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Synthesis of 1,2,3-Triazole-4-carboxamide-Containing Foldamers for Sulfate Recognition

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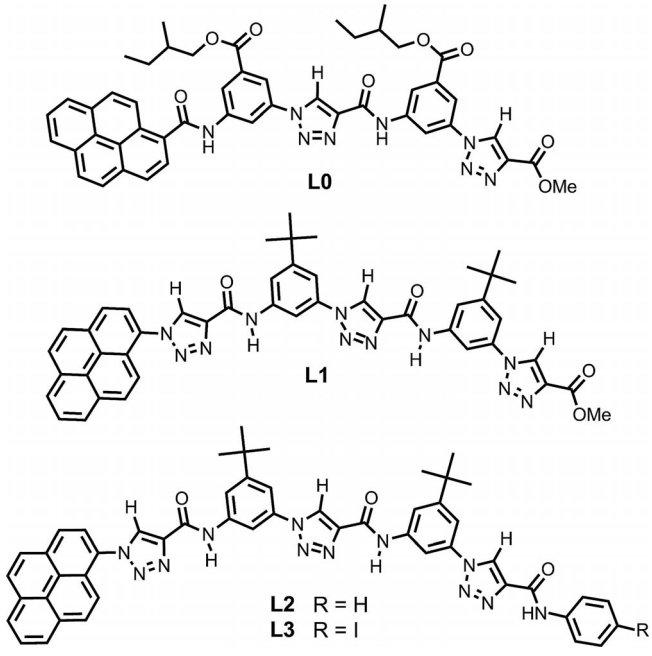
A series of triazolecarboxamide-containing foldamers were synthesized from simple starting materials by means of repeated [3+2] cycloadditions) and acid–amine coupling reactions. Foldamer–anion binding behavior and affinities were determined by ^{1}H NMR titration in [D_2]dichloromethane. The selective recognition of sulfate by these motifs was studied by one- and two-dimensional (^{1}H, ^{1}H-^{1}H COSY and NOESY) NMR spectroscopy as well as UV/Visible and fluorescence titrations. The structures of the triazolecarboxamide-containing foldamers can be optimized for highly selective recognition of sulfate anions by changing the numbers of triazolecarboxamide units and by the introduction of electron-withdrawing substituents on the terminal benzene ring. These findings indicate the importance of the structural compatibility between the receptor and anions for the highly selective anion binding as well as the electronic effect on tuning the anion-binding affinities of receptors.

Introduction

Research into anion recognition has been attracting considerable interest in recent years, due to its wide applications in many scientific areas, such as environmental science, biology, and chemistry.[1] Anions are present everywhere in living systems and cause both beneficial and deleterious effects to human beings. With regard to the various important anions, anion receptors specific to sulfate currently constitute an area of intense interest, due to the important roles the sulfate anion plays in biological systems and disease,[2] in hydrometallurgy,[3] and as a pollutant.[4] Typical anion recognition moieties containing NH groups, such as pyrrole,[5] urea,[6] amide,[7] ammonium,[8] and imidazolium systems,[9] have been widely studied as hydrogen donors to bind the anion species (N–H···X$^-$). However, it is a challenge to employ C–H groups for anion recognition because of the low acidity of the C–H bond.

In recent years, with the development of click chemistry,[10] groups such as triazole[11] or triazolium systems,[12] containing C–H bonds, have been incorporated in anion recognition. The large dipole oriented along the triazole C–H bond, as well as its polarization due to the electron-withdrawing character of the three nitrogen atoms, generates a potential C–H bond donor. Indeed, considerable efforts[13] have been devoted to the preparation of these motifs. It was shown that hosts incorporating two or more 1,2,3-triazole groups can bind anions in moderately competitive solvents solely through C–H···anion hydrogen bonds.



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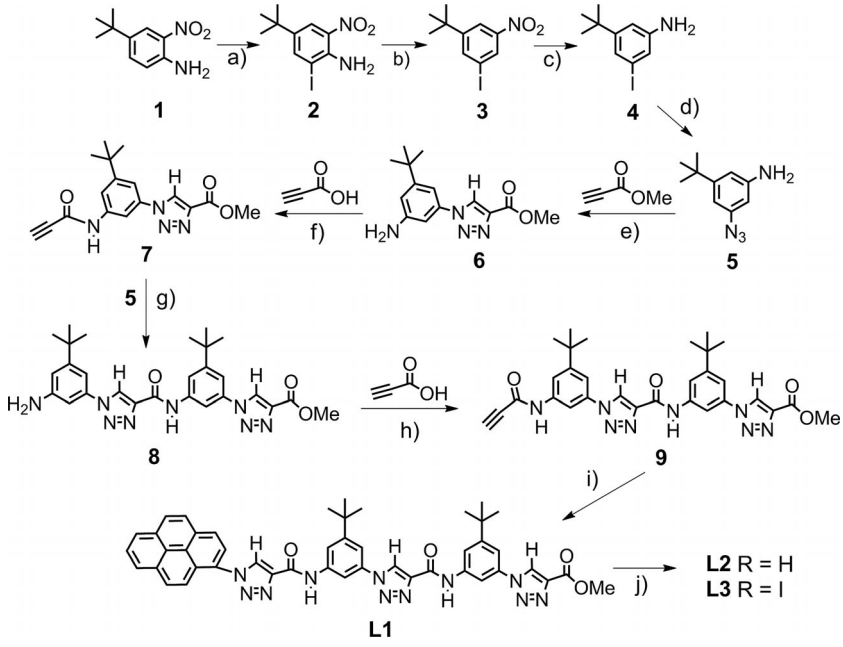
In previous studies, we have developed a versatile anion receptor building block combining the characteristics of urea and triazole – triazolecarboxamide – that can be used extensively for the construction of numerous receptor systems appended with functional groups.[14] The association of hydrogen bonding, π–π stacking, and dipole–dipole interaction in **L0** can result in changes in tetrahedral sulfate anion binding from 2:1 to 1:1 complexation,[14a] which is a good start for the construction of foldamer-like sulfate anion receptors.

