 1H, 1xH-9'(**62b**)), 4.33 (dd, $J_{11,10a}$ = 8.4 Hz, $J_{11,10b}$ = 6.7 Hz, 2H, 2xH-11(**62b**)), 4.21 (dt, $J_{11,10a}$ = 13.3 Hz, $J_{11,10b}$ = 6.6 Hz, 2H, 2xH-11(**62a**)), 3.45 (dt, $J_{1'',2''}$ = 13.3 Hz, $J_{1'',2''}$ = 6.6 Hz, 1H, 1xH-1''(**62b**)), 3.41 – 3.33 (m, 1H, 1xH-1''(**62a**)), 3.32 – 3.23 (m, 2H, 1xH-1''(**62a**), 1xH-1''(**62b**)), 3.23 – 3.05 (m, 2H, 1xH-4'(**62b**), 1xH-9'(**62a**)), 2.81 (m, 1H, 1xH-9'(**62a**)), 2.65 (dt, $J_{gem}$ = 15.0 Hz, $J_{4';5'}$ = 4.7 Hz, 1H, 1xH-4'(**62b**)), 2.36 (t, $J$ = 7.4 Hz, 8H, 2xH-2a(**62a**), 2xH-2(**62b**), 2xH-9''(**62a**), 2xH-9''(**62b**)), 2.25 – 2.09 (m, 2H, 1xH-5'(**62a**), 1xH-8'(**62b**)), 2.00 (m, 1H, 1xH-8'(**62b**)), 1.97 – 1.81 (m, 5H, 1xH-8'(**62a**), 2xH-10(**62a**), 2xH-10(**62b**)), 1.76 (m, 3H, 1xH-5'(**62a**), 1xH-6'(**62b**), 1xH-8'(**62a**)), 1.72 – 1.43 (m, 7H, 1xH-6'(**62a**), 2xH-7'(**62a**), 1xH-6'(**62b**), 2xH-7'(**62b**)), 1.43 – 1.10 (m, 65H, 1xH-6'(**62b**), 2xH-(2-10)(**62a**), 2x(H-2''-9'')(**62a**), 2x(H-2-10)(**62b**), 2xH-(2''-9'')(**62b**), 1.09-0.94 (m, 1H, 1xH-6'(**62a**)).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) $\delta$ 179.6 - 179.4 (4C, C-1(**62a**), C-10''(**62a**), C-1(**62b**), C-10''(**62b**)), 145.6 (C-11'(**62a**)), 144.6 (C-11'(**62b**)), 133.6 (C-10'(**62a**)), 133.1 (C-10'(**62b**)), 74.2 (C-4'(**62a**)), 72.0 (C-9'(**62b**)), 68.9 - 68.8 (C-1''(**62a**), C-1''(**62b**)), 49.0 (C-11(**62b**)), 47.8 (C-11(**62a**)), 35.8 - 34.1 (C-2(**62a**), C-9''(**62a**), C-2(**62b**), C-9''(**62b**), C-8'(**62a**)), 32.0, - 20.8 (C-(2-10)(**62a**)), C-(5'-8')(**62a**), C-(2''-8'')(**62a**), C-(2-10)(**62b**), C-(5'-8')(**62b**), C-(2''-8'')(**62b**)), 20.0 (C-4'(**62b**)).

## Synthesis of 11-((1-(11-mercaptoundecyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta[d][1,2,3]triazol-4-yl)oxy)undecanethiol and 11-((1-(11-mercaptoundecyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta[d][1,2,3]triazol-9-yl)oxy)undecanethiol, 63a and 63b




To a solution of **58** (5.3 mg, 8.6 μmol) in $CHCl_3$ (40 μL), a solution of **43** (4.2 mg, 18.3 μmol) in $CHCl_3$ (40 μL) was added. Reaction mixture was stirred at rt for 3.5 h, after which solvent was evaporated under vacuum to afford a mixture of **63a** and **63b** (8.1 mg, 7.5 μmol, 87 % yield) with a ratio of 1.38:1, respectively.

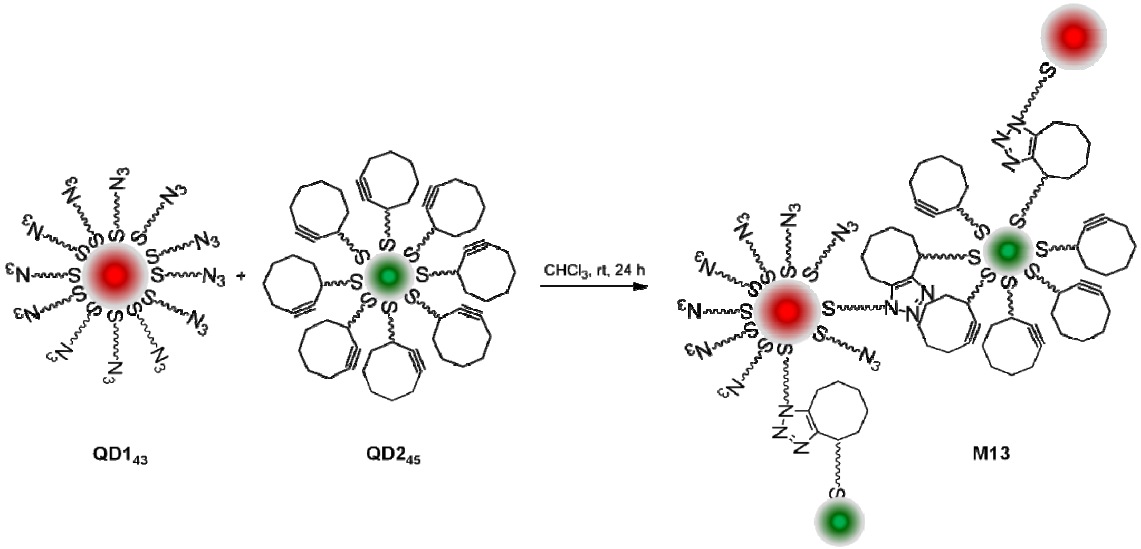
Espectroscopic data of mixture **63a** and **63b**

**$^1$H NMR** (400 MHz, $CDCl_3$) $\delta$ 4.81 (dd, $J_{4';5'a}$ = 5.3, Hz, $J_{4';5'a}$ = 3.6 Hz, 2H, 2x(1xH-4'(**63a**))), 4.63 (dd, $J_{9';8'a}$ = 8.7 Hz, $J_{9';8'b}$ = 3.4 Hz, 2H, 2x(1xH-9'(**63b**))), 4.32 (t, $J_{11,10}$ = 8.4 Hz, 4H, 2x(2xH-11(**63b**))), 4.19 (t, $J_{11,10}$ = 7.4 Hz, 4H, 2x(2xH-11(**63a**))), 3.47 – 3.21 (m, 8H, 2x(2xH-1''(**63a**), 2xH-1''(**63b**))), 3.22 – 3.05 (m, 4H, 2x(1xH-4'(**63b**), 1xH-9'(**63a**))), 2.91 – 2.77 (m, 2H, 2x(1xH-9'(**63a**))), 2.75 – 2.58 (m, 10H, 2x(1xH-4'(**63b**), 2xH-11''(**63a**), 2xH-11''(**63b**))), 2.52 (q, $J_{11'',10''}$ = 7.5 Hz, 8H, 2x(2xH-1(**63a**), 2xH1(**63b**))), 2.16 (m, 6H, 2x(1xH-5'(**63a**), 2xH-8'(**63b**))), 2.06 – 1.81 (m, 16H, 2x(1xH-5'(**63a**), 1xH-6'(**63b**), 2xH-8'(**63a**), 2xH-10(**63a**), 2xH-10(**63b**))), 1.81 – 1.72 (m, 4H, 2x(1xH-5'(**63a**), 1xH-6'(**63b**))), 1.72 – 1.46 (m, 12H, 2x(2xH-6'(**63a**), 2xH-7'(**63a**), 1xH-6'(**63b**), 2xH-7'(**63b**), 2xH-10(**63a**), 2xH-10(**63b**))), 1.40 – 1.14 (m, 68H, 2x(2xH-(2-9)(**63a**), 2x(H-2''-10'')(**63a**), 2x(H-2-9)(**63b**), (2xH-2''-10'')(**63b**)).

**$^{13}$C NMR** (101 MHz, $CDCl_3$) $\delta$ 145.3 (C-11'(**63a**), C-11'(**63b**)), 133.4 (C-10'(**63a**), C-10'(**63b**)), 74.0 (C-4'(**63a**)), 71.7 (C-9'(**63b**)), 68.8 (C-1''(**63a**)), 68.7 (C-1''(**63b**)), 49.0 (C-11(**63b**)), 47.7 (C-11(**63a**)), 39.1 (C-11''(**63a**), C-11''(**63b**)), 35.6 - 33.9 (C-2(**63a**), C-9''(**63a**), C-2(**63b**), C-9''(**63b**), C-8'(**63a**)), 31.8 - 20.6 (C-(2-10)(**63a**), C-(5'-8')(**63a**), C-(2''-8'')(**63a**), C-(2-10)(**63b**), C-(5'-8')(**63b**), C-(2''-8'')(**63b**)), 19.8 (C-4'(**63b**)).

