Published in final edited form as:

Supramol Chem. 2016 ; 28(1-2): 37–44. doi:10.1080/10610278.2015.1072199.

Anion-directed self-assembly of a 2,6-bis(2-anilinoethynyl)pyridine bis(amide) scaffold

Blakely W. Tresca^a, Orion B. Berryman^{a,b}, Lev N. Zakharov^c, Darren W. Johnson^{*,a}, and Michael M. Haley^{*,a}

^aDepartment of Chemistry & Biochemistry and the Materials Science Institute, University of Oregon, Eugene, Oregon 97403-1253, USA

^cCAMCOR, University of Oregon, 1443 East 13th Avenue, Eugene, Oregon 97403, USA

Abstract

Bis(sulfonamide) receptors based on the 2,6-bis(2-anilinoethynyl)pyridine scaffold form persistent dimers with water and halides in solution and in the solid-state. The structurally related bis(amide) receptor derived from 3,5-dinitrobenzoyl chloride is a dimer in the solid-state with two HCl molecules directing the self-assembly. The 2+2 dimer, with a twisted “S”-shaped backbone, is held together by six hydrogen bonds. Dissolution of the ($\text{H}_2^+\cdot\text{Cl}^-$)₂ adduct in CHCl_3 results, however, in a monomeric structure. DOSY and ^1H NMR experiments were used to identify the dominance of monomer in solution for both **2** and $\text{H}_2^+\cdot\text{Cl}^-$. The ‘OFF-ON’ fluorescence response of 2, 6-bis(2-anilinoethynyl)pyridine is retained with amide arms.

Keywords

self-assembly; anion binding; amide binding; host-guest; DOSY

1. Introduction

Self-assembly plays an important role in the design of supramolecular materials and host-guest complexes (1). Macromolecules resulting from self-assembly provide unique properties such as conductivity (2, 3), metal capture (4), sensing (5, 6), motion (7, 8), or logic gates (9). Self-assembled receptors or sensors are also capable of selecting guests by an “induced fit” model (10, 11), not just the restrictive lock and key method. The self-assembly of many such complexes has been effected using metal ions (12, 13), small molecules (14), and anions (15, 16). Advancing the use of anions as directing elements and/or templates in self-assembling systems requires an improved understanding of conformational preferences of the flexible receptors comprising these assemblies (5, 8).

*Corresponding authors. dwj@uoregon.edu; haley@uoregon.edu.

^bCurrent address: Department of Chemistry & Biochemistry, University of Montana, 32 Campus Drive, Missoula, Montana 59812, USA

Supplementary Information: Copies of the ^1H and ^{13}C NMR spectra of **2** as well as the ^1H NMR data for the titration, dilution and DOSY experiments in support of the results cited in this paper are available in the supporting information, available online.

Alkynes offer many characteristics that are useful to designing self-assembled receptors: linear rigidity, rotational freedom, π -electron conjugation and easy functionalization (17). We have previously reported on a family of modular arylethynyl receptors for anion binding and fluorescent sensing using 2,6-bis(2-anilinoethynyl)pyridine (18-25), -bipyridine (24, 26-28), -phenanthroline (28), -benzene (29-30), and -thiophene (24) scaffolds. The anilines are further functionalized with amide (20), sulfonamide (18, 24), or urea (19, 21-23, 25-30) groups to provide capabilities such as anion selectivity for nitrate (30) and H_2PO_4^- (26), water solubility (25) or metal coordination (27). An example of a pyridine receptor with sulfonamide arms (e.g., **1**) is shown in Figure 1. The sulfonamide receptors exhibited an exceptional capacity to bind water by self-assembling into 2+2 dimers (18, 24). The water molecules can be substituted by halides to form a 2+2 homodimer and even a 2+1+1 heterodimer ($\text{H}_2\text{O}/\text{Cl}$), as all three configurations have been observed in the solid-state. Unfortunately, the persistence of these dimers in solution made characterization of binding equilibria difficult except for determination of the dimerization constants (K_{dim}).