In this manuscript we present new triazolecarboxamide-containing foldamers for highly selective recognition of sulfate anions. By increasing the numbers of triazolecarboxamide units and modifying the terminal benzene ring, the binding stoichiometry and binding affinity can be controlled.

Results and Discussion

Unlike in the case of the previous receptor **L0**, here we designed new sulfate receptors containing two and three triazolecarboxamide units connected through benzene units in the middle as the binding motif, the photoactive pyrene ring attached to the triazole terminal as a fluorescent handle and π–π stacking unit, and a terminal benzene ring to provide convenience for the investigation of substitution effects on binding affinity. The synthesis of the triazolecarboxamide derivatives was performed by a stepwise strategy as shown in Scheme 1. Treatment of 4-*tert*-butyl-2-nitroaniline (**1**) with ICl gave compound **2**, which was treated with $NaNO_2$ in H_2SO_4 and ethanol to yield **3**. Reduction of the nitro group with $SnCl_2$ afforded iodoamine **4**. Treatment of **4** with NaN_3 and a catalytic amount of sodium ascorbate and CuI provided **5**. By repetition of a sequence based on a [3+2] cycloaddition and an acid–amine coupling reaction, compound **9** was afforded. The [3+2] cycloaddition between compound **9** and 1-azopyrene[15] gave compound **L1** in 56% yield, and subsequent reactions produced compounds **L2** and **L3** in 45% and 43% yields. The COSY and NOESY spectra were used to assign protons of the receptor **L2** in detail (Figure S1 in the Supporting Information).

L1, similar to **L0** but containing an extra triazole group (connected to the pyrene unit), also showed a 2:1 binding process with sulfate. Upon addition of 0.5 equiv. of bis(tetrabutylammonium) sulfate (TBA_2SO_4), the triazole proton ($\Delta\delta$Hf = 1.0 ppm, $\Delta\delta$Hk = 0.47 ppm, $\Delta\delta$Ha = 0.41 ppm) and the amide proton ($\Delta\delta$He = 1.39 ppm, $\Delta\delta$Hj = 1.32 ppm) showed downfield shifts (Figure 1). Upfield shifts of protons on the pyrene ring and a proton of the benzene ring close to the pyrene ring ($\Delta\delta$Hg = 0.1 ppm) were observed (smaller than that in the case of **L0**). With the addition of another 0.5 equiv. of sulfate (1.0 equiv. total), the signals of the central amide NH ($\Delta\delta$Hf = 1.39 ppm, $\Delta\delta$Hk = 0.58 ppm, $\Delta\delta$Ha = 0.66 ppm) and triazole CH protons ($\Delta\delta$He = 1.89 ppm, $\Delta\delta$Hj = 1.97 ppm) migrated further downfield, and the upfield-shifted signals moved back to their original position (Figure S2 in the Supporting Information). These results clearly indicate that in the presence of 0.5 equiv. of sulfate the formation of a 2:1 host–guest complex occurred, though with less stability than in the case of **L0**. This complex is gradually replaced by a 1:1 complex as the sulfate/**L1** ratio increases from 0.5 to 1 and, ultimately, the 1:1 complex prevails thereafter.[14a]



Scheme 1. Preparation of **L1**, **L2**, and **L3**. Reaction conditions: a) ICl, $C_2H_4Cl_2$, 95%; b) $NaNO_2$, H_2SO_4, ethanol, 82%; c) $SnCl_2$, ethanol, 81%; d) NaN_3, sodium ascorbate, CuI, *N*,*N*-dimethylethane-1,2-diamine, DMSO/H_2O (5:1), room temp., 1 h, 67%; e) $CuSO_4$, sodium ascorbate, ethanol/H_2O (2:1), room temp., 12 h, 89%; f) *N*,*N*-dicyclohexylcarbodiimide (DCC), 4-(dimethylamino)pyridine (DMAP), CH_2Cl_2, 65%; g) $CuSO_4$, sodium ascorbate, THF/H_2O (10:1), room temp., 12 h, 67%; h) DCC, DMAP, CH_2Cl_2, 53%; i) CuI, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1-azopyrene, toluene, 56%; j) trimethylaluminum, aniline/*p*-iodoaniline, toluene, 2 h.

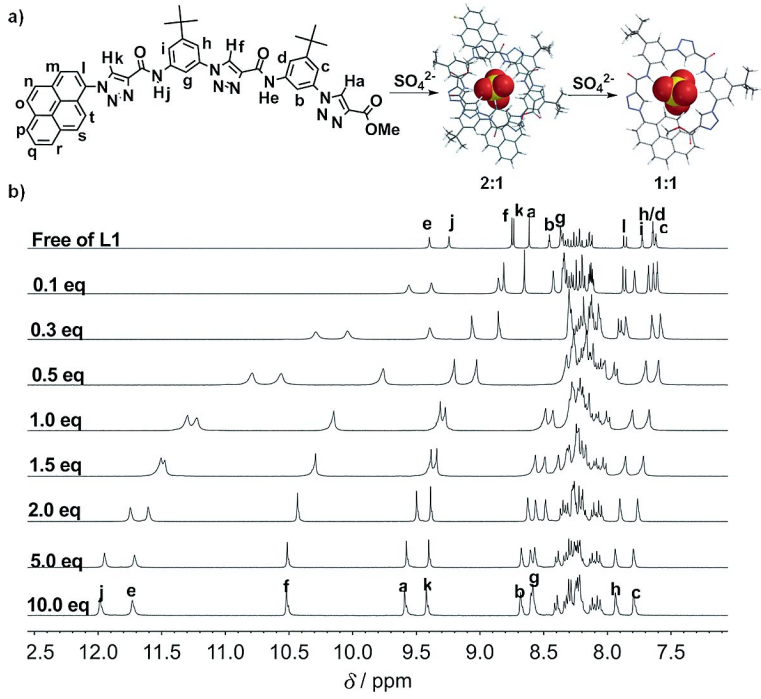


Figure 1. a) Illustration of the sulfate-binding process of receptor **L1**; b) ^{1}H NMR (CD_2Cl_2, 400 MHz) spectra of **L1** in the presence of SO_4^{2-}.

