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RESEARCH ARTICLE

A Bis-Acridinium Macrocycle as Multi-Responsive Receptor and Selective Phase Transfer Agent of Perylene

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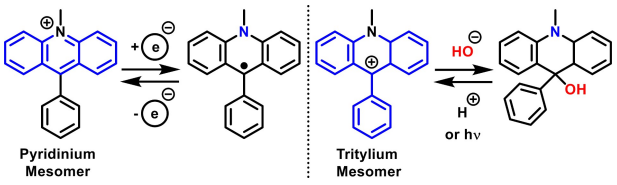
Abstract: A bis-acridinium cyclophane incorporating switchable acridinium moieties linked by a 3,5-dipyridylanisole spacer was studied as a multi-responsive host for polycyclic aromatic hydrocarbon guests. Complexation of perylene was proven to be the most effective and was characterized in particular by a charge transfer band as signal output. Effective catch and release of the guest was triggered by both chemical (proton/hydroxide) and redox stimuli. Moreover, the dicationic host was also easily switched between organic and perfluorocarbon phases for application related to the enrichment of perylene from a mixture of polycyclic aromatic hydrocarbons.

Introduction

The past decades have seen the emergence of numerous covalent artificial receptors.[1] Supramolecular chemistry and self-assembly have also allowed the formation of sophisticated receptors incorporating several recognition units.[2] These receptors have gained in complexity with the integration of switching units allowing a control of the guest-binding properties.[3] However, multi-state systems responsive to different type of stimuli are still scarce in the literature and are based on the combination of molecular switches in either the host or the guests. Such systems were recently reported to control the association/dissociation process in host-guest complexes[4] and the motion in mechanically interlocked molecules.[5]

In this context, 9-aryl-acridinium moieties are emerging building blocks[6] for the development of multi-responsive receptors of Polycyclic Aromatic Hydrocarbons (PAHs). Indeed, these building blocks are single components responsive to different stimuli (electron, light and nucleophile) thus avoiding the combination of several switches. Upon redox[7] or acid/nucleophile[8] stimulations, the acridinium fragments experience reversible and profound changes of their electronic properties and/or shape, two key parameters strongly affecting recognition processes (Scheme 1). Among the few studies reporting acridinium based switchable supramolecular systems, a family of [2]rotaxanes incorporating two acridinium stoppers was described by Abraham and coworkers.[9] The photochromic properties of the acridinium stoppers were used to trigger the shuttling of a tetracationic macrocycle. In a seminal work, Yoshizawa and coworkers recently reported the synthesis of the tetrakisacridinium receptor interacting with long hydrophilic molecules (e.g. coumarin and steroid derivatives).[10] Upon addition of nucleophiles, the formation of the corresponding tetrakisacridane macrocycle triggers the decomplexation of the guest molecules as the result of the modulation of the cavity size of the receptor.



Scheme 1. Two possible mesomeric forms of the 9-aryl-N-methyl acridinium subunit highlighting the electronic and 2D to 3D structural changes occurring upon addition of redox and pH stimuli.

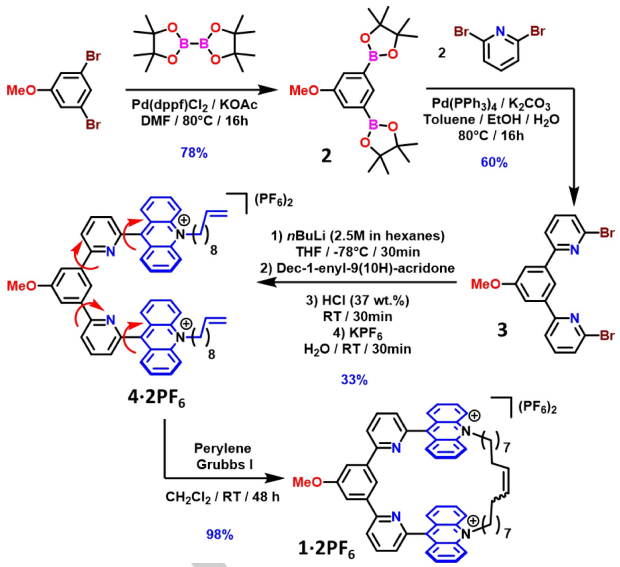
An additional interest of acridinium moieties resides in their ionic nature allowing their straightforward confinement in aqueous and organic phases according to the associated counterions.[10,11] This is of primary importance for applications in molecular

separation/purification processes which mostly exploit aqueous/organic solvents biphasic systems.[12] Perfluorocarbons (PFCs) are the least polar liquids making them non-miscible at room temperature and ambient pressure with both water and organic solvents, hydrocarbons included.[13] In reason of their extremely poor solvation ability, PFCs are appealing phases for receptors confinement.[14] They do not compete with the host-guest interactions, thus increasing their strength,[15] but also potentially limit the number and amount of competing guests or hosts in the recognition phase. These unique properties have been exploited to develop potentiometric ion sensing assays exhibiting unequalled sensitivity and selectivity ranges,[15a-b, 16] as well as a few colorimetric/fluorogenic assays.[17] Rather surprisingly, application of PFCs and fluorous supramolecular receptors to selective separation/transportation processes have been much less explored.[18] It might be ascribed to the difficulty of getting receptors with enough fluorophilicity to impart high partitioning in the fluorous phase.

