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An Anthracene Based Photoswitchable Dioxo-Tetraaza Ligand Selective for Cu^{II} and Capable of Photochemical pK_a Modulation

Giacomo Dacarro,[a] Paola Ricci,[a] Donatella Sacchi,[a] and Angelo Taglietti*[a]

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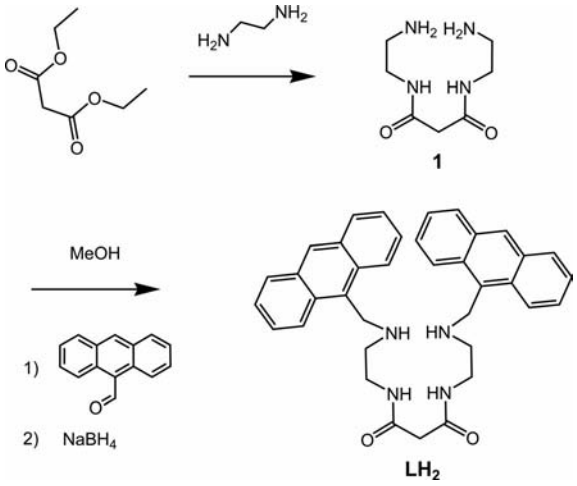
Two anthracene fragments were added to a linear dioxotetramine ligand in order to exploit a [4πs+4πs] photocycloaddition reaction and obtain a photoswitchable selective receptor for Cu^{II}, whose cavity (and binding abilities) can be closed on command. Moreover, it was demonstrated that this new ligand, *N*,*N*′-bis{2-[(anthracen-9-ylmethyl)amino]ethyl}-malonamide (LH_2), can also be used for the photoinduced release of protons in aqueous solution, as a result of photoinduced pK_a modulation.

Introduction

Switchable receptors[1] are molecular or supramolecular systems for which a stimulus is required to make the system change to have the correct shape and right features to recognize a given chemical species. The stimulus can be provided, to give the most common examples, by pH changes, electrochemical input, cation complexation or light irradiation. Photoswitchable receptors[2] have been explored in the last few decades by several groups. Such systems can be designed by joining photochromic fragments and typical binding ligands, with the goal of preparing ligands that permit the photocontrol of their structural changes, which allows to modulate the molecular recognition properties of the ligand in response to light. Anthracene has been used widely as a photochromic fragment because of its ability to undergo a typical [4πs + 4πs] photodimerization reaction, which is photo and thermally reversible.[3] Using this approach, several examples of photoswitchable receptors for cations involving mainly ethers,[4] crown ethers and coronands,[5] resorc[4]arenes,[6] and calixarenes[7] have been described in the last few years. Another intriguing example of the application of anthracene photodimerization has been reported recently by Tucker and collegues, and their ligand demonstrated barbiturate recognition through a hydrogen bond receptor moiety.[8] To the best of our knowledge, no studies have been reported regarding anthracene-based photoswitchable ligands that are selective for transition metal cations. Furthermore, no examples of the exploitation of this approach in aqueous environments have been given.

Dioxo 2-3-2 is a diamino-diamido ligand that has been used widely because of its ability to bind selectively to Cu^{II} and Ni^{II} among the divalent cations of the first metal transition series (like Mn^{II}, Fe^{II}, Co^{II} and Zn^{II}), with the deprotonation of the two amido groups.[9] The deprotonation of the two amidic functions is a highly endothermic process, and can take place only when compensated for by the formation of energetic strong bonds between the cation and the deprotonated amide group. This is possible only for the two cited cations, which can profit from strong ligand field effects, with Cu^{II} being able to form very stable complexes, as expected from the Irving Williams series.[10] Our idea was to take this well known open ligand that is able to bind selectively to Cu^{II} and Ni^{II} in water as a function of pH, and to equip it with an anthracene fragment at both extremities (see Scheme 1 for the synthesis) to enable it to photoreact to give a closed (macrocyclic) structure, as de-



Scheme 1. Synthesis of LH_2.

[a] Dipartimento di Chimica Generale, Università di Pavia,
Viale Taramelli 12, 27100 Pavia, Italy
Fax: +39-0382-529-544
E-mail: angelo.taglietti@unipv.it

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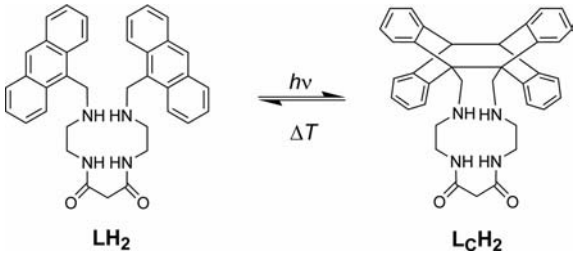
picted in Scheme 2, and to check any possible change of affinity towards the cited cations upon this structural alteration. In our consideration was the need for the photoswitching process, which leads to the macrocyclic form of the ligand, to give sensible changes in the receptor features in terms of cavity size and accessibility, but also in the basicity of the binding atoms.



Scheme 2.

