Electronic Supplementary Information (ESI)

The electrochemically tuneable recognition properties of an electropolymerised flavin derivative

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1. Synthesis

Synthesis of 2

To a solution of \(N\)-(10)-hydroxyhexyl flavin (0.45 g, 1.32 mmol) and 3-(pyrrol-1-yl) propanoic acid (0.18 g, 1.32 mmol) in DMF (25 mL), were added EDCI (0.25 g, 1.32 mmol) and DMAP (0.16 g, 1.32 mmol). The resulting solution was stirred at room temperature for 7 days. The solvent was evaporated under reduced pressure, and the residue was dissolved in DCM (100 mL) and washed with water (50 mL). The aqueous layer was further extracted with DCM (2 x 100 mL). The combined organic extracts were dried over MgSO\(_4\), filtered and evaporated. Column chromatography (silica gel, eluting with ethyl acetate/acetone, 90:10, v/v) afforded 2 as a yellow powder (66%). Mp 185-184°C (dec); \(v\)\(_{\text{max}}\) (KBr) 3436, 3103, 3028, 2926, 1721, 1675, 1578, 1539, 1502, 1462, 1400, 1351, 1264, 1168, 1092, 827, 724 cm\(^{-1}\); \(^1\)H NMR (200 MHz, acetone-d\(_6\)) \(\delta = 1.47\) (6H, m), 1.86 (2H, m), 2.43 (3H, s), 2.55 (3H, s), 2.81 (2H, t), 4.04 (2H, t), 4.19 (2H, t), 4.70 (2H, t), 5.94 (2H, t), 6.69 (2H, t), 7.77 (1H, s), 7.83 (1H, s), 10.09 (1H, s); MS (EI) m/z = 463 (M\(^+\)); HRMS (ES\(^+\)) calcd. for \(C_{25}H_{29}N_5O_4\) [M+1]\(^+\) 464.2292, found 464.2290.

Synthesis of 3

A mixture 1,4-dithiophen-2-ylbutane-1,4-dione (1.5 g, 5.8 mmol), 3-aminobenzoic acid (0.80 g, 5.8 mmol) and \(para\)-toluenesulfonic acid (0.150 g, 0.58 mmol) in dry toluene (15 mL) was heated to reflux using a Dean-Stark apparatus for 12 h. The toluene was removed using a rotary evaporator, and water (100 mL) was added. The crude product was removed by filtration, and purified on a silica gel column (eluting first with CH\(_2\)Cl\(_2\) to remove the unreacted dione and then with CH\(_2\)Cl\(_2\)/ethyl acetate 80/20, v/v) to yield the carboxylic acid derivative as an off-white powder (28%). Mp 268-269°C; \(v\)\(_{\text{max}}\) (KBr) 3065, 2958, 2843, 2646, 2532, 2843, 1700, 1588, 1487, 1454, 1294, 1196, 1046, 933, 826, 763, 698, 558 cm\(^{-1}\). \(^1\)H NMR (400 MHz, DMSO-d\(_6\)) \(\delta = 6.59\) (2H, s), 6.68 (2H, d), 6.87-
6.89 (2H, m), 7.29 (2H, dd), 7.62-7.65 (2H, m), 7.76-7.77 (1H, m), 8.07-8.11 (1H, m), 13.32 (1H, br.s); MS (EI) m/z = 351 (M+); HRMS (ES+) calcd. for C_{19}H_{13}NO_{2}S_{2} [M+1]^{+} 352.0460, found 352.0458.

To a solution of compound N-(10)-hydroxyhexyl flavin (0.5 g, 1.46 mmol) and bis-4,4'-[(2,2'-bithienyl)-N-pyrrolyl]-3-carboxybenzene (0.51 g, 1.46 mmol) in DMF (25 mL) were added EDCI (0.28 g, 1.46 mmol) and DMAP (0.18 g, 1.46 mmol). The resulting solution was stirred at room temperature for 3 days. The solvent was evaporated under reduced pressure, and the residue was dissolved in DCM (100 mL) and washed with water (50 mL). The aqueous layer was further extracted with DCM (2 x 100 mL). The combined organic extracts were dried over MgSO_{4}, filtered and evaporated. Column chromatography (silica gel, eluting with CH_{2}Cl_{2}/acetone, 90:10, v/v) afforded the product as a yellow powder (28%). Mp 233-235 °C; \( \nu_{\text{max}} \) (KBr) 3425, 3157, 3099, 2952, 2819, 1717, 1656, 1576, 1537, 1502, 1460, 1350, 1233, 1109, 843, 767, 697 cm\(^{-1}\); \(^1\)H NMR (200 MHz, CDCl\(_3\)) \( \delta = 1.55 \) (6H, m), 1.70 (2H, m), 2.45 (3H, s), 2.55 (3H, s), 4.30 (2H, t), 4.65 (2H, t), 7.35 (1H, s), 6.48 (2H, d), 6.50 (2H, s), 6.78 (2H, m), 7.00 (2H, dd), 7.49 (2H, m), 7.98 (1H, m), 8.06 (1H, s), 8.15 (1H, m), 8.40 (1H, s); MS (EI) m/z = 675 (M+); HRMS (ES+) calcd. for C\(_{37}\)H\(_{33}\)N\(_5\)O\(_4\)S\(_2\) [M+1]^{+} 676.2047, found 676.2046.

