

Supporting Information

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A Fluorescent Polymeric INHIBIT Logic Gate based on the Natural Product Quinidine

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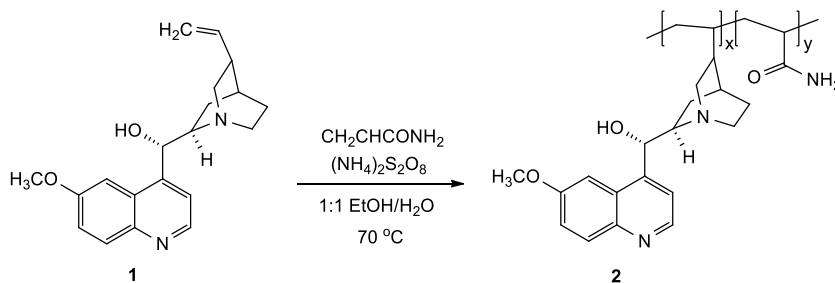
Chemicals

Ammonium persulfate (Sigma Aldrich, 99%), hydrochloric acid (Fisher Scientific, 375), ethanol (Carlo Erba, HPLC grade), methanesulfonic acid (Sigma Aldrich, 99%), 25% tetramethylammonium hydroxide in water (Fluke, 99%), quinidine sulfate dihydrate (Sigma Aldrich, 85%), sodium chloride (Sigma Aldrich, 99%) were all used as received. Silica gel on aluminium foil (with fluorescent indicator 254 nm, Fluka analytical) were used for thin-layer chromatography (TLC). 4 Å molecular cylinder sieves (Aldrich) were dried in a furnace at 330 °C for 48 hours before use and stored in an oven at ~100 °C.

Instrumentation

Melting points were measured using a Stuart SMP40 automatic melting point apparatus. An IKA C-MAG HS 7 hotplate with IKA ETS-D5 temperature probe was used for the copolymerization reactions at 70 °C. The centrifuge was an International Clinical Centrifuge Model 40652H. Fourier transform infrared (FTIR) spectra were recorded using a Shimadzu IR–Affinity-1 spectrophotometer. Nuclear Magnetic Resonance (NMR) spectra were recorded with a Bruker Avance III HD NMR equipped with an Ascend 500 11.75 Tesla superconducting magnet and 5 mm PABBO probe at operating frequencies of 500.13 MHz. for ¹H nuclei, respectively. Spectra were processed with TOPSPIN® V3.5p17 software. Chemical shifts were calibrated against tetramethylsilane (TMS) ($\delta = 0.00$ ppm). UV-visible absorption spectra were recorded on a Jasco V650 spectrophotometer connected to a PC running Windows XP and the spectra analysed with Spectra Manager Suite.® The instrumentation parameters were set to medium response, a bandwidth of 1.0 nm and a scan speed of 200 nm min⁻¹. Fluorescence measurements were recorded with a Jasco FP-8300 spectrofluorimeter analysed with Spectra Manager Suite®. Bandwidth wavelength was set at 2.5 nm, response time of 50 msec, and scanning speed 200 nm min⁻¹. Spectra were background subtracted for solvent. Quartz SUPRASIL cuvettes (101-10-40) with 10 mm pathlength with transparent windows on all four sides were used.

