1 General Methods and Procedures

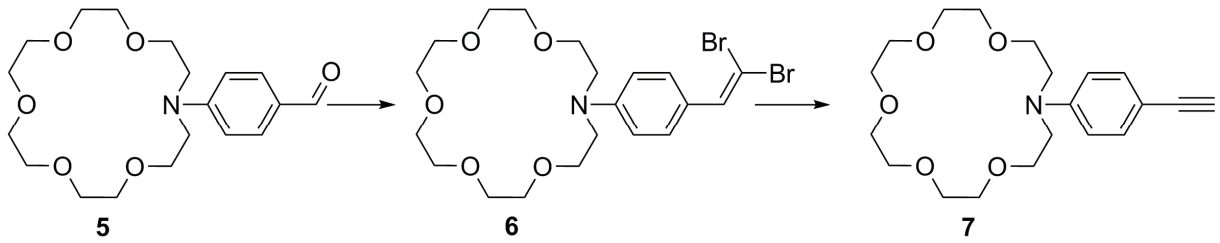
All commercially available chemicals were used without further purification. Solvents were distilled prior use. ^{1}H and ^{13}C NMR spectra were recorded on 300 MHz, 500MHz or 600MHz instruments. Data are reported as follows: chemical shifts in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, dd = double doublet), integration, coupling constant (Hz). ESI spectra were recorded using a Micromass Q-TOF micro mass spectrometer in a positive electrospray mode. IR spectra were recorded using a Thermo Nicolet NEXUS FTIR instrument.

Air/water-sensitive reactions were performed in oven-dried glassware under an argon atmosphere. Column chromatography was performed with SiO_2 (Merck Silica Gel 60 (0,04-0,063 mesh)).

2 Synthesis

The preparation of 3-azido-7-diethylaminocoumarine (**13**),[1] 3-ethinyl-7-diethylaminocoumarine (**14**),[2] *N*-phenylaza-18-crown-6 ether[3] and *N*-(4-formyl)phenylaza-18-crown-6 ether (**5**)[4] has been described previously.

N-(4-Ethinyl)phenylaza-18-crown-6 ether (**7**)



5 **6** **7**

N-4-(2,2-Dibromovinyl)phenylaza-18-crown-6 ether (**6**)

The preparation of **7** followed the literature and references therein according to a modified procedure.[5]

A suspension of zinc (1.69 g, 25.9 mmol) and carbon tetrabromide (8.59 g, 25.9 mmol) in dry CH_2Cl_2 (40 ml) was cooled to -15°C with an ice-salt bath before a solution of triphenylphosphine (6.79 g, 25.9 mmol) in dry CH_2Cl_2 was added dropwise. The resulting yellow green mixture was kept at -15°C for 30 min and was then stirred at RT for 3 h whereupon a solution of **5** (4.31 g, 11.7 mmol) in dry CH_2Cl_2 was added dropwise. The red brown mixture was stirred at RT for 2 h and then water (100 ml) was added. The organic phase was separated and washed with water (3 × 75 ml).The combined organic layer were dried with $MgSO_4$ and concentrated to give **6** as a light brown oil that was directly used for the next step.

Note that the product decomposes when concentrated to dryness resulting in a green solid. Storage at -20°C is recommended.

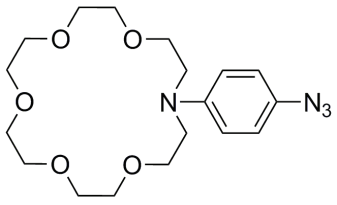
HRMS ($^{+}$ESI): m/z calcd for $(M+H)^{+}$, 522.04, 524.05, 526.04; found, 522.11, 524.11, 526.11.

6 (2.91 g, 5.56 mmol) was dissolved in 25 ml dry THF and set under argon atmosphere immediately. It was cooled to -78°C before n-butyllithium (7.5 ml, 1.6 M, solution in hexane) was added via a syringe. After stirring for 1h at -78°C the solution was allowed to warm up to room temperature and stirring was continued at this temperature for 1h before H_2O (15 ml) was added cautiously. The reaction mixture was extracted with $3\times CH_2Cl_2$ and the combined organic layers were dried with $MgSO_4$ and concentrated to give **7** as a red brown oil, which was purified via chromatography (silica gel, $CHCl_3$/MeOH, 95/5 v/v). Yield: 20%, overall.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.93 (s, 1H), 3.6 (m, 24H), 6.56 (d, 2H, *J* = 9.23 Hz), 7.28 (d, 2H, *J* = 8.85 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 51.66, 68.94, 71.15, 75.12, 85.17, 108.82, 111.62, 133.73, 148.45; HRMS ($^{+}$ESI): m/z calcd for $(M+H)^{+}$, 364.21; found, 364.26; IR(ATR, cm^{-1}): 718, 692, 1115, 2097, 2868, 3054.