Herein, the four-step synthesis of the bis-acridinium cyclophane (**1**$^{2+}$) and its recognition properties towards PAHs is reported. The chemical and redox-controlled encapsulation/release properties of the cyclophane towards perylene (**Per**) is demonstrated. This dicationic host also showed its ability to switch between CH_2Cl_2 and perfluorocarbon phases using fluorophilic supramolecular anions. In addition, the confinement of the receptor in a fluorous phase was exploited to the selective extraction of **Per** from a mixture of PAHs.

Results and Discussion

Design and Synthesis. The multi-switchable bis-acridinium cyclophane **1·2PF$_6$** was designed to target PAH guest molecules that are ubiquitous environmental pollutants, most of them being carcinogenic.[19] It is known that acridinium moieties can act as recognition units in π-donor/π-acceptor interactions with electron rich guests.[20] The targeted receptor **1·2PF$_6$** was prepared in only four steps from commercially available 3,5-dibromoanisole (Scheme 2). First, 3,5-dibromoanisole (1 eq.) was borylated under Miyaura conditions using bis(pinacolato)diboron (2 eq.), $Pd(dppf)Cl_2$ (10 mol%) and KOAc (6 eq.) in DMF. After purification, the corresponding bis(pinacolato)anisole **2** was isolated in 78% yield. Compound **2** was reacted with 2,6-dibromopyridine (4 eq.) under Suzuki conditions using $Pd(PPh_3)_4$ (20 mol%) and K_2CO_3 (2 N) in a toluene/ethanol/water mixture. After column chromatography, the semi-rigid spacer **3** was obtained in 60% yield. The dibromo derivative **3** underwent a bromo-lithium exchange using a solution of nBuLi (2 eq.) in hexanes (2.5 mol L^{-1}) followed by reaction with dec-1-enyl-9(10H)-acridone (2 eq).[21] Aromatization of the bis-acridane intermediate by acidification of the reaction mixture using HCl (37 wt.%) led to the bis-acridinium tweezer **4·2Cl**, then converted to the corresponding hexafluorophosphate salt (**4·2PF$_6$**) by anion metathesis using **KPF$_6$**. Tweezer **4·2PF$_6$** was isolated as a yellowish solid in 33% yield. The key macrocyclization step was achieved in almost quantitative yield under olefin metathesis conditions using first-generation Grubbs catalyst (10 mol%) and **Per** (3 eq.) as template.[22] Without template, the macrocyclization step did not proceed showing that **Per** effectively preorganizes both acridinium units in a face to face conformation necessary for the ring-closure step.[23]



Scheme 2. Synthesis of the cyclophane **1·2PF$_6$** from 3,5-dibromoanisole as commercially available material.

The receptor **1·2PF$_6$** and all precursors were characterized by NMR, UV-vis spectroscopies and MS spectrometry (see SI). The ^{1}H NMR spectrum of **1·2PF$_6$** (CD_3CN, 298K) revealed characteristic triplets at 5.47 and 5.44 ppm ($^3J_{gem}$ = 1.0 Hz) corresponding to the olefin protons of both expected diastereomers of the cyclophane, namely *trans* and *cis* in a 9:1 ratio (Fig. 2a). Crystals of the inclusion complex $C_6H_6 \subset$ **1·2PF$_6$** were grown by vapor diffusion of C_6H_6 into an CH_3CN solution of **1·2PF$_6$**, and its structure was solved by X-ray diffraction analysis (Fig. 1b-c).[24] The preorganization of both acridinium moieties was clearly evidenced by the optimum distance for π-stacking interactions ($d_{C9\text{-}C9}$ = 7.198 Å and $d_{N\text{-}N}$ = 7.676 Å). Overall, the cavity size (7.2 × 15.6 Å) is well-adapted to PAHs such as **Per**.

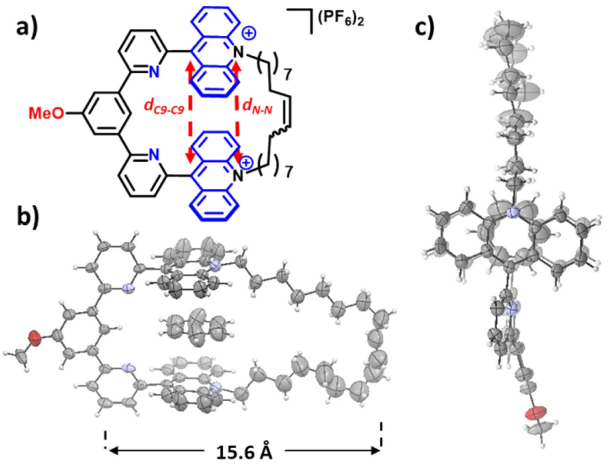


Figure 1. a) Scheme of the receptor **1·2PF$_6$**, b) Side view and c) Top view of the crystal structure of $C_6H_6 \subset$ **1**$^{2+}$ showing the inclusion of a benzene molecule (thermal ellipsoids at 50% probability level; PF_6^- anions and a benzene have been omitted for clarity).