Synthesis of 5

To a solution of compound bis-4,4'-[(2,2'-bithienyl)-N-pyrrolyl]-3-carboxybenzene (0.51 g, 1.46 mmol) and penta nol (0.12 g, 1.46 mmol) in DMF (25 mL), were added EDCI (0.28 g, 1.46 mmol) and DMAP (0.18 g, 1.46 mmol). The resulting solution was stirred at room temperature for 3 days. The solvent was evaporated under reduced pressure, and the residue was dissolved in DCM (100 mL) and washed with water (50 mL). The aqueous layer was further extracted with DCM (2 x 100 mL). The combined organic extracts were dried over MgSO\(_4\), filtered and evaporated. Column chromatography (silica gel, eluting with CH\(_2\)Cl\(_2\)/acetone, 90:10, v/v) afforded the product as a white powder (48%). Mp 75-77 °C; \( \nu_{\text{max}} \) (KBr) 3100, 2953, 2858, 1717, 1291, 1234 cm\(^{-1}\); \(^1\)H NMR (200 MHz, CDCl\(_3\)) \( \delta = 0.90 \) (3H, t), 1.38 (4H, m), 1.72 (2H, m), 1.73 (2H, m), 4.28 (2H, t), 6.53 (4H, m), 6.80 (2H, m), 7.05 (2H, dd), 7.49 (2H, m), 7.99 (1H, m), 8.14 (1H, m); MS (EI) m/z = 421 (M+); HRMS (ES+) calcd. for C\(_{24}\)H\(_{23}\)NO\(_2\)S\(_2\) [M+1]^{+} 422.5760, found 422.5765.
2. Electrochemical measurements.

All electrochemical experiments were performed using a CH Instruments 620A electrochemical workstation. The electrolyte solution (0.1 M) was prepared from recrystallised Bu$_4$NPF$_6$ using either dry acetonitrile, toluene or dichloromethane. The solution was rigorously purged with nitrogen prior to use, and all electrochemical data were recorded under a nitrogen atmosphere. A three electrode configuration was used with a platinum disc (2mm diameter) working electrode, a Ag /AgCl reference electrode and a platinum wire as the counter electrode. Scan rate (unless otherwise stated) was 0.5 V s$^{-1}$.

The redox-based enhancement in recognition was calculated using a thermodynamic cycle which can be expressed mathematically using: $K_a(\text{red})/K_a(\text{ox}) = e^{-(nF/RT)(E_{1/2}(\text{bound}) - E_{1/2}(\text{unbound}))}$. $K_a(\text{red})$ and $K_a(\text{ox})$ are the association constants in the reduced and oxidized forms, and $E_{1/2}(\text{bound})$ and $E_{1/2}(\text{unbound})$ are the half-wave redox potentials in the receptor bound and unbound states.
Selected electrochemical data for derivative 2

CVs of electropolymerised 2 (following two electropolymerisation cycles from acetonitrile) recorded in CH$_2$Cl$_2$ (0.1 M Bu$_4$NPF$_6$). Scan rate = 1 (largest current), 0.75, 0.5, 0.25 (smallest current) Vs$^{-1}$. $\Delta E_{fwhm} = 0.209$ V, $1.19 \times 10^{-7}$ C, $\Gamma = 1.23 \times 10^{-12}$ mol cm$^{-2}$ (using 1 Vs$^{-1}$ scan rate).