N-(4-Azido)phenylaza-18-crown-6 ether (**8**)

The preparation of the *N*-(4-nitro)phenylaza-18-crown ether and subsequent hydrogenation to the corresponding amine followed the literature.[6]



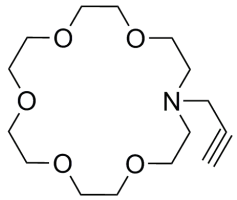
8

The synthesis of **8** followed the literature according to a modified procedure.[7] *N*-Anilino-4-aza-18-crown-6 ether (4.03 g, 11.4 mmol) was dissolved in 90 ml HCl (4M) and cooled to 0°C. A solution of $NaNO_2$ (0.784 g, 11.4 mmol) in 45 ml H_20 was added dropwise. The mixture was stirred for 10 min before a solution of NaN_3 (1.1 g, 17 mmol) in 45 ml H_20 was added drop wise. Stirring was continued for another 10 min at 0°C before the orange solution was allowed to warm up to room temperature and it was stirred for 14 h at ambient temperature. The reaction mixture was brought to pH = 7 with

Na_2CO_3, was extracted with 3×180ml $CHCl_3$ and the combined organic layers were dried with $MgSO_4$. The solvent was removed under reduced pressure to yield **8** as brown oil (1.31 g, 30.3 %). The product was used for the next reaction step without further purification.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.57-3.69 (m, 24H), 6.68 (d, 2H, J = 8.854 Hz), 6.88 (d, 2H, J = 9.042 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 51.48, 68.74, 70.70, 112.97, 119.94, 127.55, 145.98; HRMS ($^+$ESI): m/z calcd for $(M+H)^+$, 381. 21; found, 381.34, calcd for $(M-N_2)^+$ 353.21; found, 353.30; IR (ATR, cm^{-1}): 1100 , 1508, 2120, 2097, 2867.

N-Propargyl-aza-18-crown-6 ether (**9**)

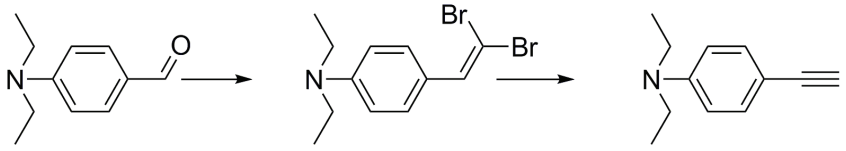


9

The synthesis followed the literature according to a modified procedure.[8] Monoaza-18-crown-6 ether[9] (0.6 g, 2.28 mmol) and propargylbromide (0.206 ml, 2.74 mmol) were dissolved in dry acetonitrile (70 ml) before Cs_2CO_3 (1.48 g, 4.56 mmol) was added. The suspension was stirred overnight at 85°C. After cooling to room temperature, the suspension was filtered and the filtrate was concentrated. The residue was purified by column chromatography on silica gel eluting with $CHCl_3$/MeOH (9/1 v/v) yielding **9** as a red oil (64 %)

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.18 (t, 1H, J = 2,45Hz), 2.82 (t, 4H, J = 5.28Hz), 3.61-3.74 (m, 22H); ^{13}C ($CDCl_3$, 75 MHz): δ = 43.42, 53.29, 68.94, 70.52, 73.61, 78.85; IR (ATR, cm^{-1}): 1115, 2867, 3189; HRMS ($^+$ESI): m/z calcd. for $(M+H)^+$,302.20; found, 302.21.

N,*N*-Diethyl-4-alkinylaniline (**12**)



10 **11** **12**

The synthesis followed the literature according to a modified procedure.[10]

1,1-Dibromo-2-(4-*N*,*N*-diethylaminophenyl)ethene (**11**): A mixture of zinc (4.9 g, 75 mmol), triphenylphosphine (19.67 g, 75 mmol), and carbon tetrabromide (24.87 g, 75 mmol) in dry dichloromethane (250 ml) was sonicated for 2 h while cooling with an ice bath. *N,N*-diethylaminobenzaldehyde (**10**) (5.30 g, 29.9 mmol) was added to the grayish suspension and it was stirred overnight resulting in a brownish suspension. The mixture was concentrated and petroleum ether (500 ml) was added, whereupon a tarry precipitate formed. It was washed with 1/1 CH_2Cl_2/light petroleum ether (2 × 100 ml). The combined organic phases were concentrated, and the residue was chromatographed on silica gel (150 g), eluting with 1/1 CH_2Cl_2/hexane to give **11** as a yellow oil (7.3 g, 21.0 mmol, 70 %). The intermediate product was kept at -20°C until the next step.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.17 (t, 6H, *J* = 6.94 Hz, C*H*$_3$), 3.37 (q, 4H, *J* = 6.94 Hz, C*H*$_2$), 6.62 (d, 2H, *J* = 7.88 Hz, Ar-*H*), 7.32 (s, 1H, C*H*), 7.49 (d, 2H, *J* = 8.21 Hz); HRMS ($^+$ESI): m/z calcd. for $(M+H)^+$, 331.96, 333.96, 335.96; found, 331.93, 333.93, 335.94.

N,N-Diethyl-4-alkinylaniline (**12**): A solution of **11** (4.3g, 12.4mmol) in dry THF (93 ml) was cooled to -78°C before n-butyllithium (19 ml, 15% in hexane) was added dropwise. It was stirred for 45 min at this temperature before the reaction mixture was allowed to warm up to RT. After stirring for 1 h at RT, water (7ml) was added slowly. The solvent was removed and the residue was taken up in diethyl ether. The organic layer was washed with water (30 ml) and brine (30 ml) and dried over $MgSO_4$. Concentration of the ether phase gave **12** as orange oil that was used in the next step without further purification (1.29 g, 6.96 mmol, 56.2 %).