Results and Discussion

Irradiation Studies and Photoproduct Characterization

The ability of LH_2 to undergo a photocyclization reaction was at first assessed by means of a spectrophotometric investigation. As a consequence of the [4π + 4π] photocycloaddition, the typical structured absorption band associated with anthracene disappears from the UV spectrum.[3] Solutions of LH_2 ($1–2 \times 10^{-5}$ M) were prepared in different solvents (acetonitrile, tetrahydrofuran, methanol) and mixtures of these solvents with water. The samples were placed in a 1 cm quartz cuvette, deaerated with argon for 10 min, and then irradiated with UV light for 5 min, then spectra were taken. Then the samples were stored in the dark for 48 h, and spectra were taken again to check for the reversibility of the photocycloaddiction reaction and the opening of the ligand. The best results were obtained for the ligand dissolved in methanol and its mixtures with water. Figure 1 shows the spectra of LH_2 [in water/methanol (1:4)], of LH_2 after 5 min of irradiation, and of LH_2 after 48 h in the dark. The back ring opening reaction was also followed over time in order to establish the mechanism of the reaction. Pure MeOH solutions of the ligand were irradiated for 5 min, stored in the dark at a controlled temperature, and then absorption spectra were taken over the following hours. As expected, a first order kinetic reaction was observed when fitting the change in intensity values for the typical anthracene absorption band (at 366 nm) vs. time.

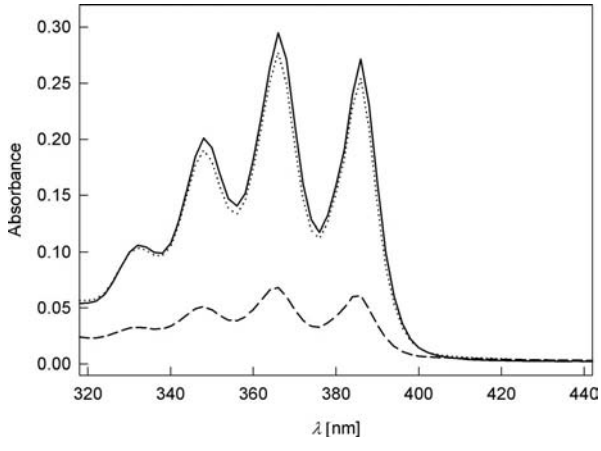


Figure 1. Spectra of 2×10^{-5} M LH_2 water/MeOH (1:4) solution (solid line), and the same solution after 5 min of irradiation at 366 nm (dashed line), and the same solution after being stored for 48 h in the dark at room temperature (dotted line).

At 293 K, a kinetic constant of 2.28×10^{-5} s^{-1} (corresponding to a half time of ca. 465 min) was calculated for the ring opening reaction. When the kinetc measurements were repeated after storing the irradiated sample at 318 K, a constant of 4.76×10^{-4} s^{-1} was found, corresponding to a half time of ca. 24 min. It is obvious that the slow ring opening reaction can be controlled by means of temperature. An estimation of the activation energy for this reaction can be calculated easily from these measurements, and has a value of 1.37 kJ mol^{-1}.

In order to rule out the occurrence of intermolecular photoaddition reactions, mass spectra were recorded on a sample before irradiation, after irradiation, and after a ring opening thermal reaction. In all cases only the presence of the molecular mass peak (569 *m*/*z*) was observed in the spectra, no peaks corresponding to intermolecular dimers were seen.

The ^1H NMR spectra of LH_2 in degassed deuterated methanol was recorded, and after this data collection the sample tube was irradiated for 10 min and the spectrum of the photoproduct was then recorded (see Supporting Information). The singlet at 8.4 ppm in the spectrum of LH_2, which is attributed to two protons on the central ring of each anthracene fragment (at the 10 position), disappears in the spectrum of the photoproduct, and is substituted by a singlet signal at $\delta = 4.47$ ppm as the protons become benzylic after removal of the aromaticity of the central rings. In the same way, the singlet at $\delta = 4.71$ ppm observed in the spectrum of LH_2, which is associated with four benzylic protons, disappears after irradiation of the sample and is substituted by a singlet at 4 ppm in the spectrum of the

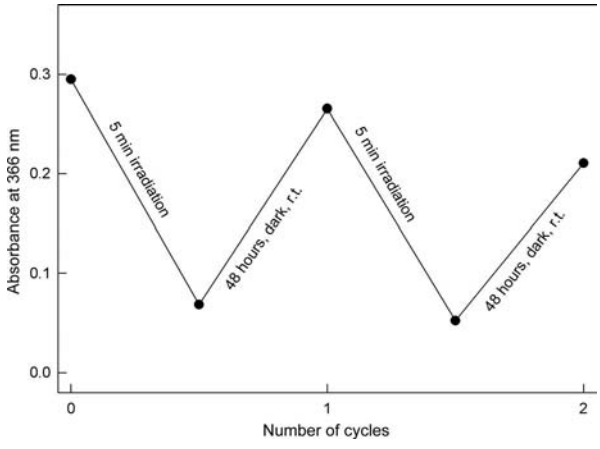


Figure 2. Fatigue studies on a 2×10^{-5} M solution of LH_2.

photoproduct as a consequence of the aliphatic nature of these protons in the photoproduct. These results are very clear, even though the NMR spectrum of the photoproduct is quite complex due to the presence of small fractions (around 10% of each) of unreacted open ligand and of irradiation by-products that are generated in this solvent.

