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Realization of a "Lockable" Molecular Switch via pH- and Redox-Modulated Cyclization

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Abstract: A switchable organic system involving four distinct states that can be interconverted by use of both pH and redox chemistry as control parameters has been developed. The key molecules involved in this system are the phenanthridine-based heterocycles 1-isobutyl-1,2,3,12b-tetrahydroimidazo[1,2-*f*]phenanthridine (TIP) and 5-[2-(isobutylamino)ethyl]phenanthridinium (AEP). These two states are interchangeable via pH control, and in addition they can also be further manipulated by oxidation or reduction to convert them to their "pH-inert" forms: 1-isobutyl-2,3-dihydro-1*H*-imidazo[1,2-*f*]phenanthridinium (DIP) and 5-[2-(isobutylamino)ethyl]-5,6-dihydrophenanthridine (AEDP), respectively. UV and ^{1}H NMR experiments carried out in a biphasic dichloromethane (DCM)/water solution were used for in situ structure determination. The results showed that the pH-modulated cyclization and phase-transfer process between the TIP and AEP states was essentially quantitative and repeatable without any significant loss in activity and that reduction or oxidation could be used to lock out these states against such acid−base-induced changes.

Introduction

The development of molecular systems capable of changing state, both reversibly and irreversibly, is of interest since they conceptually provide a route for the development of molecular scale devices.[1−3] These devices are interesting because switching on the single-molecule or cluster level[4,5] arouses the possibility of molecular-scale information processing, but the practical issues in terms of both positioning and interfacing the molecules are considerable.[6,7] Fortunately these practical barriers have not prevented vast amounts of research, in particular with the use of derivatizable organic molecules, into discrete systems that have the potential to function as molecular devices.[8−12] Devices that have been constructed to date include molecular shuttles, switches, sensors, valves, motors, and wires, for which there are numerous examples.[13−17] Systems that have a switchable functionality are particularly important as the development of robust and configurable systems will open up new avenues and possibilities including molecular information processing and storage.[18,19]

Most examples of molecular switches typically consist of two stable states distinguishable by physical or chemical properties (response), which are interchangeable through the alteration of controllable parameters (stimuli) such as pH, temperature, light, redox potential, and metal ions.[20−23] There are many examples of systems that utilize these criteria where a single stimulus provides an on/off response, such as the fluorescence quenching of aminomethylanthracenes under pH control,[24,25] UV-controlled fluorescence response of fulgide and fulgimide photochromic systems,[26,27] and the photoisomerization of azobenzene re-

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ceptors.[26−28] These systems generally require the continuous application or absence of the stimulus in order to maintain transmission of the response signal.[29] A highly desirable property in information storage systems is therefore a gated response with gain, where a second external stimulus is used to control the susceptibility of the system to the changes operated by the primary stimulus and this results in an amplified response. Good examples of such systems (without gain) are the dual-mode photoswitching of chiral helical-shaped alkenes, where the photochemical isomerization process can be turned on and off by changes in pH,[26,30] and the dual-mode bisphenolic diarylethenes, where electrochromism can control the primary photochromic cyclization process.[22] Such systems offer the possibility to "store" written information by means of write−lock−read−unlock−erase cycles. Herein we report the use of a pH-modulated cyclization to switch between two states with complementary redox activities that can then be selectively "locked" by oxidation or reduction, thus giving rise to a system with the potential for both read−write and read-only processes.[31−34]

Results and Discussion

The key molecules involved in the present system are the phenanthridine-based heterocycles 1-isobutyl-1,2,3,12b-tetrahydroimidazo[1,2-*f*]phenanthridine (TIP) **1** and 5-[2-(isobutylamino)ethyl]phenanthridinium (AEP) **3**, shown in Figure 1 along with their absorption and emission spectra. The two molecules are interchangeable and can be converted from one to the other via pH control; however, they can also be further manipulated through exploitation of their redox potentials to convert them to their "pH-inert" forms: 1-isobutyl-2,3-dihydro-1*H*-imidazo[1,2-*f*]phenanthridinium (DIP) **2** and 5-[2-(isobutylamino)ethyl]-5,6-dihydrophenanthridine (AEDP) **4**, respectively.[35] Although each of the four switchable states was isolated and characterized, a suitable method to identify each of the states and observe the switching mechanism in situ had to be devised. For this, UV and ^{1}H NMR spectroscopy were the most appropriate analytical techniques, and a series of experiments were designed to demonstrate the behavior of the system in solution. Due to the contrasting properties of the key switchable states TIP **1** (neutral, hydride donor) and AEP **3** (positive charge, hydride acceptor), it was found that the system behaved differently when in monophasic and biphasic conditions.

When a biphasic solution of AEP **3b** in D_2O and $CDCl_3$ was incrementally made more basic with sodium carbonate, the cyclization to TIP **1** and phase transfer processes could be observed by monitoring both phases with ^{1}H NMR spectroscopy. The series of spectra showed a gradual growth of the TIP **1** peaks in the chloroform phase, with respect to cyclohexane as an internal reference. After basification (>pH 12) of the aqueous phase, no AEP **3b** could be detected. Conversely, gradual reduction of TIP **1** peaks with respect to cyclohexane in the chloroform phase was observed upon acidification with DCl. The deprotonation, cyclization, and phase-transfer process was faster than could be observed on the NMR time scale; therefore, conversion essentially occurred instantly upon addition of acid or base. (See Supporting Information for ^{1}H NMR spectra.)