With an increase in the numbers of triazolecarboxamide units, as in **L2**, three amide NH and triazole CH groups in combination with one CH group from each of the two connecting benzene groups can interact with a sulfate anion in a 1:1 ratio through eight hydrogen bonds. The complexation behavior of host **L2** with the sulfate anion was studied by ^{1}H NMR titration in [D$_2$]dichloromethane at 25 °C. Figure 2 shows the ^{1}H NMR spectra of **L2** with different amounts of TBA_2SO_4. In general, π–π stacking results in upfield shifting of protons, whereas hydrogen-bonding interaction results in downfield shifting of protons. Upon the addition of 1.0 equiv. of TBA_2SO_4, the amide protons ($\Delta\delta$Hi = 1.84 ppm, $\Delta\delta$Hn = 1.88 ppm, $\Delta\delta$Hd = 1.16 ppm), the triazole protons of the triazolecarboxamide unit ($\Delta\delta$Ho = 0.92 ppm, $\Delta\delta$Hj = 0.89 ppm, $\Delta\delta$He = 0.69 ppm), and two benzene protons ($\Delta\delta$Hg = 0.02 ppm, $\Delta\delta$Hm = 0.06 ppm) showed downfield shifts, due to the multiple hydrogen bonding between sulfate and **L2**. The upfield shifts of protons Ha and Hb on the terminal benzene ring and Hp–x on the pyrene system evidently indicated the π–π stacking between these terminal aromatic rings due to folding of molecule **L2** upon complexation, as shown in Figure 2 (a, right).

The stable 1:1 **L2**·SO_4^{2-} complex allowed for a structural investigation in solution by NOESY NMR spectroscopy. Strong NOE connections were observed between Ht/v and He, between Hn and Hd, and between Ho and Hc, which supported the formation of the folded circle conformation (see the bracketed cross peaks in Figure 3). Because the distances between Hd and Hn and between Hc and Ho of the linear chain are much too long for any cross peak to be observed, these signals must correspond to contacts due to the folding of the molecular chain.[16]

To investigate the electronic effects on the binding affinities of foldamers of this kind for sulfate, iodide was introduced into the terminal benzene ring. Iodide-substituted receptor **L3** showed similar binding behavior with SO_4^{2-}. The titration curve is best fitted for a 1:1 host–guest complex, yielding an apparent binding constant of K = 2200 ± 100 M^{-1}, which is bigger than that obtained from **L2**. This result indicated that the electron-withdrawing group could enhance the binding affinity (see Figure S3 in the Supporting Information).

The binding behavior of **L2** with other anions was also investigated by ^{1}H NMR titration as shown in Figures S4–S9 in the Supporting Information. Addition of tetrabutylammonium nitrate to **L2** in [D$_2$]dichloromethane resulted in only very small perturbations in the ^{1}H NMR spectra (Figure S4 in the Supporting Information), which is due to size and geometry mismatch between nitrate and **L2**, because nitrate is big and flat. Titration of fluoride anions induced similar folding of molecular **L2** through hydrogen bonding of triazole protons and the middle benzene ring protons, whereas the amide protons Hi, Hn, and Hd disappeared due to the fast oscillation of F^- in the cavity formed by the foldamer at the same ^{1}H NMR timescale at 298 K. Cl^- and Br^- induced similar but weaker ^{1}H NMR spectra shifts. As the methyl group of the acetate anion prefers to form a hydrogen bond with the nitrogen atom of the triazole, thus repelling the two triazole C–H bonds to the outside, AcO^- binds with the half-circle formed by the central triazolecarboxamide unit and the terminal triazolecarbox-

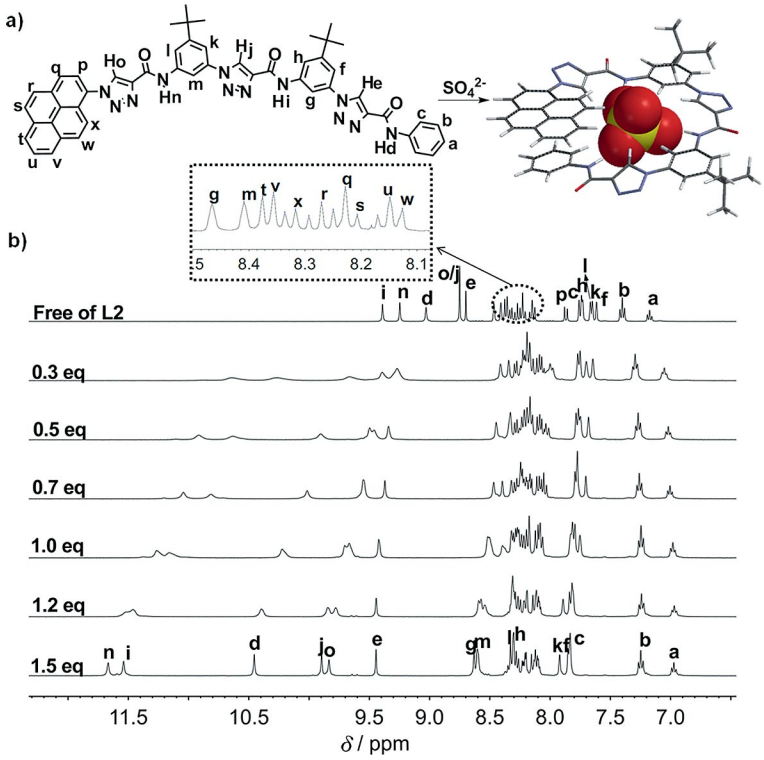


Figure 2. a) Illustration of the sulfate-binding process of receptor **L2**; b) ^{1}H NMR (CD_2Cl_2, 400 MHz) spectra of **L2** in the presence of SO_4^{2-}.