Fatigue studies were also performed. A sample of LH_2 in a water/methanol mixture was irradiated for 5 min and then stored in the dark for 2 d; this cycle was then repeated, with spectra taken after every step. As can be noticed in Figure 2, a small amount of ligand (ca. 10%) decomposes after each cycle.

Potentiometric and Complexation Studies

After determination of the protonation constants for LH_2 and evaluation of the relative distribution diagram (see Supporting Information) of the ligand in an aqueous environment (water/methanol, 1:4), the complexation tendencies of LH_2 towards Cu^{II} and Ni^{II} were investigated.

Stability constants obtained by potentiometric titrations (water/methanol, 1:4) in presence of one equivalent of LH_2 (10^{-3} M) and one of Cu^{II} (or Ni^{II}) are given in Table 1. This stoichiometric ratio was chosen as it is the ratio that was used in the mass spectra experiments (vide infra) and in the photochemical experiment (performed on the 1:1 complex, vide infra). Under these conditions only the $[M^{II}L]$ species is formed. Such a behavior is in agreement with previous investigations on the solution stability of Cu^{II} and Ni^{II} dioxotetramine complexes.[9] pH-spectrophotometric titrations were performed under the same conditions, and the spectra show the formation of d-d bands as a function of pH, which are bands that are typical of the two metal complexes. In Figures 3 and 4 the distribution diagrams obtained for the Cu^{II}/LH_2 and Ni^{II}/LH_2 systems are shown, as obtained from the potentiometric titrations, and superimposed on these diagrams is the data obtained from the pH-spectrophotometric titrations, i.e. the absorbance value for the typical absorption band of the complex (510 nm for CuL and 480 nm for NiL). It can be seen clearly in these diagrams that the sigmoid profiles of the absorbance curves are coincident with the formation of the two ML species. It is also evident that the complex with the nickel ion is formed at two pH units higher than the copper complex, as expected on the basis of previous data reported for similar systems.[9a]

Table 1. Logarithmic formation constants[a] for species relative to ligand LH_2 plus M^{2+} (1:1 molar ratio).

Equilibrium and relative species	log *K*
[1,0,2] $LH_2 + 2H^+ \leftrightarrows LH_4^{2+}$	13.98
[1,0,1] $LH_2 + H^+ \leftrightarrows LH_3^+$	7.58
[1,1,0] $LH_2 + Cu^{2+} \leftrightarrows CuLH_2^{2+}$	6.20
[1,1,–2] $LH_2 + Cu^{2+} \leftrightarrows CuL + 2H^+$	–5.80
[1,1,0] $LH_2 + Ni^{2+} \leftrightarrows NiLH_2^{2+}$	2.55
[1,1,–2] $LH_2 + Ni^{2+} \leftrightarrows NiL + 2H^+$	–10.49

[a] All constants have an uncertainty of 0.04 associated with them.

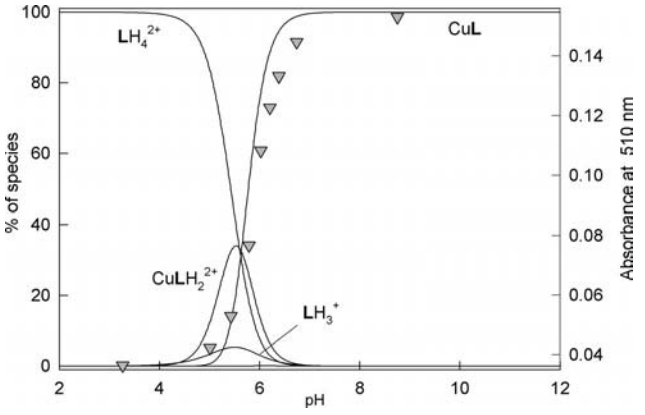


Figure 3. Distribution diagram for the system [L, Cu^{2+}, H^+] obtained from a potentiometric titration. Symbols represent the data obtained from pH-spectrophotometric titrations. The intensity of the absorbance band at 510 nm in the spectrum of the titration solution is also shown.

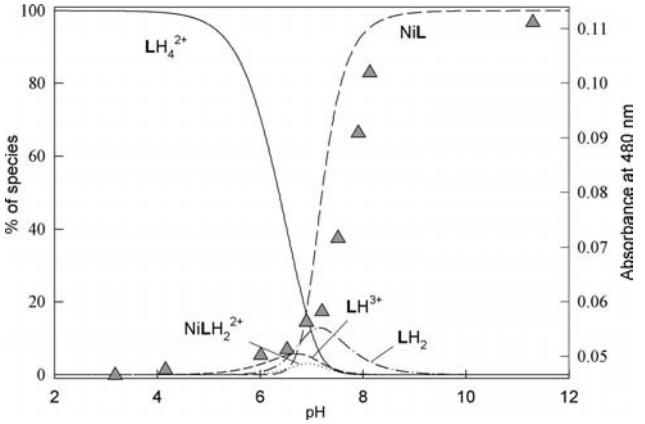


Figure 4. Distribution diagram for the system [L, Ni^{2+}, H^+] obtained from a potentiometric titration. Symbols represent the data obtained from pH-spectrophotometric titrations. The intensity of the absorbance band at 480 nm in the spectrum of the titration solution is also shown.