Synthesis and Characterisation



Poly(quinidine-co-am) 2

The procedure was based on literature synthesis for the stereoisomer; poly(quinine-co-am).^{S1} Quinidine sulfate dihydrate **1** (0.98 g, 1.3 mmol), acrylamide (0.32 g, 4.5 mmol), and ammonium persulfate (0.027 g, 0.12 mmol) were dissolved in 1:1 H₂O/EtOH (5 mL) and mixed with a magnetic stir bar in a sealed 50 mL round-bottom flask under nitrogen and heated to 70 °C. A brown off-white suspension was centrifuged and washed multiple times with ethanol. The poly(quinidine-co-am) **2** was dried under vacuum to give 208 mg of off-white flakes. The copolymer was characterised using ¹H NMR by dissolving the copolymer in DMSO-*d*₆. *R*_f = 0.15 (CH₂Cl₂), m.p. 295 °C; ¹H NMR (500 MHz, DMSO-*d*₆, ppm): δ 8.73 (d, *J* = 8.5 Hz, 1H, Ar-H), 7.96 (d, 1H, *J* = 9.1 Hz, Ar-H), 7.55 (d, 1H, *J* = 4.3 Hz, Ar-H), 7.48 (d, 1H, *J* = 6.4 Hz, Ar-H), 7.42 (d, 2H, NH₂), 5.63 (d, 3H, *J* = 7.3 Hz, -CH), 5.38 (s, 1H, OH), 3.97 (m, 3H, *J* = 8.4 Hz, -OCH₃), 2.12 (s, 3H, -CH₃) 2.68-1.08 (m, quinuclidine, polymeric backbone), 1.09 (t, 3H, *J* = 7.0 Hz, -CH₃); IR (KBr disk, cm⁻¹): 3600-3080 (C-OH, N-H, =C-H) less broad than quinidine sulfate dihydrate, 1681 (C=O), 1591, 1504, 1477 (C=C), 1157-1000 (C-OH, C-O-C).

Quinidine sulfate dihydrate **1**

m.p. 219-222 °C; ¹H NMR (500 MHz, DMSO-*d*₆, ppm): δ 8.76 (d, 1H, *J* = 4.6 Hz, Ar-H), 8.00 (d, 1H, *J* = 9.3 Hz, Ar-H), 7.62 (d, 1H, *J* = 5.5 Hz, Ar-H), 7.46 (s, 2H, Ar-H), 7.44 (d, 1H, *J* = 2.6 Hz, Ar-H), 6.10 (m, 3H, *J* = 10.3 Hz, -CH₂), 5.70 (s, 1H, -OH), 5.20 (t, 2H, *J* = 1.4 Hz, -CH₂) 3.98 (s, 3H, -OCH₃), 3.38 (s, 1H, HDO), 2.12 (d, 2H, *J* = 12.0 Hz, -CH₂), 1.86 (s, 1H, -CH), 1.60 (m, 3H, *J* = 5.8 Hz, -CH), 1.30 (q, 1H, *J* = 6.5 Hz, -CH), 0.90 (t, 1H, *J* = 7.4 Hz, -CH); IR (KBr disk, cm⁻¹): 3550-2100 (C-OH, N-H, =C-H, -C-H), 1620 (C=O), 1591, 1504, 1477 (C=C), 1155-1000 (C-OH and C-O-C).

UV-Vis absorbance and Fluorescence Analysis

Quinidine sulfate dihydrate **1** and poly(quinidine-co-am) **2** were separately dissolved in 0.03 M methanesulfonic acid (pH 1.49) to give solutions with an absorbance less than 0.20. Then up to 10 drops of 0.010 mM disodium EDTA were added to 100 mL solutions of quinidine sulfate dihydrate and poly(quinidine-co-am). Titrations were performed using acid and base (TMAH) solution of various concentrations: 1000, 100, 10, 1.0 and 0.1 mM. UV-vis measurements were blanked with water. Absorbance and fluorescence measurements were recorded after each aliquot of acid with a pH electrode.

Fluorescence titrations of the monomer and copolymer were performed applying the Henderson-Hasselbalch equation,

$$\text{pH} = \text{p}K_a + \log \frac{[A^-]}{[HA]}$$

in which $\text{p}K_a$ represents the acid dissociation constant, $[A^-]$ is the concentration of the conjugate base and $[HA]$ is the concentration of the weak acid. The fluorescence intensity was plotted against pH and linearised version fitting $y = mx + c$ where the x-axis is the pH plotted against $\log \frac{[I_{\text{max}} - I]}{[I - I_{\text{min}}]}$ on the y-axis.

Fluorescence quantum yields were determined in water according to the equation below using quinine sulfate in 0.1 M H_2SO_4 as a standard.^{S2}

$$Q_S = Q_R \times \frac{I_S}{I_R} \times \frac{A_R}{A_S} \times \frac{\eta_S^2}{\eta_R^2}$$

where Q_S and Q_R are the quantum yield of the sample and reference (quinine sulfate, $\Phi_F = 0.55$), I_S and I_R are the area under curve for the sample and reference, A_R and A_S are the absorbance of the reference and sample, and η_S^2 and η_R^2 are the refractive indices, respectively. Typical values were 1.33 for the refractive indices and absorbances of 0.10 ± 0.05 for samples excited at 350 nm.

