

# **Anion Binding Induces Helicity in a Hydrogen Bonding Receptor: Crystal Structure of a**

## **2,6-Bis(anilinoethynyl)pyridinium Chloride**

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## RECEPTOR SYNTHESIS AND CHARACTERIZATION

**General:**  $\text{CDCl}_3$ ,  $\text{CD}_2\text{Cl}_2$ ,  $d_7$ -DMF and  $d_8$ -toluene were obtained from Cambridge Isotope Laboratories, Inc., Andover, MA, and used without further purification. All other materials were obtained from TCI-America, Sigma-Aldrich, Acros and Strem and used as received. All glassware was flame dried immediately prior to use. Nuclear Magnetic Resonance  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on a Varian INOVA 300 (299.935) and 125 (125.751) MHz spectrometer respectively. Variable temperature  $^1\text{H}$  NMR experiments were performed on a Bruker DRX-600 spectrometer with a 5mm QNP probe. Chemical shifts ( $\delta$ ) are expressed as ppm downfield from tetramethylsilane using either the residual solvent peak as an internal standard ( $\text{CDCl}_3$   $^1\text{H}$ : 7.27 ppm,  $^{13}\text{C}$ : 77.00 ppm). Signal patterns are indicated as br, broad; s, singlet; d, doublet; t, triplet; m, multiplet. Coupling constants ( $J$ ) are given in hertz. Melting points were determined with a Meltemp II apparatus or a TA Instruments DSC 2920 Modulated DSC. Column chromatography was performed on Whatman reagent grade silica gel (230-400 mesh).

**2,6-bis(anilinoethynyl) pyridine  $\alpha$ -chloroacetamide intermediate.** A solution of chloroacetyl chloride (571 mg, 5.1 mmol) in  $\text{CH}_2\text{Cl}_2$  (10 mL) was added to a stirred, deoxygenated solution of alkynyl pyridine **2** (395 mg, 0.94 mmol) and  $\text{Et}_3\text{N}$  (379 mg, 3.76 mmol) in  $\text{CH}_2\text{Cl}_2$  (10 mL). The reaction was stirred for 12 h at rt under  $\text{N}_2$  and then concentrated in vacuo.  $\text{CH}_2\text{Cl}_2$  was added and the organic layer was washed thrice with water, dried over  $\text{MgSO}_4$ , and concentrated in vacuo. The crude material was filtered through a 2.5 cm silica plug (1:1 hexanes:EtOAc) and concentrated to afford the  $\alpha$ -chloroacetamide intermediate (476 mg, 89%) as a pale brown solid. Mp: 193 °C.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.23 (br s, 2H), 8.30 (d,  $J$  = 8.3 Hz, 2H), 7.72 (t,  $J$  = 8.3 Hz, 1H), 7.64 (d,  $J$  = 2.1 Hz, 2H), 7.52 (d,  $J$  = 8.1 Hz, 2H), 7.43 (dd,  $J$  = 8.1, 2.1 Hz, 2H), 4.27 (s, 4H), 1.31 (s, 18H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  163.62, 147.46, 143.19, 136.83, 135.83, 129.32, 127.87, 126.20, 119.07, 111.15, 94.78, 84.80, 43.21, 34.41, 31.10. IR (neat)  $\nu$  3363, 2962, 2868, 2207, 1691, 1523  $\text{cm}^{-1}$ . UV-Vis ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\text{max}}$  ( $\epsilon$ ) 254 (52,600), 293 (27,700), 335 (27,600) nm. MS (CI pos)  $m/z$  (%): 578 ( $\text{M}^+$ +4, 15), 577 ( $\text{M}^+$ +3, 23), 576 ( $\text{M}^+$ +2, 75), 575 ( $\text{MH}^+$ , 38), 574 ( $\text{M}^+$ , 100);  $\text{C}_{33}\text{H}_{33}\text{Cl}_2\text{N}_3\text{O}_2$  (574.54).

