Supporting Information for

Rotamerism-Driven Large Magnitude Host-Guest Binding Change in a Crown Ether Derivatized Pyridinium-Phenolate Series

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1. Materials and General Characterization Methods.

All reagents for synthesis, N,N,N´,N´-tetramethylguanidine (TMG), potassium thiocyanate (KSCN), tetrabutylammonium tetrafluoroborate (n-Bu_4NBF_4) were purchased from Aldrich. The solvents for synthesis were dried and purified by standard procedures. THF were freshly distilled from sodium/benzophenone and DMF was dried over 3 Å molecular sieves. The acetonitrile employed for UV-Vis absorption and electrochemistry was Fluka spectroscopic grade.

All melting points were taken on a Kofler bench. IR spectra (cm^{-1}) were recorded on a Bruker Vertex 70 spectrometer. ^1H NMR (400 MHz) and ^{13}C NMR (100.6 MHz) spectra were measured with a Bruker Avance (Serie 400) spectrometer at 295 K. High resolution MS were measured with an Agilent Technologies 6510 (Q-TOF) Spectrometer using a dual ESI source.

The cyclic voltammetry experiments (using a computer-controlled Radiometer Voltalab 6 potentiostat with a three-electrode single-compartment cell; the working electrode was a platinum disk; a saturated calomel electrode (SCE) used as a reference was placed in a separate compartment) were performed at 300 K, in N_2-degassed acetonitrile with a constant concentration (0.1 M) of n-Bu_4BF_4. Ferrocene was used as an internal reference.

The absorption measurements were carried out with a Perkin Elmer Lambda 2 double beam UV-Vis spectrophotometers. The linearity of absorbance at λ_{MAX} as a function of concentration was checked to assert that all chromophores do not aggregate for concentration below 0.1 mM in acetonitrile.

The pK_a values of the chromophores have been determined by UV-Visible absorption methods. The measurements are performed in aqueous medium (acetonitrile / water: 1v / 1v). A large excess of tetramethyl guanidine base (0.02 M) is initially added in the solution containing the chromophore. Aliquots of a concentrated solution of hydrochloric acid (0.2M) are gradually added to decrease the pH. A typical evolution of the absorption spectrum of **T-C** as function of the pH is illustrated in the **Figure 1**.