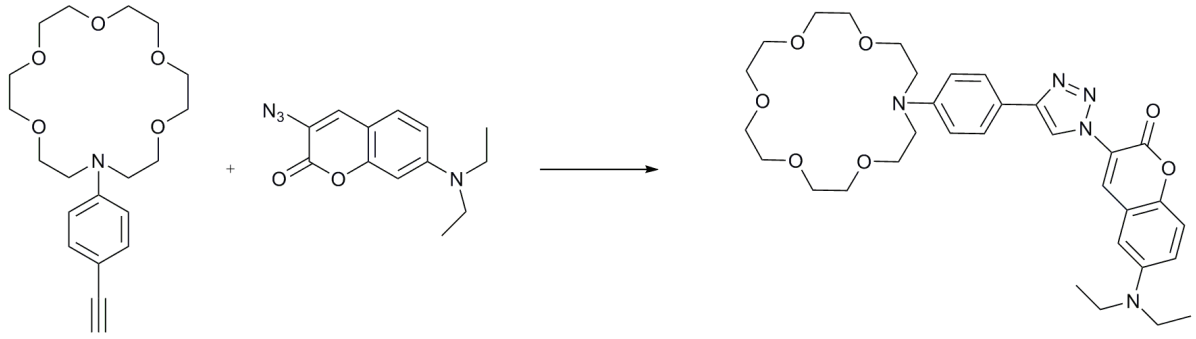
^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.16 (t, 6H, *J* = 7.25Hz), 2.97 (s, 1H), 3.37 (q, 4H, *J* = 7.25Hz,), 6.57 (d, 2H, *J* = 9.14Hz), 7.34 (d, 2H, *J* = 9.14Hz), ^{13}C ($CDCl_3$, 75 MHz): δ = 12.46, 44.26, 74.41, 85.01, 107.47, 110.94, 133.39, 147.73, HRMS ($^+$ESI): m/z calcd. for $(M+H)^+$, 174.13; found, 174.16.

2.3 General Procedure of the CuAAC reaction:

All reactions were performed on a mmol-scale. To a solution of azide (1 eq) and alkyne (1 eq) in THF/H_2O (3/1) was added CuI (5 mol%) and sodium ascorbate (2.5 mol%). It was stirred overnight at 50°C.

The THF was removed under reduced pressure and the residue was taken up in $CHCl_3$. It was washed with water and the organic phase was dried over $MgSO_4$. The organic phase was concentrated and the residue was chromatographed on silica gel eluting with CH_2Cl_2/MeOH (95/5).

N-4-[1-(7-Diethylaminocoumarin-3-yl)-1*H*-1, 2, 3-triazol-4-yl)]phenylaza-18-crown-6 ether (**1**):

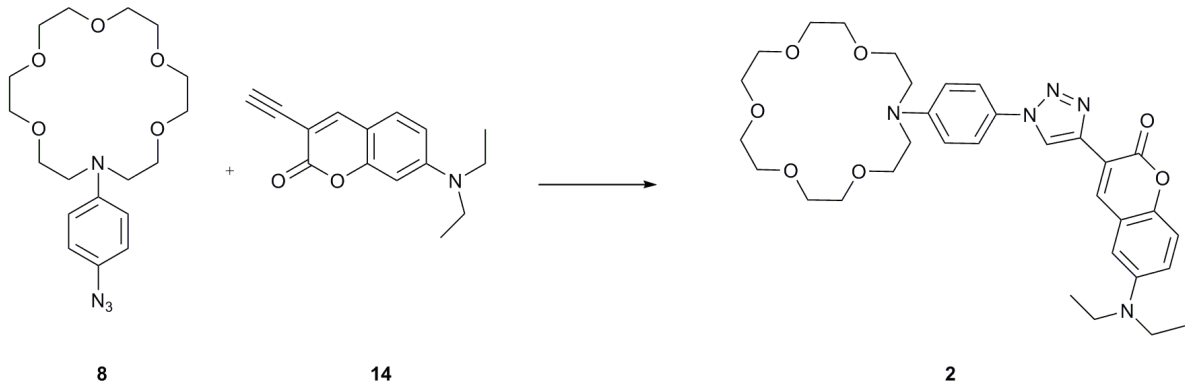


7 **13** **1**

Scheme S1. Synthetic route towards **1**.

Yield: 49 %, ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.23 (t, 6H, *J* = 7.25Hz), 3.44 (q, 4H, *J* = 7.25Hz,), 3.64-3.67 (m, 20H), 3.72 (t, 4H, *J* = 5.68Hz), 6.55 (s, 1H), 6.66 (dd, 1H), 6.75 (d, 2H, *J* = 8.52Hz), 7.41 (d, 1H, *J* = 8.83Hz), 7.74 (d, 2H, *J* = 8.83Hz), 8.15 (s, 1H), 8.38 (s, 1H); ^{13}C ($CDCl_3$, 75 MHz): δ = 13.53, 46.05, 52.38, 69.78, 71.89, 98.08, 108.27, 110.91, 112.67, 118.12, 119.22, 119.70, 127.96, 130.95, 135.34, 148.82, 149.06, 152.40, 156.79, 158.02; HRMS ($^+$ESI): m/z calcd. for $(M+H)^+$, 622.32; found, 623.33; UV/Vis (Acetonitrile), λ_{max} (ε) = 410 nm (21228 M^{-1} cm^{-1}), λ_{max} (ε) = 288 nm (20211 M^{-1} cm^{-1}).