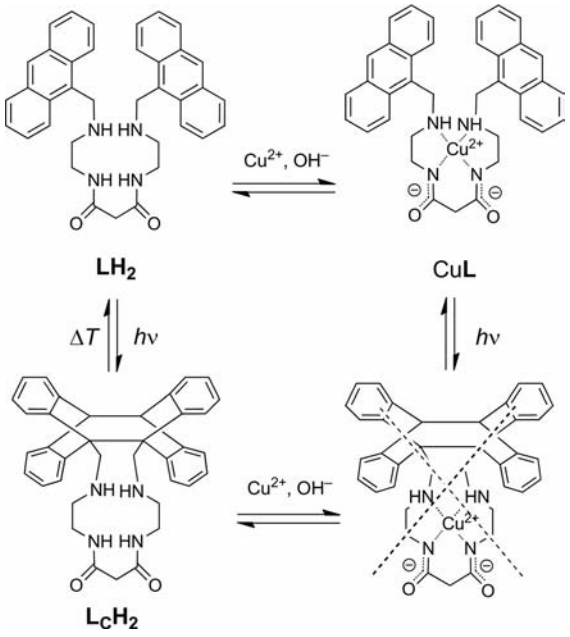
Thus, ligand LH_2 can act as a selective receptor for Cu^{II} at pH 6.5–7; at these pH values complexation of Cu^{II} is quantitative, while affinity for Ni^{II} (and for other previously cited divalent cations) is negligible. To check this, we performed titrations with a solution of LH_2 [10^{-3} M, water/methanol (1:4)] buffered at pH 6.8 [0.05 M 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES)]. Titration with a solution containing Ni^{II}, Mn^{II}, Fe^{II} Co^{II} and Zn^{II} gave no absorption bands in the UV/Vis spectra of the solution that could be assigned to a complex, while the spectra of the titration solution containing Cu^{II} clearly showed the formation of the CuL complex, with the development of a typical absorption band centred at 510 nm, the intensity of which reached a plateau after the addition of 1 equiv. of cation (see Supporting Information).

We tried to repeat the whole set of potentiometric experiments with irradiated samples, but unfortunately the thermal reaction leading back to the open ligand did not allow

us to obtain meaningful data as the concentration of photocyclized ligand decreases over the time scale needed for the experiment (at least 2 h).

To check the photocyclized ligand's affinity for Cu^{II}, we performed similar titration experiments with Cu^{II} and L_cH_2 that was obtained from the irradiation of a 10^{-3} M water/methanol (1:4) deareated solution of LH_2, which was buffered to pH 6.8 with HEPES. In this case, no formation of the typical absorbance band for a complex was observed in the spectra of the titration solution, while it was noticed that there was an increase in the intensity of the typical copper aquo-ion absorption band as the titration proceeded (see Supporting Information). This implies that the photocyclized ligand is not able to bind with copper cations in the investigated pH range. Moreover, a pH-spectrophotometric titration was carried with the photocyclizated L_cH_2 product in presence of 1 equiv. of Cu^{II} in order to exclude the possibility of complex formation between L_cH_2 and copper ions at high pH values. In this case, no development of absorption bands between 500 and 600 nm that are typical of dioxotetraminic deprotonated complexes of copper,[1b,1i,1l,9a,9b,9d] were observed in spectra of the titration solution that were recorded in the investigated pH range (3–11), if one excludes a small shoulder appearing at pH > 6, which is ascribed to a small percentage of open ligand that is generated by a thermal back reaction (see Figure S4 in the Supporting Information). To evaluate this result we performed mass spectroscopy experiments with the following solutions: (a) a solution of CuL [10^{-5} M, water/methanol (1:4)] adjusted to pH 7; (b) a solution containing ligand LH_2 [10^{-5} M, water/methanol (1:4)] and 1 equiv. of copper triflate; (c) a solution containing the irradiated ligand, L_cH_2 [10^{-5} M, water/methanol (1:4)] and 1 equiv. of copper triflate; (d) a mixture of solutions (a) and (c). In the spectra of solutions (a) and (b) we observed a single peak at m/z = 633 (with the expected Cu^{II} isotopic pattern) that was assigned to the $[CuL + H]^+$ ion, while in the spectrum for solution (c) only the peak associated with the free ligand (as $L_cH_3^+$) at m/z = 569 was observed, and in the spectrum of sample (d) both peaks were present. These results confirm the following: (i) the presence of only the 1:1 deprotonated complex CuL under the conditions of our experiments; (ii) the fact that the photocyclized ligand is not able to bind to copper ions under these pH conditions. As suggested from molecular modeling performed with PM3 calculations[11] (see Supporting Information), the inability to bind copper in the cyclic ligand should be due to the lack of preorganization in the L_cH_2 ligand. The enthalpic contribution required to rearrange the diamidic framework in the strained cyclic ligand and the endoergonic demand for deprotonation, overcomes the energetic advantages of complexation. Additionally, the rearrangement of the photocyclizated L_cH_2 molecule to a conformation suitable for metal coordination may also suffer from severe steric constraints and should be characterized by a very high kinetic barrier. The overall result is that the macrocyclic effect, which one could expect to occur when changing from the open ligand to the cyclic one, and which should allow for complexation of cations at low pH,[9a] is not observed. On the contrary, no complex formation is observed even at high pH values.