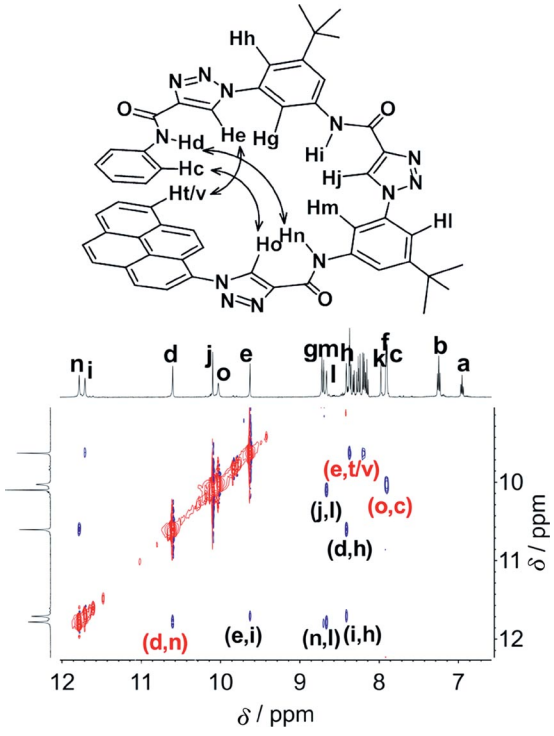


Figure 3. Intramolecular NOE contacts in the **L2**·SO_4^{2-} complex and partial NOESY spectrum (600 MHz) of **L2** + SO_4^{2-} in CD_2Cl_2 at 288 K (mixing time: 1 s).

amide connected with the pyrene group, as indicated by the more strongly downfield shifts of protons Hi and Hn relative to Hd (Figure S8 in the Supporting Information). The stability constant of the F^- complex (79 ± 8 M^{-1}) was calculated by fitting the chemical shifts of proton He (as shown in Figure S5 in the Supporting Information), and the stability constants of the Cl^- (39 ± 6 M^{-1}), Br^- (5.3 ± 0.8 M^{-1}), AcO^- (18 ± 2 M^{-1}), SO_4^{2-} (1300 ± 100 M^{-1}), and $H_2PO_4^-$ (590 ± 50 M^{-1}) complexes were obtained by analysis of the signal shifts of amide NH (Hi) with use of a 1:1 binding model with the WinEQNMR2[17] software, as summarized in Figure 4. With increasing halide size, the binding stability decreased, whereas **L2** showed the greatest selectivity towards sulfate, due to the association effects of eight hy-

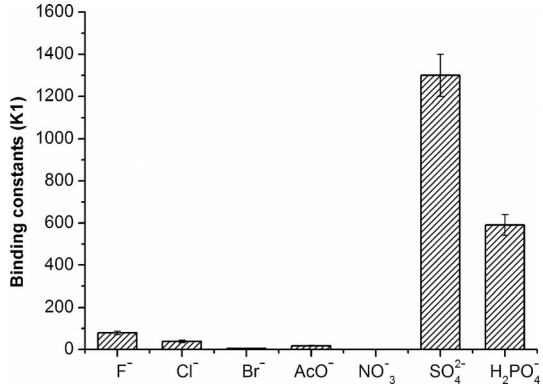


Figure 4. Comparison of the binding constants of **L2** with various anions (determined by ^{1}H NMR spectroscopy) in CD_2Cl_2 at room temperature.

drogen bonds and the π–π stacking between the terminal groups.

UV/Vis experiments were carried out in CH_2Cl_2 to evaluate the binding properties of **L2** towards sulfate (Figure S11 in the Supporting Information): **L2** exhibits weak increases in the absorption of the pyrene band (λ_{max} = 344 nm) and the triazolecarboxamide band (λ_{max} = 277 nm). The binding stoichiometry of the sulfate–**L2** interactions was calculated to be 1:1 from the Job's plot (Figure S12 in the Supporting Information). **L2** exhibits an emission band of pyrene at λ_{max} = 386 nm (Figure S13 in the Supporting Information), which is quenched upon the addition of SO_4^{2-} due to electron transfer from the electron-rich sulfate anions to the pyrene chromophore.

Conclusions

In summary, we have successfully optimized the structures of triazolecarboxamide-containing foldamers for selective recognition of sulfate anions and demonstrated that the binding stoichiometry and binding affinity can be tuned by increasing the numbers of triazolecarboxamide units and by modification of the terminal benzene ring. The structural compatibility between the receptor and anions greatly influenced the binding strength and selectivity. The triazolecarboxamide units can give rise to quite strong oxyanion receptors; this system could open the way to the construction of numerous receptor systems when triazolecarboxamides are preorganized into shape-persistent macrocyclic structures in the future.

Experimental Section

Materials and Characterization: All reagents were obtained from commercial suppliers and used as received unless otherwise noted. Column chromatography was performed on silica gel (160–200 mesh), and thin-layer chromatography (TLC) was performed on precoated silica gel plates with observation under UV light. Nuclear magnetic resonance (NMR) spectra were recorded with a Bruker Avance DPS 400 spectrometer at room temperature (298 K). Chemical shifts were referenced to the residual solvent peaks. Matrix-assisted laser desorption/ionization reflectron time-of-flight (MALDI-TOF) mass spectrometry was performed with a Bruker Biflex III mass spectrometer. Electronic absorption spectra were measured with a JASCO V-579 spectrophotometer. Fluorescence excitation and emission spectra were recorded with a Hitachi F-4500 instrument. Compound **1** was synthesized by literature procedures.[18]

Compound 2: Iodomonochloride (25 g, 154 mmol) was slowly added at 70 °C under N_2 to a solution of compound **1** (27.16 g, 140 mmol) in dichloroethane (150 mL). The mixture was stirred for an additional 3 h and cooled to room temperature. The crude reaction mixture was washed with saturated NaCl solution. The aqueous layer was extracted with CH_2Cl_2 and the combined organic extracts were washed with brine and water, dried ($MgSO_4$), and concentrated under reduced pressure. The crude residue was subjected to flash silica gel column chromatography (CH_2Cl_2/petroleum ether 1:2) to yield solid **2** (95%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (d, J = 2.2 Hz, 1 H), 7.96 (d, J = 2.2 Hz, 1 H), 6.51 (s, 2 H), 1.29 ppm (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.8, 141.9, 141.3, 131.5, 123.2, 87.6, 34.0, 31.20 ppm. MS (EI): m/z = 320. $C_{10}H_{13}IN_2O_2$ (320.13): calcd. C 37.52, H 4.09, N 8.75; found C 37.65, H 4.13, N 8.69.