N-4-[4-(7-Diethylaminocoumarin-3-yl)-1*H*-1, 2, 3-triazol-1-yl)]phenylaza-18-crown-6 ether (**2**):

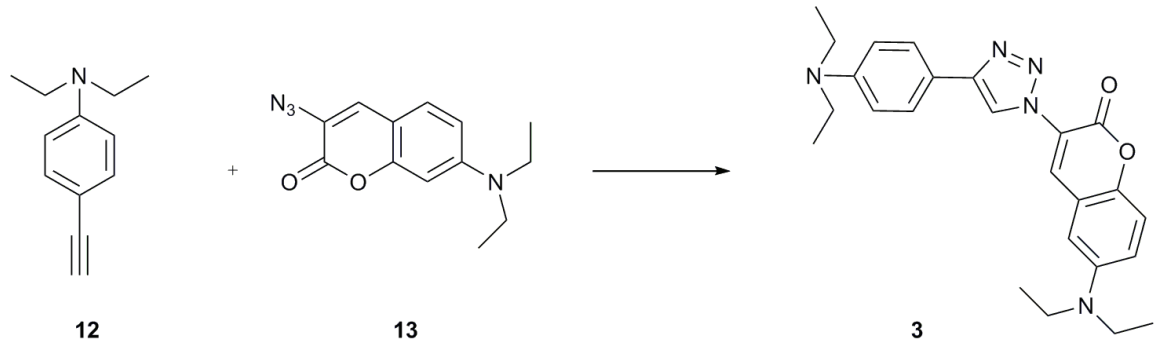


8 **14** **2**

Scheme S2. Synthetic route towards **2**.

Yield: 55 %, ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 1.23 (t, 6H, *J* = 7.25Hz), 3.44 (q, 4H, *J* = 7.25Hz,), 3.63-3.67 (m, 20H), 3.72 (t, 4H, *J* = 5.68Hz), 6.53 (s, 1H), 6.62 (dd, 1H), 6.76 (d, 2H, *J* = 8.48Hz), 7.41 (d, 1H, *J* = 8.85Hz), 7.76 (d, 2H, *J* = 8.48Hz), 8.60 (s, 1H), 8.64 (s, 1H); ^{13}C ($CDCl_3$, 150 MHz): δ = 12.54, 44.94, 51.51, 68.58, 70.84, 97.13, 108.83, 109.44, 110.87, 111.93, 120.54, 122.12, 126.56, 129.60, 138.51, 142.06, 148.26, 150.82, 156.11, 160.79; HRMS ($^{+}$ESI): m/z calcd. for $(M+H)^{+}$, 622.32; found, 623.35; UV/Vis (Acetonitrile), λ_{max} (ε) = 413 nm (40057 M^{-1} cm^{-1}), λ_{max} (ε) = 293 nm (18136 M^{-1} cm^{-1}).

N,N-Diethyl-4-[1-(7-diethylaminocoumarin-3-yl)-1*H*-1, 2, 3-triazol-4-yl)]aniline(**3**):

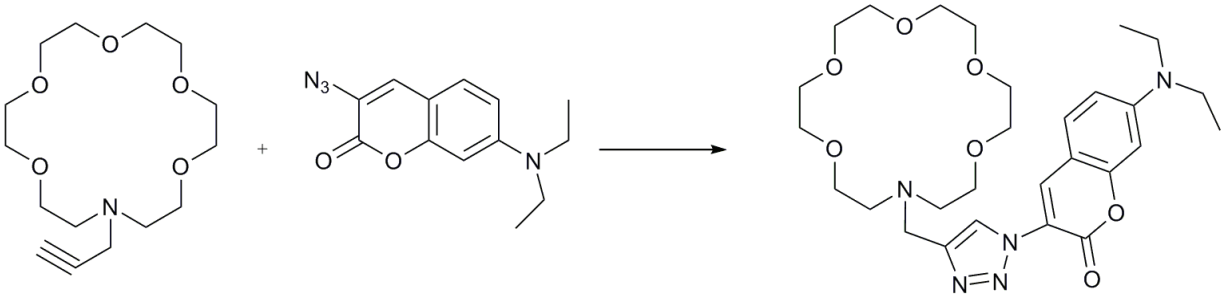


12 **13** **3**

Scheme S3. Synthetic route towards **3**.

Yield: 60 %, ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.17-1.27 (m, 12H), 3.37-3.50 (m, 8H), 6.57 (s, 1H), 6.68 (dd, 1H), 6.75 (d, 2H, *J* = 8.48Hz), 7.42 (d, 1H, *J* = 8.85Hz), 7.76 (d, 2H, *J* = 8.1Hz), 8.44 (s, 1H), 8.65 (s, 1H), ^{13}C ($CDCl_3$, 75 MHz): δ = 12.43, 12.62, 29.69, 44.39, 44.98, 97.08, 107.28, 109.99, 111.80, 117.31, 117.57, 118.61, 127.06, 129.91, 134.15, 147.75, 148.25, 151.41, 155.72, 157.01; HRMS ($^{+}$ESI): m/z calcd. for $(M+H)^{+}$, 431.23; found, 432.32; UV/Vis (acetonitrile), λ_{max} (ε) = 410 nm (29501 M^{-1} cm^{-1}), 248 nm (22823 M^{-1} cm^{-1}).

N- [1-(7-Diethylaminocoumarin-3-yl)-1*H*-1, 2, 3-triazol-4-yl)] methyleneaza-18-crown-6 ether(**4**):



9 **13** **4**

Scheme S4. Synthetic route towards **4**.

Yield: 23 %, ^{1}H NMR ($CDCl_3$, 300 MHz): δ =1.14 (t, 6H, *J* = 7.16Hz), 2.70 (m, 4H), 3.36 (q, 4H, *J* = 7.16Hz,), 3.54-3.68 (m, 20 H), 3.79 (s, 2H), 6.42 (s, 1H), 6.60 (dd, 1H), 7.40 (d, 1H, *J* = 9.04Hz), 8.24 (s, 1H), 8.33 (s, 1H); ^{13}C ($CDCl_3$, 75 MHz): δ = 12.76, 45.34, 49.51, 53.78, 67.91, 69.72, 97.16, 107.21, 110.60, 124.15, 129.08, 130.67, 131.26, 136.14, 152.12, 156.27, 127.46 ; HRMS ($^{+}$ESI): m/z calcd. for $(M+H)^{+}$,560.31; found,560.43; UV/Vis (acetonitrile), λ_{max} (ε) = 408 nm (10534 M^{-1} cm^{-1}), 246 nm (11149 M^{-1} cm^{-1}).