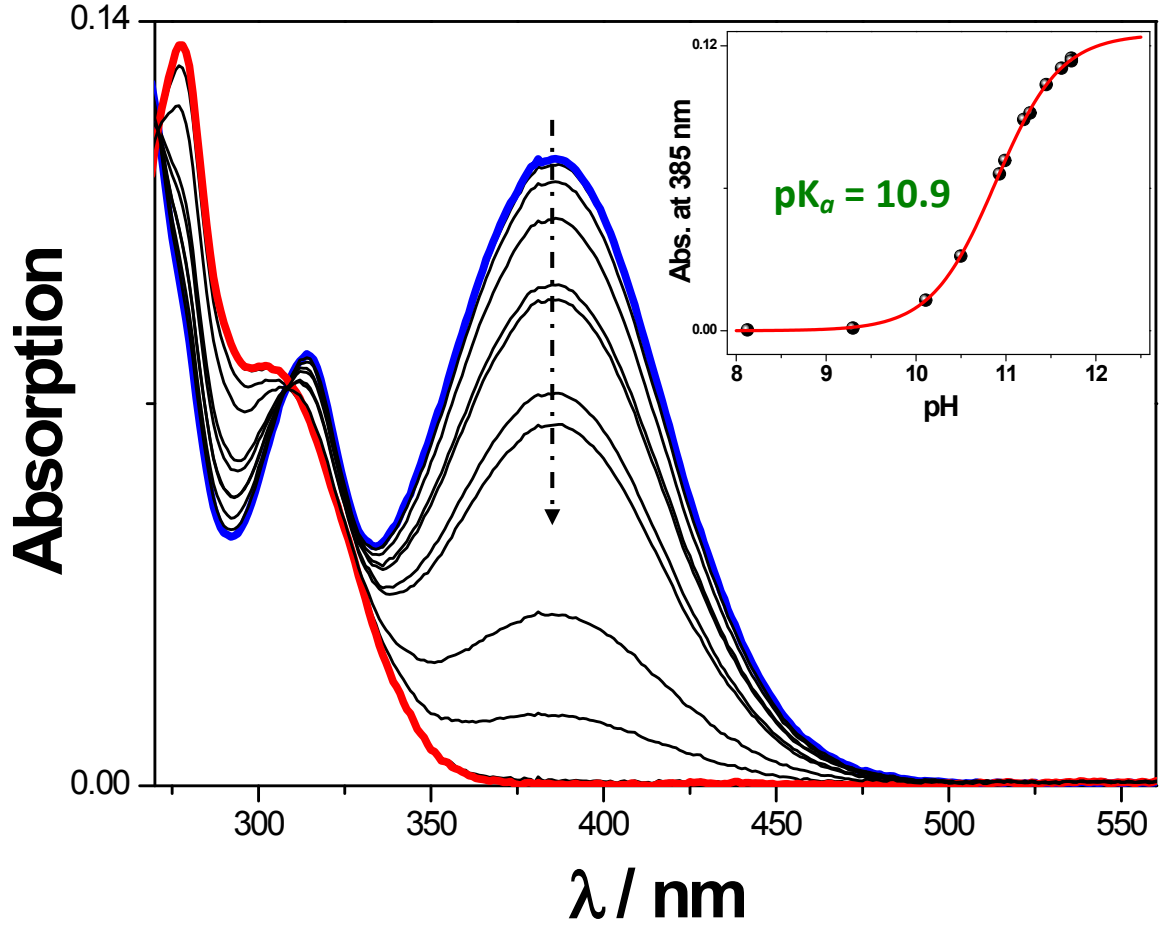
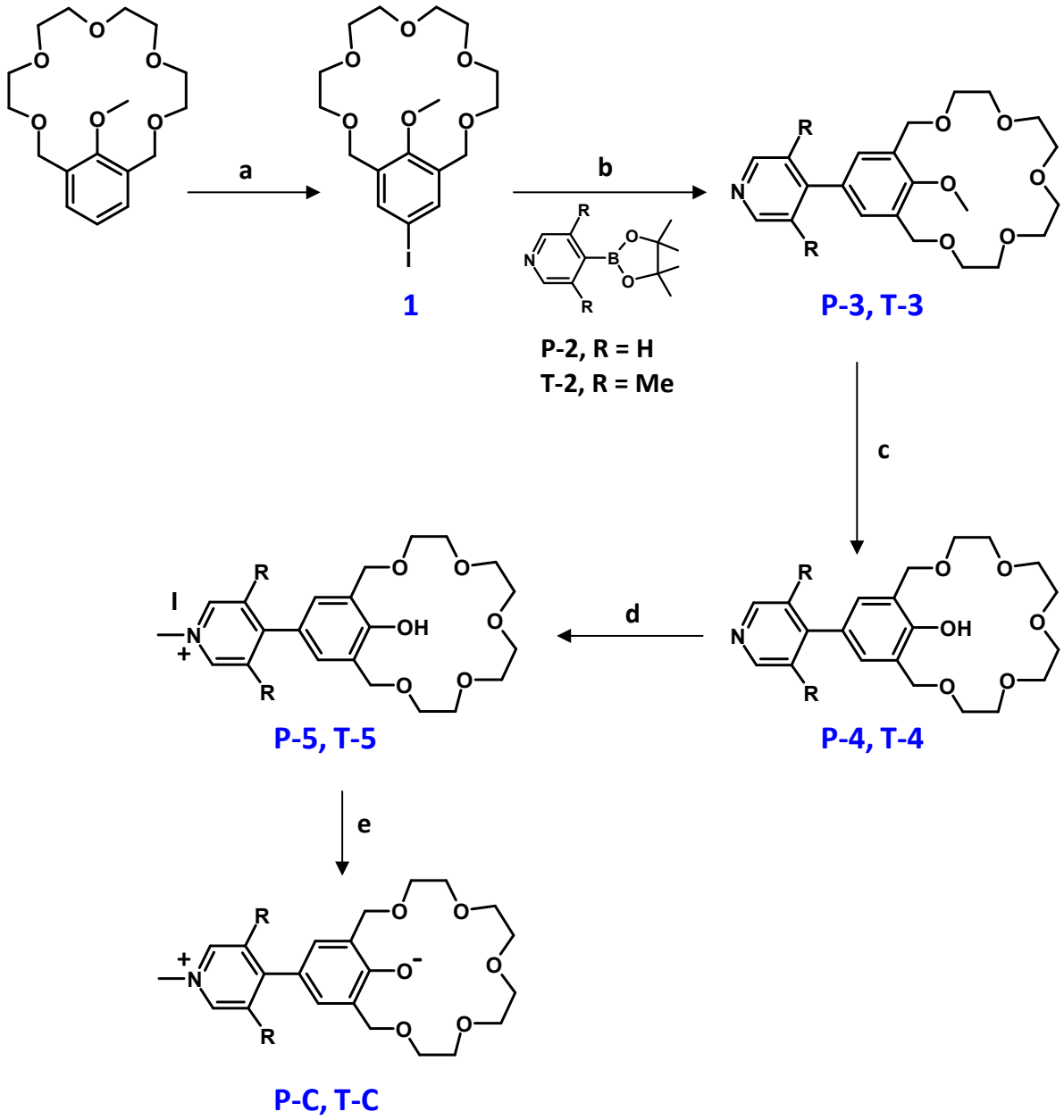