References

- S1. C. Van Bruggen, D. Punihaole, A. R. Keith, A. J. Schmitz, J. Tolar, R. R. Frontiera and T. M. Reineke, *Proc. Natl. Acad. Sci.*, 2020, **117**, 32919.
- S2. J. R. Lakowicz, *Principles of Fluorescence Spectroscopy*, 2nd ed.; Springer, New York, 1999.

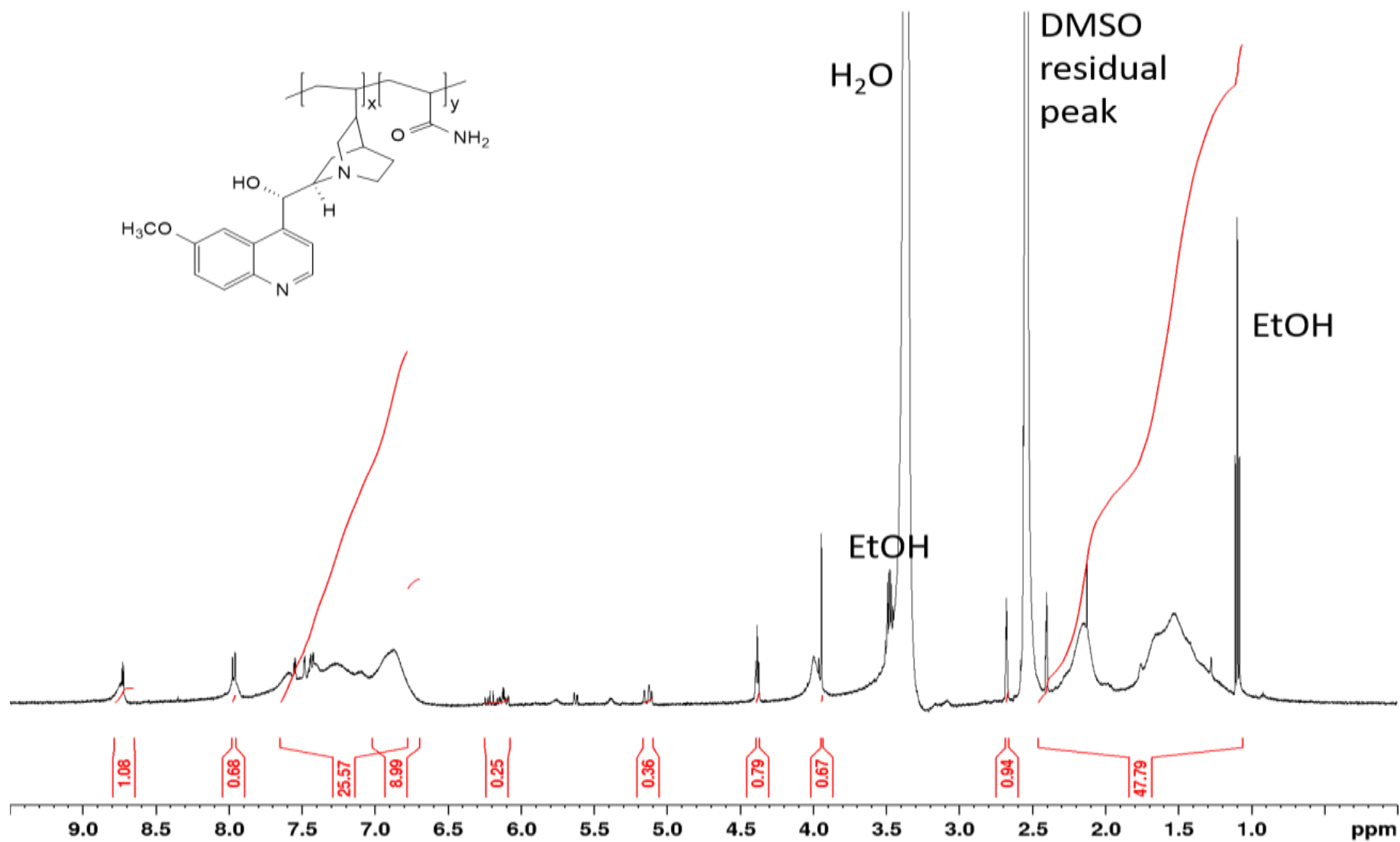


Fig. S1 ^1H NMR spectrum of 2 poly(quinidine-co-am) in $\text{DMSO-}d_6$.