## VI.3.3.2. Quantum dot SPAAC

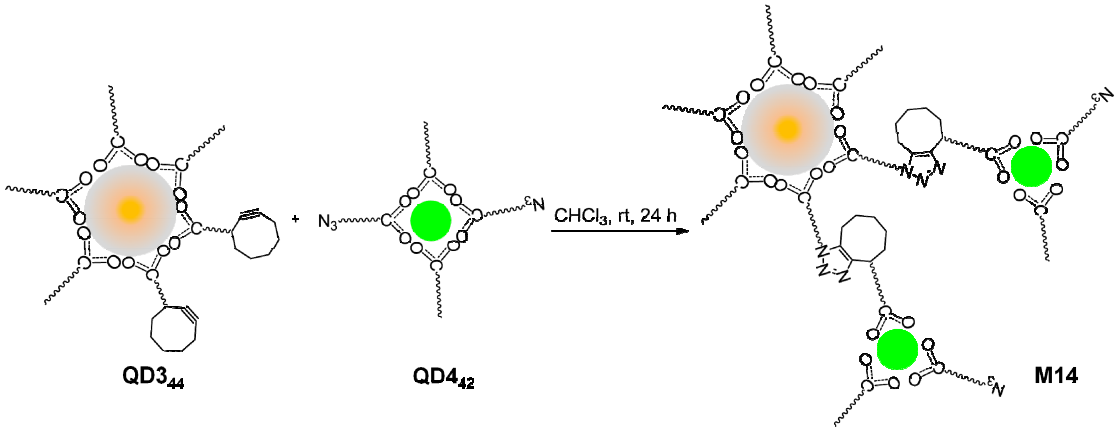
### Synthesis of M13




To a solution of **QD1$_{43}$** (50 μmol) in $CHCl_3$ (100 μL), a solution of **QD2$_{45}$** (55 μmol) in $CHCl_3$ (100 μL) was added and mixture was stirred for 24 h at rt. To monitor PL changes, 10 μL of solution were taken from the mixture every 1 h for the first 10 h, and at 24 h, and diluted in 2 mL of $CHCl_3$. Each aliquot was analyzed by fluorescence spectroscopy. Initial and final mixtures were also analized by TEM.

For NMR monitoring, different initial concentrations were mixed: **QD1$_{43}$** (2.31 mmol) and **QD2$_{45}$** (2.70 mmol) were dispersed in of $CDCl_3$ (0.7 mL).

### Synthesis of M14




To a solution of **QD3$_{44}$** (490·μmol) in $CHCl_3$ (100 μL), a solution of **QD4$_{42}$** (2.1 mmol) in $CHCl_3$ (100 μL) was added and mixture was stirred for 24 h at rt. To monitor PL changes, 10 μL of solution were taken from the mixture every 1 h for the first 10 h, and at 24 h, and diluted in 2.5 mL

of $CHCl_3$. Each aliquot was analyzed by fluorescence spectroscopy. Initial and final mixtures were also analized by TEM.

For NMR monitoring, different initial concentrations were mixed: **$QD3_{44}$** (1.71 mmol) and **$QD4_{42}$** (1.88 mmol) were dispersed in of $CDCl_3$ (0.7 mL).

Espectroscopic data of **M14**

**1D DOSY NMR** (400 MHz, $CDCl_3$) $\delta$ 5.35 (m, OA), 4.81 (m, 1,4-H-4'), 4.62 (m, 1,5-H-4'), 4.30 (m, 1,4- and 1,5-H-11), 3.52 and 3.26 (m, 1,4- and 1,5-H-1''), 2.21 - 0.90 (m, 1,4- and 1,5-[H-(2'-8'), H-(2''-9''), H-(2-10)], OA).

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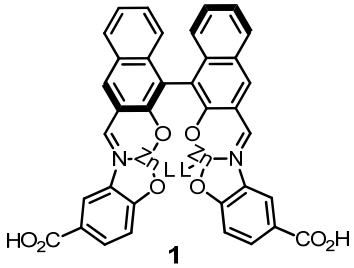
# Chapter VII

## Annex

# VII.1. FORMULA INDEX



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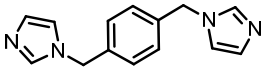

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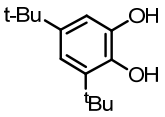

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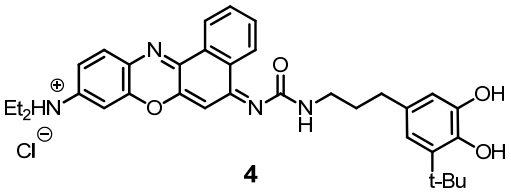

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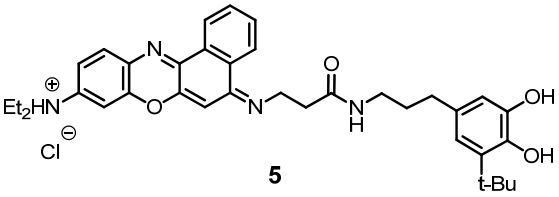

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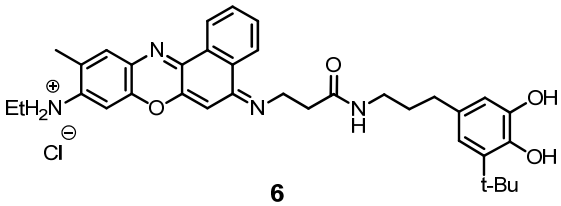

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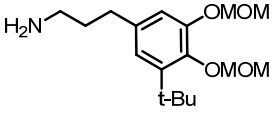

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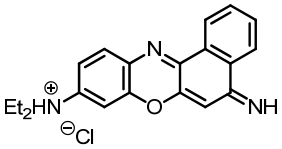
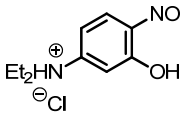


**8**



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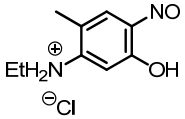

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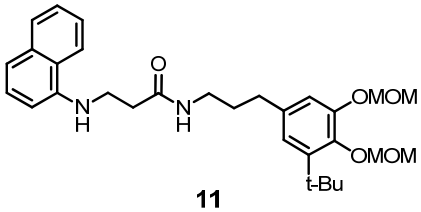

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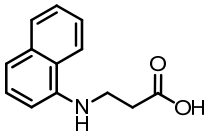

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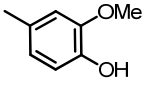

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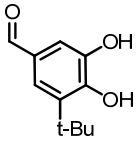

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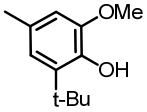

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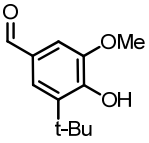

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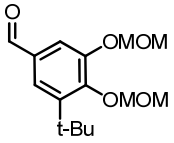

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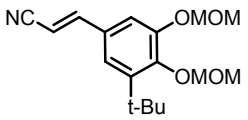


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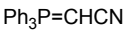


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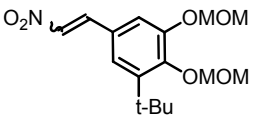


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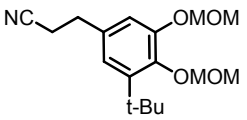


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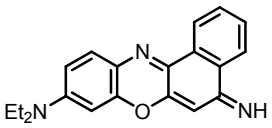


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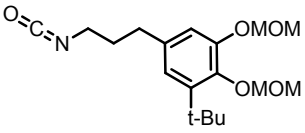


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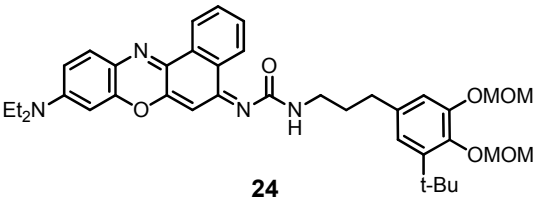


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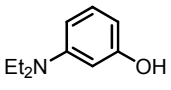


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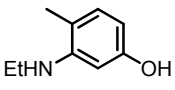


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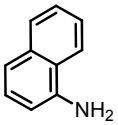


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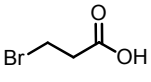


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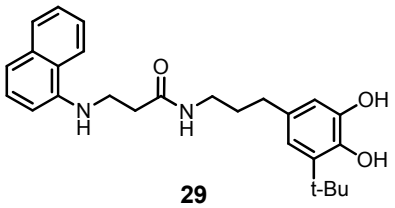