Figure 1. pH dependence of the absorption spectrum of **T-C**.
(solvent : ACN/Water 1v/1v)

2. Synthesis of the chromophores.

The detailed synthesis and characterization of model chromophores **P-M** and **T-M** have been previously reported in ref. [1]. The synthetic route for the synthesis of crown ether derivatives is depicted in the following scheme:



(a) I_2, $Ag_2CO_2CF_3$, $CHCl_3$, r.t., overnight, 90%. **(b)** $PdP(Ph_3)_4$, Cs_2CO_3, THF, reflux, overnight, 70.5 % (**P-3**) and 55.5 % (**T-3**) . **(c)** EtSH, NaH, DMF, 100°C, overnight, 78% (**P-4**) and 64 % (**T-4**). **(d)** MeI, acetone, reflux, overnight, 95 % (**P-5**) and 63.5 % (**T-5**). **(e)** Ag_2O, MeOH, r.t., 72 % (**P-C**) and 66 % (**T-C**).

The intermediate compounds, namely 2'-methoxy-1',3'-xylyl-18-crown-5,[2] 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine[3] and 3,5-dimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine[4] were prepared using previously reported procedures[2-4]. $Pd(PPh_3)_4$ was prepared according to reference [5] and used directly or within three months at longest while stored under N_2 at - 30 °C.

The known 2'-methoxy-1',3'-xylyl-18-crown-5 was first *para* iodinated by treatment with iodine in dichloromethane in presence of silver trifluoroacetate (step **a** in scheme). Then, the following four step, namely the cross-coupling reactions, the oxygen deprotections of biaryls, the quaternizations of pyridine and the deprotonations were performed under the previously described conditions[4].