Moreover, when we irradiated a solution of the neutral copper complex CuL [10^{-4} M, water/methanol (1:4)] to obtain photocyclization, even after long irradiation times (up to 30 min) negligible changes were observed in the anthracene absorption band in the spectrum of the solution. Once again, a steric explanation can be offered; the copper ion imposes a square planar structure on the donating atom set[12] and a minimum fixed distance between the two anthracene fragments, which prevents the fragments from coming close enough to each other to allow the photocyclization reaction to occur. The overall behaviour of LH_2 and L_cH_2 towards photocyclization and copper binding is outlined in Scheme 3.



Scheme 3.

Photochemical Modulation of pK_a

In order to evaluate the variations in the basicity features of the ligand arising from the photocyclization reaction, we had to overcome the problems due to the thermal back reaction, which precluded the possibility of potentiometric investigations. We decided to prepare an array of solutions containing a fixed amount of ligand and a fixed excess of acid, as in the potentiometric esperiment setup. To each of these solutions a known quantity of base was added, and the pH and absorption spectra of the solutions were measured. If carefully done, this operation allows us to deduce some points (grey triangles in Figure 5) comparable to the potentiometric titration experiments (the continuous line in Figure 5 represents the experimental data obtained from potentiometric titration of LH_2). pH values were found to equal to those recorded during the potentiometric experiment for a given amount of added base. The solutions were

then irradiated for 10 min, and pH and absorption spectra were measured again (this was done mainly to check that there was a decrease in the intensity of the anthracene absorption band, which indicted that the photocyclization yield was more than 80%). As reported in Table 2, some pH values show sensible variations after irradiation. If we report on the graph the new pH values (Figure 5, open diamonds), we can imagine that a new potentiometric curve is passing through these new points that is pertinent to the photocyclized ligand with the same amount of base added to the solution. We used the Hyss program to simulate a potentiometic curve passing through the new data points obtained after photocyclization, and to do this we tried several values for the basicity constant. There is clear evidence, looking at the distribution diagram for the free ligand (see Supporting Information), that the variations in pH upon photocyclization are observed only in the pH range in which the diprotonated species is present in a significant amount (below pH 7).

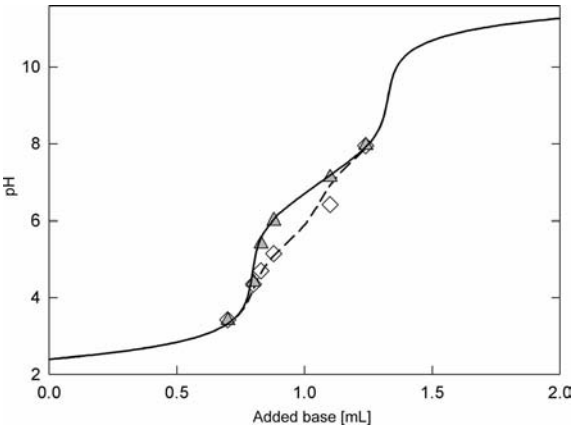


Figure 5. Solid line represents the fitting of the potentiometric data obtained from measurements with free ligand LH_2 as described in the text. Filled triangles represent data points (i.e. pH values) obtained by adding to 6 identical ligand solutions the proper amount of base. Empty diamonds represents pH values measured for the same 6 solutions after 10 min of irradiation. The dashed line represents a calculated potentiometric curve that gives the best fit for the 6 new pH values obtained after irradiation.

Table 2. pH values for 10^{-3} M solutions of ligand LH_2 after the addition of known amounts of acid and base,[a] prior to and after irradiation to form the photoproduct L_cH_2.

Before irradiation (LH_2)	After irradiation (L_cH_2)
3.40	3.42
4.41	4.35
5.40	4.70
6.00	5.15
7.12	6.41
7.96	7.95

[a] Calculated with Gran's method, see ref.[14].

In these calculations we essentially changed the β_2 value. When β_2 is lowered by one logaritmic unit ($\log\beta_2$ changes from 13.98 to 13) the dashed line reported in Figure 5 is calculated, which can be seen to be a rather satisfactory approximation to an hypothetical potentiometric dataset comprising the pH data obtained after irradiation of the ligand solution. We can explain this finding in the following way: when the two protonated amines of the ligand come in close contact as a result of the photocyclization reaction, electrostatic repulsion is produced that lowers the stability of the diprotonated ligand, i.e. the basicity of the second amminic group is reduced. pH changes are reversible, and the pH values of the solutions return to their original values following the thermal opening of the ligand. The effect is known as reversible pK_a modulation[13] upon photoswitching, and results in a decrease in the pH of the solution. The photocyclizated ligand is less basic than the open one as a consequence of the proximity of the two basic amino groups. Thus, when a solution of the diprotonated open ligand, with a pH between 4 and 7, is photocyclized the basicity of the solution is lowered, and this effect can be exploited for the photocontrolled release of protons in solution. Moreover, from the new β_2 value, we can calculate a new distribution diagram that shows how the photoreaction lowers the concentration of diprotonated species in solution in the pH interval between 4 and 7 (see Figure S1 in the Supporting Information).