In addition to hydrogen bonds, anion- π interactions are underutilized (31-33) and have the potential to improve selectivity for soft anions, such as iodide (34) and nitrate (30, 35). We previously reported some of the first examples of hydrogen bond assisted (31) and unassisted (36) anion- π halide receptors. Aromatic interactions featuring anions have the added benefit of sometimes producing a unique color change due to charge transfer, which offers additional sensing opportunities. Inspired by our previous work with anion- π interactions and the self-assembly of sulfonamides such as **1**, we sought to design a new receptor that would combine these properties for new selectivity and increased fluorescent response. Herein we report the synthesis and binding properties of bis(amide) receptor **2** derived from 2,6-bis(2-anilinoethynyl)pyridine and electron-poor 3,5-dinitrobenzoyl chloride, the latter unit intended to promote anion- π interactions.

2. Results and discussion

2.1 Synthesis

Precursor **3** has been previously reported as a versatile building block for selective, fluorescent receptors. The large family of compounds cited above, along with **3**, are accessible by Sonogashira cross-coupling a suitable 2-ethynylaniline to a haloarene core (18-25). Amide condensation of **3** with the commercially available 3,5-dinitrobenzoyl chloride furnishes bis(amide) **2** in moderate yield (Scheme 1) after recrystallization from hot EtOAc.

2.2 Absorbance and fluorescence

The electronic absorption spectrum of **2** (Figure 2, left) is characteristic of the 2,6-bis(2-anilinoethynyl)pyridine backbone. The freebase receptor has a broad absorbance with shoulders at 290 nm and 315 nm. Protonation with TFA or HCl results in a yellow solution. In the absorbance spectrum of H_2^+Cl^- , a new peak appears at 395 nm with a slight decrease in absorbance below 340 nm. The TFA^- salt has a shoulder at 380 nm and an increased absorbance at 308 nm.

Electron-poor receptor **1** is non-emissive as the free-base and the additional nitro groups on **2** should further quench fluorescence. Prior studies in our lab showed that electron poor receptors like **1** exhibit a highly desirable ‘OFF-ON’ fluorescence response to acids such as HCl and trifluoroacetic acid (TFA) (21). Whereas receptor **2** has no appreciable fluorescence in O₂-containing CHCl₃ (Figure 2, right), the addition of HCl affords a yellow solution that possesses a yellow emission when irradiated with a handheld UV lamp. When exciting at 395 nm, the fluorescence maximum of **H2⁺·Cl⁻** is 505 nm, which matches with the λ_{max} of **H1⁺·Cl⁻**. The fluorescence emission of **H2⁺·TFA⁻** was unexpectedly similar in intensity to **H2⁺·Cl⁻**, although the λ_{max} was hypsochromically shifted to 477 nm. In comparison, sulfonamide **1** exhibited the same λ_{max} for Cl⁻ and TFA⁻, but the TFA⁻ salt had less than 50% the emission intensity of the Cl⁻ salt. The increased response from **H2⁺·TFA⁻** is unusual because of the weak binding of TFA and breaks from the normally observed quenching. The fluorescence mechanism for this family of receptors is expected to include significant rigidification of the alkyne backbone due to anion binding. We next sought to examine whether a change in the anion binding structure could explain this anomaly.

2.3 X-Ray crystallography

Single crystals of **H2⁺·Cl⁻** suitable for X-ray diffraction analysis were grown by slow evaporation of an HCl-saturated CH₂Cl₂ solution. **H2⁺·Cl⁻** crystallized as a dimeric structure in the triclinic space group *P*-1 with two CH₂Cl₂ molecules. Figure 3 shows the ORTEP representation of a single protonated receptor bound to one chloride. The asymmetric bis(amide) **2** adopts an “S” conformation with only one arm appearing to bind a Cl⁻ ion, as the other arm is rotated away from the binding pocket. Interestingly, this result is in contrast to our earlier studies that showed that the sulfonamides (18, 24) and ureas (19) derived from pyridine scaffold **3** both bind halides in a “U”-shaped conformation.