Compound 3: $NaNO_2$ (10 g, 145 mmol) was slowly added at 0 °C to a suspension of compound **2** (22.33 g, 70 mmol) in concentrated sulfuric acid (60 mL). After additional stirring for 15 min at 0 °C, the mixture was allowed to reach room temperature and stirred at this temperature for an additional 3 h. The black viscous mixture was slowly added to ethanol (500 mL) at reflux. After complete addition, most of the solvent was evaporated and the mixture was poured into dichloromethane/water (500/500 mL). The organic phase was extracted with CH_2Cl_2, washed with water and brine, and dried with $MgSO_4$. The crude residue was subjected to flash silica gel column chromatography (CH_2Cl_2/petroleum ether 1:15) to yield solid **3** (82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.37 (s, 1 H), 8.20 (s, 1 H), 8.01 (s, 2 H), 1.35 ppm (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.2, 148.5, 140.7, 129.6, 120.0, 93.5, 35.2, 30.9 ppm. MS (EI): m/z = 304. $C_{10}H_{12}INO_2$ (305.11): calcd. C 39.36, H 3.96, N 4.59; found C 39.51, H 4.01, N 4.53.

Compound 4: $SnCl_2{\cdot}2H_2O$ (9.06 g, 40.0 mmol) was added to a solution of compound **3** (2.44 g, 8 mmol) in ethanol (5 mL). The reaction mixture was heated at reflux until the reaction was complete (indicated by TLC analysis). The solvent was removed under reduced pressure and the crude residue was partitioned between ethyl acetate and KOH (2 M). The aqueous layer was extracted with ethyl acetate and the combined organic extracts were washed with brine and water, dried ($MgSO_4$), and concentrated under reduced pressure. The crude residue was subjected to flash silica gel column chromatography (ethyl acetate in petroleum ether, 20%) to yield solid **4** (82.9%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.11 (s, 1 H), 6.88 (s, 1 H), 6.65 (s, 1 H), 3.69 (s, 2 H), 1.25 ppm (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.5, 147.4, 125.0, 121.1, 112.0, 95.3, 34.6, 31.2 ppm. MS (EI): m/z = 275. $C_{10}H_{14}IN$ (275.13): calcd. C 43.65, H 5.13, N 5.09; found C 43.69, H 5.07, N 5.22.

Compound 5: Compound **4** (1.1 g, 4 mmol), NaN_3 (520 mg, 8 mmol), sodium ascorbate (44.6 mg, 0.2 mmol), CuI (76 mg, 0.4 mmol), and *N*,*N*′-dimethylethane-1,2-diamine (53 mg, 0.6 mmol) were added to degassed DMSO/H_2O (5:1, 10 mL). The reaction mixture was stirred at room temp. for 1 h. The crude reaction mixture was taken up in a mixture of brine and EtOAc. The aqueous phase was extracted with EtOAc. The combined organic phases were concentrated in vacuo and the residue was purified by flash chromatography over silica gel (CH_2Cl_2 in petroleum ether, 25%) to yield solid **5** (67.2%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.49 (s, 1 H), 6.45 (s, 1 H), 6.18 (s, 1 H), 1.27 ppm (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.4, 147.5, 140.4, 109.3, 106.7, 102.8, 34.4, 31.2 ppm. MS (EI): m/z = 190. $C_{10}H_{14}N_4$ (190.25): calcd. C 63.13, H 7.42, N 29.45; found C 63.22, H 7.54, N 29.33.

Compound 6: $CuSO_4{\cdot}5H_2O$ (24.5 mg, 0.1 mmol) and sodium ascorbate (40 mg, 0.2 mmol) were added to a solution of compound **5** (570 mg, 3 mmol) and methyl propiolate (252 mg, 3 mmol) in ethanol/H_2O (2:1). The mixture was stirred at room temp. for 12 h. Ethanol was removed in vacuo and CH_2Cl_2 was added. The organic phase was washed with water and dried ($MgSO_4$). The residue was purified by silica gel chromatography (ethyl acetate in petroleum ether, 25%) to afford **6** (89%) as a solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.47 (s, 1 H), 7.05 (s, 1 H), 6.93 (s, 1 H), 6.8 (s, 1 H), 1.33 ppm (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.1, 154.8, 147.6, 139.9, 137.1, 125.5, 113.1, 108.2, 104.7, 52.4, 34.7, 31.1 ppm. MS (EI): m/z = 274. $C_{14}H_{18}N_4O_2$ (274.32): calcd. C 61.30, H 6.61, N 20.42; found C 61.38, H 6.57, N 20.31.

Compound 7: Propiolic acid (100 mg, 1.4 mmol) and DCC (290 mg, 1.4 mmol) were combined in CH_2Cl_2 (10 mL), the solution was stirred for 10 min, and then compound **6** (384 mg, 1.4 mmol) and DMAP (5 mg) were added. The reaction mixture was stirred for 30 min, and then the precipitate was filtered off and the solvent was removed in vacuo. The residue was purified by silica gel chromatography (CH_2Cl_2/methanol 50:1) to afford **7** (65%) as a solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.56 (s, 1 H), 8.01 (s, 1 H), 7.61 (s, 1 H), 7.53 (s, 1 H), 4.0 (s, 3 H), 2.98 (s, 1 H), 1.36 ppm (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.0, 154.7, 150.1, 140.4, 138.5, 136.6, 125.9, 117.9, 114.6, 109.9, 74.8.6, 52.4, 35.3, 31.0, ppm. MS (EI): *m*/*z* = 326. $C_{17}H_{18}N_4O_3$ (326.35): calcd. C 62.57, H 5.56, N 17.17; found C 62.51, H 5.63, N 17.31.