***5-Iodo-2-methoxy-1,3-xylyl-18-crown-5* (1).**

To a solution of 100 mg (0.3 mmol) of 2'-methoxy-1',3'-xylyl-18-crown-5 in chloroform (3.6 mL) were added, under Ar, first $AgCO_2CF_3$ (81 mg, 1.2 equiv), then, a solution of I_2 (93.3 mg,1.2 equiv) in chloroform (3.6 mL). The reaction mixture was stirred at room temperature overnight. The suspended silver salts were then filtered off. The filtrate was successively washed with aqueous saturated solution of Na_2SO_3 and water. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. Purification by column chromatography (cyclohexane/AcOEt 1:9 then AcOEt/MeOH 9:1) afforded pure **1** as a colourless solid (125 mg, 90%). M.P. 96 °C.^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.38-3.52 (m, 8H), 3.54-3.70 (m, 8H), 4.11 (s 3H), 4.50 (s, 4H), 7.58 (s 2H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 65.2 (1C), 68.4 (2C), 68.7 (2C), 70.2 (4C), 70.8 (2C), 86.4 (1C), 134.5 (2C), 140.6 (2C), 159.6 (1C) ppm. IR (KBr): ν = 781, 848, 868, 946, 990, 1024, 1098, 1223, 1241, 1268, 1349, 1429, 1469, 2867 cm^{-1}. HRMS (ESI-Q-Tof) : calcd for $C_{17}H_{29}INO_6$ $[M+NH_4]^{+}$ 470.1034 ; found 470.1033.

Suzuki-Miyaura cross-coupling reaction.

Under an atmosphere of Ar, to a solution of **1** (1 equiv.) in anhydrous THF (50 mL per mmol of **1**) were successively added, Cs_2CO_3 (1.2 equiv.), boronic ester **P-2** or **T-2** (1.2 equiv.), and $Pd(PPh_3)_4$ (0.08 equiv.) were. The reaction mixture was refluxed overnight. The suspension was then filtered through *Celite* with CH_2Cl_2. The solution was concentrated under reduced pressure and the residue was purified by chromatography on silicagel to afford pure **P-3** and **T-3**.

***5-(Pyridin-4'-yl)-2-methoxyl-1,3-xylyl-18-crown-5* (P-3).**

After purification by chromatography on silicagel (cyclohexane/AcOEt, 1:9 then AcOEt/MeOH, 9:1), compound **P-3** (125 mg, 70 %) was obtained as colourless crystals from **1** (200 mg, 0.4 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.43-3.54 (m, 8H), 3.57-3.70 (m, 8H), 4.20 (s, 3H), 4.65 (s, 4H), 7.59 (s, 2H), 7.64 (d, $^{3}J_{H,H}$ = 6.0 Hz, 2H), 8.65 (d, $^{3}J_{H,H}$ = 6.0 Hz, 2H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 65.3 (1C), 68.8 (2C), 69.2 (2C), 70.2 (2C), 70.25 (2C), 70.8 (2C), 121.5 (2C), 130.6 (2C), 132.7(1C), 132.8 (2C), 147.8 (1C), 150.0 (2C), 160.7 (1C) ppm. HRMS (ESI-Q-Tof) : calcd for $C_{22}H_{33}N_2O_6$ $[M+NH_4]^{+}$ 421.2333 ; found 421.2330.

***5-[2',6'-Dimethyl-(pyridin-4'-yl)]-2-methoxyl-1,3-xylyl-18-crown-5* (T-3).**

After purification by chromatography on silicagel (cyclohexane/AcOEt, 1:9 then AcOEt/MeOH, 9:1), compound **T-3** (352 mg, 55.5 %) was obtained as colourless crystals from **1** (667 mg, 1.5 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.07 (s, 6H), 3.45-3.60 (m, 8H), 3.60-3.70 (m, 8H), 4.19 (s, 3H), 4.60 (s, 4H), 7.04 (s, 2H), 8.33 (sl, 2H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 17.6 (2C), 65.1 (1C), 68.6 (2C), 69.2 (2C), 70.3 (4C), 70.8 (2C), 131.1 (2C), 131.7 (2C), 132.4 (2C), 132.6 (1C), 148.3 (2C), 148.6 (1C), 158.9 (1C) ppm.HRMS (ESI-Q-Tof) : calcd for $C_{24}H_{37}N_2O_6$ $[M+NH_4]^{+}$ 449.2646 ; found 449.2657.

Phenols deprotection.