Recognition Properties. NMR and UV-vis studies were employed to probe the recognition properties of **1·2PF$_6$** toward

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PAHs, namely **Per**, anthracene (**Ant**) and naphthalene (**Naph**). The ^{1}H NMR (CD_3CN, 298 K) of the 1:1 mixture (c = 1.5 × 10^{-3} mol L^{-1}) of **1·2PF$_6$** and **Per** revealed a chemical shift of all protons in comparison to the individual host and guest (Fig. 2). More especially, upfield shifts of the acridinium protons ($\Delta\delta(H_{1/8})$ = –0.42, $\Delta\delta(H_{3/6})$ = –0.41, and $\Delta\delta(H_{4/5})$ = –0.57 ppm) of **1·2PF$_6$** for the trans isomer as well as of the **Per** protons ($\Delta\delta(H_{1/6/7/12})$ = –0.58, $\Delta\delta(H_{2/5/8/11})$ = –0.52 and $\Delta\delta(H_{3/4/9/10})$ = –0.44 ppm) suggested π–π interactions between the guest and the acridinium subunits. The inclusion complex **Per** ⊂ **1·2PF$_6$** was confirmed by the downfield shifts of the inner proton $H_{o'}$ of the 1,3-dipyridylanisyl spacer ($\Delta\delta(H_{o'})$ = 0.42 ppm) and the olefin protons ($\Delta\delta(H_{trans})$ = 0.22 and $\Delta\delta(H_{cis})$ = 0.08 ppm). In addition, the existence of the inclusion complex was confirmed by control experiments using the 9-pyridyl-N-acridinium moiety as host (see SI, Figure S4.1). Indeed, the ^{1}H NMR spectrum (CD_3CN, 298 K) of the 1:1 mixture of 9-pyridyl-N-acridinium and **Per** showed no chemical shifts of any proton signals suggesting a macrocyclic effect and the cooperative assistance between both acridinium moieties in **1·2PF$_6$**.

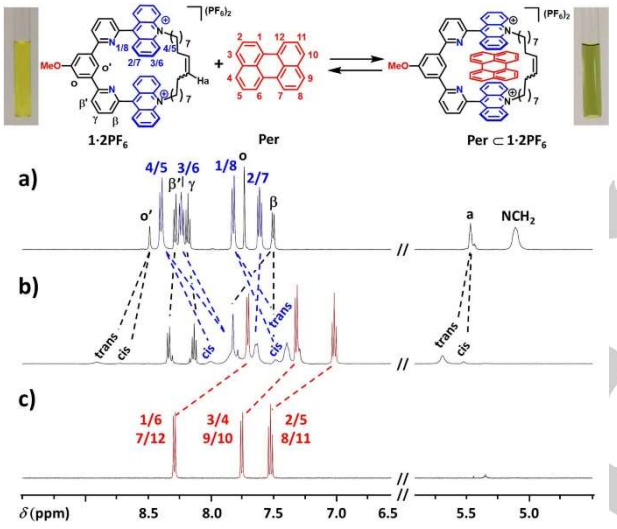


Figure 2. ^{1}H NMR (500 MHz, CD_3CN, 298 K, c = 1.5 × 10^{-3} mol L^{-1}) spectra of (a) **1·2PF$_6$**, (b) the 1:1 mixture of **Per** and **1·2PF$_6$**, and (c) **Per**. The photographs of the solution of **1·2PF$_6$** and the 1:1 mixture of **Per** and **1·2PF$_6$** are shown.

Of particular interest, complex formation gave rise to a new electronic transition in the visible region (λ_{max} = 606 nm; ε_{606} ~ 670 L mol^{-1} cm^{-1})[25] attributed to a charge transfer band from **Per** to the acridinium units of the receptor, responsible for the color change from yellow to green (Fig. 2-3). This optical output was only observed for the complexation of **Per** and account of its higher π-donor character in comparison to **Ant** and **Naph**. The poor solubility of **Per** did not allow NMR or UV-Vis titration experiments in CH_3CN. In order to get higher solubility of both **1^{2+}** and **Per** in a common solvent, namely CH_2Cl_2, **1·2PF$_6$** was converted to the corresponding tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (BArF) salt, **1·2BArF** (see SI). Monitored by UV-Vis spectroscopy, titration experiments in CH_2Cl_2 allowed the estimation of an association constant of 1200 ± 38 L mol^{-1} between **Per** and **1·2BArF** (fitted to a 1:1 binding model, see SI, Fig. S4.3).[26] Remarkably, this binding constant is 18 and 400 times higher than the binding constant determined between **1·2BArF** and **Ant** (Ka = 66 ± 3 L mol^{-1}, see SI Fig. S4.5-6) and **Naph** (Ka = 3 ± 0.08 L mol^{-1}, see SI Fig. S4.7-4.8) respectively.[27]