3 UV/Vis absorption Measurements

UV/Vis measurements were recorded on a Perkin Elmer Lambda 950 spectrophotometer using 1 cm path length quartz cuvettes. Titrations of the compounds **1** - **4** ($c = 5 \cdot 10^{-5}$ mol/l) were carried out in acetonitrile and recorded 5 min after the addition of 0.01 ml of volumetric standard solutions of respectively $NaPF_6$ or KPF_6 ($c = 5 \cdot 10^{-4} - 5 \cdot 10^{-2}$ mol·l^{-1}) in acetonitrile. To ensure complete reaction towards the corresponding complex, titration was continued until no change in the UV/Vis absorption spectra was observed.

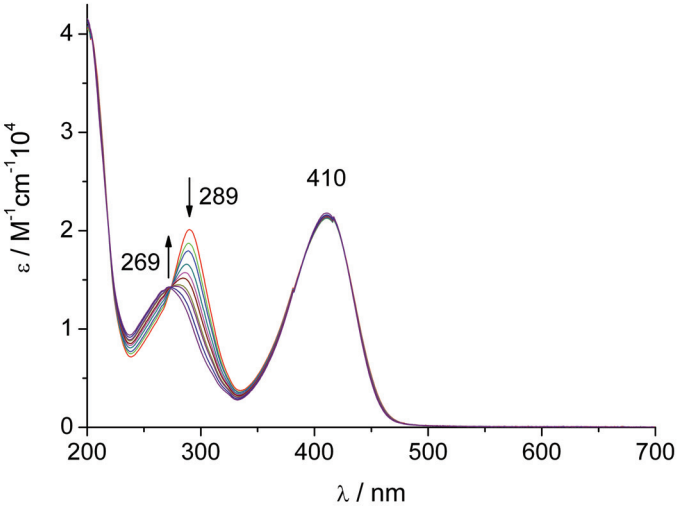


Figure S1. UV/Vis spectra of **1** ($c = 5 \cdot 10^{-5}$ mol/l) in acetonitrile in the presence of 0-2.4 mM K^+.

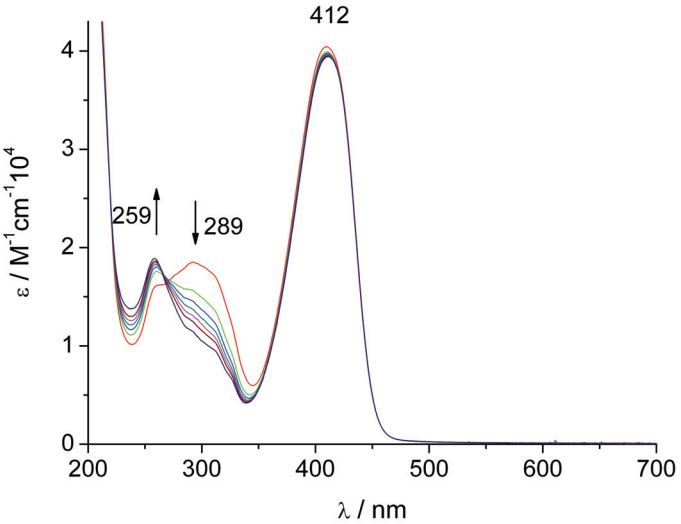


Figure S2. UV/Vis spectra of **2** ($c = 2.5 \cdot 10^{-5}$ mol/l) in acetonitrile in the presence of 0-3.27 mM K^+.

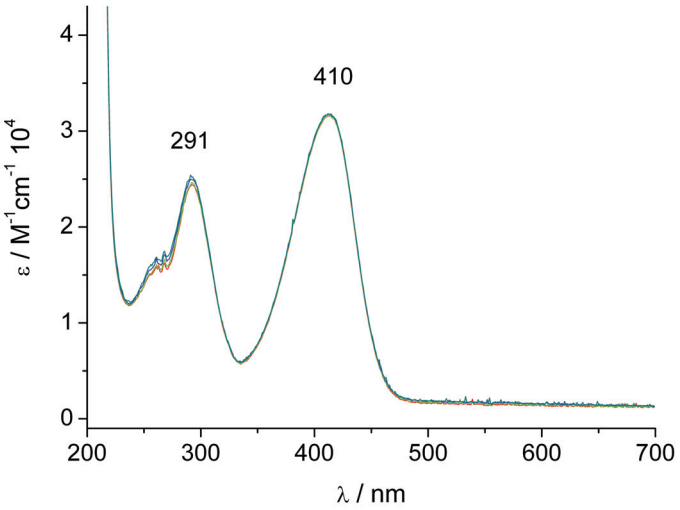


Figure S3. UV/Vis spectra of **3** ($c = 5 \cdot 10^{-6}$ mol/l) in acetonitrile in the presence of 0-2.4 mM K^+