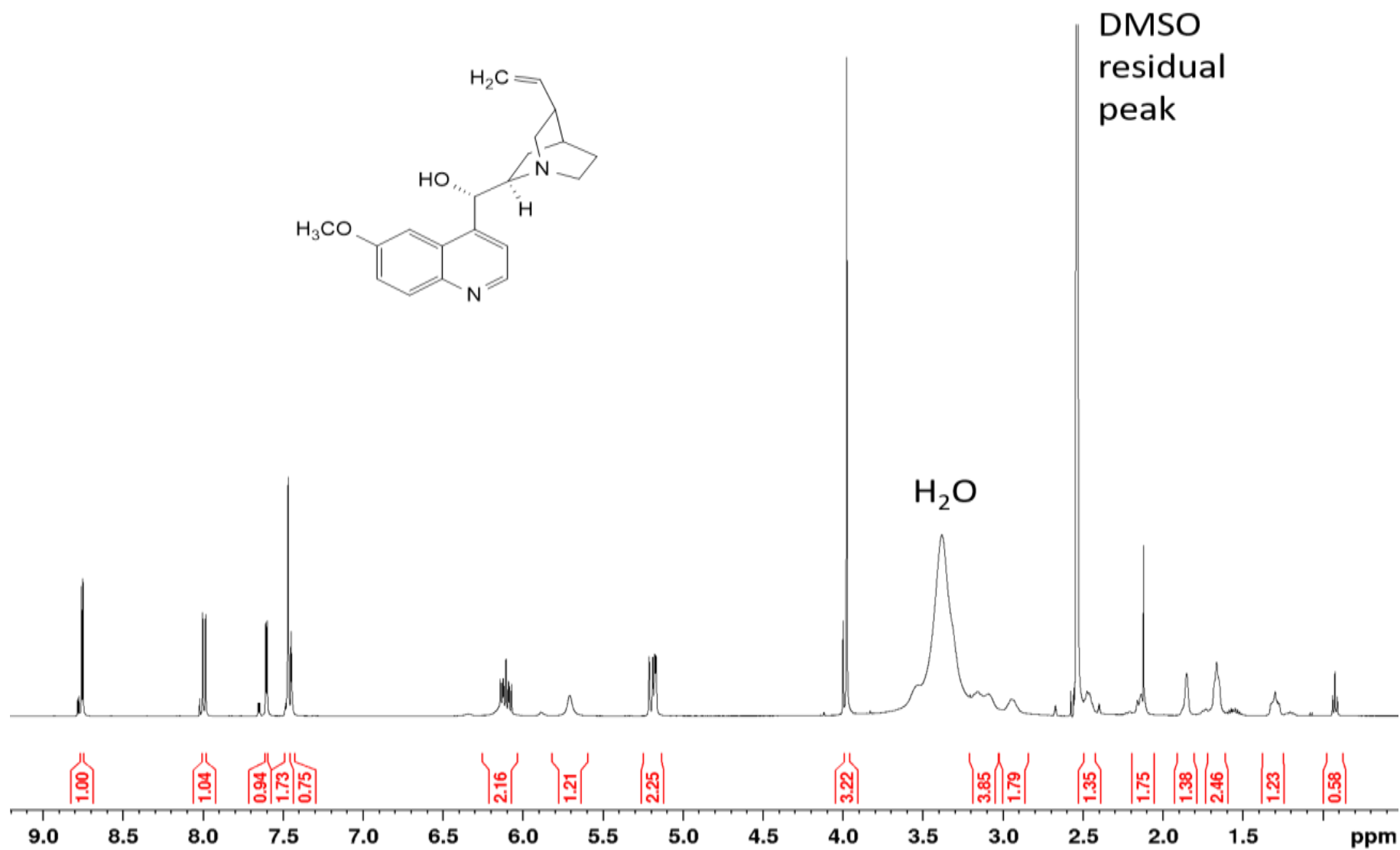


Fig. S2 ¹H NMR spectrum of 1 quinidine sulfate dihydrate in DMSO-*d*₆.