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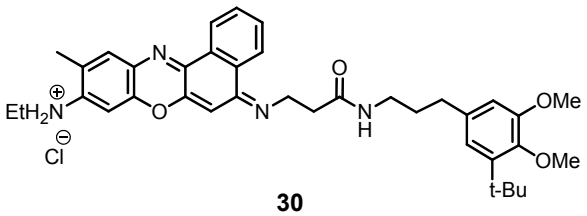


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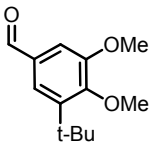


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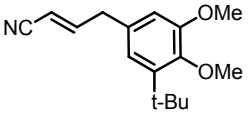


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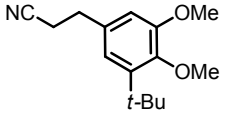


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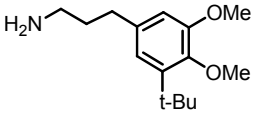


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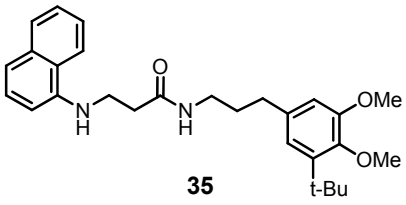


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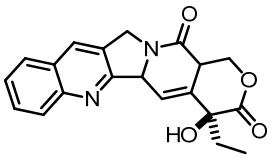

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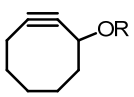

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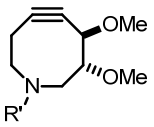

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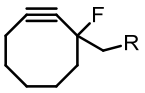

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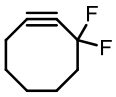

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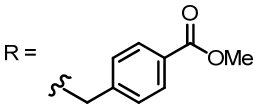

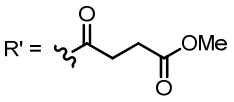

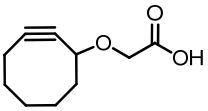

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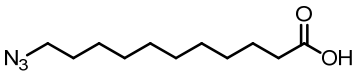

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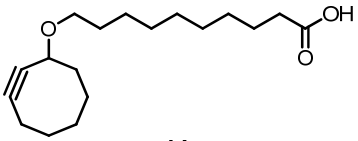

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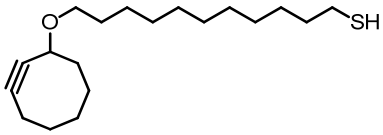

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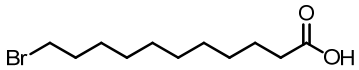

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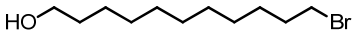

**47**

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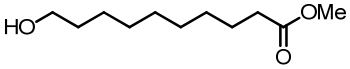
**52**



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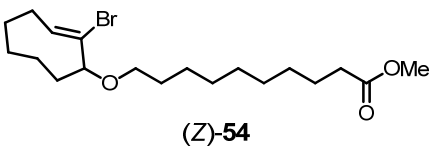
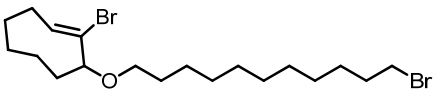


(*Z*)-**54**



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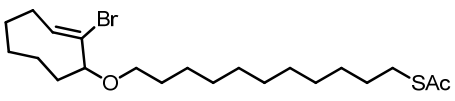
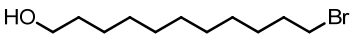
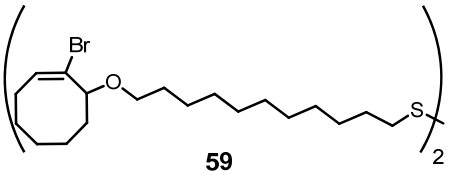


(*Z*)-**56**



**57**


58

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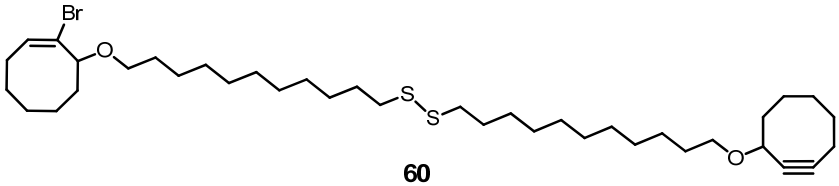


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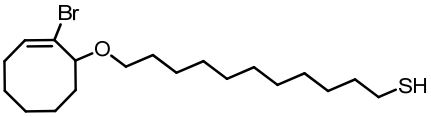


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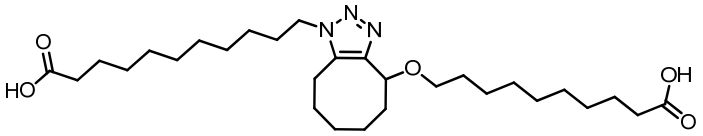
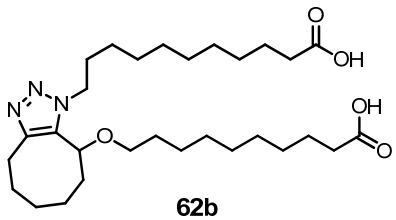
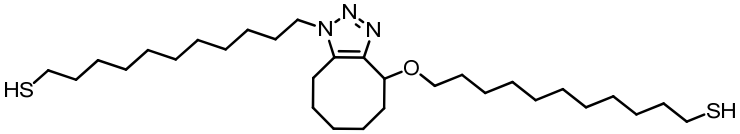