Under an atmosphere of Ar, EtSH (7 equiv.) was added dropwise to NaH (8 equiv.) suspended in DMF (14 mL per mmol of **P-3** or **T-3**). On completion of the H_2 emission, **P-3** or **T-3** (1 equiv.) was introduced in the reaction mixture. After an overnight stirring at 100 °C, H_2O (2.5 mL per mmol of **P-3** or **T-3**), aqueous HCl (1M, 8 mL per mmol of **P-3** or **T-3**), and a phosphate buffer (0.5 M, pH = 2) were successively added. The aqueous layer was extracted three times with Et_2O. The combined organic layers (pH = 6.5) were extracted twice with H_2O and dried over $MgSO_4$. The solution was concentrated under reduced pressure and the residue was purified by chromatography on silicagel (cyclohexane/AcOEt) to afford pure **P-4** or **T-4**.

***5-(Pyridin-4'-yl)-2-hydroxy-1,3-xylyl-18-crown-5* (P-4).**

After purification by chromatography on silicagel (cyclohexane/AcOEt, 1:9), compound **P-4** (24 mg, 78 %) was obtained as colourless crystals from **P-3** (32 mg, 0.08 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.63-3.81 (m, 16H), 4.74 (s, 4H), 7.45 (s, 2H), 7.48 (d, $^{3}J_{H,H}$ = 7.0 Hz, 1H), 7.49 (d, $^{3}J_{H,H}$ = 7.0 Hz, 1H), 8.39 (s, 1H), 8.59 (d, $^{3}J_{H,H}$ = 7.0 Hz, 2H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 69.4 (2C), 70.1 (2C), 70.3 (2C), 70.38 (2C), 70.7 (2C), 121.0 (2C), 125.6 (2C), 128.2 (2C), 129.0 (1C), 147.8 (1C), 150.0 (2C), 157.0 (1C) ppm. HRMS (ESI-Q-Tof) : calcd for $C_{21}H_{27}NNaO_6$ $[M+Na]^+$ 412.1731 ; found 412.1736.

***5-[2',6'-Dimethyl-(pyridin-4'-yl)]-2-hydroxy-1,3-xylyl-18-crown-5* (T-4).**

After purification by chromatography on silicagel (cyclohexane/AcOEt, 1:9), compound **T-4** (68 mg, 64 %) was obtained as colourless crystals from **T-3** (109 mg, 0.25 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.90-20.5 (sl, 1H), 2.03 (s, 6H), 3.60-3.80 (m, 16H), 4.69 (s, 4H), 6.87 (s, 2H), 8.25 (sl, 1H), 8.31 (sl, 1H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 17.5 (2C), 69.3 (2C), 70.1 (2C), 70.4 (2C), 70.5 (2C), 70.7 (2C), 125.2 (2C), 128.7 (1C), 129.3 (2C), 129.8 (1C), 131.4 (1C), 148.2 (2C), 149.1 (1C), 155.3 (1C) ppm. IR (KBr): ν = 879, 1023, 1160, 1247, 1263, 1354, 1469, 2865, 3363 cm^{-1}. HRMS (ESI-Q-Tof) : calcd for $C_{23}H_{31}NaO_6$ $[M+Na]^{\cdot+}$ 440.2044 ; found 440.2046.

Alkylation of pyridine.

Under an atmosphere of Ar, to a suspension of the biaryl compounds **P-4** or **T-4** (1 equiv.) in acetone (16 mL per mmol of **P-4** or **T-4**), iodomethane (4 equiv.) was added dropwise. The reaction mixture was refluxed overnight. The solvent was then removed under reduced pressure. The residue was washed first with Et_2O then with AcOEt. The crude iodides **P-5** or **T-5** were not further purified.