We also noticed that the rate of the thermal back reaction is a function of the starting pH of the solution, i.e. it is influenced by the abundance of the diprotonated species. Back reactions taking place in all the studied solutions were followed by evaluating the intensity of the anthracene absorbance band in the spectra as function of time. Preliminary results seem to indicate that the first-order rate constant for the thermal back reaction increases as the solution becomes more acidic, changing from 3.16×10^{-5} s^{-1} (a value quite close to the value obtained for the reaction in pure methanol) for the solution at pH 7.95, to 1.84×10^{-4} s^{-1} for the solution at pH 4.35, suggesting that destabilization due to electrostatic repulsion in the diprotonated photocyclizated ligand plays a key role in the thermal back reaction.

Conclusions

Ligand LH_2 behaves, as expected, as a selective receptor towards Cu^{II} when in solution at pH values close to 7. This ability, which is shared by many ligands with similar donating atom sets, can be switched off by a simple photochemical input, and then switched on again by a thermal back reaction that can be controlled by altering the temperature and pH of the solution. Ligand LH_2 can also be used for photoinduced release of protons in aqueous solution. To the best of our knowledge, this is the first time in which the [4πs + 4πs] photodimerization reaction of anthracene in aqueous solution has been exploited to photocontrol the binding abilities of a ligand towards a transition metal cation, and to obtain reversible pK_a modulation.[13] Of course, these preliminary findings have to be expanded on to include simpler systems such linear polyamines, an investigation that is currently being undertaken in our laboratory.

Experimental Section

Materials and Instruments: All commercially available compounds were purchased from Aldrich or Fluka and used as received. ^{1}H NMR spectra were recorded on a Bruker AMX 400 spectrometer. The UV/Vis spectroscopic studies were recorded on a Varian Cary 100 UV/Vis spectrophotometer or on a HP 8452 diode array spectrophotometer. Mass spectra were recorded with an Electrospray Ionization instrument Thermo-Finnigan LCQ Advantage Max. For pH spectrophotometric titrations, an ORION 420A pH-meter equipped with an HANNA Instruments electrode was used. For the determination of protonation and complexation equilibrium constants an automated titration apparatus Radiometer Titralab TIM 900 was used. Irradiation of solutions was obtained by placing the samples in a Helios Italquartz Photochemical Multirays Reactor equipped with ten 15-W UV lamps (λ = 366 nm).

Synthetic Procedures

***N*,*N*′-Bis(2-aminoethyl)malonamide (1):** Diethyl malonate (7×10^{-3} mol) was placed in a flask with a large excess of freshly distilled ethylenediamine (100 mL) under an argon atmosphere. The solution was stirred for one week at room temperature, and after this period ethylendiamine was eliminated by rotary evaporation with a high vacuum pump. A white solid product was obtained after washing of the residue with several fractions of diethyl ether; yield 94% (1.23 g). ESI-MS: *m*/*z* (%) = 189.1 $[M + H]^+$ (100). ^{1}H NMR (400 MHz, [D$_6$]DMSO, 25 °C): δ = 8 (s, 2 H, CON*H*), 3 (s, 2 H, COCH_2CO; t, 4 H, CONHCH_2), 2.5 (t, 4 H, CH_2NH$_2$), 1.7 (broad signal, 4 H, NH_2) ppm.

***N*,*N*′-Bis{2-[(anthracen-9-ylmethyl)amino]ethyl}malonamide (LH_2):** To *N*,*N*′-bis(2-aminoethyl)malonamide (507.1 mg, 2.7×10^{-3} mol) dissolved in methanol (70 mL) a solution of 9-anthraldehyde (1.113 g, 5.4×10^{-3} mol) dissolved in methanol (100 mL) was slowly added at room temperature in the dark, and the reaction solution was then stirred overnight. A yellow solid was obtained and separated by filtration. The yellow solid was redissolved in methanol and treated with of $NaBH_4$ (1.03 g), which was added in small portions over a 2 h period. After this time the reaction mixture was stirred in the dark at 40 °C for 4 h. The reaction mixture was then filtered, and the solvent eliminated by rotary evaporation. The obtained solid was then suspended in water, and extracted with four portions of CH_2Cl_2 (40 mL each). The organic phase was dried with Na_2SO_4. After filtration and removal of the solvent by rotary evaporation a yellow oil was obtained, which solidified after repeated washing with diethyl ether; yield 65% (0.999 g). ESI-MS: *m*/*z* (%) = 569.4 $[M + H]^+$ (100). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 8.4 (s, 2 H), 8.3 (d, $^3J_{H,H}$ = 8.8 Hz, 4 H), 8 (d, $^3J_{H,H}$ = 8.8 Hz, 4 H), 7.5 (m, 8 H, aromatic protons), 7.2 (s, 2 H, CON*H*) 4.4 (s, 4 H, AnCH_2NH), 3.3 (dt, 4 H, CONHCH_2), 3 (s, 2 H, COCH_2CO), 2.9 (t, 4 H, CH_2NHCH$_2$An) ppm.