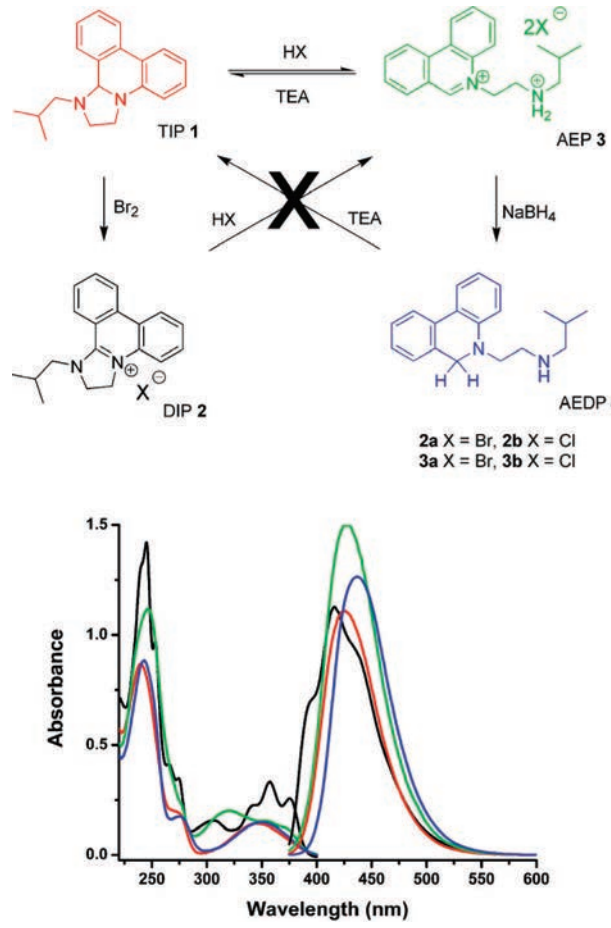

Figure 1. Reaction scheme and absorption (left) and emission (right) spectra for each of the four switchable states: (i) TIP, red curve: (ii) DIP, black curve; (iii) AEP, green curve; (iv) AEDP, blue curve. For absorption spectra, concentrations were 4×10^{-5} M in acetonitrile. See Supporting Information for emission spectra conditions.

Cyclization and phase transfer under biphasic conditions was also followed over a number of cycles by UV spectroscopy (Figure 2). AEP **3a** showed absorbance maxima at 366 and 324 nm, and TIP **1** showed an absorbance maximum at 348 nm. As each form was only soluble in one of the two phases—TIP **1** in the organic phase and AEP **3** in the aqueous phase—this allowed both structural and quantitative data to be obtained for each phase. The pH of a biphasic solution of AEP **3a** was repeatedly switched from ~3 to ~9 over a total number of three cycles, and UV spectra were recorded for each phase throughout. The absorbance at the selected absorbance maxima for each phase can be seen to switch from high to low inversely as pH is altered: When the pH is low, the absorbance of the aqueous phase at 324 nm is at its highest, whereas the absorbance of the organic phase is effectively zero as the molecule exists completely in the open AEP form. When the pH is high, the absorbance of the organic phase at 348 nm is at its highest and the absorbance of the aqueous phase is effectively zero as the molecule exists

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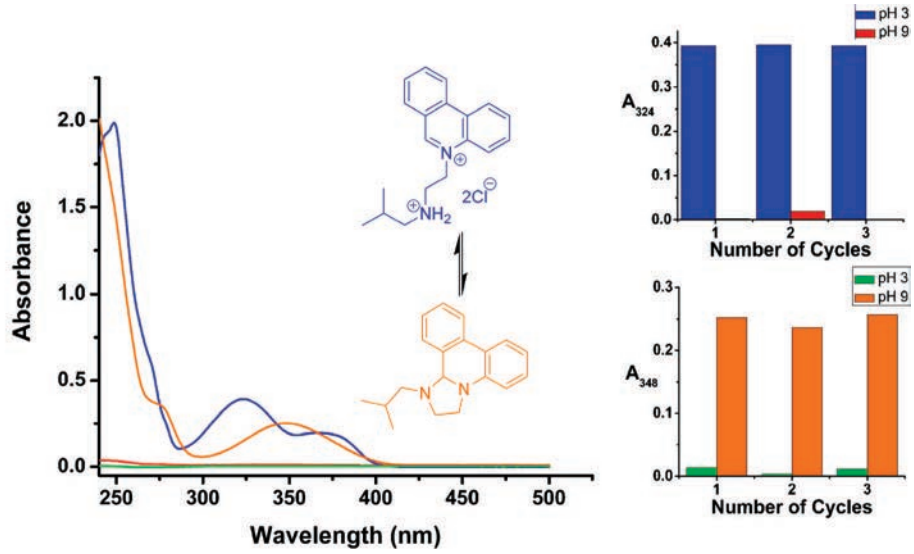

Figure 2. Absorption spectra of dichloromethane (DCM) and aqueous phases at varying pH: (i) AEP in aqueous phase, pH ~3, blue curve; (ii) blank DCM phase, pH ~3, red curve; (iii) blank aqueous phase, pH ~9, green curve; (iv) TIP in DCM phase, pH ~9, orange curve. (Inset, top) Absorbance changes of aqueous phase at 324 nm. (Inset, bottom) Absorbance changes of DCM phase at 348 nm.