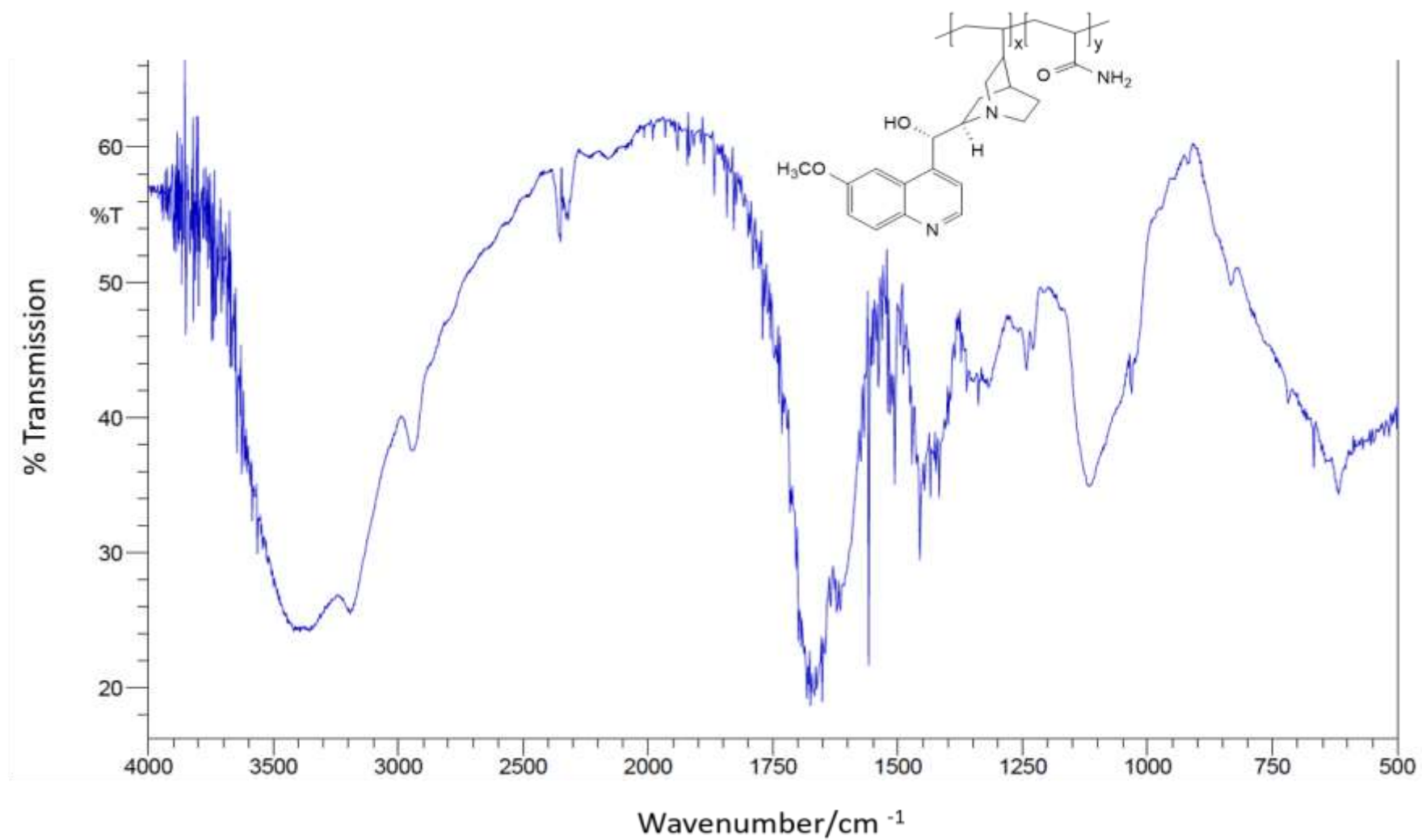


Fig. S3 IR spectrum of **2** poly(quinidine-co-am) as a KBr disk.

