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PAPER

Interaction studies between photochromic spiropyrans and transition metal cations: the curious case of copper†

Manuel Natali and Silvia Giordani*

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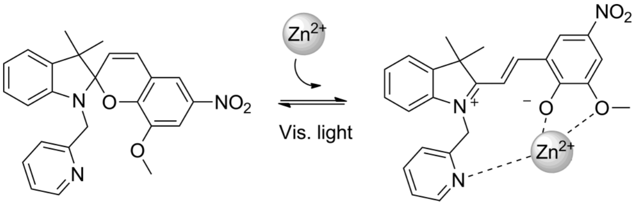
A series of four spiropyrans bearing different substituents on the indolic nitrogen were synthesized and their capability of binding mono and bivalent transition metal cations in solution was assessed *via* UV-visible absorption spectroscopy. All the compounds responded selectively to the presence of Cu(II) ions producing intense absorption bands in the visible region of their spectra. Bidimensional ^{1}H-NMR and MALDI-TOF MS spectroscopies revealed the formation of SP dimers mediated by Cu(II). This is the first example of cross-coupling mediated by copper(II) in mild conditions causing the symmetric dimerization of spiropyran dyes.

Introduction

The development and synthesis of artificial receptors tailored to respond to a wide variety of clinically and environmentally important species have been of great interest in the last two decades.[1–3] Spiropyrans, reported for the first time in the early fifties,[4] are members of the well-established class of photochromic compounds. They respond to a multitude of optical and chemical stimuli. Ultraviolet light promotes the heterolytic cleavage of the spiro C–O bond, followed by *cis-trans* isomerisation with generation of a metastable merocyanine. The reverse process of ring-closing takes place upon irradiation with visible light or thermal bleaching. Both solvatochromism and acidochromism have been reported.[5–7] They also respond reversibly to metal cations producing an optical signal,[8] and occupy a dignified niche in the vast universe of chemosensors. Due to the intriguing nature of their molecular recognition and signal transduction mechanisms, great interest has arisen in the scientific community leading to the construction of spiropyran based sensors that cover a disparate range of analytes such as metal ions,[9–19] aminoacids,[20,21] and nucleosides.[22,23] Fascinated by the potentiality of this class of compounds, we recently designed new spiropyran based probes for the detection of metal cation that showed remarkable selectivity and sensitivity.[24,25]

Indeed, the binding constant of the metal ligation process was affected by irradiation with visible light yielding the uptake/release of the cation fully reversible and controllable. As we reported, the substituents decorating the spiropyran skeleton are crucial factors in obtaining a good degree of selectivity towards a specific analyte while retaining reversibility of the metal coordination process (Scheme 1). In more recent studies we expanded the library of our molecules and produced new candidates for ion sensing, retaining the same spiropyran skeleton we chose previously but changing the functional groups. Among these new spirochromenes, four molecules showed outstanding selectivity towards Cu(II) ions. Thrilled by this odd result, we delved into studying their properties in order to produce a rational and plausible explanation. Helped by analytical techniques such as bidimensional ^{1}H-NMR, MALDI-TOF HRMS, and UV-visible absorption spectroscopy we have been able to shade light on this unique case. We report herein the synthesis and the activity evaluation of four spiropyran-based cation receptors: this is the curious case of copper.



Scheme 1 Spiropyran-based selective and reversible Zn(II) sensor.