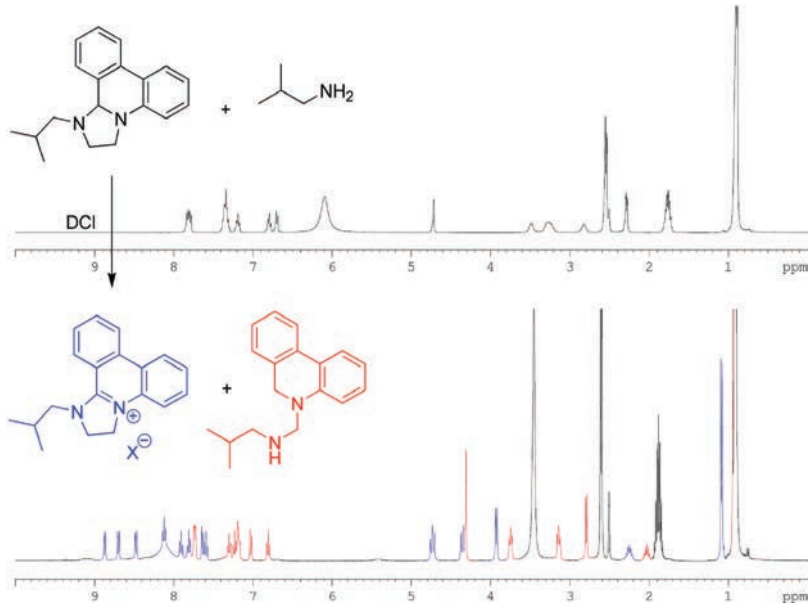

Figure 3. ^{1}H NMR spectra of monophasic DMSO solution containing (top) TIP **1** and excess isobutylamine before DCl addition and (bottom) equimolar amounts of DIP **2** (blue) and AEDP **4** (red) and excess isobutylamine hydrochloride after DCl addition.

completely in the closed TIP form. It can be seen quite clearly from these experiments that the cyclization and phase-transfer process is rapid and essentially quantitative and repeatable without any significant loss of activity.

When incremental pH alterations were made to a monophasic solution of TIP **1** in perdeuterated dimethyl sulfoxide (DMSO-d_6), the same quantitative conversion to AEP **3** was not observed; instead a 1:1 mixture of DIP **2b** and AEDP **4** was formed. ^{1}H NMR spectroscopy was again used to observe this process in solution: A monophasic solution of TIP **1** was prepared by addition of isobutylamine (0.40 mmol, 4.0 equiv) to a solution of 5-(2-bromoethyl)phenanthridinium bromide (0.10 mmol, 1.0 equiv) in DMSO-d_6 (1.0 mL). In this case the amine acts as the nucleophile and base according to the mechanism proposed by Parenty et al.[35] to give a solution of TIP **1**, amine hydrobromide salt, and excess amine. Addition of DCl (0.125 mmol, 1.25 equiv) resulted in complete conversion of TIP **1** to equimolar amounts of DIP **2b** and AEDP **4** (Figure 3.). The same pH-dependent equilibrium exists between TIP **1** and AEP **3** under both monophasic and biphasic conditions, so it must be the phase-transfer mechanism that holds the key for the different outcomes. The presence of a competing "irreversible hydride transfer" reaction between TIP **1** and AEP **3** that is only possible under monophasic conditions is responsible for the conversion to the mixture of DIP **2b** and AEDP **4** rather than to AEP **3**.[35] When the monophasic solution is completely basic (excess isobutylamine), the equilibrium favors the TIP **1** form, but as the acid is added, the increase in pH shifts the position of the equilibria within the reaction mixture from 100% TIP **1** toward a mixture of TIP **1** and AEP **3**. The two forms, now coexisting in situ in the same phase, can now undergo the hydride transfer reaction to form the corresponding

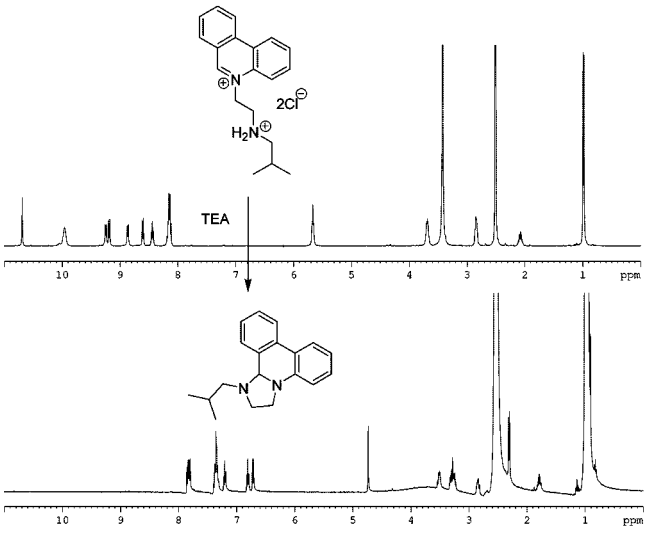

Figure 4. ^{1}H NMR spectra of monophasic DMSO solution containing (top) AEP **3b** before triethylamine addition and (bottom) TIP **1** and excess triethylamine after triethylamine addition.