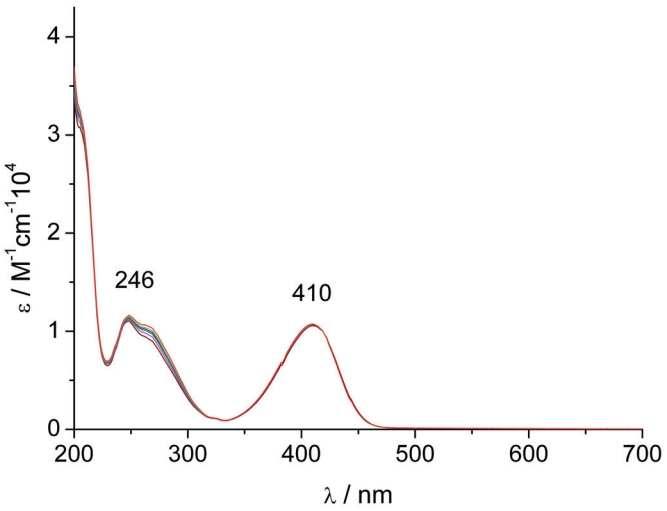


Figure S4. UV/Vis spectra of **4** ($c = 5 \cdot 10^{-5}$ mol/l) in acetonitrile in the presence of 0-3.7 mM K^+.

4 Fluorescence measurements

Fluorescence titration spectra of the compounds **1** and **2** ($c = 5 \cdot 10^{-6}$ mol·l^{-1}) in acetonitrile were recorded 5 min after the addition of 0.02 ml of volumetric standard solution of $NaPF_6$ or KPF_6 ($c = 5 \cdot 10^{-5}$ -$5 \cdot 10^{-2}$ mol·l^{-1}), respectively. Fluorescence titrations of **1** were carried out exciting at 410 nm. The change in fluorescence intensity of **2** was measured by excitation at 412 nm. Titration was continued until no change in fluorescence enhancement was observed. Fluorescence Quantum yields were determined using a PL Quantum Yield measurement System C9920-2 of Hamamatsu, Japan.

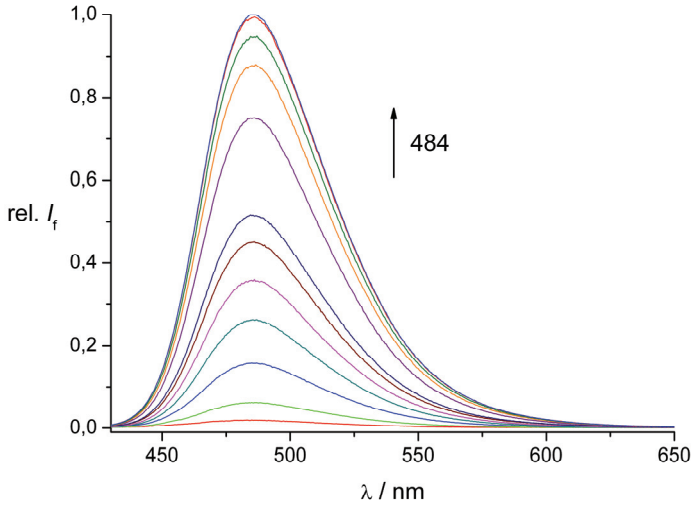


Figure S 5. Fluorescence spectra of **1** in acetonitrile in the presence of 0 - 1.2 mM Na^+.

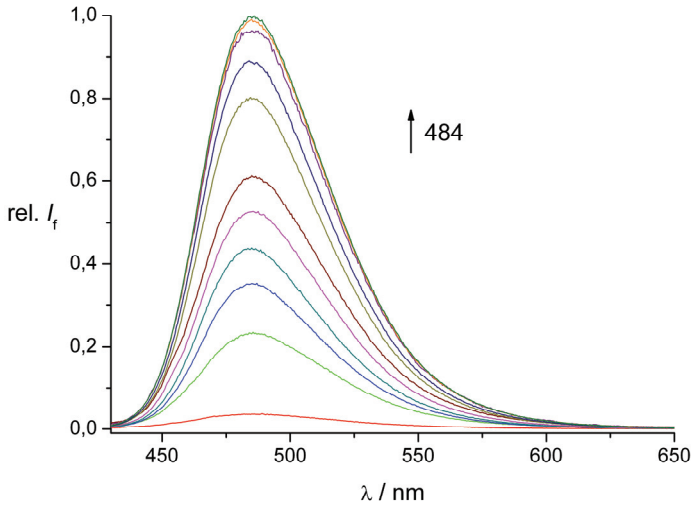


Figure S 6. Fluorescence spectra of **1** in acetonitrile in the presence of 0 - 2.5 mM K^+.

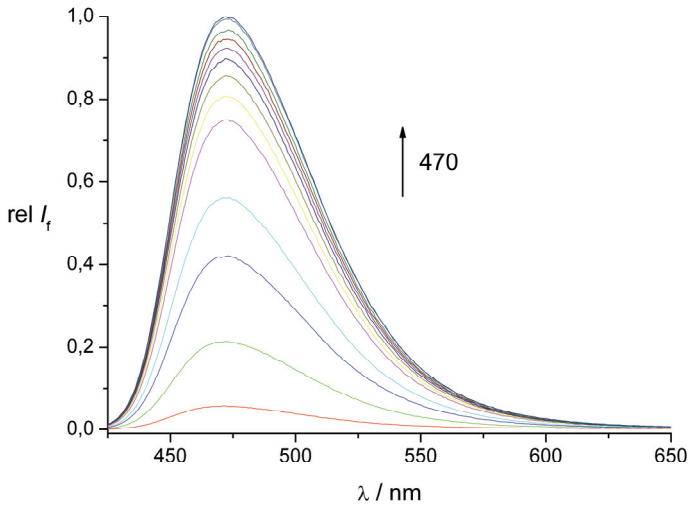


Figure S 7. Fluorescence spectra of **2** in acetonitrile in the presence of 0 - 5.0 mM Na^+.