Classical molecular dynamics simulation shed light on the dynamic behavior of the **Per** ⊂ **1^{2+}** complex in CH_2Cl_2. In the course of the calculated trajectory (10 μs), **Per** exchanges eleven times between the center of the cavity of host **1^{2+}** and bulk CH_2Cl_2 (see SI, Fig. S8.1-2) with an average residence time of about 650 ns (from 23 ns to 2151 ns). The calculated free energy difference of –26.8 kJ mol^{-1} between the associated and dissociated complex is in good agreement with the experimental value of –17.6 kJ mol^{-1}.

Multi-Switching Properties. To demonstrate the chemical switching from the bis-acridinium macrocycle, the macrocyclic bis-acridane **5** was prepared in quantitative yield by addition of a solution of KOH (1 mol L^{-1}) to a solution of **1·2PF$_6$** in CH_3CN (see structure in Fig. 3).[28] Compound **5** exhibited no binding ability for **Per** in CD_2Cl_2 as demonstrated by ^{1}H NMR spectroscopy (see SI, Fig. S5.3-S5.4). This behavior can be rationalized by the drastic geometrical change of the acridane units and by the loss of aromaticity of the recognition units in **5** in comparison to its bis-acridinium precursor **1·2PF$_6$** (see SI).[29] The reversible conversion between **5** and the receptor **1·2PF$_6$** upon addition of protons (trifluoroacetic acid, TFA) or hydroxides (KOH) was evidenced by ^{1}H NMR and UV-vis studies (see SI, Fig. S5.1-2 and S5.6-7).

The chemical switching of macrocycle **5** to **1·2PF$_6$** to efficiently release/catch **Per** was then probed by UV-vis spectroscopy following the variation in intensity of the **Per** to acridinium charge-transfer band (Fig. 3). Quantitative restoration of the **Per** ⊂ **1^{2+}** complex was achieved upon addition of 4.8 eq. of TFA. In other words, the dihydroxylated macrocycle **5** behaves as a proton-activated latent receptor for **Per**. In addition, **Per** was reversibly released upon addition of 9 eq. of tetrabutylammonium hydroxide (TBAOH, Fig. 3 inset).

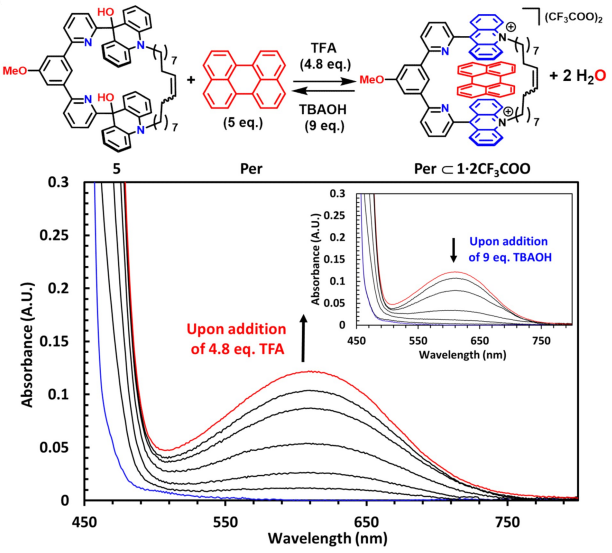


Figure 3. UV-Vis spectra (CH_2Cl_2, l = 0.1 cm, 298 K) of a mixture of **5** (c = 1.5 × 10^{-3} mol L^{-1}) with 5 eq. of **Per** upon addition of TFA (0.8, 1.6, 2.4, 3.2, 4.0 and 4.8 eq.); Insert: UV-Vis spectra (CH_2Cl_2, l = 0.1 cm, 298 K) of a mixture of **1·2CF$_3$COO** (c = 1.5 × 10^{-3} mol L^{-1}) with 5 eq. of **Per** upon addition of TBAOH (1.5, 3, 4.5, 6, 7.5 and 9 eq.).