Figure 4 shows the (**H2⁺·Cl⁻**)₂ dimer. Consistent with the *P*-1 space group, the monomers are aligned with opposite axes and are centrosymmetric with an inversion center between the monomers. The bridging Cl⁻ atoms in (**H2⁺·Cl⁻**)₂ are held by three hydrogen bonds: a N_{pyr}–H⁺ contact, one N_{amide}–H H-bond from one receptor, and another N_{amide}–H contact from the second receptor. The hydrogen bond distances are (N_{pyr}···Cl) 3.024(4) Å, (N_{amide}···Cl) 3.276(4), and (N_{amide}···Cl_b) 3.426(5) Å. The closest face-to-face arene-arene contacts are 4.004 Å between the pyridine and an opposing benzene ring. A long π – π interaction (3.705 Å) and long bridging hydrogen bond in the Cl⁻-centered dimer are indicative of weak dimerization. The packing also reveals a lone pair– π interaction (3.203 Å) between –NO₂ on one receptor and the 3,5-dinitroarene on another.

We have previously observed that **1** adopts unusual conformations to accommodate larger guests that do not fit in the idealized binding pocket. In addition, the sulfonamide receptors form strong dimers with water or halide anions providing seven or six bridging hydrogen bonds, respectively. The sulfonamide receptors are able to form face-to-face dimers because the bend of the sulfonyl bridge places the terminal arene out of the way with a 230° bend through the N–S bond. Conversely, bis(amide) **2** is planar through the C(=O)–N bond and risks a steric clash if it adopts the “U” confirmation. For **H2⁺·Cl⁻**, the weak Cl⁻ bridging

contacts discourage the formation of strong dimers in solution and likely contribute to the decreased fluorescence selectivity.

2.4 ^1H and DOSY NMR studies

The existence and strength of a $\text{H2}^+\cdot\text{Cl}^-$ dimer in solution was probed using ^1H NMR dilution experiments and titration of a competing guest, tetrabutylammonium chloride (TBACl). Figure 5 shows the stacked ^1H NMR spectra of **2** and $\text{H2}^+\cdot\text{Cl}^-$ (prepared by bubbling gaseous HCl through a stock solution of **2**) in CDCl_3 at 1.0 mM. The amide NH appears at 8.92 ppm as a broad singlet and shifts to 10.04 ppm upon forming the chloride complex. Based on our prior experience with the water-bound dimers of **1** in solution (18,24), we expected to observe some broadening and shifting of the water peak from its typical value of 1.55 ppm to ca. 3-4 ppm; however, the shift of the resonance remained unchanged.

We next eliminated the formation of a halide-water bridged dimer by observing the shift of the amide and arene protons while adding TBACl. The titration of free base **2** with TBACl from 0–18 equivalents is shown in Figure 6. The aromatic peaks remain static and the amide peak shifts downfield with a large excess of Cl^- . The change in the amide proton ($\delta = 0.22$ ppm) is unusual for such an electron-poor amide and coincides with a weak hydrogen bond. The binding isotherm for the titration with Cl^- was perfectly linear (Figure S1) over the range we observed. Based on the concentration of **2**, a linear isotherm and the limits of solubility, the association constant for Cl^- is too low for accurate determination by ^1H NMR. The weak association to Cl^- further supports our hypothesis that water is not an appropriate bridge for dimerization of **2**.

X-ray crystallography pointed towards $\text{H2}^+\cdot\text{Cl}^-$ as a much more likely candidate for dimerization in solution. The ^1H NMR spectrum of $\text{H2}^+\cdot\text{Cl}^-$ in Figure 5 was remarkably similar to the spectrum of **2** at equimolar concentration. The water peak remains in place at 1.55 ppm with slight broadening due to the change in ionic strength. The pyridine protons and the amide proton have the largest shifts from **2** to $\text{H2}^+\cdot\text{Cl}^-$. Surprisingly, we do not observe a large shift for the 3,5-dinitroarene peaks as could be expected from anion- π interactions. The 3,5-substitution pattern is optimized for forming anion- π interactions over the alternative C–H hydrogen bond, but neither appears to be significant here. A last test for the presence of an anion- π interaction was to subject **2** to the larger Br^- and I^- ions as their TBA salts. Iodide is noteworthy for forming colored charge-transfer complexes in the presence of electron poor arenes; however, we did not observe this characteristic color change and thus eliminated anion- π or weak- σ interactions as major contributors.