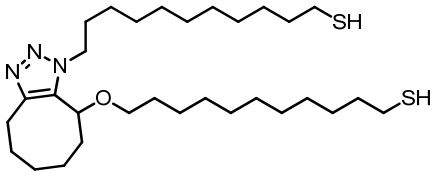

62a




62b



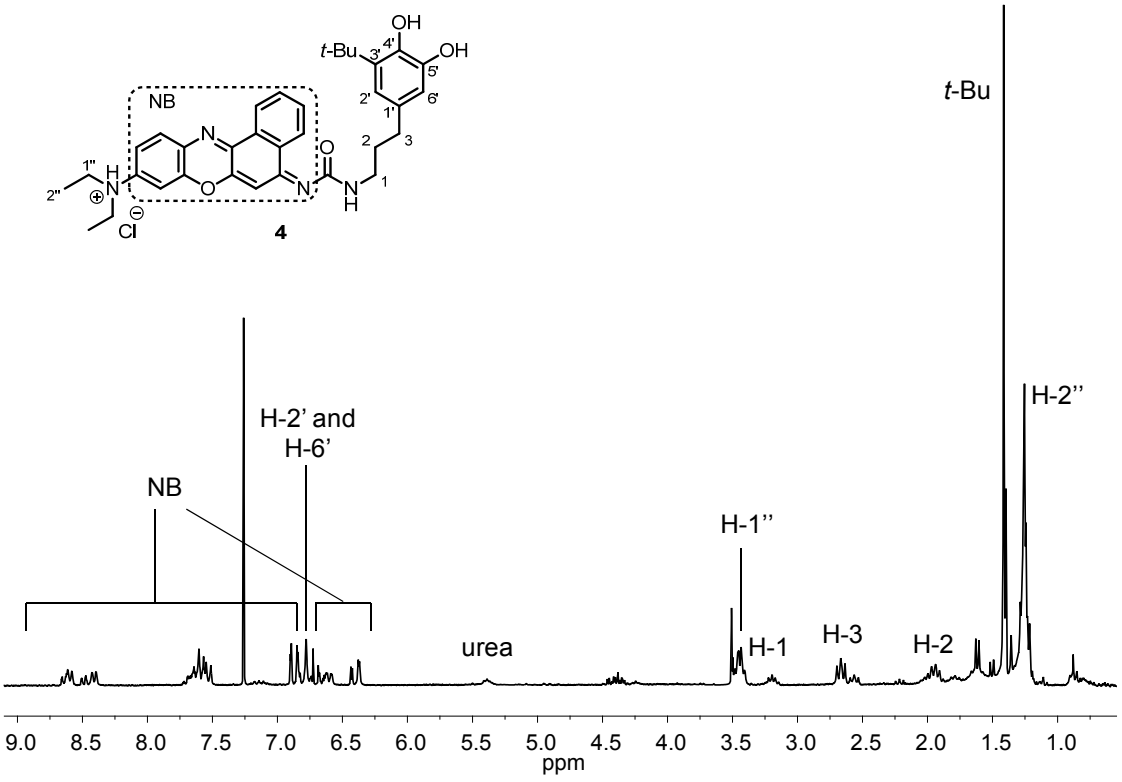

63a




63b

# VII.2. SELECTED NMR SPECTRA

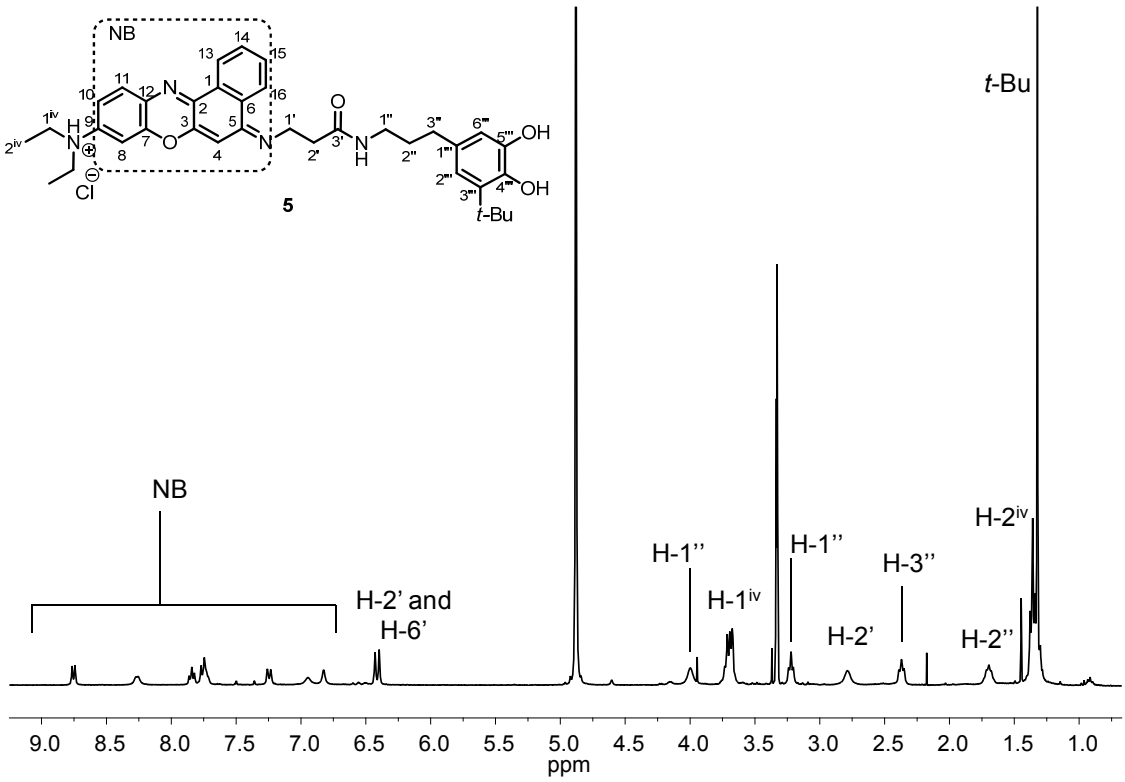
**Ligand 4:** 5-(((3-(3-(tert-butyl)-4,5-dihydroxyphenyl)propyl)carbamoyl)imino)-N,N-diethyl-5H-benzo [a]phenoxazin-9-aminium chloride



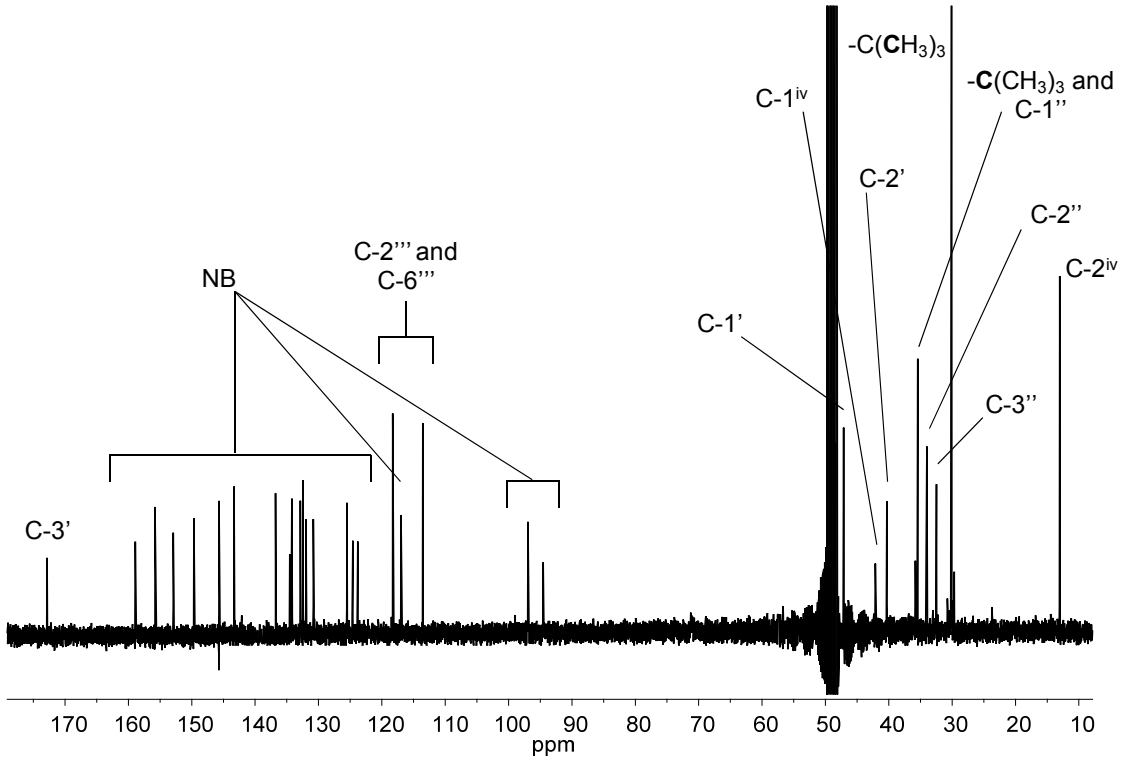

4

**$^1$H NMR** ($CDCl_3$, 400 MHz)

**Ligand 5:** 5-((3-((3-(3-(tert-butyl)-4,5-dihydroxyphenyl)propyl)amino)-3-oxopropyl)imino)-N,N-diethyl-5H-benzo[a]phenoxazin-9-aminium chloride