**2,6-bis(anilinoethynyl) pyridine  $\alpha$ -thioacetate amide (**1**).** Potassium thioacetate (16 mg, 0.14 mmol) was added to a stirred, deoxygenated solution of the  $\alpha$ -chloro amide intermediate (see above) (34 mg, 0.06 mmol) in DMF (3 mL). The reaction was stirred for 12 h at rt under  $\text{N}_2$  and then concentrated in vacuo. The crude material was filtered through a 2.5 cm silica plug (1:1 hexanes:EtOAc) and purified via Chromatotron (2:1 hexanes: EtOAc) to afford **1** (35 mg, 92%) as a spongy light yellow solid. Recrystallization by diffusion (hexanes:EtOAc) afforded colorless crystals. Mp: 94 °C.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  8.75 (br s, 2H), 8.28 (d,  $J$  = 8.7 Hz, 2H), 7.75 (br s, 3H), 7.58 (d,  $J$  = 2.4 Hz, 2H), 7.39 (dd,  $J$  = 8.7, 2.4 Hz, 2H), 3.76 (s, 4H), 2.34 (s, 6H), 1.28 (s, 18H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  195.20, 166.16, 146.81, 143.31, 136.59, 136.54, 129.38, 127.68, 126.57, 119.45, 110.79, 94.31, 85.15, 34.27, 33.99, 31.05, 30.13. IR (neat)  $\nu$  3339, 3058, 2962, 2868, 2208, 1693, 1518  $\text{cm}^{-1}$ . UV-Vis ( $\text{CH}_2\text{Cl}_2$ ):  $\lambda_{\text{max}}$  ( $\epsilon$ ) 253 (48,200), 291 (24,500), 330 (21,600) nm. MS (CI pos)  $m/z$  (%): 656 ( $\text{M}^+$ +2, 19), 655 ( $\text{MH}^+$ , 44), 654 ( $\text{M}^+$ , 100);  $\text{C}_{37}\text{H}_{39}\text{N}_3\text{O}_4\text{S}_2$  (653.85).

**General preparation of  $\text{H1}^+\text{Cl}^-$ .** 2,6-bis(anilinoethynyl) pyridine  $\alpha$ -thioacetate amide (**1**) (2 mg, 0.0031 mmol) is dissolved in 600 microliters of deuterated solvent. A pipette with 2 ml bulb was used to pass HCl gas through the solution 25 times. Further deuterated solvent was added as needed to the resulting bright yellow solution to return to the original sample volume.

## **VARIABLE TEMPERATURE DATA**

### **$^1\text{H}$ NMR chemical shifts of **1** at 300 K**

$^1\text{H}$  NMR (600 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta$  8.85 (br, 2H), 8.26 (d,  $J$  = 8.8 Hz, 2H), 7.88 (br, 1H), 7.77 (d,  $J$  = 12 Hz, 2H), 7.62 (s, 2H), 7.46 (dd,  $J$  = 12 Hz, 2H), 3.83 (br, 4H), 2.37 (s, 6H), 1.32 (s, 18H).

$^1\text{H}$  NMR (600 MHz,  $d_7$ -DMF):  $\delta$  9.77 (s, 2H), 8.07 (t,  $J$  = 6 Hz, 1H), 8.02 (br, 2H), 7.90 (d,  $J$  = 7.8 Hz, 2H), 7.70 (d,  $J$  = 2.3 Hz, 2H), 7.57 (dd,  $J$  = 8.7 Hz, 2H), 4.05 (s, 4H), 2.44 (s, 6H), 1.35 (s, 18H).

$^1\text{H}$  NMR (600 MHz,  $d_8$ -toluene):  $\delta$  8.83 (s, 2H), 8.76 (d,  $J$  = 8.8 Hz, 2H), 7.62 (d,  $J$  = 2.3, 2H), 7.46 (d,  $J$  = 7.8 Hz, 2H), 7.16 (dd,  $J$  = 8.8 Hz, 2H), 7.06 (t,  $J$  = 7.8 Hz, 1H), 3.38 (s, 4H), 1.84 (s, 6H), 1.13 (s, 18H).