Compound 8: $CuSO_4$ (24.5 mg, 0.1 mmol) and sodium ascorbate (40 mg, 0.2 mmol) were added to a solution of compound **7** (326 mg, 1 mmol) and compound **5** (190 mg, 1 mmol) in THF/H_2O (10:1, 15 mL). The mixture was stirred at room temp. for 12 h. THF was removed in vacuo and CH_2Cl_2 was added. The organic phase was washed with water and dried ($MgSO_4$). The residue was purified by silica gel chromatography (CH_2Cl_2/ethyl acetate 5:1) to afford **8** (67%) as a solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.17 (s, 1 H), 8.6 (s, 1 H), 8.55 (s, 1 H), 8.28 (s, 1 H), 7.65 (s, 1 H), 7.60 (s, 1 H), 7.09 (s, 1 H), 6.92 (s, 1 H), 6.82 (s, 1 H), 4.01 (s, 3 H), 1.41 (s, 9 H), 1.34 ppm (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.1, 158.1, 154.8, 154.7, 143.2, 140.4, 138.6, 137.1, 136.8, 126.0, 124.3, 117.7, 114.3, 113.4, 109.6, 108.1, 104.5, 52.4, 35.3, 31.1 ppm. MS (MALDI-TOF): *m*/*z* = 539.1 [M + Na]. $C_{27}H_{32}N_8O_3$ (516.60): calcd. C 62.77, H 6.24, N 21.69; found C 62.59, H 6.17, N 21.72.

Compound 9: Propiolic acid (100 mg, 1.4 mmol) and DCC (290 mg, 1.4 mmol) were combined in CH_2Cl_2 (10 mL), the solution was stirred for 10 min, and then compound **6** (384 mg, 1.4 mmol) and DMAP (5 mg) were added. The reaction mixture was stirred for 30 min, and then the precipitate was filtered off and the solvent was removed in vacuo. The residue was purified by silica gel chromatography (CH_2Cl_2/ethyl acetate 5:1) to afford **9** (55%) as a solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.17 (s, 1 H), 8.62 (s, 1 H), 8.60 (s, 1 H), 8.28 (s, 1 H), 8.05 (s, 1 H), 7.86 (s, 1 H), 7.65 (s, 1 H), 7.61 (d, *J* = 5.9 Hz, 2 H), 7.52 (s, 1 H), 4.01 (s, 3 H), 2.99 (s, 1 H), 1.41 (s, 9 H), 1.38 ppm (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 161.0, 157.3, 154.8, 140.4, 138.6, 136.8, 126.0, 124.5, 117.9, 117.8, 114.7,114.4, 110.0, 109.6, 74.8, 52.4, 35.3, 31.1 ppm. MS (MALDI-TOF): *m*/*z* = 591.2 [M + Na]. $C_{30}H_{32}N_8O_4$ (568.63): calcd. C 63.37, H 5.67, N 19.71; found C 63.24, H 5.62, N 19.77.

Compound L1: CuI (38 mg, 0.2 mmol) and DBU (0.7 mL, 4.0 mmol) were added to a solution of compound **9** (568 mg, 1 mmol) and 1-azopyrene (243 mg, 1 mmol) in toluene (50 mL). The mixture was stirred at room temp. for 5 h, and then the solvent was removed in vacuo and the residue was purified by silica gel chromatography (CH_2Cl_2/ethyl acetate 10:1) to afford **L1** (56%) as a solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.38 (s, 1 H, NH), 9.20 (s, 1 H, NH), 8.71 (s, 1 H, CH), 8.67 (s, 1 H, CH), 8.60 (s, 1 H, CH), 8.35 (s, 1 H), 8.32–8.08 (m, 9 H), 7.81 (d, *J* = 9.1 Hz, 1 H), 7.73 (s, 1 H), 7.66 (s, 2 H), 7.62 (s, 1 H), 4.00 (s, 3 H, OCH_3), 1.44 (s, 9 H, CH_3), 1.40 ppm (s, 9 H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2, 161.1, 158.2, 157.9, 154.7, 138.6, 130.2, 129.4, 129.2, 126.8, 126.3, 125.9, 124.7, 124.5, 123.2, 117.7, 109.8, 109.5, 52.3, 35.3, 31.16 ppm. MS (MALDI-TOF): *m*/*z* = 834.1 [M + Na], 850.2 [M + K]. $C_{30}H_{32}N_8O_4$ (568.63): calcd. C 63.37, H 5.67, N 19.71; found C 63.50, H 5.69, N 19.65.

Compound L2: Trimethylaluminum (2 M solution in toluene, 0.25 mL, 0.5 mmol) was added dropwise to a solution of aniline (46.5 mg, 0.5 mmol) in dry toluene (30 mL). The solution was stirred at room temperature for 30 min, and then a solution of **L1** (405 mg, 0.5 mmol) in toluene was added at room temperature and the reaction mixture was heated to 100 °C for 2 h. The reaction mixture was cooled to room temperature, quenched cautiously with water (0.1 mL), and stirred at room temperature for 10 min. Evaporation of the solvent gave a residue, and then the residue was purified by silica gel chromatography (CH_2Cl_2/ethyl acetate 10:1) to afford **L2** (45%) as a solid. ^{1}H NMR (400 MHz, CD_2Cl_2): δ = 9.39 (s, 1 H, NH), 9.25 (s, 1 H, NH), 9.03 (s, 1 H, NH), 8.75 (s, 2 H, CH), 8.70 (s, 1 H, CH), 8.47 (s, 1 H), 8.41 (s, 1 H), 8.38–8.15 (m, 9 H), 7.76 (s, 1 H), 7.74 (s, 1 H), 7.73 (s, 1 H), 7.67 (d, *J* = 6.9 Hz, 2 H), 7.62 (s, 1 H), 7.40 (t, *J* = 7.7 Hz, 2 H), 7.17 (t, *J* = 7.4 Hz, 1 H),1.45 (s, 9 H, CH_3), 1.43 ppm (s, 9 H, CH_3). ^{13}C NMR (100 MHz, CD_2Cl_2): δ = 159.4, 159.2, 159.0, 156.0, 155.9, 145.2, 144.7, 144.5, 140.2, 140.1, 139.0, 138.2, 134.0, 132.4, 131.8, 131.4, 130.9, 130.6, 130.3, 128.2, 127.7, 126.2, 125.9, 125.7, 124.7, 121.8, 121.2, 119.2, 119.0, 115.3, 111.0, 109.3, 36.5, 32.2 ppm. MS (MALDI-TOF): *m*/*z* = 895.3 [M + Na]. $C_{51}H_{44}N_{12}O_3$ (872.99): calcd. C 70.17, H 5.08, N 19.25; found C 70.34, H 5.14, N 19.14.