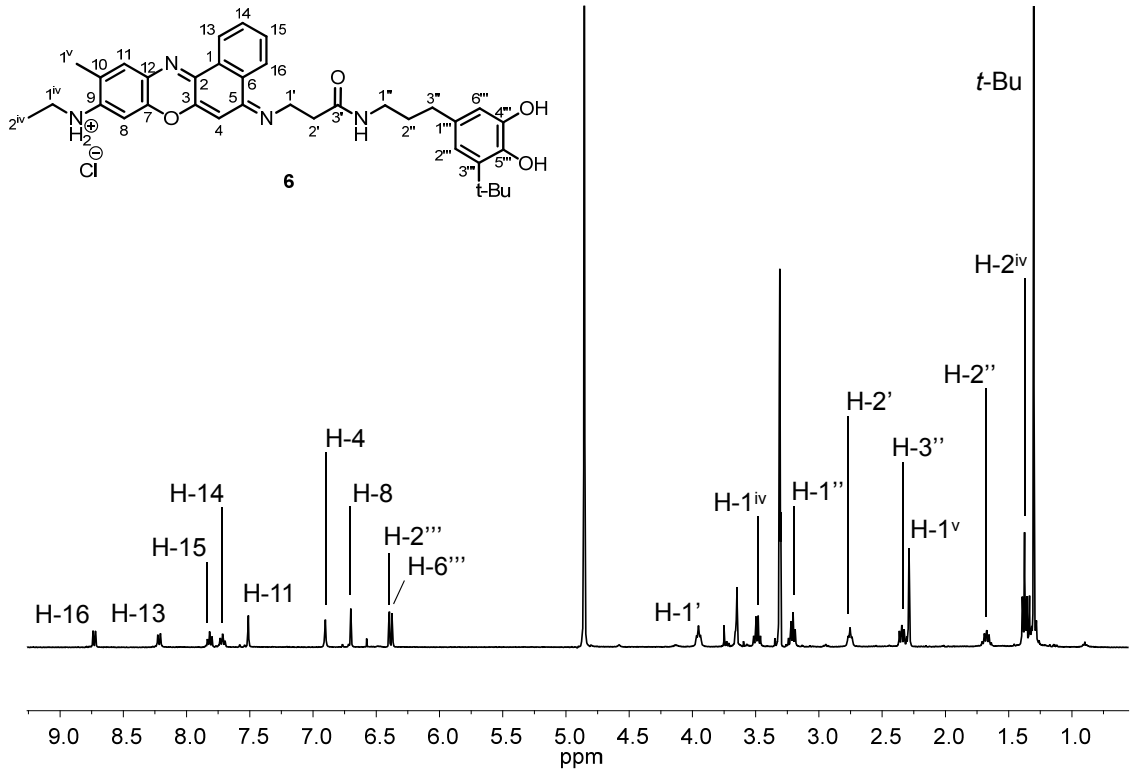



**$^{1}$H NMR** (MeOH-$d_4$, 360 MHz)

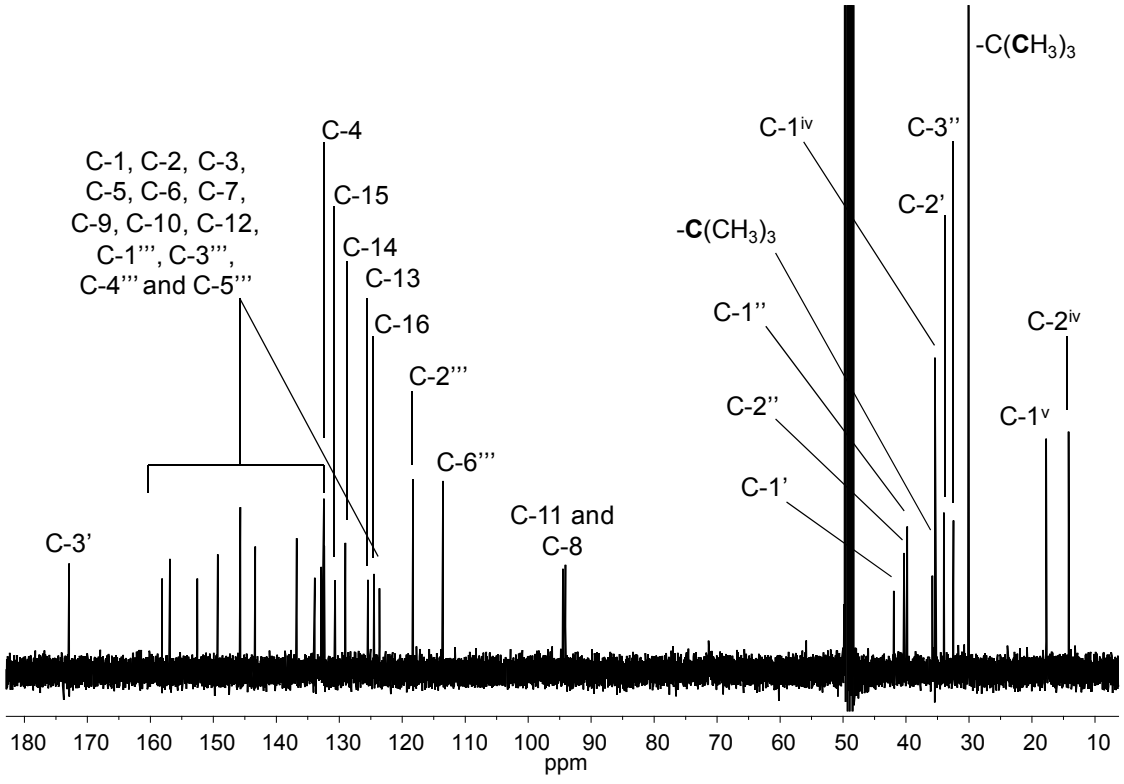



**$^{13}$C NMR** (MeOH-$d_4$, 90 MHz)

**Ligand 6:** 5-((3-((3-(3-(tert-butyl)-4,5-dihydroxyphenyl)propyl)amino)-3-oxopropyl)imino)-N-ethyl-10-methyl-5H-benzo[a]phenoxazin-9-aminium chloride

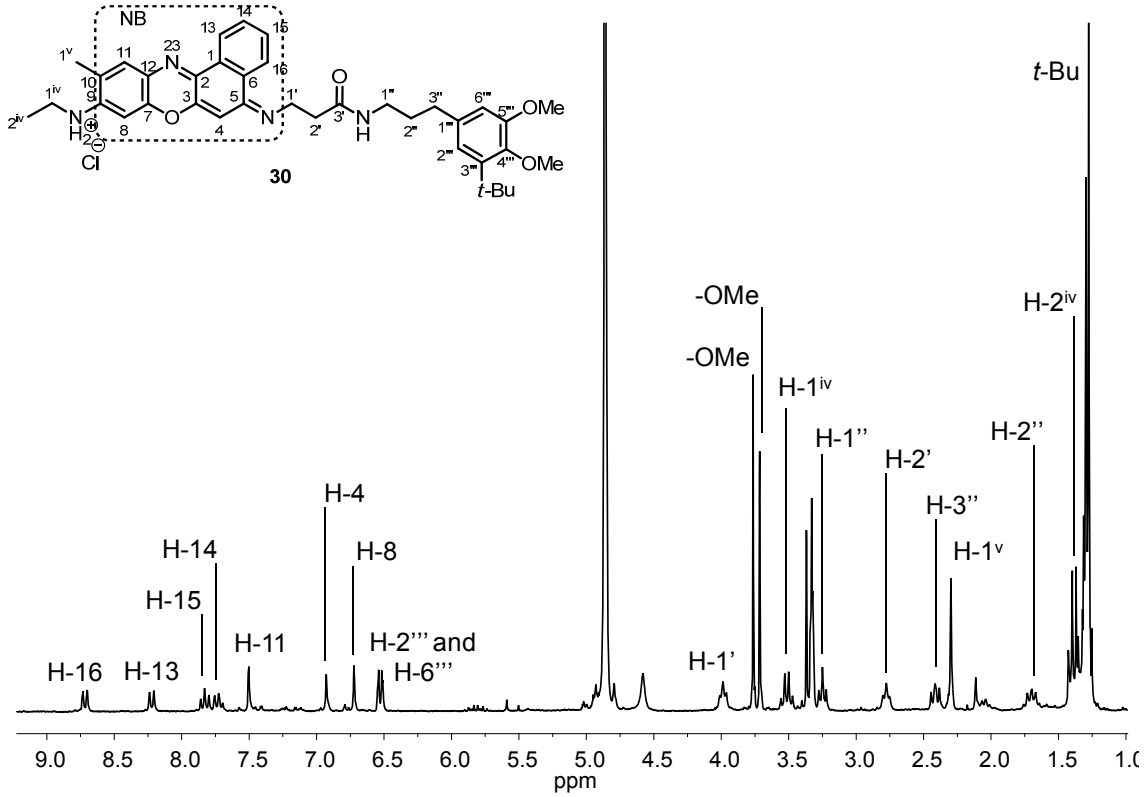



**$^{1}$H NMR** (MeOH-$d_4$, 400 MHz)

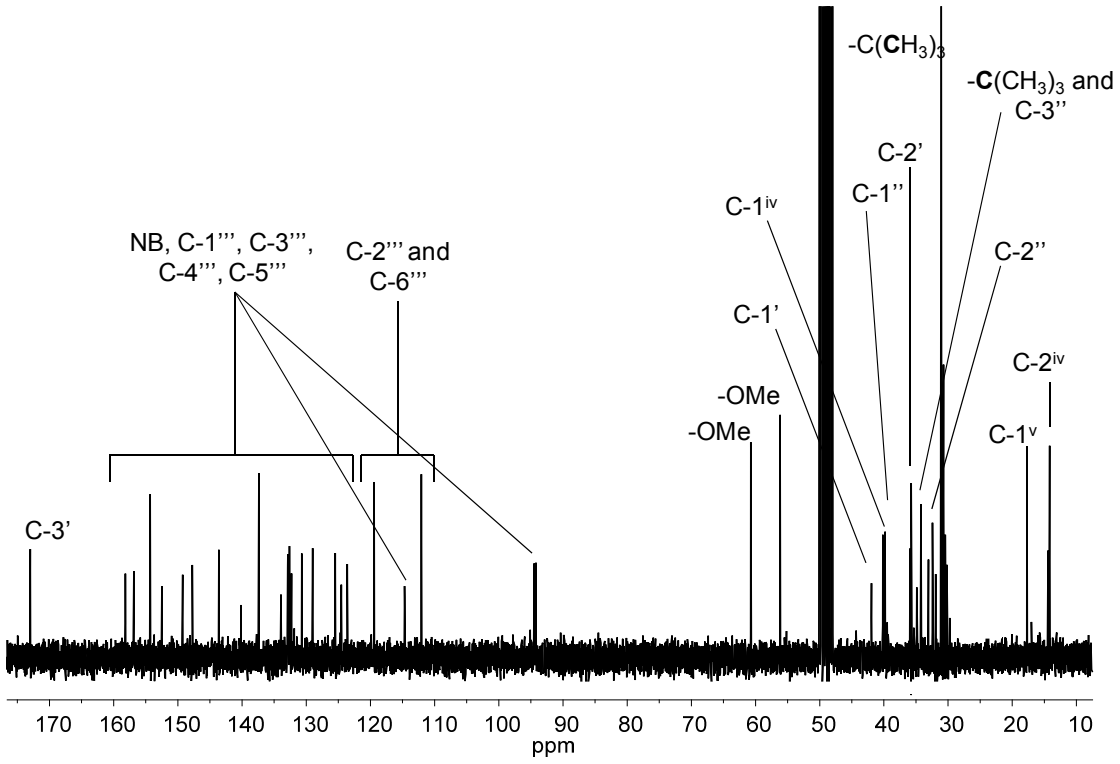



**$^{13}$C NMR** (MeOH-$d_4$, 100 MHz)

**Ligand 30:** 5-((3-((3-(3-(tert-butyl)-4,5-dimethoxyphenyl)propyl)amino)-3-oxopropyl)imino)-N-ethyl-10-methyl-5H-benzo[a]phenoxazin-9-aminium chloride