CVs of electropolymerised 2 (following four electropolymerisation cycles from acetonitrile) recorded in CH$_2$Cl$_2$ (0.1 M Bu$_4$NPF$_6$). Scan rate = 1 (largest current), 0.75, 0.5, 0.25 (smallest current) Vs$^{-1}$. $\Delta E_{fwhm} = 0.225$ V, $1.59 \times 10^{-7}$ C, $\Gamma = 1.65 \times 10^{-12}$ mol cm$^{-2}$ (using 1 Vs$^{-1}$ scan rate).

CVs of electropolymerised 2 (following eight electropolymerisation cycles from acetonitrile) recorded in CH$_2$Cl$_2$ (0.1 M Bu$_4$NPF$_6$). Scan rate = 1 (largest current), 0.75, 0.5, 0.25 (smallest current) Vs$^{-1}$. $\Delta E_{fwhm} = 0.245$ V, $2.37 \times 10^{-7}$ C, $\Gamma = 2.45 \times 10^{-12}$ mol cm$^{-2}$ (using 1 Vs$^{-1}$ scan rate).
CVs showing the electropolymerisation of 2 (two cycles) recorded in CH₃CN (0.1 M Bu₄NPF₆). Scan rate = 0.5 Vs⁻¹

CVs showing the electropolymerisation of 2 (four cycles) recorded in CH₃CN (0.1 M Bu₄NPF₆). Scan rate = 0.5 Vs⁻¹
CVs showing the electropolymerisation of 2 (eight cycles) recorded in CH$_3$CN (0.1 M Bu$_4$NPF$_6$). Scan rate = 0.5 Vs$^{-1}$

CVs of electopolymerised 2 (following two electropolymerisation cycles from acetonitrile) recorded in CH$_2$Cl$_2$ (0.1 M Bu$_4$NPF$_6$) showing six successive cycles. Scan rate = 1 Vs$^{-1}$
Selected electrochemical data for derivative 3

CVs showing the electropolymerisation of 3 (~2 x 10^-4 M) (eight cycles) recorded in a 0.1 M Bu₄NPF₆ CH₃CN/ toluene (1:1) solution. Scan rate = 0.5 Vs⁻¹

CVs of electropolymerised 3 (following eight electropolymerisation cycles from acetonitrile) recorded in CH₂Cl₂ (0.1 M Bu₄NPF₆). Scan rate = 1 (largest current), 0.75, 0.5, 0.25 (smallest current) Vs⁻¹. ΔE_fwhm = 0.177 V, 4.643 x 10⁻⁸ C, Γ = 4.8 x 10⁻¹³ mol cm⁻² (parameters calculated using 1 Vs⁻¹ scan rate).

The Γ value of 4.8 x 10⁻¹³ mol cm⁻² and the peak current/scan rate linearity suggest a sub-monomolecular coverage.

CV studies recorded in toluene/CH₃CN (1:1) between -0.8 V and +2.0 V, showing the oxidation of the electropolymerised films of 3 (——) and in the presence of a 3 x 10⁻² M solution of 4 (-----). Scan rate = 0.5 Vs⁻¹.
CVs of electropolymerised 3 (following eight electropolymerisation cycles from acetonitrile/toluene 1:1, between -0.5 and +1.5 V) recorded in acetonitrile/toluene (1:1) (0.1 M Bu4NPF6). Scan rate = 1 (largest current), 0.75, 0.5 0.25, 0.125 (smallest current) Vs⁻¹.

CV studies showing the reduction of the electropolymerised films (fabricated by 8 cycles between -0.5 and +1.5 V in acetonitrile/toluene, 1:1) of 3 in acetonitrile/toluene, 1:1 (—) and in the presence of a 3 x 10⁻² M solution of 4, first scan (……), second scan (+ + +). Scan rate = 0.5 Vs⁻¹.
CV studies showing the reduction of the electropolymerised films (fabricated by 8 cycles between -0.5 and +1.5 V in acetonitrile/toluene, 1:1) of 3 in acetonitrile/toluene, 1:1 (—) and in the presence of a 3 x 10^{-2} M solution of 4 (-----). Scan rate = 0.5 V s^{-1}.

Selected electrochemical data for derivative 5

CVs showing the electropolymerisation of 5 (~2 x 10^{-4} M) (eight cycles) recorded in a 0.1 M Bu_{4}NPF_{6} CH_{3}CN/ toluene (1:1) solution. Scan rate = 0.5 V s^{-1}

CV studies showing the oxidation of the as-deposited electropolymerised films of 5 in CH_{3}CN/toluene 1,1 (v/v) (—) and in the presence of a 3 x 10^{-2} M solution of 4 (-----).