The redox-switchable properties of **1·2PF$_6$** were investigated by cyclic voltammetry experiments in $C_2H_4Cl_2$ (Fig. 4). At 100 mV s^{-1}, **1·2PF$_6$** exhibits a reduction wave at a potential (E_{c1}) of –0.946 V *vs* Fc+/Fc and a reoxidation wave at –0.828 V *vs* Fc+/Fc (E_{a1}). This observation is in agreement with two quasi reversible one-electron injection processes (ΔE_p = 118 mV) leading to the formation of the diradical **1^0** at $E_{1/2}$ = –0.887 V *vs* Fc+/Fc.[30] This observation is supported by the scan rate study performed from 50 to 800 mV s^{-1} (see SI, Fig. S6.1). Indeed, the plot of the cathodic and anodic intensity as a function of the square root of the scan rate (I_c and I_a = f($\nu^{1/2}$)) shows a perfect linear relationship (see SI, Fig. S6.2 and S6.4). Noteworthy, the slight shift of the cathodic potential (E_{c1}) corroborates a process under diffusion control. In addition, spectro-electrochemical experiments were undertaken to provide evidences of the reduction of both acridinium units at the same potential. Upon reduction, the original spectrum of **1·2PF$_6$** was converted to the spectrum of **1^0** (see SI, Fig S6.6) revealing four maxima at 357 (20200), 367 (24100), 492 (8400) and 531 nm (8350). Upon re-oxidation, the spectrum of **1·2PF$_6$** was substantially restored thus demonstrating the clean chemical reversibility of this electrochemical process (see SI, Fig S6.7).

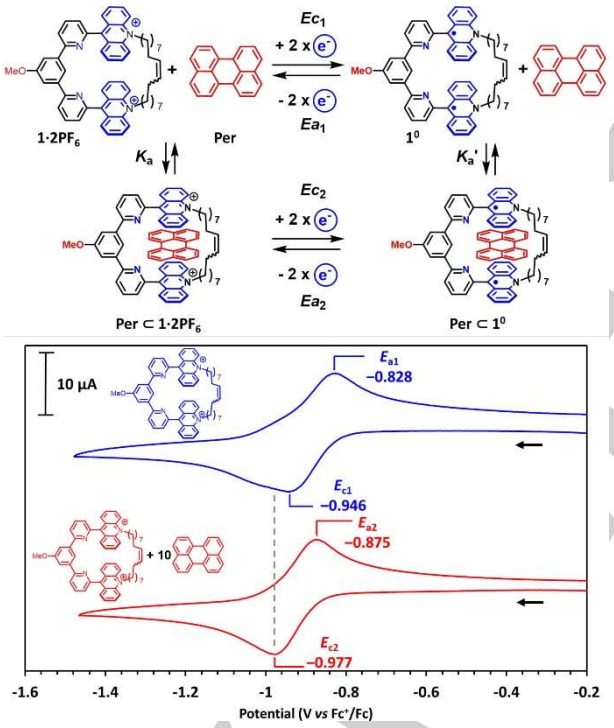
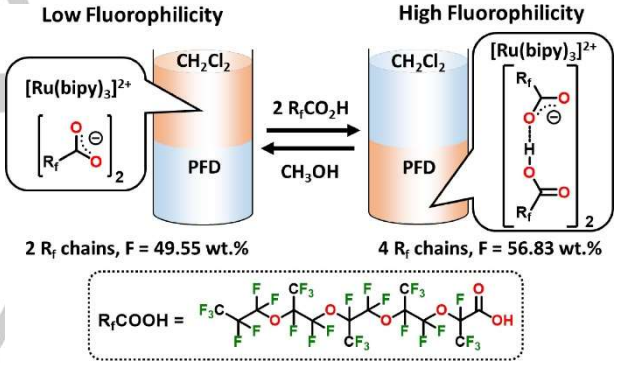


Figure 4. Cyclic voltammograms ($C_2H_4Cl_2$, WE: Pt, CE: Pt, RE: Ag, 100 mV s^{-1}) of a solution of **1·2PF$_6$** (c = 1 × 10^{-3} mol L^{-1}) before (blue) and after addition of 10 eq. of **Per** (red) in the presence of $TBAPF_6$ as supporting electrolyte (c = 0.1 mol L^{-1}).

After addition of an excess of **Per** (10 eq.) corresponding to 74% complex formation, a cathodic shift of the reduction (E_{c2} = –0.977 V *vs* Fc$^+$/Fc) and re-oxidation processes (E_{a2} = –0.875 V *vs* Fc$^+$/Fc) were observed ($E_{1/2}$ = –0.926 V *vs* Fc$^+$/Fc). This observation corroborates the formation of the host-guest complex since the electron rich guest transfers some of its electronic density to the acridinium moieties making them more difficult to reduce. The half-wave potential difference ($\Delta E_{1/2}$) was found to be –39 mV and allowed the estimation of a binding constant (*K*a') of 54 L mol^{-1} between the reduced receptor **1^0** and **Per**. This 20 times lower association constant compared to the constant found between **1·2PF$_6$** and **Per** (*K*a = 1 200 ± 21 L mol^{-1} in $C_2H_4Cl_2$ in the presence of 0.1 mol L^{-1} of $TBAPF_6$; see SI, Fig. S4.9) clearly evidences the destabilization of the host-guest complex upon reduction. This binding constant corresponds to 34% complex formation between the **1^0** and **Per** showing that the host-guest association-dissociation can be controlled to a different extent using either a redox or a chemical stimulus.[31]

Phase transfer in perfluorocarbons. Interested in applying the receptor in selective transportation processes, perfluorcarbons (PFCs) were envisioned as potential liquid phases for the receptor confinement.[32] In 2011, some of us reported the transfer of a $[Ru(bipy)_3]^{2+}$ dication from CH_2Cl_2 to a perfluorodecalin (PFD) phase by a markedly increase of the fluorine content coming from the associated counter-ions (Scheme 3).[33] These counter-ions are heteromeric supramolecular fluorous carboxylates-carboxylic acid anions easily formed in PFCs by an ionic H-bond interaction thus doubling the number of fluorous chains.[34] The back transfer from the PFD to CH_2Cl_2 was achieved by adding a tiny amount of a H-bond competitor, namely CH_3OH, to the biphasic system thus disrupting the supramolecular anion.