### **$^1\text{H}$ NMR chemical shifts of $\text{H1}^+\text{Cl}^-$ at 300 K**

$^1\text{H}$  NMR (600 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta$  9.51 (s, 2H), 8.27 (t,  $J$  = 8.0 Hz, 1H), 8.13 (d,  $J$  = 8.8 Hz, 2H), 7.85 (d,  $J$  = 8.0 Hz, 2H), 7.65 (s, 2H), 7.54 (dd,  $J$  = 8.8 Hz, 2H), 4.23 (s, 4H), 2.34 (s, 6H), 1.33 (s, 18H).

$^1\text{H}$  NMR (600 MHz,  $d_8$ -toluene):  $\delta$  9.95 (s, 2H), 8.53 (d,  $J$  = 8.0 Hz, 1H), 7.63 (br, 2H), 7.08 (br, 6H), 4.68 (s, 4H), 1.89 (s, 6H), 1.18 (s, 18H).

### **$^1\text{H}$ NMR chemical shifts of $\text{H1}^+\text{Cl}^-$ at 222 K**

$^1\text{H}$  NMR (600 MHz,  $d_8$ -toluene):  $\delta$  10.13 (s, 2H), 8.54 (br, 2H), 7.68 (br, 1H), 7.08 (br, 4H), 6.90 (br, 2H), 4.65 (s, 4H), 1.80 (s, 6H), 1.19 (s, 18H).

### **$^1\text{H}$ NMR chemical shifts of $\text{H1}^+\text{Cl}^-$ at 205 K**

$^1\text{H}$  NMR (600 MHz,  $\text{CD}_2\text{Cl}_2$ ):  $\delta$  9.52 (s, 2H), 8.27 (t,  $J$  = 8.0 Hz, 1H), 7.92 (d,  $J$  = 8.8 Hz, 2H), 7.83 (br, 2H), 7.85 (s, 2H), 7.49 (d,  $J$  = 8.1 Hz, 2H), 4.17 (s, 4H), 2.32 (s, 6H), 1.23 (s, 18H).

## CRYSTALLOGRAPHY

***X-ray Crystallography.*** The X-ray diffraction data for **2,6-bis(anilinoethynyl) pyridine  $\alpha$ -thioacetate amide (1)**, and **H<sup>1+</sup>Cl<sup>-</sup>** were collected on a Bruker Smart Apex diffractometer at -173 K using MoK $\alpha$  radiation ( $\lambda = 0.71073 \text{ \AA}$ ). Absorption corrections were applied by SADABS<sup>S1</sup>. Crystal structure were solved by direct methods. The structure of **1** was determined in the non-centrosymmetrical space group *Pc* and it was found that the investigated crystal of **1** is a racemic twin with a ratio of two phases 25/75. Some of the *t*-Bu groups in **1** are disordered over two positions. All non-H atoms in both structures were refined with anisotropic thermal parameters except those in the disordered *t*-Bu groups in **1** which were refined with isotropic thermal parameters and C-C distances of  $1.53 \text{ \AA}$  were used in the refinement as a target for the C-C bonds in these groups. H atoms in both structures were refined in calculated positions in a rigid group model except H atoms on N atoms involved in H-bonds. These H atoms were found from the F-maps and refined with isotropic thermal parameters and with restrictions; the N-H distance of  $1.00 \text{ \AA}$  was used as a target for the N-H bonds. In the crystal structure of **1** two dichloromethane solvent molecules fill the empty spaces created between main molecules. It was found that these positions are not fully occupied by dichloromethane solvent molecules; the refinement shows that occupation factors for both solvent molecules are close to 0.5 and such occupation factors were used in the final refinement of **1**. All calculations were performed using Bruker SHELXTL 6.10 package.<sup>S2</sup>

## References

- S1. Sheldrick, G. M.; SADABS: University of Göttingen, Germany, 1995.
- S2. Bruker; SHELXTL 6.10; Bruker AXS Inc.: Madison, Wisconsin, USA, 2000.