DIP **2** and AEDP **4** products. This reaction is not possible under biphasic conditions as the redox-incompatible forms are separated by the phase-transfer process even when the pH allows both forms.

The cyclization process could be carried out under monophasic conditions by using a pH swing or jump,[30,36] as the proton-transfer and cyclization processes are faster than the hydride transfer. TIP **1** and AEP **3** will therefore interconvert rather than disproportionate to DIP **2** and AEDP **4**. This was demonstrated by a ^{1}H NMR spectroscopy experiment where an excess of triethylamine (~12 equiv) was added to a solution of AEP **3** in DMSO-d_6 (Figure 4). The large excess of triethylamine causes a jump to highly basic pH, thus allowing conversion of AEP **3** to TIP **1** without observing any of the potential products of the hydride transfer reaction. Although this proves that the reversible cyclization step can occur in a single phase, it is thought that the biphasic system is a more robust technique for achieving repeatable "clean" switching between states.

We have also investigated the solution electrochemistry of compounds DIP **2a** and AEP **3b** using cyclic (CV) and square wave (SWV) voltammetries. CV data for compound **2a** gave rise to a pseudoreversible redox wave, whereas the redox wave for **3b** was irreversible (Figure 5). SWV estimates the reduction potential of **2a** and **3b** to be $E = -1.3$ and -0.6 V, respectively, indicating that the DIP-based system is significantly harder to reduce than the AEP species. The large difference in reduction potentials of these compounds is in agreement with our spectroscopic data, confirming the possibility of hydride transfer between TIP **1** and AEP **3**.

It is this complementary redox activity that allows selective "locking" of the system in its open or closed state by reduction or oxidation. A set of biphasic experiments monitored by UV and ^{1}H NMR spectroscopy (similar to those mentioned previously) were used to demonstrate this: When an excess of $NaBH_4$ was added to a biphasic solution of AEP **3a**, the complete conversion and phase transfer to a new product with an absorbance maximum at 357 nm was observed by UV spectroscopy (Figure 6). With the chromophore structures of TIP **1**

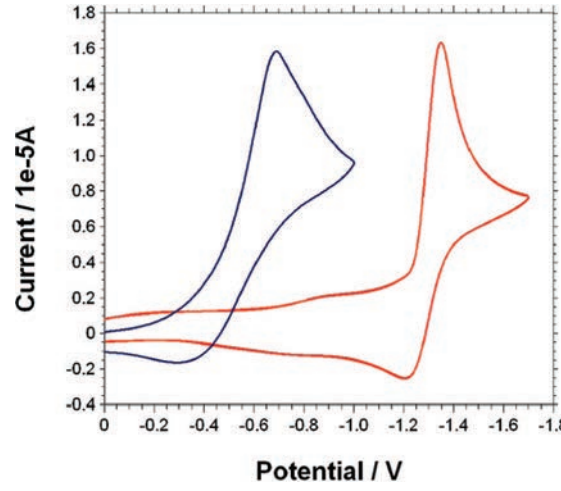

Figure 5. Cyclic voltammograms of compounds **3b** (blue line) and **2a** (red line) in acetonitrile (1.8×10^{-3} M). Scan rate = 100 mV s^{-1}.