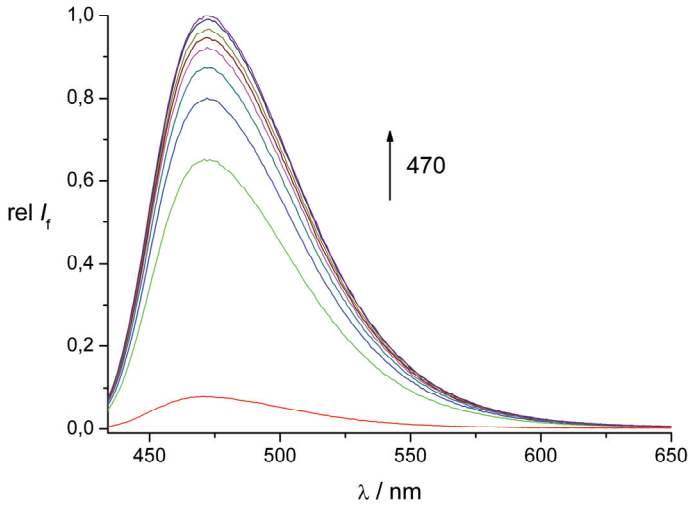


Figure S 8. Fluorescence spectra of **2** in acetonitrile in the presence of 0 - 4.2 mM K^+.

Fluorescence spectra in aqueous solutions were carried out in buffered saline solutions (10 mM Tris-buffer, pH = 7.2) using a 1 mM ligand solution in DMSO. The water used was purified by a Milli-Q-Deioniser from Millipore®. To obtain physiological conditions, the salt solutions contained constant concentrations of $CaCl_2$ (2 mM) and $MgCl_2$ (2 mM). The physiological solutions were varied with regard to the concentrations of respectively KCl or NaCl and constant ionic strength was adjusted to a typical ionic strength in physiological systems (180 mM) by choline chloride.

The dye was exposed to different saline solutions containing 0, 5, 10, 20, 40, 80, 160 mM KCl or NaCl, respectively (Table S1 and S2). Each salt solution was mixed with 1 mM DMSO solution of **1** (990/10 v/v) to give a final ligand concentration of 10 μM. For each measurement, a freshly prepared dye mixture was used and every experiment was repeated with n = 4. Fluorescence response of **1** was recorded exciting at 424 nm

Table S1. Composition of the different aqueous solutions under simulated physiological conditions with regard to K^+- selectivity.

KCl/ mM	Choline Cl/ mM	$MgCl_2$/ mM	$CaCl_2$/ mM
0	180	2	2
5	175	2	2
10	170	2	2
20	160	2	2
40	140	2	2
80	100	2	2
160	20	2	2

Table S2. Composition of the different aqueous solutions under simulated physiological conditions with regard to Na^+- selectivity.

NaCl/ mM	Choline Cl/ mM	$MgCl_2$/ mM	$CaCl_2$/ mM
0	180	2	2
5	175	2	2
10	170	2	2
20	160	2	2
40	140	2	2
80	100	2	2
160	20	2	2

5 pH measurements

Investigation of pH – sensitivity was carried out at different pH values from 2 to 10.5 in the absence of metal salt. The water used was purified by a Milli-Q-Deioniser from Millipore®. The pH was adjusted to the desired pH range with 0.1 M HCl or Tetrabutylammonium hydroxide (40 wt% in water), respectively.

Each aqueous solution was mixed with 1 mM DMSO solution of **1** (990/10 v/v) to give a final ligand concentration of 10 μM. For each measurement, a freshly prepared dye mixture was used.

Plotting of fluorescence intensity at different pH values gives the $pK_a = 4.5$, as depicted in Fig. S9.