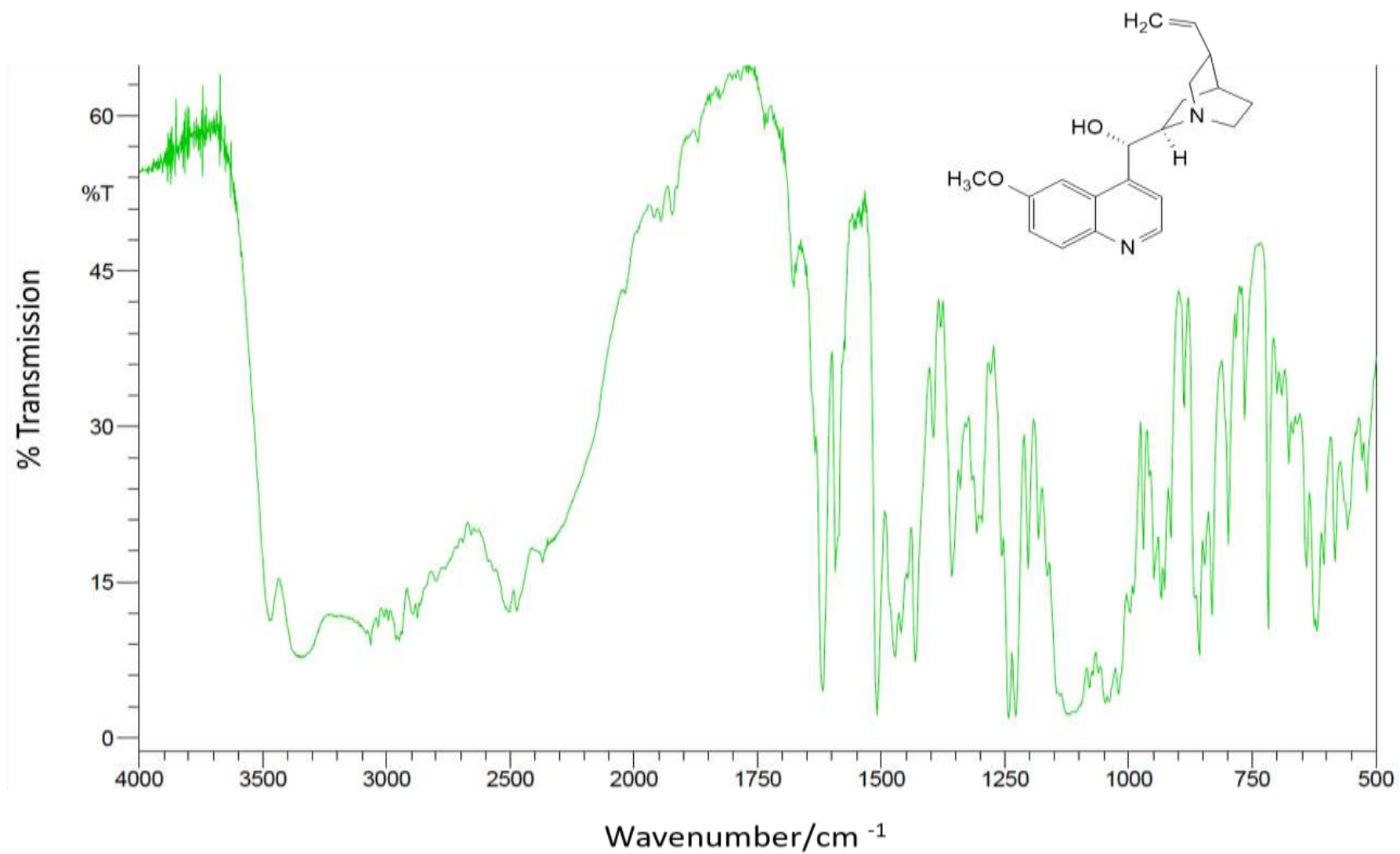


Fig. S4 IR spectrum of **1** quinidine sulfate dihydrate as a KBr disk.