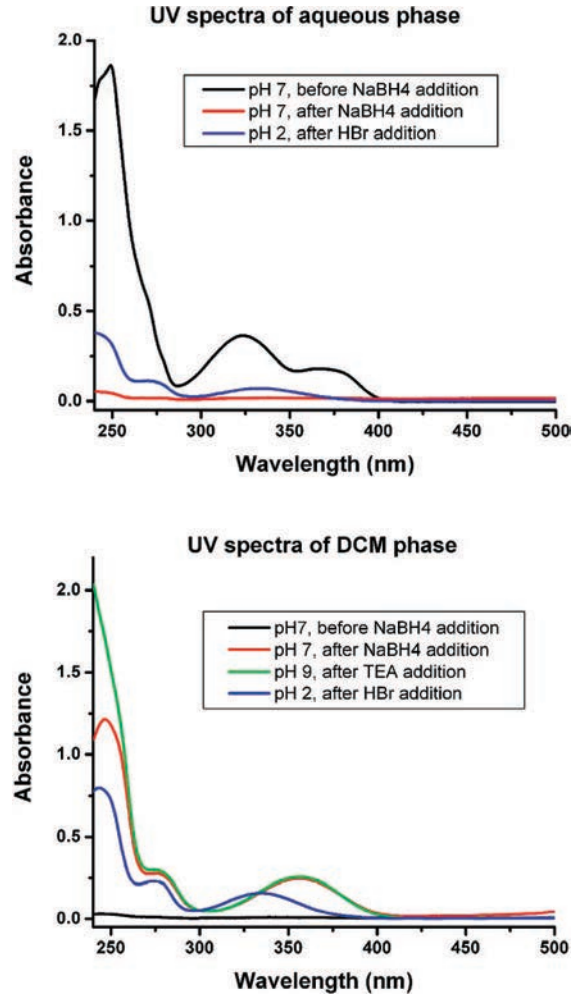

Figure 6. UV spectra of aqueous (top) and DCM (bottom) phases during reduction of AEP **3** to AEDP **4** under biphasic conditions: (i) before $NaBH_4$ addition, black curve; (ii) after $NaBH_4$ addition, red curve; (iii) after TEA addition, green curve; (iv) after excess HBr addition, blue curve.

and AEP **4** being so similar, their absorbance maxima are very close (348 and 357 nm, respectively), thus making the distinction by UV spectroscopy alone a little ambiguous. The same experiment was therefore carried out with ^{1}H NMR spectroscopy

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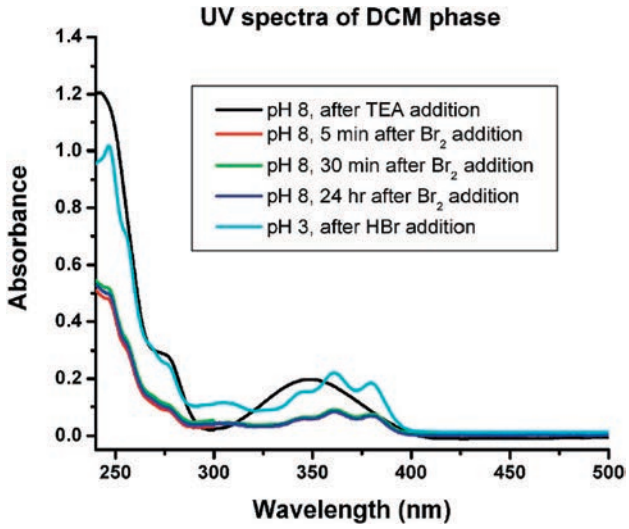

Figure 7. UV spectra of DCM phase during bromine oxidation of TIP **1** to DIP **2** under biphasic conditions: (i) after TEA addition to form TIP **1** from aqueous AEP **3** solution, black curve; (ii) 5 min after Br_2 addition, red curve; (iii) 30 min after Br_2 addition, green curve; (iv) 24 h after Br_2 addition, blue curve; and (v) after excess HBr addition, cyan curve.

used to follow the reduction step. The ^{1}H NMR spectra of AEDP **4** and TIP **1** are very different, and the reduction of AEP **3a** to AEDP **4** could be unambiguously identified by the presence of the characteristic methylene singlet at 4.33 ppm in the ^{1}H NMR spectrum. Alteration of the pH after reduction does not yield absorption bands correlating to either AEP **3** or TIP **1**, thus demonstrating that cyclization could no longer be induced by changes in pH. The changes in the UV spectrum upon reacidification after the reduction can be explained simply by protonation of the diamine product AEDP **4**.

When bromine was added to a biphasic solution of TIP **1**, the oxidation to DIP **2** could be seen by the appearance of new absorbance maxima at 380, 361, and 347 nm in the UV spectrum (Figure 7). The UV spectrum of DIP **2** is very distinctive and completely different than the spectra of any of the other states. However, the same reaction was carried out with ^{1}H NMR spectroscopy to characterize the product, and the characteristic ring triplets at 5.01 and 4.64 ppm in the ^{1}H NMR spectrum unambiguously identified DIP **2** as the sole oxidation product. Alteration of the pH after oxidation does not yield UV absorption bands correlating to either AEP **3** or TIP **1**, again demonstrating that the reversible cyclization process had been inhibited. The changes in the UV spectrum upon reacidification after the oxidation can be explained by protonation and phase transfer of excess triethylamine from the organic phase.

Conclusions

The cyclization process in this heterocyclic molecular system can operate reversibly in both monophasic and biphasic conditions via pH control, and reduction and oxidation can be used to irreversibly inhibit this process. The preferred use of biphasic conditions allows clean reversible operation of pH-modulated cyclization and repetition over a number of cycles. The selective "locking" oxidation and reduction steps of the TIP **1** and AEP **3** molecules are also equally efficient, and conversion to the "pH-inert" DIP **2** and AEDP **4** forms is quantitative. This combination of two separate control parameters creates a switchable system with a gated response where one parameter controls the other, thus allowing for read−write and read-only behavior. This renders it particularly interesting in the development of molecular devices that combine write−read−erase and write−read−lock mechanisms. Although the biphasic solution based methodologies used here demonstrate the dual functionality of this system very well, it is hoped that immobilizing the substrates on surfaces will enhance or alter its performance and allow us to create a truly functional molecular device. In further work we will therefore extend the investigations of the switching/locking potential by anchoring the amine tail group to a surface via a long hydrocarbon chain in the formation of SAMs. Other areas considered for future applications of this system include embedding it within liquid crystals or membranes[37] or grafting onto other functional materials such as polyoxometalates.[38−40]