In a dilution experiment with $\text{H2}^+\cdot\text{Cl}^-$, the addition of CDCl_3 down to $[\text{2}] = 0.2$ mM resulted in an upfield shift of the amide proton. The small shift (0.15 ppm) was completely mitigated by bubbling additional gaseous HCl into the sample. A second dilution with the addition of HCl saturated CDCl_3 resulted in no change of the peaks down to $[\text{2}] = 0.03$ mM. The possibility remains for a dimer to be present throughout the dilution and it is simply too strong to break, but more likely the monomer persists over this concentration range

(otherwise $K_{\text{dim}} > 10^5 \text{ M}^{-1}$, which is unreasonably high for a dimer held together by only two weak hydrogen bonds).

Diffusion Ordered Spectroscopy (DOSY) is a NMR technique to measure the diffusion constant of each NMR active species via a gradient pulse sequence (37). The diffusion constant scales with molecule size by equation 1:

$$D = k_b T / 6 \pi \eta R \quad (1)$$

and correlates with molecular weight (38). D is the diffusion constant, η is the viscosity, and R is the radius of a spherical particle. Samples for DOSY were prepared in water-saturated CDCl_3 using the HCl salt $\mathbf{H2}^+\cdot\text{Cl}^-$ (0.93 mM) and **2** (1.11 mM). The diffusion constant for $\mathbf{H2}^+\cdot\text{Cl}^- = 4.13 \pm 0.34 \times 10^{-10} \text{ D}$ and **2** = $4.55 \pm 0.47 \times 10^{-10} \text{ D}$ at 298 K. The difference is statistically insignificant at the 95% confidence interval. Diffusion of residual solvent (CHCl_3) was the same in both samples, excluding a significant change in solvent viscosity. These results again indicate that **2** and $\mathbf{H2}^+\cdot\text{Cl}^-$ are monomeric in solution.

3. Conclusion

Substitution of 3,5-dinitrophenyl amides on the 2,6-bis(2-anilinoethynyl)pyridine scaffold affords a receptor that retains the strong 'OFF-ON' fluorescence response of the sulfonamide and urea receptors, while also improving upon background fluorescence. The propensity (or not) to form dimers with HCl highlights the difference in conformation of the amide from its sulfonamide cousin. In addition, solution studies elucidated a greater preference for monomers with the amide arms. The low affinity for Cl^- and increased response to TFA indicate this may be a good strategy for increasing oxoanion selectivity.

4. Experimental

4.1 General

2,6-Bis(2-ethynylaniline)pyridine **3** was synthesized using previously reported procedures (19, 23). ^1H and ^{13}C NMR spectra were obtained on an Inova 500 MHz (^1H 500.10 MHz, ^{13}C 125.75 MHz) or Bruker Avance-III-HD 600 MHz (^1H 599.98 MHz, ^{13}C 150.87 MHz) spectrometer with a Prodigy multinuclear broadband BBO CryoProbe. Chemical shifts (δ) are expressed in ppm relative to tetramethylsilane (TMS) using residual non-deuterated solvent (CDCl_3 : ^1H 7.26 ppm, ^{13}C 77.0 ppm). UV-Vis spectra were recorded on a Hewlett-Packard 8453 UV-Vis spectrophotometer using a 265 nm high-pass filter. Fluorescence spectra were recorded on a Horiba Jobin-Yvon FluoroMax-4 fluorescence spectrophotometer equipped with an integrating sphere in O_2 -containing solvents. Unless otherwise specified, all reagents were purchased and used as received. Dry solvents were obtained from distillation using published literature procedures directly before use.