Results and discussion

The four spiropyrans **SP1**, **SP2**, **SP3**, and **SP4** discussed in this article are those depicted in Scheme 2. Although these structures have been known for quite a long time,[26–28] very little has been reported regarding their coordinative behaviour.[29]

In the endeavour of designing molecules capable of acting as efficient, sensitive and reversible metal ion detectors, we chose these known structures as a starting point. The reason is mainly due to the simplicity of their structures. As we mentioned before, the functional groups decorating the spiropyran backbone are key elements that can facilitate metal-ion binding and promote

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Trinity College Dublin, School of Chemistry, College Green, Dublin, 2, Ireland. E-mail: giordans@tcd.ie; Fax: +353 (0)1 896 1422; Tel: +353 (0)1 671 2826

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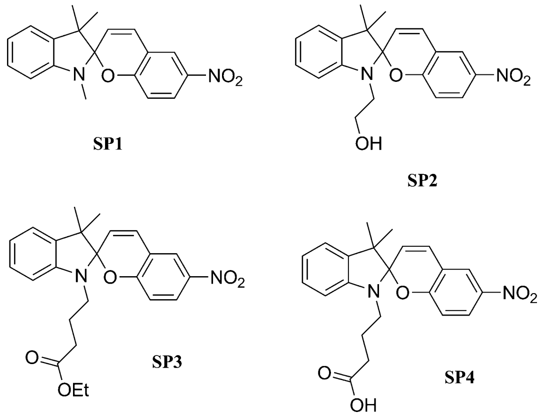


Scheme 2

photoinduced control of the metal ligation. In these four compounds, only two functional groups are present on each structure. The indolic nitrogen offers a functionalizable site and several examples of N-modified spirochromenes for metal chelation applications are known.[29,30] If a group with good coordinating properties and sufficient conformational flexibility is placed in this position, the presence of a metal cation may induce the spiro C–O bond cleavage and promote its ligation through a bidentate system formed by the chelating group itself and the merocyanine phenolate anion. With this in mind we chose three different aliphatic tethers bearing a terminal group with binding properties such as a carboxylic acid (**SP4**), an ethyl ester (**SP3**), and a hydroxy group (**SP2**). Compound **SP1** is functionalized with a methyl group that cannot be considered a binding site. However a bivalent metal can be coordinated by two merocyanine units through their phenolate anions.[31] It is known that the presence of a strongly electron-withdrawing group in the 6′ position stabilizes the open merocyanine form whereas an electron-donating group produces a more stable photostationary closed form. Since the nitro group is a very strong electron withdrawing function, the ring opening-close in these structures should be easily photocontrollable as well as the uptake-release of a metal by their open merocyanines.

Spiropyrans **SP1–SP4** were synthesized according to known procedures.[28,32–34] In order to establish whether the combination of the different functional groups were capable of offering metal-ion recognition, systematic binding studies were performed on our spiropyrans with eleven different metal cations. Biologically and environmentally relevant metal ions such as Zn(II), Cu(II), Ni(II), Co(II), Mn(II), Cd(II), Fe(II), Mg(II), Ca(II), Na(I) and K(I) were tested. The investigations were carried out *via* different spectroscopic techniques such as UV-vis absorption and emission spectroscopy, ^{1}H-NMR, and MALDI-TOF HRMS.

UV-vis absorption studies

The addition of the eleven monovalent and bivalent cations to spiropyrans solutions in acetonitrile gave unexpected results. The first compound analysed was **SP1** (Fig. 1). The absorption spectrum of this derivative shows three maxima in the ultraviolet region at 263 nm, 293 nm, and 341 nm respectively. The presence of 1 equivalent of ten of the eleven metals did not produce any variation of the spiropyran spectrum. However, addition of 1 equivalent of copper perchlorate caused a sudden colour change from slightly pink to deeply orange in few seconds.

This event was accompanied by the appearance of an intense absorption band localized in the visible region with maximum intensity at 496 nm. Other two maxima of the same intensity were visible in the UV region at 263 nm and 305 nm respectively (Fig. 1a).