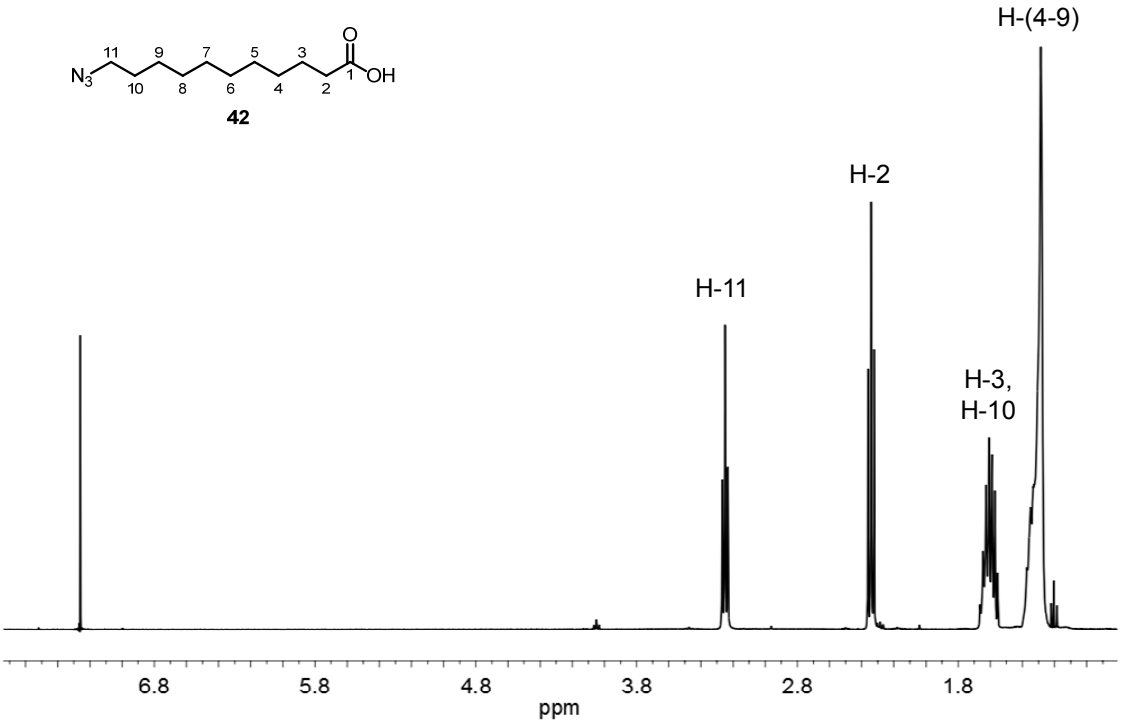



**$^{1}$H NMR** ($CDCl_3$, 250 MHz)



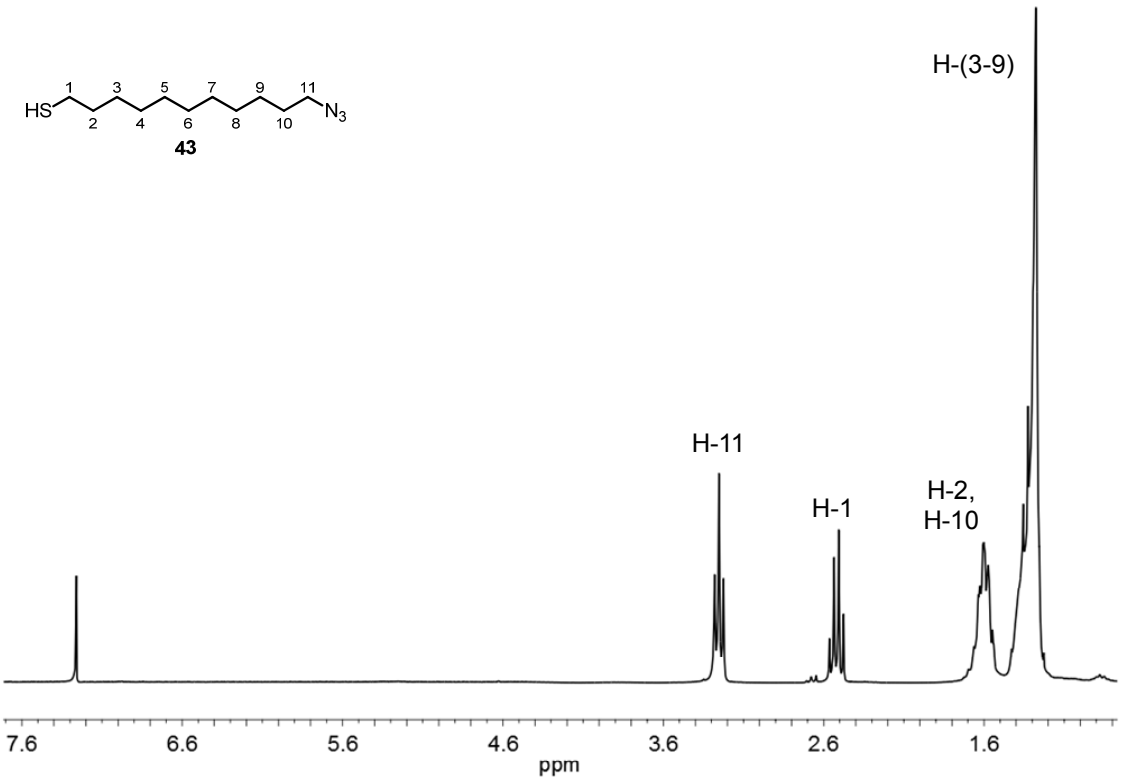

**$^{13}$C NMR** ($CDCl_3$, 63 MHz)

**Ligand 42**: 11-azidoundecanoic acid



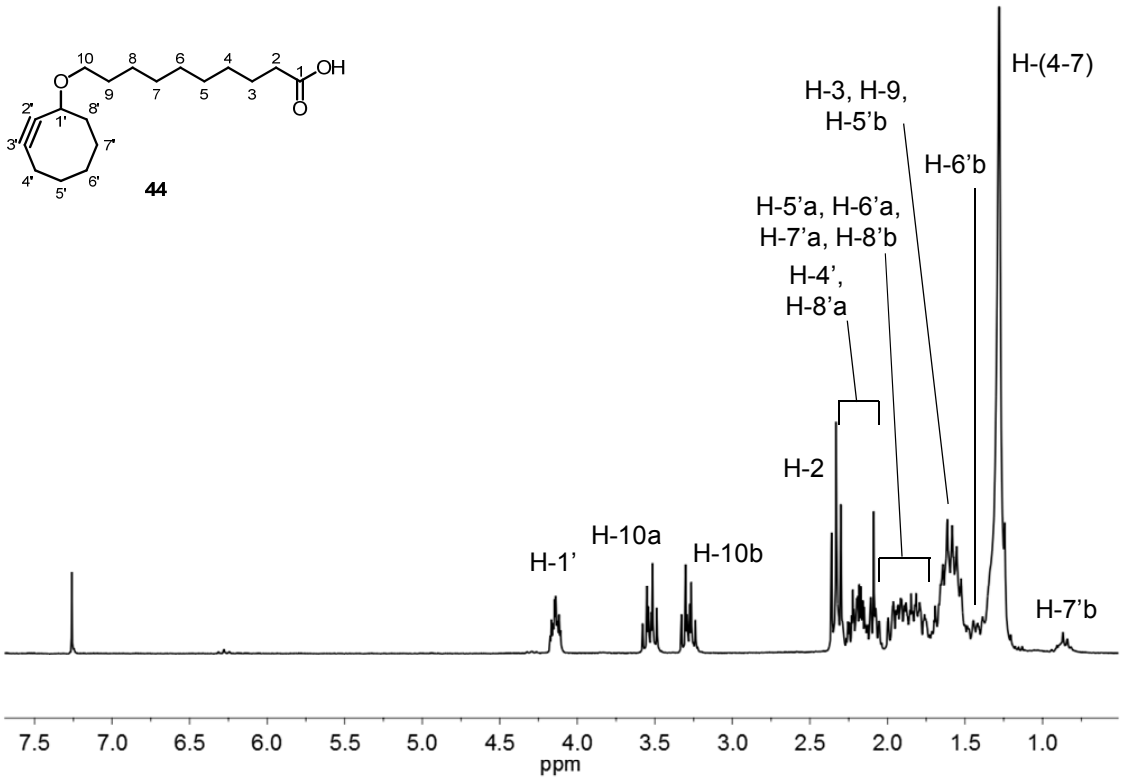

**$^1$H NMR** ($CDCl_3$, 250 MHz)

**Ligand 43:** 11-azidoundecanethiol



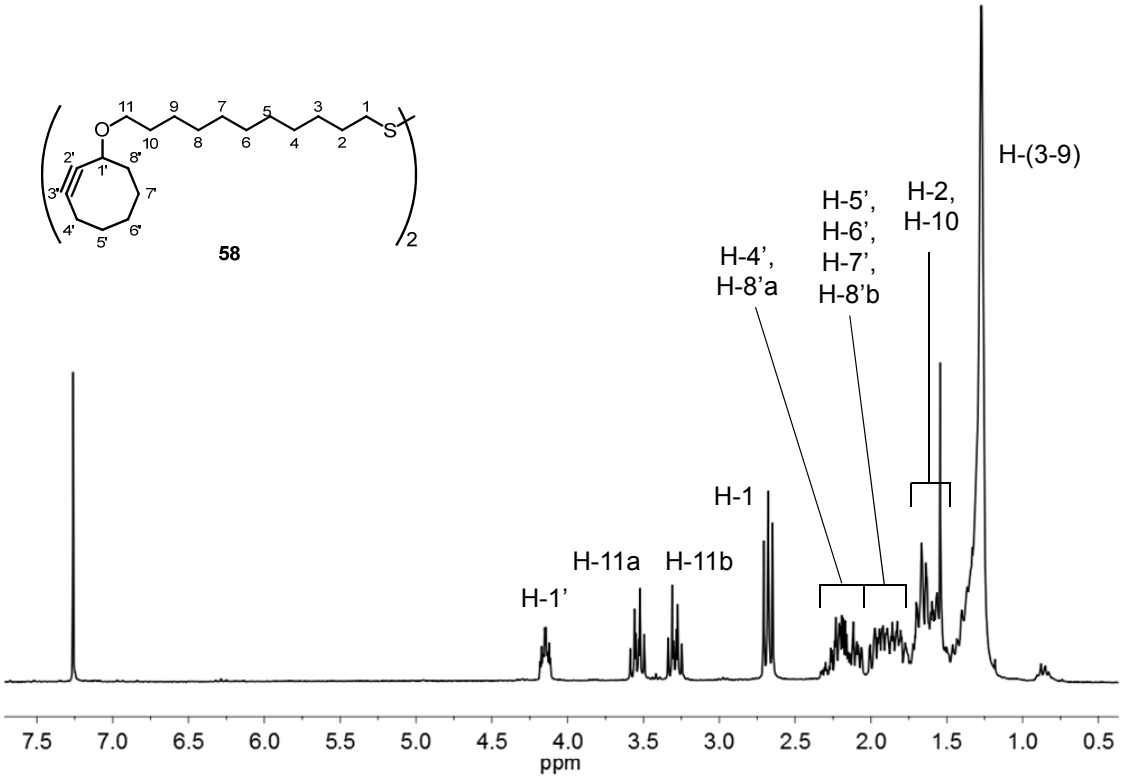

**$^1$H NMR** ($CDCl_3$, 250 MHz)

**Ligand 44:** 10-(cyclooct-2-ynyloxy)decanoic acid

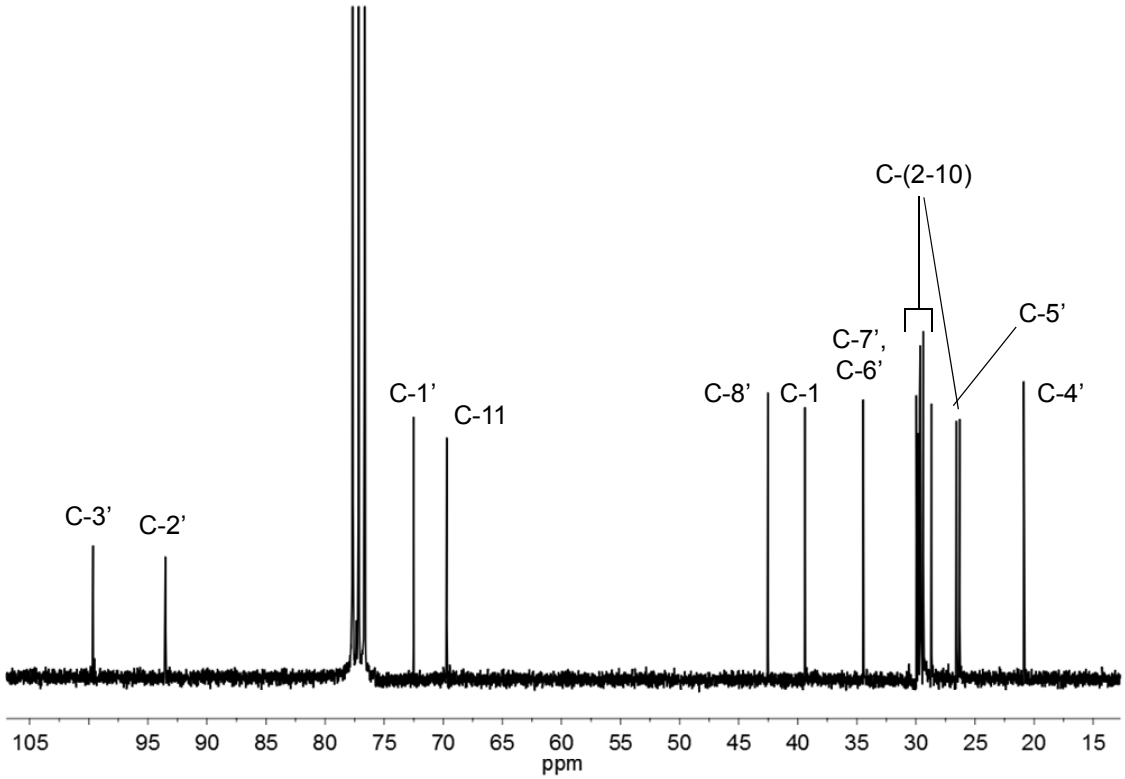