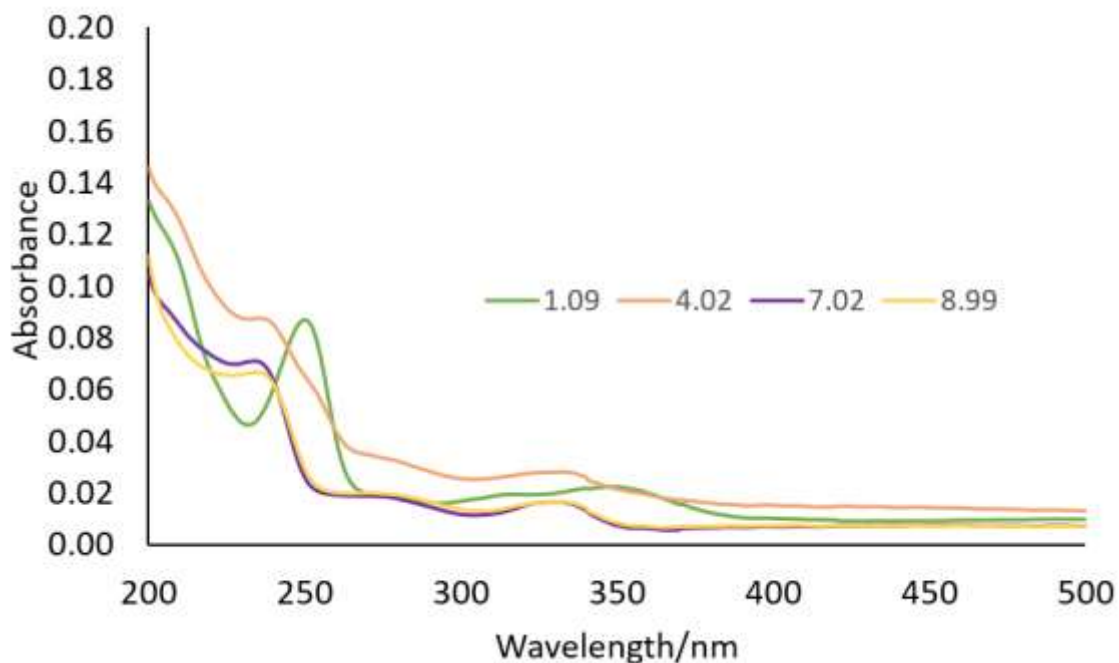


Fig. S5 Absorbance spectra of 0.046 g/L poly(quinidine-co-am) **2** in water titrated from 10^{-9} to 10^{-1} M H^+ .