4.2 Synthesis of **2**

To a vigorously stirred, biphasic mixture of dianiline **3** (100 mg, 0.24 mmol), EtOAc (10 mL), H_2O (10 mL) and K_2CO_3 (70.8 mg, 0.51 mmol) was added 3,5-dinitrobenzoyl chloride

(111 mg, 0.48 mmol) in EtOAc (2 mL) dropwise via syringe over 2 min. A precipitate formed after 10 min. After stirring vigorously for 16 h, the precipitate was isolated and recrystallized from hot EtOAc to yield **2** (62 mg, 45%) as a pale yellow powder. MP >210°C (dec) ¹H NMR (600 MHz, CDCl₃): δ 9.07 (s, 4H), 8.91 (s, 2H), 8.80 (s, 2H), 8.36 (d, *J* = 8.7 Hz, 2H), 7.84 (t, *J* = 7.7 Hz, 1H), 7.57–7.60 (m, 4H), 7.53 (d, *J* = 8.7 Hz, 2H), 1.39 (s, 18H); ¹³C NMR (151 MHz, CDCl₃): δ 176.28, 159.95, 148.65, 148.47, 143.15, 137.67, 137.60, 136.31, 128.73, 128.49, 127.50, 126.23, 121.31, 119.57, 111.08, 96.22, 85.16, 34.79, 31.31; IR (KBr) ν 3389 (NH), 2207 (C≡C), 1655 (C=O); HRMS (ESI) for C₄₃H₃₅N₇O₁₀ [M+H]⁺: calcd 810.2524, found 810.2555.

4.3 Crystal data for **2**

Diffraction intensities were collected at 173(2) K on a Bruker Apex2 CCD diffractometer using MoK α radiation. The space group was determined based on intensity statistics. Absorption correction was applied by SADABS (39). The structure was solved by direct methods and Fourier techniques and refined on F^2 using full matrix least-squares procedures. All non-H atoms were refined with anisotropic thermal parameters. H atoms were refined in calculated positions in a rigid group model except those at the N atoms involved in H-bonds. Positions of these H atoms were found on the residual density map and they were refined with isotropic thermal parameters. In the crystal structure there are two solvent CH₂Cl₂ molecules. All calculations were performed by the Bruker SHELXTL (v. 6.10) package (40).

Crystal data: C₄₅H₄₀Cl₅N₇O₁₀, *M* = 1016.09, 0.20 × 0.10 × 0.02 mm, *T* = 173(2) K, Triclinic, space group *P*-1, *a* = 11.032(2) Å, *b* = 13.691(2) Å, *c* = 15.767(3) Å, α = 98.225(4), β = 91.235(3), γ = 95.894(3), *V* = 2342.9(7) Å³, *Z* = 2, *D*_c = 1.440 Mg/m³, μ (Mo) = 0.375 mm⁻¹, *F*(000) = 1048, 2 θ _{max} = 50.0°, 16887 reflections, 8166 independent reflections [*R*_{int} = 0.0689], *R*1 = 0.0727, *wR*2 = 0.1380 and GOF = 1.050 for 8166 reflections (616 parameters) with *I* > 2 σ (*I*), *R*1 = 0.1622, *wR*2 = 0.1730 and GOF = 1.050 for all reflections, max/min residual electron density +0.587/−0.412 eÅ⁻³. CCDC 1406414.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was funded initially by the National Science Foundation (CHE-0718242) and subsequently supported by the National Institutes of Health (R01-GM087398) and the Oregon Nanoscience and Microtechnologies Institute. This publication was made possible, in part, by the Biomolecular Mass Spectrometry Core of the Environmental Health Sciences Core Center at Oregon State University, grant P30ES00210, National Institute of Environmental Health Sciences, National Institutes of Health. NIH grant R01-GM087398 funded early stage intellectual property that was licensed by SupraSensor Enterprises, a company co-founded by D.W.J. and M.M.H. O.B.B. is also a shareholder in this company.