**$^1$H NMR** ($CDCl_3$, 400 MHz)

**Ligand 45 in its protected form, 58:** 1,2-bis(11-(cyclooct-2-ynyloxy)undecyl)disulfane

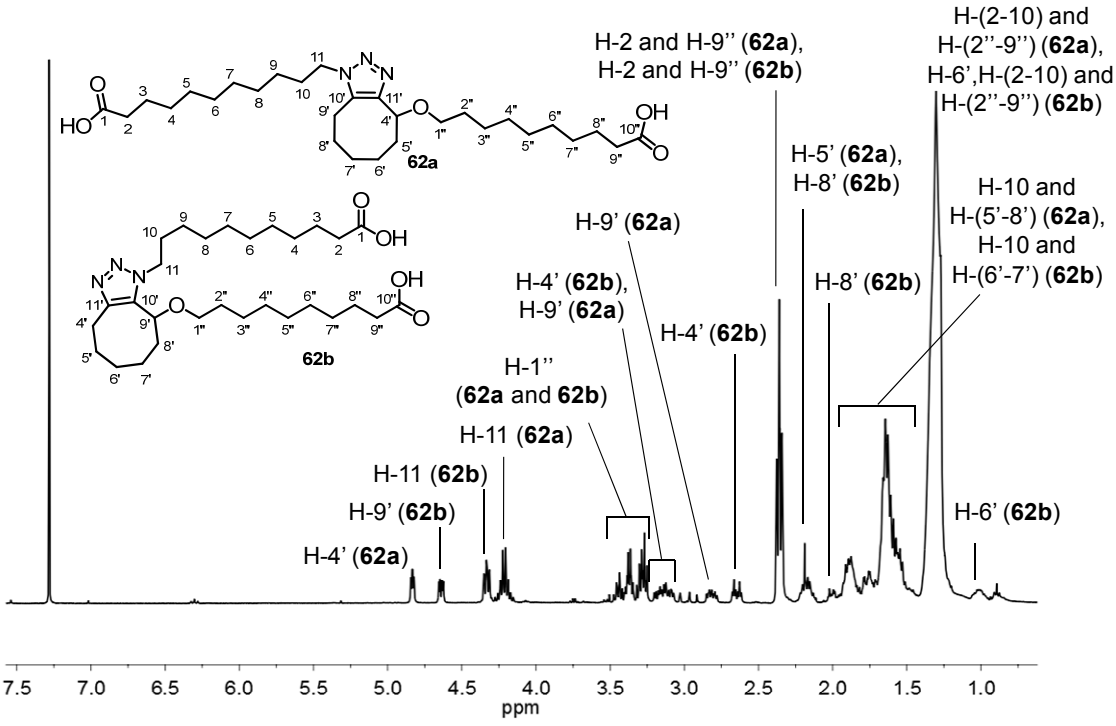



**$^1$H NMR** ($CDCl_3$, 250 MHz)

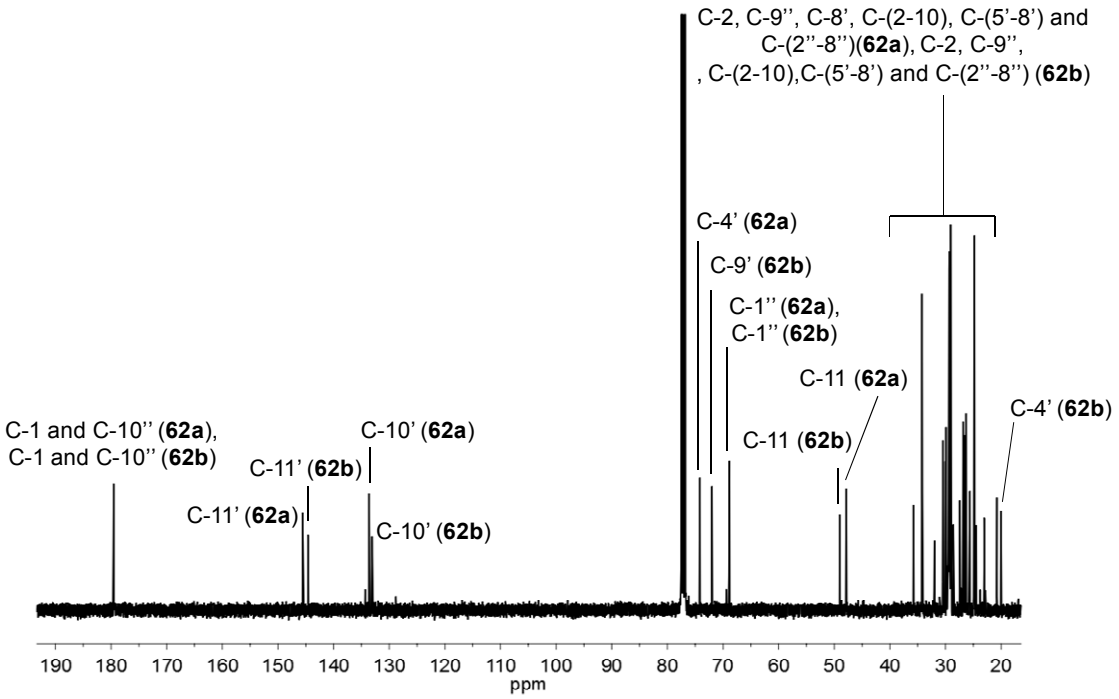



**$^{13}$C NMR** ($CDCl_3$, 63 MHz)

**Free quantum dot SPAAC, 62a and 62b:** 11-(4-((9-carboxynonyl)oxy)-4,5,6,7,8,9-hexahydro-1H-cycloocta[d] [1,2,3]triazolyl)undecanoic acid and 11-(9-((9-carboxynonyl)oxy)-4,5,6,7,8,9-hexahydro-1H-cycloocta[d][1,2,3]triazol-1-yl)undecanoic acid

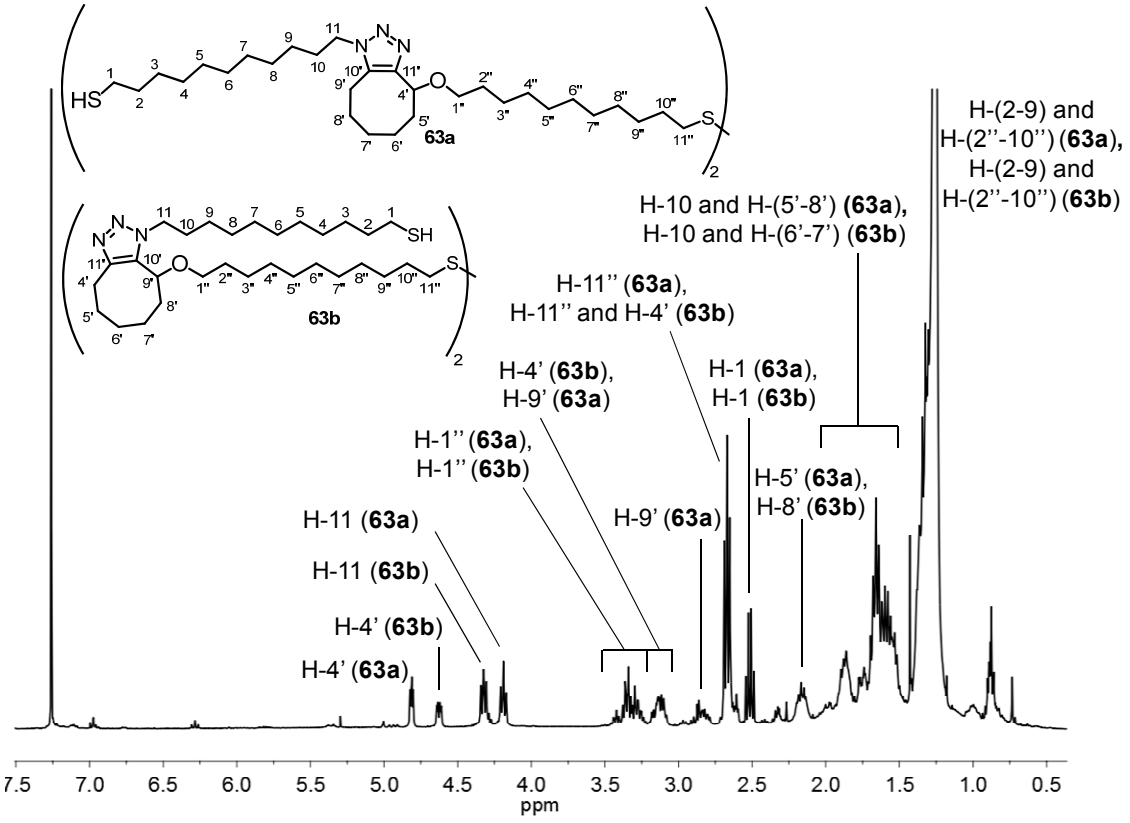