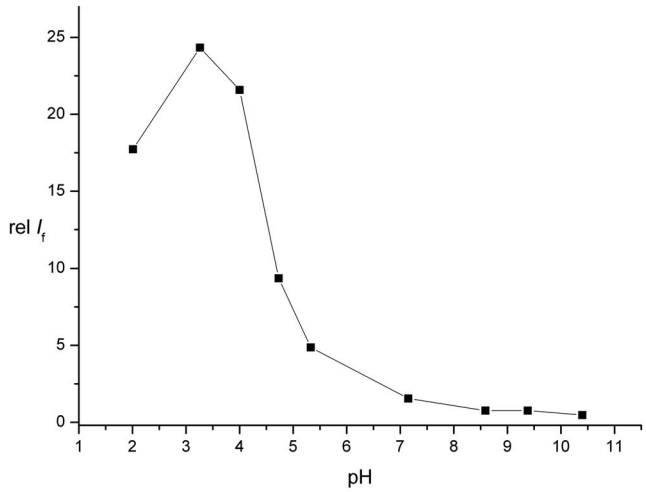
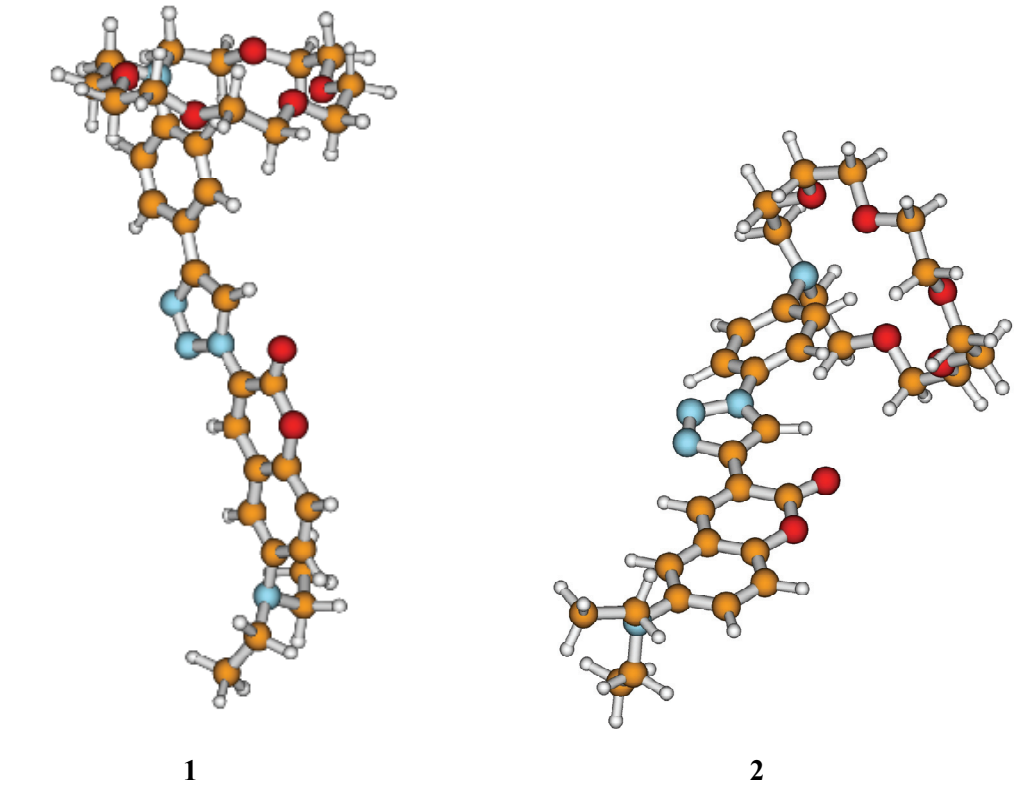


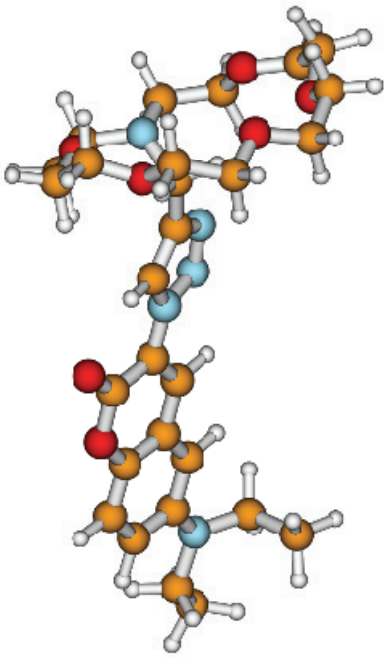
Figure S 9. pH response curve of **1** in water. Excitation at 424 nm, emission at 498 nm.

6 Theoretical calculations

All structures are optimized using the Gaussian03 program package[11] employing the B3LYP functional[12] together with a 6-31G* basis set as implemented in Gaussian 03. Frequency analyses were performed to confirm that the optimized geometries are minima on the potential energy surface.



1 **2**



4

Figure S10: B3LYP/6-31G* -optimized geometry of **1**, **2** and **4**.

7 References

[1] K. Sivakumar, F. Xie, B. M. Cash, S. Long, H. N. Barnhill and Q. Wang, *Org. Lett.*, **2004**, *6*, 4603-4606.

[2] a) J.-S. Wu, W.-M. Liu, X.-Q. Zhuang, F. Wang and S.-T. Lee, *Org. Lett*., **2007**, *9*, 33-36. b) D.-N. Lee, G.-J. Kim, H.-J. Kim, *Tetrahedron Lett.,* **2000**, *50*, 4766-4768.

[3] D. Jiménez, R. Martínez-Máñez, F. Sancenón, and E.García-Breijo*, Eur. J. Inorg. Chem.* **2005,** 2393-2403

[4] J. P. Dix and F. Vögtle, *Chem. Ber*. **1980**, *113*, 457.

[5] J. D.Lewis, J. M. Moore, *Dalton Trans.,* **2004**, 1376-1385.

[6] J. W. Sibert, V. Lynch, *Inorg. Chem*., **2007**, *46*, 10913-10925.

[7] P. A. S. Smith and J. H. Boyer, *Org. Synth.,* **1963,** *4*, 74.

[8] E. Tamanini, S. E. J. Rigby, M. Motevalli, M. H. Todd, M. Watkinson, *Chem. Eur. J.* **2009**, *15*, 3720-3728.

[9] M. Hirokazu; S. Furuyoshi, Y. Nakatsuji, M. Okahara. *Bull. Chem. Soc. Jpn.***1983**, *56*, 212-218.

[10] R. Wortmann, C. Glania, P. Krämer, R. Matschiner, J. J. Wolff, S. Kraft, B. Treptow, E. Barbu, D. Längle and G. Görlitz, *Chem. Eur. J.*, **1997**, *3*, 1765-1773.

[11] M. J. Frisch, G. W. Trucks, H. B. Schlegel et al., Gaussian 03, revision c.02, Gaussian, Inc., Wallingford, CT, 2004.

[12] A. D. Becke, *J. Chem. Phys*., **1993**, *98*, 5648.