References

1. Whitesides GM, Grzybowski B. Science. 2002; 295:2418. [PubMed: 11923529]
2. Yoshizawa M, Klosterman JK. Chem Soc Rev. 2014; 43:1885. [PubMed: 24169958]

3. Park JS, Karnas E, Ohkubo K, Chen P, Kadish KM, Fukuzumi S, Bielawski CW, Hudnall TW, Lynch VM, Sessler JL. *Science*. 2010; 329:1324. [PubMed: 20829481]
4. Carnes ME, Collins MS, Johnson DW. *Chem Soc Rev*. 2014; 43:1825. [PubMed: 24346298]
5. Ren C, Zhang J, Chen M, Yang Z. *Chem Soc Rev*. 2014; 43:7257. [PubMed: 25060777]
6. Zhang Z, Kim DS, Lin CY, Zhang H, Lammer AD, Lynch VM, Popov I, Miljani OŠ, Anslyn EV, Sessler JL. *J Am Chem Soc*. 2015; 137:7769. [PubMed: 25965790]
7. Knipe PC, Thompson S, Hamilton AD. *Chem Sci*. 2015; 6:1630.
8. Spence GT, Beer PD. *Acc Chem Res*. 2013; 46:571. [PubMed: 23190374]
9. Kim DS, Lynch VM, Park JS, Sessler JL. *J Am Chem Soc*. 2013; 135:14889. [PubMed: 24011216]
10. Black SP, Sanders JKM, Stefankiewicz AR. *Chem Soc Rev*. 2014; 43:1861. [PubMed: 24132207]
11. Park JS, Yoon KY, Kim DS, Lynch VM, Bielawski CW, Johnston KP, Sessler JL. *Proc Natl Acad Sci USA*. 2011; 108:20913. [PubMed: 22160675]
12. Han M, Michel R, He B, Chen YS, Stalke D, John M, Clever GH. *Angew Chem Int Ed*. 2012; 52:1319.
13. Gong HY, Rambo BM, Nelson CA, Lynch VM, Zhu X, Sessler JL. *Chem Commun*. 2012; 48:10186.
14. Gong HY, Rambo BM, Karnas E, Lynch VM, Sessler JL. *Nat Chem*. 2010; 2:406. [PubMed: 20414243]
15. Riddell IA, Ronson TK, Clegg JK, Wood CS, Bilbeisi RA, Nitschke JR. *J Am Chem Soc*. 2014; 136:9491. [PubMed: 24905797]
16. Moyer BA, Custelcean R, Hay BP, Sessler JL, Bowman-James K, Day VW, Kang SO. *Inorg Chem*. 2012; 52:3473. [PubMed: 23134587]
17. Vonnegut CL, Tresca BW, Johnson DW, Haley MM. *Chem-Asian J*. 2015; 10:522. [PubMed: 25586943]
18. Berryman OB, Johnson CA, Zakharov LN, Haley MM, Johnson DW. *Angew Chem Int Ed*. 2008; 47:117.
19. Carroll CN, Berryman OB, Johnson CA, Zakharov LN, Haley MM, Johnson DW. *Chem Commun*. 2009; 2520.
20. Johnson CA II, Berryman OB, Sather AC, Zakharov LN, Haley MM, Johnson DW. *Cryst Growth Des*. 2009; 9:4247.
21. Carroll CN, Coombs BA, McClintock SP, Johnson CA, Berryman OB, Johnson DW, Haley MM. *Chem Commun*. 2011; 47:5539.
22. Engle JM, Lakshminarayanan PS, Carroll CN, Zakharov LN, Haley MM, Johnson DW. *Cryst Growth Des*. 2011; 11:5144.
23. Engle JM, Carroll CN, Johnson DW, Haley MM. *Chem Sci*. 2012; 3:1105. [PubMed: 25328662]
24. Berryman OB, Johnson CA II, Vonnegut CL, Fajardo KA, Zakharov LN, Johnson DW, Haley MM. *Cryst Growth Des*. 2015; 15:1502.
25. Watt MM, Engle JM, Fairley KC, Robitshek TE, Haley MM, Johnson DW. *Org Biomol Chem*. 2015; 13:4266. [PubMed: 25758666]
26. Gavette JV, Mills NS, Zakharov LN, Johnson CA, Johnson DW, Haley MM. *Angew Chem Int Ed*. 2013; 52:10270.
27. Gavette JV, Klug CM, Zakharov LN, Shores MP, Haley MM, Johnson DW. *Chem Commun*. 2014; 50:7173.
28. Gavette JV, Evoniuk CJ, Zakharov LN, Carnes ME, Haley MM, Johnson DW. *Chem Sci*. 2014; 5:2899. [PubMed: 24976946]
29. Tresca BW, Zakharov LN, Carroll CN, Johnson DW, Haley MM. *Chem Commun*. 2013; 49:7240.
30. Watt MM, Zakharov LN, Haley MM, Johnson DW. *Angew Chem Int Ed*. 2013; 52:10275.
31. Berryman OB, Hof F, Hynes MJ, Johnson DW. *Chem Commun*. 2006:506.
32. Watt MM, Collins MS, Johnson DW. *Acc Chem Res*. 2013; 46:955. [PubMed: 22726207]
33. Wheeler SE, Bloom JWG. *J Phys Chem A*. 2014; 118:6133. [PubMed: 24937084]
34. Adriaenssens L, Gil-Ramírez G, Frontera A, Quiñero D, Escudero-Adán EC, Ballester P. *J Am Chem Soc*. 2014; 136:3208. [PubMed: 24494711]