Despite the structural difference between **SP1** and the other members of this group, the addition of the same amount of Cu $(ClO_4)_2$ caused the same colour changes in acetonitrile solutions of **SP2**, **SP3**, and **SP4**. The absorption spectrum of a **SP2** shows bands in the UV region at 266 nm, 301 nm, and 340 nm. After addition of copper(II), the UV-vis spectrum of the same solution showed an intense absorption band, flat on its top with maximum intensity at 515 nm and a shoulder at 493 nm. Weak absorption shoulders were observed at 410–414 nm in the spectra of solutions containing the same molecule and either iron(II) or zinc(II) indicating little interactions with these two cations as well (Fig. 1b). The absorption maxima recorded at 269 nm, 299 nm, and 340 nm for a metal-free solution of compound **SP3** were similar to those of **SP1** and **SP2**. Addition of zinc(II) perchlorate and iron(II) perchlorate caused the appearance of two shoulders in the spiropyran spectra at 410 nm and 400 nm respectively (Fig. 1c). Addition of copper(II) perchlorate caused an intense absorption band to appear in the range of 450–600 nm with maximum intensity at 517 nm (Fig. 1c). Even compound **SP4** which is functionalized with a carboxylated tether did not show any interaction with any of the tested metal salts except for a copper(II) perchlorate. The presence of this metal in fact caused analogous changes in the compound absorption spectra which resemble the changes observed for the other compounds in this group. The absorption band risen from addition of copper had its maximum localized at 514 nm. The response of the four spiropyrans to different concentrations of Cu $(ClO_4)_2$ was investigated. In all experiments similar events were observed. The sequential addition from 0.1 to 1 equivalent of copper(II) caused different bands to appear at different wavelengths which resolved eventually in those reported in Fig. 1. However, in all cases different isosbestic points were observed. These results are shown in Fig. 2. Addition of 0.4 equivalents of copper(II) to a solution of **SP1** caused the appearance of two bands with maxima at 481 nm and 503 nm which coalesced into a broad absorption with maximum at 496 nm in the presence of higher concentrations of the metal (Fig. 2a). In the same spectra two isosbestic points are localized at 277 nm and 348 nm. Increasing the concentration of copper(II) in a solution of **SP2** caused two similar bands to appear in the visible region with maximum intensity at 488 nm and 515 nm. Three isosbestic points were observed at 279, 338, and 361 nm (Fig. 2b). The same number of isosbestic points was observed for the solutions containing either **SP3** or **SP4**. In the first case they were localized at 277, 335, and 360 nm (Fig. 2c) while in the second case at 278, 332, and 365 nm (Fig. 2d). Two bands with maxima at 481 nm and 515 nm were observed in the spectra of compound **SP3** at low concentration of copper(II). These two bands coalesced partially at higher concentrations of the metal evolving in two absorptions at 491 nm and 517 nm observed after the addition of 1 equivalent of copper (Fig. 2c). Analogously, compound **SP4** responded to low concentrations of copper(II)