CuL: LH_2 (48.4 mg, 8.51×10^{-5} mol) was dissolved in EtOH (5 mL), and copper triflate (30.4 mg, 8.51×10^{-5} mol) was added to the solution. Then an aqueous solution of 0.86 M KOH (198 μL, 1.7×10^{-4} mol) was added to the solution. The solution was then heated to 50 °C and stirred for 30 min. To precipitate out the complex, diethyl ether was added to the cold mixture. A light pink crude product was then filtered off, redissolved in EtOH and recrystallized by slow diffusion of diethyl ether into the ethanolic solution; yield 41% (22 mg). ESI-MS: *m*/*z* (%) = 630.1 $[CuL + H]^+$

pH-Spectrophotometric Titrations: Spectra were recorded in the interval 300–900 nm. pH variations were obtained by addition of standard 0.1 M NaOH solution (microliters) to a solution of the fully protonated ligand [20 mL, 10^{-3} M in MeOH/H_2O (80:20), with 0.05 M $NaNO_3$ as the ionic medium], with the addition of 1 equiv. of $M^{II}(OTf)_2$. The fully protonated ligand was obtained by adding a known excess of acid to the ligand solution. The pH of the dioxane/H_2O solvent mixtures were calculated with the Nernst equation: E [mV] = E^0 + 59 log[H^+], where E^0 was determined by Gran's method.[14]

Potentiometric Titrations: Equilibrium constants for protonation and complexation reactions were determined by pH-metric measurements recorded on MeOH/H_2O (80:20) solutions of the ligand at 25 °C with 0.05 M $NaNO_3$ as the ionic medium. Data were collected with fully automatic equipment that has already been described.[15] The HYPERQUAD software package[16] was used to process the potentiometric data.

Photoinduced pH-Change Experiments: A 10^{-3} M MeOH/H_2O (80:20) solution of ligand was divided into 6 samples (20 mL each), and the proper amount of base was then added and the pH of the solution measured. Then the solutions were irradiated for 10 min, and spectra taken to check for photocyclization. Then the pH of the solution was measured again. Solutions were then stored in the dark at T = 298 K, and new spectra were taken after fixed intervals in order to evaluate the thermal kinetics of the back reaction.

Spectrophotometric Titrations with Cations at Fixed pH: Spectra were recorded in the interval 300–900 nm. 3–10 M solutions of LH_2 in MeOH/H_2O (80:20) and in 0.05 M of HEPES were adjusted to the desired pH with a standard base. The resulting solutions were titrated with standard solutions of cations (obtained from the corresponding triflate or nitrate salts). Spectra of the photocyclized product LcH_2 were collected in the same way, after adding buffer and adjusting the pH of the irradiated ligand solution (irradiation was performed for 10 min).

Supporting Information (see footnote on the first page of this article): Distribution diagrams for ligands LH_2 and LcH_2, UV/Vis spectrophotometric titrations for ligand LH_2 with Cu^{II} in buffered pH solution before and after irradiation, UV/Vis pH-spectrophotometric titrations of 1:1 mixtures of Cu^{II} and ligand LH_2 before and after irradiation, UV/Vis spectra of complex CuL before and after irradiation, sketch of the molecular model of LH_2 obtained from PM3 calculations, ^{1}H NMR spectra of the ligand before and after irradiation.

[1] a) T. Gottschalk, P. D. Jarowski, F. Diederich, *Tetrahedron* **2008**, *64*, 8307–8317; b) G. Dacarro, P. Pallavicini, A. Taglietti, *New J. Chem.* **2008**, *32*, 1839–1842; c) E. J. O'Neill, B. D. Smith, *Coord. Chem. Rev.* **2006**, *250*, 3068–3080; d) S. G. Tajc, B. L. Miller, *J. Am. Chem. Soc.* **2006**, *128*, 2532–2533; e) Y. Liu, G. Chen, Y. Chen, F. Ding, T. Liu, Y. Zhao, *Bioconjugate Chem.* **2004**, *15*, 300–306; f) T. Gottschalk, B. Jaun, F. Diederich, *Angew. Chem.* **2007**, *119*, 264–268; g) R. M. Fairchild, K. T. Holman, *J. Am. Chem. Soc.* **2005**, *127*, 16364–16365; h) D. Monti, L. La Monica, A. Scipioni, G. Mancini, *New J. Chem.* **2001**, *25*, 780–782; i) L. Fabbrizzi, F. Foti, S. Patroni, P. Pallavicini, A. Taglietti, *Angew. Chem.* **2004**, *116*, 5183–5187; j) A. Aurora, M. Boiocchi, G. Dacarro, F. Foti, C. Mangano, P. Pallavicini, S. Patroni, A. Taglietti, R. Zanoni, *Chem. Eur. J.* **2006**, *12*, 5535–5546; k) T. Gottschalk, B. Jaun, F. Diederich, *Angew. Chem. Int. Ed.* **2007**, *46*, 260–264; l) L. Fabbrizzi, F. Foti, S. Patroni, P. Pallavicini, A. Taglietti, *Angew. Chem. Int. Ed.* **2004**, *43*, 5073–5077.