***4-[17'-Hydroxy-2',5',8',11',14'-pentaoxa<15>metacyclophanyl]pyridinium iodide* (P-5).**

Compound **P-5** (32 mg, 98 %) was obtained as colourless crystals from **P-4** (24 mg, 0.06 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.69 (s, 8H), 3.73-3.82 (m, 4H), 3.88-3.96 (m, 4H), 4.29 (s, 3H), 4.77 (s, 4H), 7.86 (s, 2H), 8.27 (d, $^{3}J_{H,H}$ = 7.0 Hz, 2H), 8.51 (d, $^{3}J_{H,H}$ = 7.0 Hz, 2H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 47.8 (1C), 69.8 (4C), 69.9 (2C), 70.4 (2C),

70.5 (2C), 123.5 (2C), 123.7 (2C), 126.3 (1C), 130.2 (2C), 144.7 (2C), 153.8 (1C), 160.4 (1C) ppm. HRMS (ESI-Q-Tof) : calcd for $C_{22}H_{30}NO_6$ $[M^*]^+$ 404.2068 ; found 404.2067.

***3,5-Dimethyl-4-[17'-hydroxy-2',5',8',11',14'-pentaoxa<15>metacyclophanyl]pyridinium iodide* (T-5).**

Compound **T-5** (17 mg, 63.5 %) was obtained as colourless hygroscopic crystals from **T-4** (20 mg, 0.05 mmol). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.29 (s, 6H), 3.55-3.82 (m, 16H), 4.58 (s, 3H), 4.72 (s, 4H), 6.91 (s, 2H), 8.41 (sl, 1H), 8.84 (s, 2H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 18.3 (2C), 48.4 (1C), 69.5 (2C), 70.0 (2C), 70.1 (2C), 70.4 (2C), 70.7 (2C), 124.4 (1C), 126.2 (2C), 128.1 (2C), 138.0 (2C), 142.4 (2C), 157.0 (1C), 159.0 (1C) ppm.

Deprotonation.

Ag_2O (2 equiv.) was added to a solution of **P-5** or **T-5** in MeOH (11 mL per mmol of **5a-b**). After 10 min stirring, excesses of both Ag_2O and AgI precipitated. The suspension was then centrifugated. The supernatant organic phase was centrifugated once more and was then evaporated under reduced pressure to afford the pure pyridinium phenolates **P-C** or **T-C**.

***4-[20'-(17'-Oxydo)-2',5',8',11',14'-pentaoxa<15>metacyclophanyl]pyridinium* (P-C).**

Compound **P-C** (17.5 mg, 72 %) was obtained as red-brown crystals from **P-5** (32 mg, 0.06 mmol). ^{1}H NMR (400 MHz, CD_3OD): δ = 3.38-3.52 (m, 8H), 3.57-3.64 (m, 4H), 3.70-3.76 (s, 4H), 4.04 (s, 3H), 4.58 (s, 4H), 7.75 (s, 2H), 7.83 (d, $^3J_{H,H}$ = 7.0 Hz, 2H), 8.16 (d, $^3J_{H,H}$ = 7.0 Hz, 2H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD): δ = 46.3 (1C), 70.3 (4C), 71.2 (2C), 71.5 (2C), 71.6 (2C), 114.5 (1C), 120.0 (2C), 130.4 (2C), 131.9 (2C), 144.2 (2C), 156.1 (1C), 176.6 (1C) ppm. IR (KBr): ν = 495, 529, 827, 1017, 1074, 1090, 1103, 1186, 1312, 1381, 1454, 1482, 1590, 2862, 3272, 3272, 3499 cm^{-1}. HRMS (ESI-Q-Tof) : calcd for $C_{22}H_{29}NNaO_6$ $[M+Na]^{\cdot+}$426.1887 ; found 426.1885.

***3,5-Dimethyl-4-[20'-(17'-oxydoy)-2',5',8',11',14'-pentaoxa<15>metacyclophanyl]pyridinium* (T-C).**

Compound **T-C** (10 mg, 65 %) was obtained as red crystals from **T-5** (20 mg, 0.03 mmol). ^{1}H NMR (400 MHz, CD_3OD): δ = 2.33 (s, 6H), 3.49 (s, 8H), 3.53-3.63 (m, 4H), 3.64-3.78 (m, 4H), 4.25 (s, 3H), 4.63 (s, 4H), 6.97 (s, 2H), 8.51 (s, 2H) ppm. ^{13}C NMR (100.6 MHz, CD_3OD): δ = 18.8 (2C), 47.7 (1C), 70.0(2C), 70.4 (2C), 71.5 (4C), 71.6 (2C), 118.9 (1C),