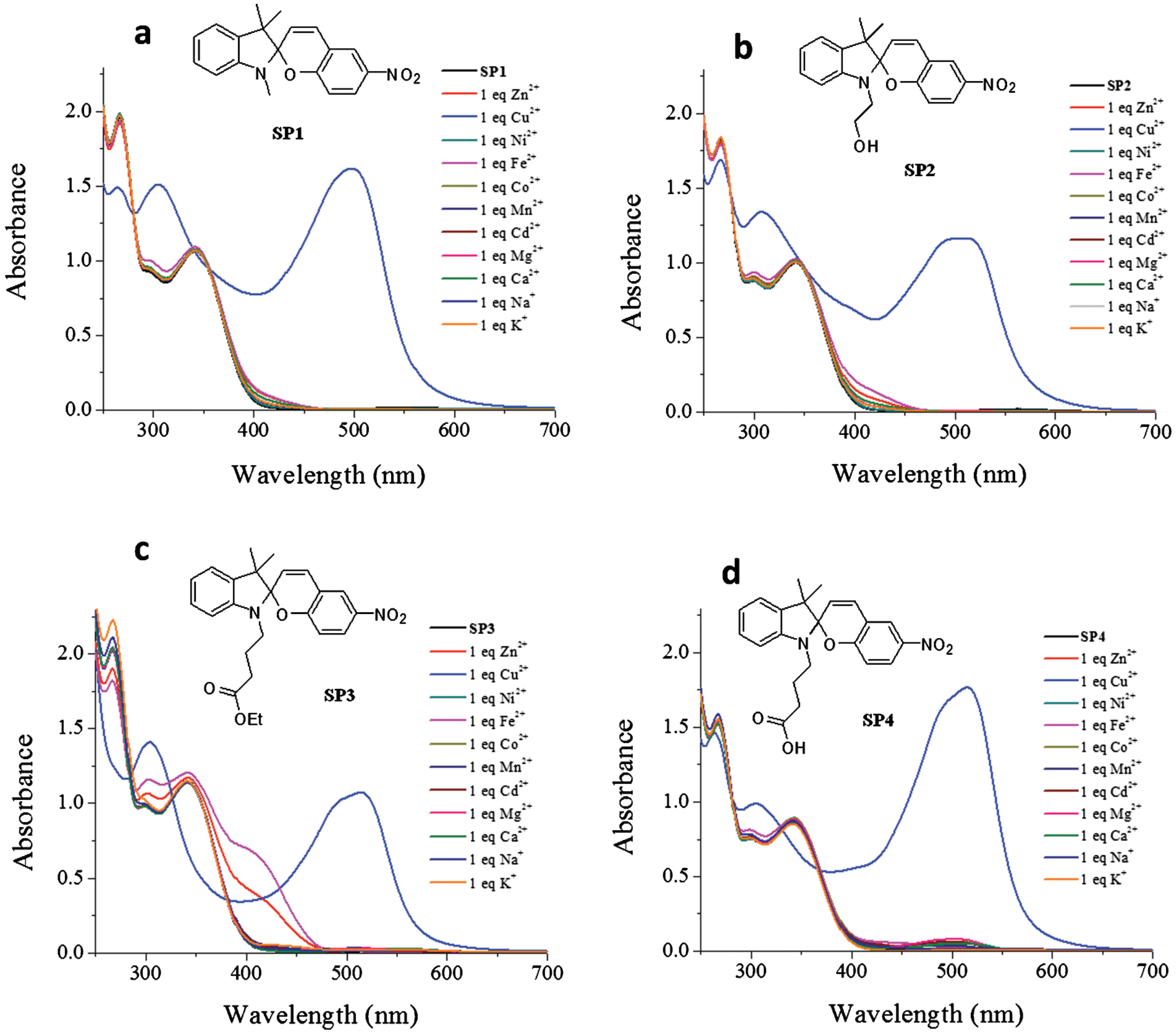


Fig. 1 Absorption spectra of **SP1** (a), **SP2** (b), **SP3** (c), and **SP4** (d) before and after the addition of 1 equivalent of different metal perchlorates and chlorides (1.0×10^{-4} M, acetonitrile, 293 K).

with two absorption maxima at 482 nm and 517 nm in the visible region that shifted at 491 nm and 512 nm respectively (Fig. 2d).