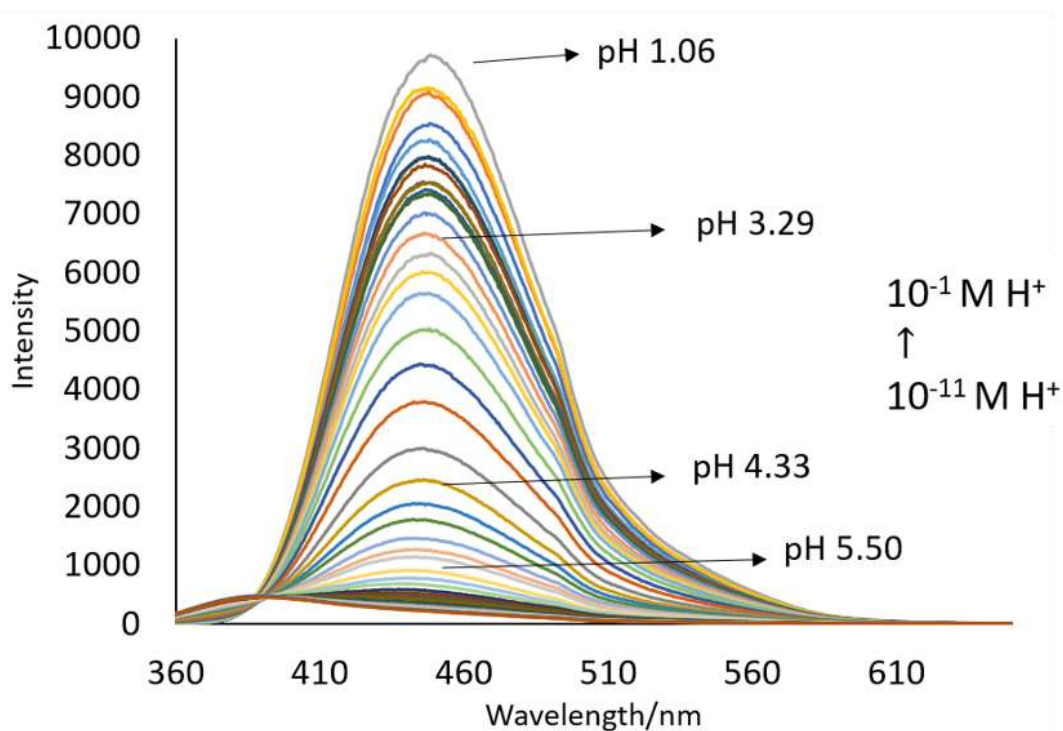


Fig. S6 Emission spectra of 0.046 g/L poly(quinidine-co-am) **2** in water $\lambda_{ex} = 350$ nm titrated from 10^{-11} to 10^{-1} M H^+ .

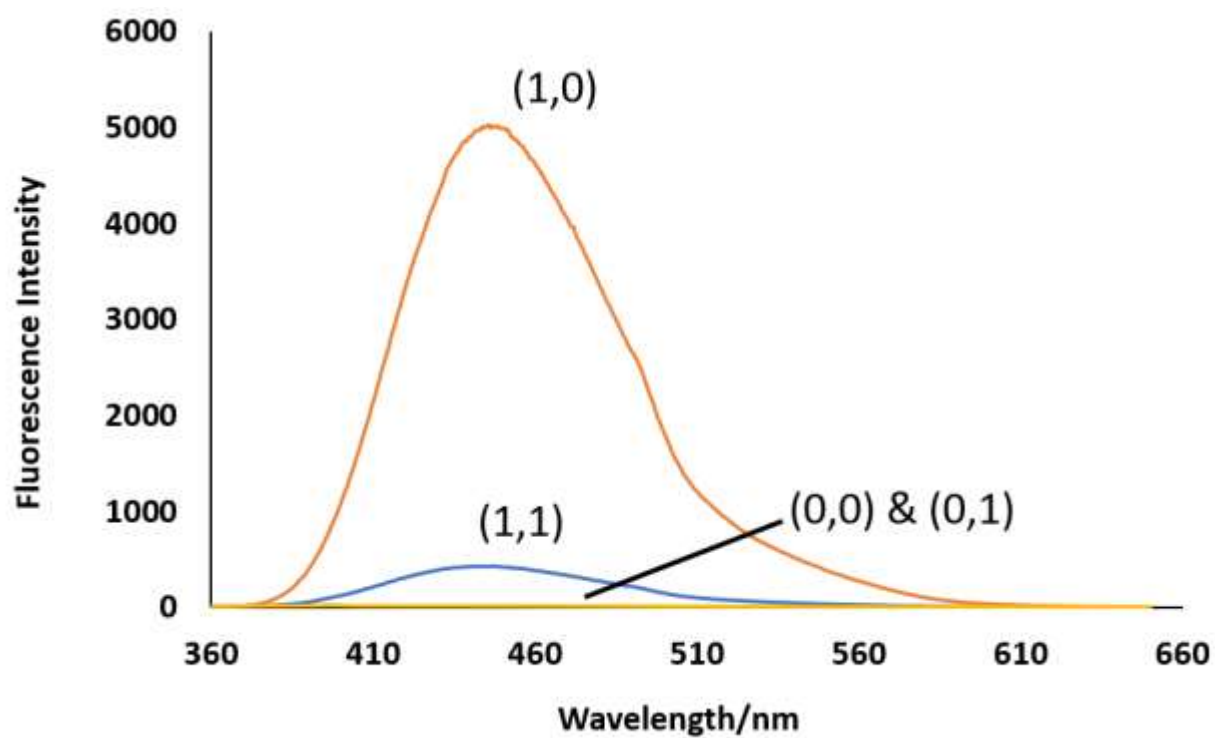


Fig. S7 Emission spectra of 30 μM quinidine **1** in water excited at 350 nm for the four input states associated with INHIBIT logic as specified in Table 2.