Experimental Section

Instruments and Materials. All reactions for synthesis and isolation of the products were carried out with clean oven-dried glassware. All starting materials and solvents were commercially available (reagent grade) and were used as supplied, from Sigma−Aldrich and Alfa Aesar Chemical Companies, without further purification. ^{1}H and ^{13}C NMR were recorded on a Bruker DPX 400 spectrometer operating at 400 and 100 MHz, respectively. Chemical shifts (δ) are given in parts per million (ppm) relative to the residual solvent peak. Coupling constants (J) are given in hertz. The multiplicities are expressed as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Infrared spectral analyses were performed on a Jasco 410 spectrophotometer, via a KBr disk; peaks are quoted in wavenumbers (cm^{-1}) and their relative intensities are reported as follows: s = strong, m = medium, w = weak. UV−vis spectroscopy was performed on a Shimadzu UV-310PC UV−vis−near-IR scanning spectrophotometer. Fluorescence spectroscopy was performed on a Shimadzu spectrofluorophotometer RF-5301PC. Mass spectra were obtained on a JEOL JMS 700 spectrometer operating in fast atom bombardment (FAB), electron ionization (EI), or chemical ionization (CI) mode. All of the compounds **1-4** used could be synthesized in two steps from the starting material 5-(2-bromoethyl)phenanthridinium bromide, prepared by the methodology of Parenty and Cronin.[41]

Preparation of 1-Isobutyl-1,2,3,12b-tetrahydroimidazo-[1,2-*f*]phenanthridine (1). In an NMR tube, 5-(2-bromoethyl)phenanthridinium bromide (30 mg, 0.082 mmol, 1.0 equiv) was suspended in $CDCl_3$ (1 mL) and D_2O (1 mL). Isobutylamine (8 μL, 0.082 mmol, 1.0 equiv) and 5% Na_2CO_3(aq) were then added, and the solution was shaken for 1 min. The $CDCl_3$ layer was then characterized by ^{1}H and ^{13}C NMR spectroscopy. The product was not isolated due to its low stability in air. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.67 (d, 2H, J = 7.7 Hz), 7.38 (d, 1H, J = 7.7 Hz), 7.30−7.21 (m, 2H), 7.15 (t, 1H, J = 7.7 Hz), 6.78 (t, 1H, J = 7.7 Hz), 6.58 (d, 1H, J = 7.7 Hz), 4.78 (s, 1H), 3.41 (m, 2H), 3.27 (m, 1H), 2.85 (m, 1H), 2.33 (m, 2H), 1.78 (m, 1H), 0.98 (d, 3H, J = 6.6 Hz), 0.90 (d, 3H, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 144.02 (C), 133.18 (C), 131.99 (C), 129.19 (CH), 127.80 (CH), 127.23 (CH), 124.74 (CH), 123.27 (CH), 122.75 (CH), 121.89 (C), 118.24 (CH), 112.66

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(CH), 79.73 (CH), 62.01 (CH_2), 51.61 (CH_2), 44.88 (CH_2), 28.21 (CH), 21.18 (CH_3), 20.92 (CH_3).

Preparation of 1-Isobutyl-2,3-dihydro-1*H*-imidazo[1,2-*f*]-phenanthridin-4-ylium Bromide (2a). 5% Na_2CO_3 aqueous solution (10 mL) was added to a suspension of 5-[2-(isobutylamino)ethyl]phenanthridinium chloride; hydrochloride (**3b**) (351 mg, 1.0 mmol, 1.0 equiv) in ethyl acetate (20 mL). The resultant biphasic solution was stirred at room temperature for 20 min. Layers were separated and the organic layer was washed with water (3 × 10 mL) and brine (1 × 10 mL). NBS (178 mg, 1.0 mmol, 1.0 equiv) was added and the reaction stirred for 3 h. The resultant suspension was filtered, washing the residue thoroughly with diethyl ether. The residue was dried under vacuum and collected as a pale yellow solid (357 mg, 1.0 mmol, 100%). mp: 251−253 °C; ^{1}H NMR (DMSO, 400 MHz): δ 8.92 (d, 1H, J = 8.0 Hz), 8.75 (d, 1H, J = 8.0 Hz), 8.51 (d, 1H, J = 8.0 Hz), 8.15 (t, 1H, J = 8.0 Hz), 7.93 (t, 1H, J = 8.0 Hz), 7.84 (t, 1H, J = 8.0 Hz), 7.67 (d, 1H, J = 8.0 Hz), 7.62 (t, 1H, J = 8.0 Hz), 4.74 (t, 2H, J = 10.6 Hz), 4.35 (t, 2H, J = 10.6 Hz), 3.95 (d, 2H, J = 7.6 Hz), 2.28 (m, 1H), 1.11 (d, 6H, J = 6.4 Hz); ^{13}C NMR (DMSO, 100 MHz): δ 153.22 (C), 135.15 (CH), 134.82 (C), 132.93 (C), 131.38 (CH), 129.35 (CH), 127.76 (CH), 125.11 (CH), 124.27 (CH), 123.88 (CH), 119.81 (C), 115.88 (CH), 115.60 (C), 56.88 (CH_2), 52.31 (CH_2), 45.89 (CH_2), 27.47 (CH), 19.73 (2 × CH_3); MS (FAB): 277 (M^+) (100), 219 (10), 176 (9).