Reversibility of the spiropyran-copper interactions

The solutions containing the four spiropyrans and 1 equivalent of copper were irradiated with visible light for 10 min and the corresponding UV-vis spectra were recorded. The absorption maxima in the spectrum of **SP1** underwent remarkable changes in its features after irradiation. First the two absorption maxima in the ultraviolet region at 263 nm and 305 nm shifted bathochromically to 271 nm and 308 nm and their intensity increased after irradiation with visible light. The broad absorption in the visible region decreased in intensity and shifted hypsochromically from 496 nm to 452 nm. A small shoulder was barely visible at 378 nm (Fig. 3a). The changes that took place in the absorption of a solution of **SP2** and copper perchlorate after irradiation with visible light resembled those observed for **SP1**. The maximum at 347 nm redshifted slightly to 352 nm retaining its intensity while the peak at 414 nm redshifted to 417 nm and underwent a significant intensity decrease. The maximum absorption located at 504 nm dropped to an intensity value which was 1/3 of the non-irradiated solution one and blueshifted to 472 nm (Fig. 3b). Analogously, the absorption maximum at 517 nm of a solution of **SP3**-Cu$(ClO_4)_2$ decreased in intensity and blueshifted to 478 nm. The peak 266 nm of non-irradiated solution moved upward after irradiation with visible light and shifted to 271 nm while the two smooth absorption bands at 302 nm and 329 nm coalesced in one unique absorption band higher in intensity whose maximum was located at 310 nm (Fig. 3c). Finally, a solution containing **SP4** and Cu$(ClO_4)_2$ responded to visible light irradiation with a blue shift of the maximum at 514 nm to a new absorption band appeared at 480 nm concomitant with a loss of intensity of the 50%. Additionally a new absorption band was observed at 391 nm while the two peaks at 264 and 306 nm redshifted to 271 and 311 nm respectively. The maximum at 271 nm was lower in intensity with respect to that at 264 nm while the appearance of the new peak at 311 nm was accompanied by an intensity increase (Fig. 3d). The interaction between the members of this group of spiropyran-based receptors and copper(II) perchlorate underwent