Scheme 3. Concept of fluorophilicity amplification applied to the phase-switching of the $[Ru(bipy)_3]^{2+}$ dication between CH_2Cl_2 and PFD phases.[31]

Based on these results, the easy confinement of **1^{2+}** in a fluorous phase was hypothesized using highly fluorophilic supramolecular anion (Fig. 5a-b). Accordingly, a stock solution of **1·2(R$_f$COO-H-OOCR$_f$)** (c = 0.55 × 10^{-3} mol L^{-1}) in perfluoromethylcyclohexane (PFMC, 6 mL) was conveniently prepared by stirring a solution of bis-acridane **5** (c = 1.88 × 10^{-3} mol L^{-1}) in CH_2Cl_2 (2 mL) with a solution of commercially available perfluoro-2,5,8,11-tetramethyl-3,6,9,12-tetraoxopentadecanoic acid (R$_f$COOH, R$_f$ = $CF_3CF_2CF_2O[(CF_3)CFCF_2O]_3(CF_3)CF$) in PFMC ($c$ = 7.5 × 10^{-3} mol L^{-1}, 6 mL). The formation of **1·2(R$_f$COO-H-OOCR$_f$)** and its phase transfer were followed by UV-Vis spectroscopy and a transfer of 90% of **1·2(R$_f$COO-H-OOCR$_f$)** into the fluorous phase was determined (see SI, Fig. S7.1-2).[35] The receptor **1·2(R$_f$COO-H-OOCR$_f$)** proved to be highly fluorophilic as revealed by a back extraction from the PFMC phase to a fresh CH_2Cl_2 solution of only 0.3 % (see SI, Fig. S7.3). Addition of a small amount of CH_3OH (a volume of ~ 4% of CH_3OH compared to that of PFMC) as a H-bond competitor led to the quantitative back transfer of the receptor from the PFMC to the CH_2Cl_2 phase, thus supporting the

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formation of supramolecular H-bonded anions in the fluorous phase.

Figure 5. a) Conversion of the bis-acridane **5** to the highly fluorophilic bis-acridinium **1·2(R$_f$COO-H-OOCR$_f$)**; b) Photograph of a biphasic system taken after stirring and decantation of a stock solution of **1·2(R$_f$COO-H-OOCR$_f$)** in PFMC (c = 0.55 × 10^{-3} mol L^{-1}, 6 mL, stir bar in the bottom of the tube) and fresh CH_2Cl_2 (3 mL); c) Photographs and schematic representation of the extraction/release of **Per** using **1·2(R$_f$COO-H-OOCR$_f$)**; i) magnetic stirring (30 min, 1000 rpm, stir bar present in the bottom of the tube) of an aliquot of the PFMC stock solution (1 mL) and a solution of **Per** (c = 4 × 10^{-3} mol L^{-1}) in CH_2Cl_2 (1 mL); ii) an aliquot (0.5 mL) of the PFMC solution containing **Per** ⊂ **1·2(R$_f$COO-H-OOCR$_f$)** was taken and fresh CH_2Cl_2 (2 mL) was added; iii) manual shaking for 60 s and decantation.

The reversible extraction/release of **Per** between both CH_2Cl_2 and PFMC phases was then probed (Fig. 5c and see SI, Fig. S7.4-9). A solution of **Per** (c = 4 × 10^{-3} mol L^{-1}, 1 mL) in CH_2Cl_2 was stirred with a solution of **1·2(R$_f$COO-H-OOCR$_f$)** in PFMC (c = 0.55 × 10^{-3} mol L^{-1}, 1 mL) leading to the fast color change of the fluorous phase from yellow to green (see SI, Fig. S7.4). After 30 min of stirring, UV-Vis titration of the PFMC phase allowed the estimation of the concentration of **Per** ⊂ **1·2(R$_f$COO-H-OOCR$_f$)** to ~ 0.21 × 10^{-3} mol L^{-1} corresponding to ~ 38% complex formation (see SI, Fig. S7.5-6). In the fluorous phase, **Per** is almost exclusively present in the form of the inclusion complex. Under similar conditions but in the absence of **1·2(R$_f$COO-H-OOCR$_f$)**, the **Per** concentration in the PFMC was as low as 1.3 × 10^{-6} mol L^{-1} (see SI, section 7.2). From these data an association constant between **Per** and **1·2(R$_f$COO-H-OOCR$_f$)** of 4.66 × 10^5 L mol^{-1} was estimated in PFMC, c.a. 390 times higher than in CH_2Cl_2 (see SI, section 7.3). Release of the complexed **Per** was achieved by replacing the CH_2Cl_2 phase containing the excess **Per** by fresh CH_2Cl_2 (four times the volume of the PFMC phase). After manual shaking, fading of the green color of the fluorous phase was observed with concomitant appearance of the characteristic yellowish color of **Per** in the CH_2Cl_2 phase (see SI, Fig. S7.7-9). The recorded UV-Vis spectra of each phase confirmed the complete release of **Per** in CH_2Cl_2.