128.6 (2C), 131.3 (2C), 138.6 (2C), 143.7 (2C), 161.5 (1C), 167.2 (1C) ppm. IR (KBr): ν□ = 1015, 1106, 1178, 1307, 1335, 1354, 1415, 1468, 1596, 1641, 2868, 3487 cm^{-1}. HRMS (ESI-Q-Tof) : calcd for $C_{24}H_{34}NO_6$ $[M+H]^{+}$ 432.2380 ; found 432.2382.

3. Cyclic voltamogramms of the chromophores.

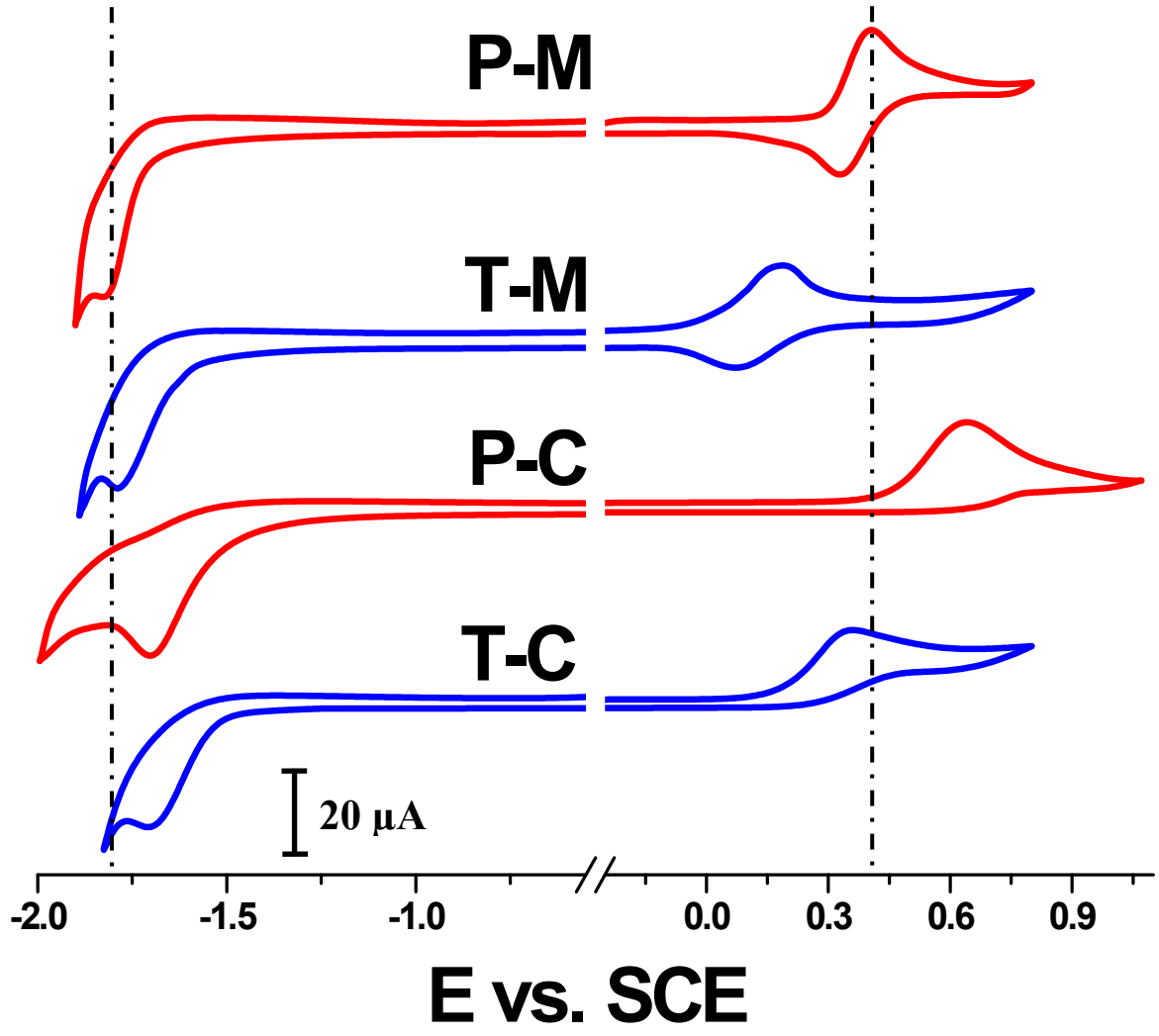


Figure S1. Cyclic voltamogramms of chromophores in acetonitrile + $(nBu)_4NBF_4$ (0.1 M) on platinum electrode at 100 mV s^{-1} (concentration of chromophores: 10^{-3} M).

4. Effects of the complexation with K^+ on the CVs of the ligands.

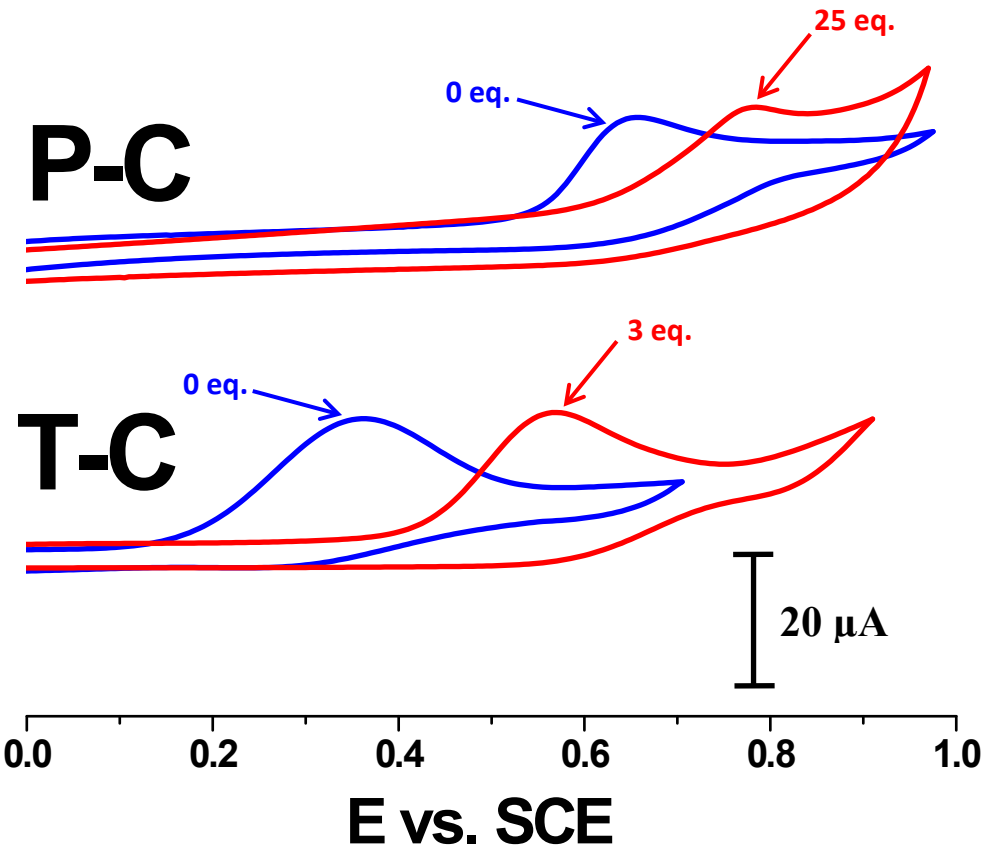


Figure S2. Experimental CVs for acetonitrile solutions of ligands in presence of KSCN. (v = 100 mV s^{-1} and concentration of ligands : 10^{-3} M).

5. References.

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