**$^{1}$H NMR** ($CDCl_3$, 400 MHz)

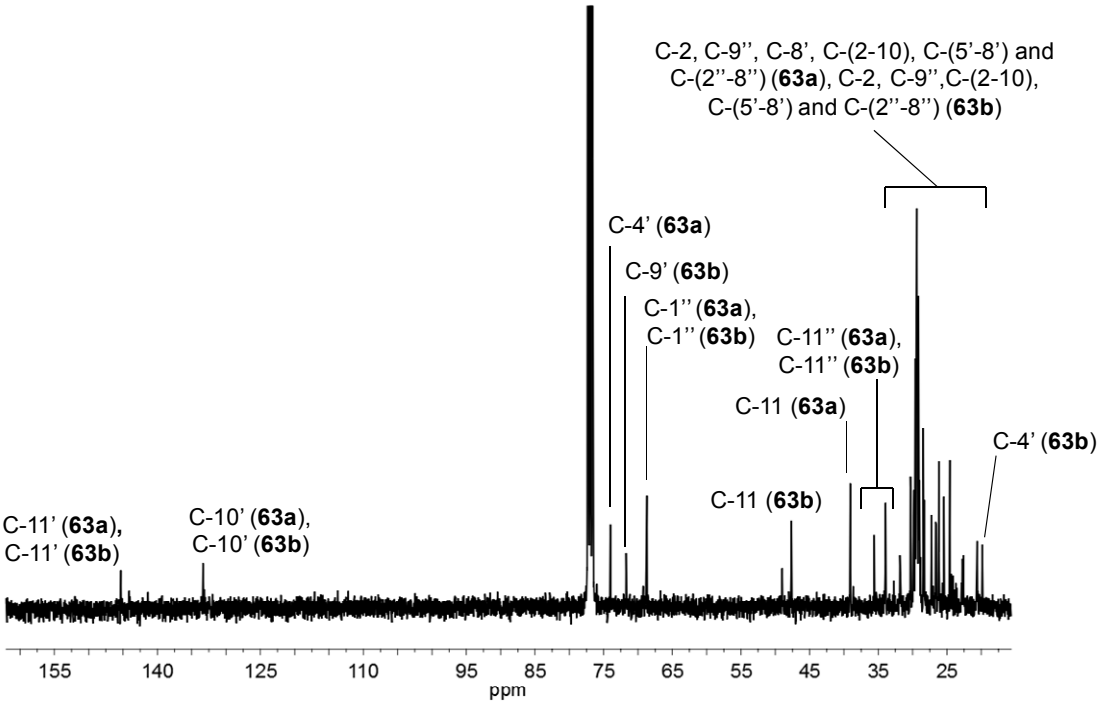



**$^{13}$C NMR** ($CDCl_3$, 101 MHz)

**Free quantum dot SPAAC, 63a and 63b:** 11-((1-(11-mercaptoundecyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta [d][1,2,3]triazol-4-yl)oxy)undecanethiol and 11-((1-(11-mercaptoundecyl)-4,5,6,7,8,9-hexahydro-1H-cycloocta[d][1,2,3]triazol-9-yl)oxy)undecanethiol




**$^{1}$H NMR** ($CDCl_3$, 400 MHz)




**$^{13}$C NMR** ($CDCl_3$, 101 MHz)