Finally, the ability of the fluorous system to selectively extract and release **Per** from a mixture of PAHs was evaluated (see SI, section 7.5). A biphasic system composed of a solution of **1·2(R$_f$COO-H-OOCR$_f$)** (c = 1.88 × 10^{-3} mol L^{-1}) in PFMC (1 mL) and an equimolar solution of **Per**, **Ant** and **Naph** (c = 2 × 10^{-3} mol L^{-1} each) in CH_2Cl_2 (2 mL) was stirred for 60 min. After decantation, an aliquot of the greenish PFMC phase (0.5 mL) was transferred in a test tube and extracted with two aliquots of fresh CH_2Cl_2 (1 mL + 0.5 mL). Analysis of the combined CH_2Cl_2 phase by UV-vis spectroscopy and GC (see SI, Fig. S7.11-S7.13) revealed a **Per** concentration (c ~ 114 × 10^{-6} mol L^{-1}) far superior than **Ant** (c = 6.1 × 10^{-6} mol L^{-1}) and **Naph** (c = 9.4 × 10^{-6} mol L^{-1}). These concentrations correspond to concentrations in the PFMC phase before release of ~ 342 × 10^{-6} mol L^{-1}, 18.3 × 10^{-6} mol L^{-1} and ~ 28.2 × 10^{-6} mol L^{-1} for **Per**, **Ant** and **Naph**, respectively. Under similar conditions without **1·2(R$_f$COO-H-OOCR$_f$)**, the extraction of **Per**, **Ant** and **Naph** in the PFMC phase led to concentrations of ~ 1.1 × 10^{-6} mol L^{-1}, 5.1 × 10^{-6} mol L^{-1} and ~ 27.1 × 10^{-6} mol L^{-1}, respectively. This observation confirms that the amount of **Naph** recovered in the CH_2Cl_2 phase with and without **1·2(R$_f$COO-H-OOCR$_f$)** is essentially due to its innate partitioning. In addition, the partition coefficient (K = c_{PFMC}/c_{CH2Cl2}) of **Naph** between CH_2Cl_2 and PFMC is higher than that of **Ant** and much higher than that of **Per**. The recyclability of the fluorous phase was also assessed by conducting three consecutive extraction/release experiments from a CH_2Cl_2 phase containing a 1/1/1 molar ratio of **Per**, **Ant** and **Naph** (see SI for detailed procedure, Fig. S7.19-22, Tables S7.4-5). Combined UV-Vis spectroscopy and GC analysis showed that the fluorous phase could be reused two times with the same efficiency, both in terms of yield of extracted/released **Per** (17.1%, 16.5% and 17.0% for the first, second and third extraction/release processes, respectively) and selectivity (**Per**/**Ant**/**Naph** molar ratios of 9.5/1/1.05, 8.7/1/1.1, 10.6/1/1.06 for the first, second and third extraction/release processes, respectively). Overall, these experiments demonstrate the ability of fluorous solvents combined with supramolecular receptor for selective transportation processes.

Conclusion

The efficient synthesis of a multi-responsive cyclophane incorporating two acridinium moieties as recognition units was described. Its ability to form host-guest complexes with perylene on account of π-donor/ π-acceptor interactions was shown in solution. Upon addition of hydroxide anions, the chemical switching properties of this system lead to the formation of the corresponding bis-acridane derivative. This derivative is unable to interact with perylene thus demonstrating the ability of the cyclophane to work as an ON/OFF switch. The electrochemical switching properties of the bis-acridinium cyclophane clearly evidenced a decrease of the host-guest interactions upon reduction. Finally, the phase switching behavior of the macrocycle between a perfluorocarbon and an organic layer was explored and successfully applied to the straightforward enrichment of perylene from a mixture of polycyclic aromatic hydrocarbons. The multifunctional properties associated to the cyclophane receptor integrating multi-responsive acridiniums units are promising and will be further explored in the context of selective transportation processes and functional materials.

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Keywords: Multi-Responsive Receptor • Phase Transfer • Acridinium • Perfluorocarbons • Host-Guest Chemistry

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[21] Dec-1-enyl-9(10H)-acridone was synthesized from commercially available materials, namely 9(10H)-acridone and 10-bromodecene, under basic conditions using NaH (60 wt.%) as base (see SI).

[22] The decenyl chain revealed to be optimum for the formation of the receptor. Attempts using shorter hexenyl and octenyl chains led to the formation of a mixture of products, namely the desired macrocycle and a cyclic side product with a methylene missing.