[2] a) S. Shinkai, in: *Molecular Switches* (Ed.: B. L. Feringa), Wiley-VCH, Weinheim, **2001**, pp. 281–307; b) Y. Liu, S. Kang, Y. Chen, Y. Yang, J. Huskens, *J. Inclusion Phenom. Macrocyclic Chem.* **2006**, *56*, 197–201; c) A. Mulder, A. Jukovic, F. W. B. van Leeuwen, A. L. Spek, J. Huskens, D. N. Reinhoudt, *Chem.*

Eur. J. **2004**, *10*,1114–1123; d) F. Wurthner, J. Rebek Jr., *J. Chem. Soc. Perkin Trans. 2* **1995**, 1727–1734; e) M. V. Alfimov, O. A. Fedorova, S. P. Gromov, *J. Photochem. Photobiol. A: Chem.* **2003**, *158*, 183–198; f) R. Rojanathanes, T. Tuntulani, W. Bhanthumnavin, M. Sukwattanasinitt, *Org. Lett.* **2005**, *7*, 3401–3404; g) M. Takeshita, M. Irie, *J. Org. Chem.* **1998**, *63*, 6643–6649; h) J. Malval, I. Gosse, J. Morand, R. Lapouyade, *J. Am. Chem. Soc.* **2002**, *124*, 904–905; i) R. Mathevet, G. Jonusauskas, C. Rulliere, J. Letard, R. Lapouyade, *J. Phys. Chem.* **1995**, *99*, 15709–15713.

[3] a) H. D. Becker, *Chem. Rev.* **1993**, *93*, 145–172; b) H. Bouas-Laurent, A. Castellan, J.-P. Desvergne, R. Lapouyade, *Chem. Soc. Rev.* **2000**, *29*, 43–55; c) H. Bouas-Laurent, A. Castellan, J.-P. Desvergne, R. Lapouyade, *Chem. Soc. Rev.* **2001**, *30*, 248–263; d) A. Beyeler, P. Belser, L. De Cola, *Angew. Chem.* **1997**, *109*, 2878–2881; e) A. Beyeler, P. Belser, L. De Cola, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2779–2781.

[4] a) G. McSkimming, J. H. R. Tucker, H. Bouas-Laurent, J.-P. Desvergne, *Angew. Chem.* **2000**, *112*, 2251–2253; b) J.-P. Desvergne, H. Bouas-Laurent, *J. Chem. Soc., Chem. Commun.* **1978**, 403–404; c) G. McSkimming, J. H. R. Tucker, H. Bouas-Laurent, J.-P. Desvergne, *Angew. Chem. Int. Ed.* **2000**, *39*, 2167–2169.

[5] a) G. McSkimming, J. H. R. Tucker, H. Bouas-Laurent, J. P. Desvergne, S. J. Coles, M. B. Hursthouse, M. E. Light, *Chem. Eur. J.* **2002**, *8*, 3331–3342; b) H. Bouas-Laurent, A. Castellan, M. Daney, J.-P. Desvergne, G. Guinand, P. Marsau, M.-H. Riffaud, *J. Am. Chem. Soc.* **1986**, *108*, 315–317.

[6] C. Schafer, J. Mattay, *Photochem. Photobiol. Sci.* **2004**, *3*, 331–333.

[7] a) T. Tsudera, A. Ikeda, S. Shinkai, *Tetrahedron* **1997**, *53*, 13609–13620; b) T. Jin, *Chem. Commun.* **2000**, 1379–1380.

[8] a) Y. Molard, D. M. Bassani, J.-P. Desvergne, N. Moran, J. H. R. Tucker, *J. Org. Chem.* **2006**, *71*, 8523–8531; b) Y. Molard, D. M. Bassani, J.-P. Desvergne, P. N. Horton, M. B. Hursthouse, J. H. R. Tucker, *Angew. Chem.* **2005**, *117*, 1096–1099; c) Y. Molard, D. M. Bassani, J.-P. Desvergne, P. N. Horton, M. B. Hursthouse, J. H. R. Tucker, *Angew. Chem. Int. Ed.* **2005**, *44*, 1072–1075.

[9] a) L. Fabbrizzi, M. Licchelli, P. Pallavicini, A. Perotti, A. Taglietti, D. Sacchi, *Chem. Eur. J.* **1996**, *2*, 167; b) M. Kodama, E. Kimura, *J. Chem. Soc., Dalton Trans.* **1979**, 325–329; c) P. Comba, S. P. Gavrish, R. W. Hay, P. Hilfenhaus, Y. D. Lampeka, P. Lightfoot, A. Peters, *Inorg. Chem.* **1999**, *38*, 1416–1421; d) P. Comba, S. P. Gavrish, Y. D. Lampeka, P. Lightfoot, A. Peters, *J. Chem. Soc., Dalton Trans.* **1999**, 4099–4102.

[10] J. E. Huheey, E. A. Keiter, R. L. Keiter, *Inorg. Chem.* **1993**, *32*, 348.

[11] *Hyperchem Package*, version 6.03 for Windows.

[12] H. A. O. Hill, K. A. Raspin, *J. Chem. Soc. A* **1968**, 3036–3039.

[13] S. H. Kawai, S. L. Gilat, J.-M. Lehn, *Eur. J. Org. Chem.* **1999**, *9*, 2359–2366.

[14] G. Gran, *Analyst* **1952**, *77*, 661–671.

[15] N. Marcotte, A. Taglietti, *Supramol. Chem.* **2003**, *15*, 617–625.

[16] P. Gans, A. Sabatini, A. Vacca, *Talanta* **1996**, *43*, 1739–1753.

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