Preparation of 1-Isobutyl-2,3-dihydro-1*H*-imidazo[1,2-*f*]-phenanthridin-4-ylium Chloride (2b). To a suspension of 5-(2-bromoethyl)-phenanthridinium bromide (350 mg, 0.95 mmol, 1.0 equiv) in ethyl acetate (20 mL) was added 5% Na_2CO_3(aq) (10 mL) and isobutylamine (95 μL, 0.95 mmol, 1.0 equiv). The resultant biphasic solution was stirred at room temperature under nitrogen for 30 min. Layers were separated and the organic layer was washed with water (1 × 10 mL) and brine (1 × 10 mL). NCS (126 mg, 0.95 mmol, 1.0 equiv) was added and the reaction stirred for 1 h in the dark. The resultant suspension was filtered, washing the residue thoroughly with diethyl ether. The residue was dried under vacuum and collected as a pale yellow powder (39 mg, 0.12 mmol, 13.1%). mp: 277−279 °C; ^{1}H NMR (DMSO, 400 MHz): δ 8.93 (d, 1H, J = 8.0 Hz), 8.76 (d, 1H, J = 8.0 Hz), 8.52 (d, 1H, J = 8.0 Hz), 8.16 (t, 1H, J = 8.0 Hz), 7.93 (t, 1H, J = 8.0 Hz), 7.85 (t, 1H, J = 8.0 Hz), 7.68 (d, 1H, J = 8.0 Hz), 7.63 (t, 1H, J = 8.0 Hz), 4.74 (t, 2H, J = 10.6 Hz), 4.35 (t, 2H, J = 10.6 Hz), 3.95 (d, 2H, J = 7.6 Hz), 2.28 (m, 1H), 1.11 (d, 6H, J = 6.4 Hz); ^{13}C NMR (DMSO, 100 MHz): δ 153.13 (C), 135.12 (CH), 134.76 (C), 132.87 (C), 131.35 (CH), 129.34 (CH), 127.72 (CH), 125.08 (CH), 124.25 (CH), 123.85 (CH), 119.75 (C), 115.86 (CH), 115.51 (C), 56.88 (CH_2), 52.31 (CH_2), 45.87 (CH_2), 27.49 (CH), 19.75 (2CH_3).

Preparation of 5-[2-(Isobutylamino)ethyl]phenanthridinium Bromide Hydrobromide (3a). To a suspension of 5-(2-bromoethyl)phenanthridinium bromide (1.00 g, 2.72 mmol, 1.0 equiv) in DCM (40 mL) were added isobutylamine (270 μL, 2.72 mmol, 1.0 equiv) and 5% Na_2CO_3 (30 mL). The reaction mixture was stirred for 1.5 h under nitrogen before it was transferred to a separating funnel. Phases were separated and the organic phase was washed with water (1 × 10 mL) and then extracted into 10% HBr (2 × 25 mL). The acidic extract was concentrated under vacuum and the residue was triturated with acetone to afford a pale yellow crystalline solid as the product (1.01 g, 2.29 mmol, 84.3%). mp 244−245 °C; ^{1}H NMR (D_2O, 400 MHz) δ 9.89 (s, 1H), 8.73 (d, 1H, J = 8.2 Hz), 8.64 (d, 1H, J = 8.2 Hz), 8.34 (d, 1H, J = 8.2 Hz), 8.22 (d, 1H, J = 8.2 Hz), 8.17 (t, 1H, J = 8.2 Hz), 7.99 (t, 1H, J = 8.2 Hz), 7.89 (m, 2H), 5.35 (t, 2H, J = 6.9 Hz), 3.72 (t, 2H, J = 6.9 Hz), 2.87 (d, 2H, J = 7.1 Hz), 1.91 (m, 1H), 0.86 (d, 6H, J = 6.9 Hz); ^{13}C NMR (D_2O, 100 MHz) δ 155.62 (CH), 138.97 (CH), 135.39 (C), 132.77 (CH), 132.60 (C), 132.48 (CH), 130.62 (CH), 130.48 (CH), 126.34 (C), 124.97 (CH), 124.32 (C), 122.72 (CH), 118.38 (CH), 55.50 (CH_2), 53.29 (CH_2), 45.57 (CH_2), 25.64 (CH), 19.03 (CH_3).