35. Adriaenssens L, Estarellas C, Vargas Jentzsch A, Martinez Belmonte M, Matile S, Ballester P. J Am Chem Soc. 2013; 135:8324. [PubMed: 23672588]
36. Berryman OB, Sather AC, Hay BP, Meisner JS, Johnson DW. J Am Chem Soc. 2008; 130:10895. [PubMed: 18661980]
37. Morris, GA. Diffusion-Ordered Spectroscopy. John Wiley and Sons; Chichester, UK: 2009.
38. Lamm JH, Niermeier P, Mix A, Chmiel J, Neumann B, Stammeler HG, Mitzel NW. Angew Chem Int Ed. 2014; 53:7938.
39. Sheldrick, GM. Bruker/Siemens Area Detector Absorption Correction Program. Bruker AXS; Madison, WI: 1998.
40. SHELXTL-6.10. Program for Structure Solution, Refinement and Presentation. BRUKER AXS Inc.; 5465 East Cheryl Parkway, Madison, WI 53711-5373 USA:

Figure 1. Sulfonamide **1** (left) and X-ray crystal structure of **(H1⁺·Cl⁻)₂** (right). Three hydrogen bonds to each Cl⁻ are shown. Nitroarenes are tilted up by the sulfonyl oxygens and a 2+2 dimer forms with Cl⁻ (or H₂O).

Figure 2.

Absorbance (left) and emission (right) spectra of **2** and H2^+ as Cl^- and TFA^- salt ($[\text{2}] = 10 \mu\text{M}$, **2** and $\text{H2}^+\bullet\text{TFA}^-$ Ex = 380 nm, $\text{H2}^+\bullet\text{Cl}^-$ Ex = 395; in wet, O_2 -containing CHCl_3).

Figure 3.
Top view of the X-ray crystal structure of $\text{H}_2^+\cdot\text{Cl}^-$ showing the asymmetric unit with atom labels. Hydrogens not involved in hydrogen bonds and two CH_2Cl_2 molecules have been omitted for clarity.

Figure 4.
Dimeric structure of $(\text{H}_2^+ \cdot \text{Cl}^-)_2$ which is stitched together by three hydrogen bonds to each Cl atom.

Figure 5. ^1H NMR spectra of **2** (1.0 mM, bottom) and $\text{H}2^+\cdot\text{Cl}^-$ (1.0 mM, top) in CDCl_3 . Water peak broadening is due to excess HCl.

Figure 6. Stacked plot showing **2** titrated with Cl^- in water saturated CDCl_3 ($[\mathbf{2}] = 1.0 \text{ mM}$). The amide peak shifts downfield slightly, while other protons remain unchanged.

Scheme 1.
Synthesis of bis(amide) **2**.