[23] During purification of **1·2PF$_6$**, **Per** was first removed by flushing the column with CH_2Cl_2.

[24] Crystal data for **1·2PF$_6$**: $[C_{61}H_{62}N_4O][PF_6]\cdot1.5(C_6H_6)$, yellow plate, crystal size 0.27 × 0.20 × 0.02 mm^3, triclinic, space group *P*-1 (No. 2), a = 8.7996(4) Å, b = 14.9178(13) Å, c = 24.2132(10) Å, α = 91.091(6)°, β = 92.696(4)°, γ = 102.548(6)°, V = 3097.8(4) Å^3, Z = 2, ρ_{calc} = 1.366 Mg m^{-3}, T = 120.0(1) K, $R_1(F^2 > 2\sigma F^2)$ = 0.140, wR_2 = 0.337. CCDC 2003776.

[25] The molar extinction coefficient at 606 nm (ε_{606}) was estimated from the determination of the binding constant (*Ka*) (Fig S4.3) showing 76% complex formation at the end of the titration.

[26] The 1:1 stoichiometry of the host-guest complex was determined by the minimum standard deviation after fitting to a 1:1, 2:1 and 1:2 binding model. Indeed, the interpretation of Job Plot titrations could be sometimes misleading in supramolecular chemistry (see F. Ulatowski, K. Dąbrowa, T. Bałakier, J. Jurczak, *J. Org. Chem.* **2016**, *81*, 1746–1756).

[27] Estimation of the binding constants between **Ant** and **Naph** were determined by ^{1}H NMR titration experiments in CD_2Cl_2.

[28] As expected, compound **5** was obtained as a mixture of two isomers, namely trans and cis, in a 9:1 ratio.

[29] The dearomatization of the acridinium units in **1·2PF$_6$** was observed by ^{1}H NMR experiments (400 MHz, DMSO-d_6, 298 K) with the upfield shifts of the acridane protons ($\Delta H_{1/8}$ = –0.80 ppm, $\Delta H_{2/7}$ = –0.62 ppm, $\Delta H_{3/6}$ = –1.52 ppm and $\Delta H_{4/5}$ = –1.60 ppm) and of the methylene protons ($\Delta H_{N\text{-}CH2}$ = –1.43 ppm). In addition, the change of hybridization of the C_9 atom from C_{sp2} in **1·2PF$_6$** (δ = 156.7 ppm) to a C_{sp3} in **5** (δ = 79.6 ppm) was confirmed by ^{13}C NMR experiments (125 MHz, DMSO-d_6, 298 K). Finally, the UV-Vis spectrum (CH_2Cl_2, l = 1 cm, 298 K, c = 5 × 10^{-4} mol L^{-1}) of **5** shows an absorbance only in the UV region at 317 nm (14 600) confirming this dearomatization.

[30] Electrochemical experiments performed on **1·2PF$_6$** in DMF showed a reversible behaviour (ΔEp = 66 mV, see SI, Fig. S6.8-6.10). Consequently, the quasi-reversible electron injection observed in $C_2H_4Cl_2$ results in a solvent effect (see E. Ahlberg, O. Hammerich, V. D. Parker, *J. Am. Chem. Soc.* **1981**, *103*, 844–849).

[31] Interaction of **Per** with the reduced receptor **1^0** was also investigated by Classical Molecular Dynamics simulations (PMF and RDF calculations).

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The free energy profile as a function of the centers of mass (COM) distance of **Per** and $\mathbf{1^0}$ shows that the complexed state is about 8.4 kJ mol^{-1} higher in energy than the uncomplexed state (see SI, Fig. S8.1). MD simulation indicates that **Per** can enter the cavity of $\mathbf{1^0}$ but they underestimate the stability of the complexed state.

[32] Receptor $\mathbf{1^{2+}}$ proved to be insoluble in water as a chloride, sulfate and nitrate salt. Consequently, perfluorocarbons (PFCs) were considered as potential orthogonal phase to both water and organic solvents.

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[35] Protonation of the pyridines of the receptor was not observed even in concentrated HCl and pure H_2SO_4.

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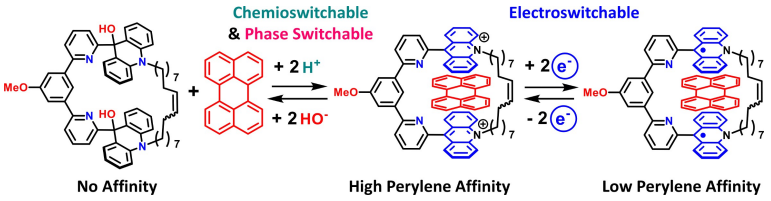

A bis-acridinium cyclophane binds selectively and reversibly perylene upon chemical or redox stimuli in organic media. In addition, its straightforward phase-transfer into a perfluorocarbon was exploited for the enrichment of perylene from a mixture of PAHs.

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