Preparation of 5-[2-(Isobutylamino)ethyl]phenanthridinium Chloride Hydrochloride (3b). 5-(2-Bromoethyl)phenanthridinium bromide (250 mg, 0.68 mmol, 1.0 equiv) was added to a biphasic solution of isobutylamine (67.5 μL, 0.68 mmol, 1.0 equiv) in ethyl acetate (20 mL) and 5% Na_2CO_3 aqueous solution (20 mL). The solution was stirred at room temperature for 3 h before it was transferred to a separating funnel, where the phases were separated and the organic phase was washed with water (2 × 5 mL) and brine (1 × 5 mL). Concentrated HCl (3 drops) was then added to the organic layer to form the hydrochloride salt. Evaporation of the solvent and trituration of the residue with diethyl ether yielded the product as a pale yellow solid (187 mg, 0.53 mmol, 78.3%). mp 234−235 °C; ^{1}H NMR (DMSO, 400 MHz) δ 10.72 (s, 1H), 10.08 (s, 2H), 9.25 (d, 1H, J = 8.0 Hz), 9.18 (d, 1H, J = 8.0 Hz), 8.89 (d, 1H, J = 8.0 Hz), 8.60 (d, 1H, J = 8.0 Hz), 8.43 (t, 1H, J = 8.0 Hz), 8.15 (m, 3H), 5.69 (t, 2H, J = 6.2 Hz), 3.69 (m, 2H), 2.84 (m, 2H), 2.10 (septet, 1H, J = 6.8 Hz), 0.99 (d, 6H, J = 6.8 Hz); ^{13}C NMR (DMSO, 100 MHz) δ 157.39 (CH), 138.15 (CH), 134.69 (C), 133.29 (C), 133.06 (CH), 132.02 (CH), 130.29 (CH), 130.18 (CH), 126.08 (C), 125.12 (CH), 123.81 (C), 123.14 (CH), 119.95 (CH), 54.29 (CH_2), 53.10 (CH_2), 45.52 (CH_2), 25.39 (CH), 20.30 (2CH_3); IR (KBr, cm^{-1}) 3412 (s), 2959 (m), 2706 (m), 1627 (s), 1535 (m), 1451 (s), 761 (s); MS (EI): 280.3 (11) (M^+), 278.3 (5), 235.2 (36), 194.2 (100), 180.2 (30), 165.1 (23); HRMS (FAB) for M^+ calcd 279.1861, obsd 279.1862.

Preparation of 5-[2-(Isobutylamino)ethyl]-5,6-dihydrophenanthridine (4). In an NMR tube, 5-(2-bromoethyl)phenanthridinium bromide (30 mg, 0.085 mmol, 1.0 equiv) was dissolved in D_2O (1 mL). $CDCl_3$ (1 mL) was then added, followed by sodium cyanoborohydride (6.4 mg, 0.102 mmol, 1.2 equiv), and the reaction was shaken until a biphasic solution formed. The aqueous phase was removed and the organic layer was washed with a 5% Na_2CO_3 in D_2O solution (2 × 1 mL). The organic layer was concentrated under vacuum to give the product as a yellow oil (20 mg, 0.713 mmol, 71.3%). ^{1}H NMR (DMSO, 400 MHz) δ 7.74 (d, 1H, J = 8.0 Hz), 7.73 (d, 1H, J = 8.0 Hz), 7.30 (t, 1H, J = 8.0 Hz), 7.23 (t, 1H, J = 8.0 Hz), 7.18 (m, 2H), 6.83 (d, 1H, J = 8.0 Hz), 7.75 (t, 1H, J = 8.0 Hz), 4.32 (s, 2H), 3.38 (t, 2H, J = 8.0 Hz), 2.76 (t, 2H, J = 8.0 Hz), 2.37 (d, 2H, J = 7.6 Hz), 1.65 (septet, 1H, J = 6.8 Hz), 0.87 (d, 6H, J = 6.8 Hz); ^{13}C NMR (DMSO, 100 MHz) δ 145.98 (C), 132.62 (C), 131.58 (C), 129.12 (C), 129.08 (CH), 127.50 (CH), 126.92 (CH), 125.65 (CH), 123.56 (CH), 122.06 (CH), 117.36 (CH), 112.28 (CH), 57.68 (CH_2), 51.85 (CH_2), 50.05 (CH_2), 45.20 (CH_2), 28.01 (CH), 20.79 (2CH_3); IR (KBr, cm^{-1}) 3424 (w), 3067 (w), 2954 (m), 2352 (w), 2251 (w), 1602 (m), 1496 (s), 1444 (s), 1289 (w), 1103 (w), 749 (s); MS (EI) 280.2 (M^+) (31), 235.1 (79), 194.0 (100), 180.0 (63), 165.1 (41), 152.0 (19), 86.1 (32); HRMS (EI) for M^+ calcd 280.1939, obsd 280.1936.

UV Spectroscopy Experiments. The experiments designed to show interconversion of the various states by use of UV

spectroscopy were all set up in 500 mL Erlenmeyer flasks with an aqueous solution of AEP **3a** (5×10^{-5} M, 100 mL) and DCM (100 mL). Aqueous solutions of AEP **3a** were prepared by dilution of fresh stock solutions, 5×10^{-3} M (22 mg, 0.05 mmol in 10 mL of deionized water). The other reactants were added as required, and aliquots of both the aqueous and organic phases were analyzed by UV spectroscopy after each addition. Full experimental details and spectra for each individual experiment are available in the Supporting Information.

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Supporting Information Available: Spectral data for compounds **1**−**4**, square wave voltammograms of compounds **2a** and **3b**, experimental methods, and additional spectroscopic results. This material is available free of charge via the Internet at http://pubs.acs.org.

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