Compound L3: Trimethylaluminum (2 M solution in toluene, 0.25 mL, 0.5 mmol) was added dropwise to a solution of *p*-iodoaniline (110 mg, 0.5 mmol) in dry toluene (30 mL). The solution was stirred at room temperature for 30 min, and then a solution of **L1** (405 mg, 0.5 mmol) in toluene was added at room temperature and the reaction was heated to 100 °C for 2 h. The reaction was cooled to room temperature, quenched cautiously with water (0.1 mL), and stirred at room temperature for 10 min. Evaporation of the solvent gave a residue, and then the residue was purified by silica gel chromatography (CH_2Cl_2/ethyl acetate, 10:1) to afford **L3** (43%) as a solid. ^{1}H NMR (400 MHz, [D_6]DMSO): δ = 11.00 (s, 1 H, NH), 10.88 (s, 1 H, NH), 10.70 (s, 1 H, NH), 9.55 (s, 1 H, CH), 9.53 (s, 1 H, CH), 9.45 (s, 1 H, CH), 8.61 (s, 1 H), 8.57 (s, 1 H), 8.52 (d, *J* = 8.2 Hz, 1 H), 8.46–8.31 (m, 6 H), 8.18 (t, *J* = 8.2 Hz, 1 H), 8.10 (s, 1 H), 8.04 (s, 1 H), 7.79 (d, *J* = 9.3 Hz, 1 H), 7.74–7.67 (m, 6 H), 1.38 (s, 9 H, CH_3), 1.36 ppm (s, 9 H, CH_3). ^{13}C NMR (100 MHz, [D_6]DMSO): δ = 159.3, 159.2, 158.9, 154.2, 154.1, 144.1, 143.7, 140.4, 140.3, 139.1, 138.0, 137.0, 132.8, 130.8, 130.6, 130.4, 129.8, 129.6, 128.9, 127.9, 127.8, 127.5, 127.0, 126.7, 125.8, 124.9, 124.7, 123.9, 123.4, 121.5, 118.8, 114.0, 110.6, 88.4, 35.8, 31.6 ppm. MS (MALDI-TOF): *m*/*z* = 1021.3 [M + Na]. $C_{51}H_{43}IN_{12}O_3$ (998.88): calcd. C 61.32, H 4.34, N 16.83; found C 61.48, H 4.26, N 16.71.

Supporting Information (see footnote on the first page of this article): Synthesis information for all key intermediates and final product, UV/Vis spectra and fluorescence spectra of compound **L2** with sulfate anions, the ^{1}H NMR and ^{13}C NMR spectra for key intermediates, ^{1}H NMR spectra of **L2** with various anions.

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[1] a) V. Amendola, D. Esteban-Gomez, L. Fabbrizzi, M. Licchelli, *Acc. Chem. Res.* **2006**, *39*, 343–353; b) P. A. Gale, *Chem. Soc. Rev.* **2010**, *39*, 3746–3771; c) T. Gunnlaugsson, M. Glynn, G. M. Tocci, P. E. Kruger, F. M. Pfeffer, *Coord. Chem. Rev.* **2006**, *250*, 3094–3117; d) R. Martinez-Manez, F. Sancenon, *Chem. Rev.* **2003**, *103*, 4419–4476; e) M. Wenzel, J. R. Hiscock, P. A. Gale, *Chem. Soc. Rev.* **2012**, *41*, 480–520; f) Y. Hua, A. H.

Flood, *Chem. Soc. Rev.* **2010**, *39*, 1262–1271; g) P. A. Gale, N. Busschaert, C. J. E. Haynes, L. E. Karagiannidis, I. L. Kirby, *Chem. Soc. Rev.* **2014**, *43*, 205–241; h) F. D. Riccardis, I. Izzo, D. Montesarchio, P. Tecilla, *Acc. Chem. Res.* **2013**, *46*, 2781–2790; i) A. V. Jentzsch, A. Hennig, J. Mareda, S. Matile, *Acc. Chem. Res.* **2013**, *46*, 2791–2800.

[2] a) J. W. Pflugrath, F. A. Quiocho, *Nature* **1985**, *314*, 257–260; b) J. W. Pflugrath, F. A. Quiocho, *J. Mol. Biol.* **1988**, *200*, 163–180.

[3] S. G. Galbraith, Q. Wang, L. Li, A. J. Blake, C. Wilson, S. R. Collinson, L. F. Lindoy, P. G. Plieger, M. Schroder, P. A. Tasker, *Chem. Eur. J.* **2007**, *13*, 6091–6107.

[4] B. A. Moyer, R. Custelcean, B. P. Hay, J. L. Sessler, K. Bowman-James, V. W. Day, S. O. Kang, *Inorg. Chem.* **2013**, *52*, 3473–3490.

[5] a) Q. G. Wang, Y. S. Xie, Y. B. Ding, X. Li, W. H. Zhu, *Chem. Commun.* **2010**, *46*, 3669–3671; b) D. Seidel, V. Lynch, J. L. Sessler, *Angew. Chem. Int. Ed.* **2002**, *41*, 1422–1425; *Angew. Chem.* **2002**, *114*, 1480.

[6] a) D. Esteban-Gomez, L. Fabbrizzi, M. Licchelli, *J. Org. Chem.* **2005**, *70*, 5717–5720; b) J. W. Steed, *Chem. Soc. Rev.* **2009**, *38*, 506–519.

[7] a) K. H. Choi, A. D. Hamilton, *J. Am. Chem. Soc.* **2001**, *123*, 2456–2457; b) S. O. Kang, J. M. Llinares, D. Powell, D. VanderVelde, K. Bowman-James, *J. Am. Chem. Soc.* **2003**, *125*, 10152–10153; c) K. Bowman-James, *Acc. Chem. Res.* **2005**, *38*, 671–678; d) S. O. Kang, R. A. Begum, K. Bowman-James, *Angew. Chem. Int. Ed.* **2006**, *45*, 7882–7894; *Angew. Chem.* **2006**, *118*, 8048.

[8] a) M. A. Hossain, J. M. Llinares, S. Mason, P. Morehouse, D. Powell, K. Bowman-James, *Angew. Chem. Int. Ed.* **2002**, *41*, 2335–2338; *Angew. Chem.* **2002**, *114*, 2441; b) F. M. Menger, K. K. Catlin, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2147–2150; *Angew. Chem.* **1995**, *107*, 2330; c) K. S. Kim, J. Y. Lee, S. J. Lee, T. K. Ha, D. H. Kim, *J. Am. Chem. Soc.* **1994**, *116*, 7399–7400.

[9] a) A. G. Avent, P. A. Chaloner, M. P. Day, K. R. Seddon, T. Welton, *J. Chem. Soc., Dalton Trans.* **1994**, 3405–3413; b) X. Chen, S. Kang, M. J. Kim, J. Kim, Y. S. Kim, H. Kim, B. Chi, S. J. Kim, J. Y. Lee, J. Yoon, *Angew. Chem. Int. Ed.* **2010**, *49*, 1422–1425; *Angew. Chem.* **2010**, *122*, 1464; c) N. J. Singh, E. J. Jun, K. Chellappan, D. Thangadurai, R. P. Chandran, I. C. Hwang, J. Yoon, K. S. Kim, *Org. Lett.* **2007**, *9*, 485–488; d) K. Chellappan, N. J. Singh, I. C. Hwang, J. W. Lee, K. S. Kim, *Angew. Chem. Int. Ed.* **2005**, *44*, 2899–2903; *Angew. Chem.* **2005**, *117*, 2959.

[10] a) C. W. Tornoe, C. Christensen, M. Meldal, *J. Org. Chem.* **2002**, *67*, 3057–3064; b) V. V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2002**, *41*, 2596–2599; *Angew. Chem.* **2002**, *114*, 2708.

[11] a) H. Juwarker, J. M. Lenhardt, D. M. Pham, S. L. Craig, *Angew. Chem. Int. Ed.* **2008**, *47*, 3740–3743; *Angew. Chem.* **2008**, *120*, 3800; b) S. Lee, Y. R. Hua, H. Park, A. H. Flood, *Org. Lett.* **2010**, *12*, 2100–2102; c) Y. R. Hua, R. O. Ramabhadran, E. O. Uduehi, J. A. Karty, K. Raghavachari, A. H. Flood, *Chem. Eur. J.* **2011**, *17*, 312–321; d) R. O. Ramabhadran, Y. R. Hua, Y. J. Li, A. H. Flood, K. Raghavachari, *Chem. Eur. J.* **2011**, *17*, 9123–9129; e) Y. J. Li, A. H. Flood, *Angew. Chem. Int. Ed.* **2008**, *47*, 2649–2652; *Angew. Chem.* **2008**, *120*, 2689.

[12] a) A. Kumar, P. S. Pandey, *Org. Lett.* **2008**, *10*, 165–168; b) B. Schulze, C. Friebe, M. D. Hager, W. Gunther, U. Kohn, B. O. Jahn, H. Gorls, U. S. Schubert, *Org. Lett.* **2010**, *12*, 2710–2713; c) Q. Y. Cao, T. Pradhan, M. H. Lee, K. No, J. S. Kim, *Analyst* **2012**, *137*, 4454–4457; d) J. J. Cai, B. P. Hay, N. J. Young, X. P. Yang, J. L. Sessler, *Chem. Sci.* **2013**, *4*, 1560–1567.

[13] a) Y. L. Li, A. H. Flood, *J. Am. Chem. Soc.* **2008**, *130*, 12111–12122; b) Y. R. Hua, A. H. Flood, *J. Am. Chem. Soc.* **2010**, *132*, 12838–12840; c) K. P. McDonald, Y. R. Hua, S. Lee, A. H. Flood, *Chem. Commun.* **2012**, *48*, 5065–5075; d) Y. Hua, Y. Liu, C.-H. Chen, A. H. Flood, *J. Am. Chem. Soc.* **2013**, *135*, 14401–14412; e) S. Lee, C.-H. Chen, A. H. Flood, *Nature Chem.* **2013**, *5*, 704–710; f) F. Garcia, M. R. Torres, E. Matesanz, L. Sanchez, *Chem. Commun.* **2011**, *47*, 5016–5018; g) N. G. White, P. D. Beer, *Org. Biomol. Chem.* **2013**, *11*, 1326–1333; h) J. L. Sessler, J. J. Cai, H.-Y. Gong, X. P. Yang, J. F. Arambula, B. P. Hay, *J. Am. Chem. Soc.* **2010**, *132*, 14058–14060.

[14] a) Y.-J. Li, L. Xu, W.-L. Yang, H.-B. Liu, S.-W. Lai, C.-M. Che, Y.-L. Li, *Chem. Eur. J.* **2012**, *18*, 4782–4790; b) L. Xu, Y. Li, Y. Yu, T. Liu, S. Cheng, H. Liu, Y. Li, *Org. Biomol. Chem.* **2012**, *10*, 4375–4380.

[15] N. Niamnont, N. Kimpitak, K. Wongravee, P. Rashatasakhon, K. K. Baldridge, J. S. Siegel, M. Sukwattanasinitt, *Chem. Commun.* **2013**, *49*, 780–782.

[16] J. Sanchez-Quesada, C. Seel, P. Prados, J. De Mendoza, *J. Am. Chem. Soc.* **1996**, *118*, 277–278.

[17] M. J. Hynes, *J. Chem. Soc., Dalton Trans.* **1993**, 311–312.

[18] D. K. Frantz, A. Linden, K. K. Baldridge, J. S. Siegel, *J. Am. Chem. Soc.* **2012**, *134*, 1528–1535.

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