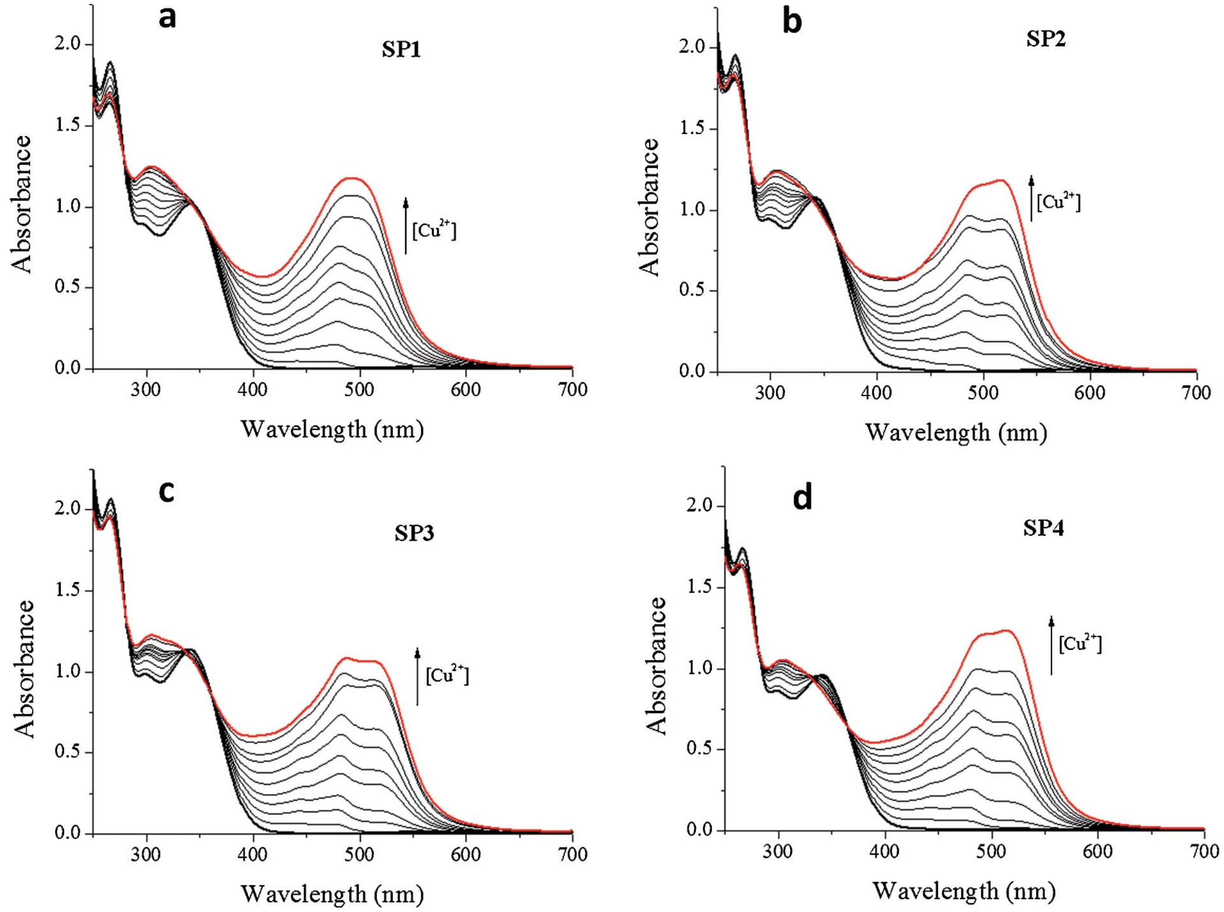


Fig. 2 Absorption spectra of **SP1** (a), **SP2** (b), **SP3** (c), and **SP4** (d) (1.0×10^{-4} M, acetonitrile, 293 K) after increasing the concentration from 0.1 to 1 eq of Cu $(ClO_4)_2$.

visible changes upon irradiation with visible light. If a complex was actually formed between the spirochromenes and copper(II), these results would indicate only a partial release of the metal guest from the receptors sites as the original spectra of metal free solutions of spiropyrans were not recovered after irradiation with visible light. Overall, a very selective response to copper(II) was observed with all the members of this group regardless to the substituent present on the indolic half of the molecules.

Mass spectroscopy analysis

As mentioned above, spiropyrans can form complexes with transition metals whose composition can vary depending on the structure of the switchable molecule. Complexes where the ratio SP-M^{2+} is either 2 : 1 or 1 : 1 are often observed. When the ratio is 2 : 1, two open merocyanines usually cooperate in the coordination of a metal cation by means of their phenolate anions. Thus, sandwich-like complexes are formed and the metal guest is trapped between the two molecules. Considering the unusual results observed with these spiropyrans, a similar explanation would be plausible. Since all compounds responded to the presence of copper(II) perchlorate in the same manner regardless to the substituent on the indolic moiety, we thought that sandwich like complexes formed between to molecular switches and the metal guests where the interaction between the three parts was only due by the coordination between two phenolate and the metal while the substituent on N is completely extraneous to the binding. In order to confirm this hypothesis we carried out MALDI-TOF MS studies on the solutions containing **SP1**, **SP2**, **SP3**, and **SP4** in the presence of an equimolar amount of $Cu(ClO_4)_2$. Calculation of the theoretical mass of spiropyran-copper complex 1 : 1 affords a value of 385 *m*/*z* for the molecular ion [**SP1**-Cu^{2+}]$^+$. If two molecules of compound **SP1** form a sandwich like complex with one Cu^{2+} cation the resulting molecular ion [**SP1–SP1**-Cu^{2+}]$^+$ mass would be 707 *m*/*z*. In Fig. 4a the spectrum of **SP1** in the presence of copper shows a peak whose value of 643 *m*/*z* corresponds exactly to a [**SP1–SP1**]$^+$ dimer with no copper in it and a weight loss of one proton. Peaks at 642 and 644 *m*/*z* were also detected indicating different protonation states of the molecule. The small peak at 322 *m*/*z* correspond to monomer [**SP1**]$^+$. A peak indicating the molecular ion [**SP2–SP2**]$^+$ at 702 *m*/*z* was found in mass spectroscopy analysis carried out on the **SP2** solution containing copper (Fig. 4b). This peak indicates the mass of two **SP2** molecules with a weight loss of one proton. In this experiment other peaks were found at 330, 352, 423, 702, and 704 *m*/*z*. That at 352 corresponds to the molecular ion [**SP2**]$^+$. Also in this case it seems that the metal does not form a complex while the peaks at 702 and 704 *m*/*z* may indicate different protonation states of the same molecule. In the analysis of the solution containing **SP3** and the same cation, the presence of a spiropyran-spiropyran

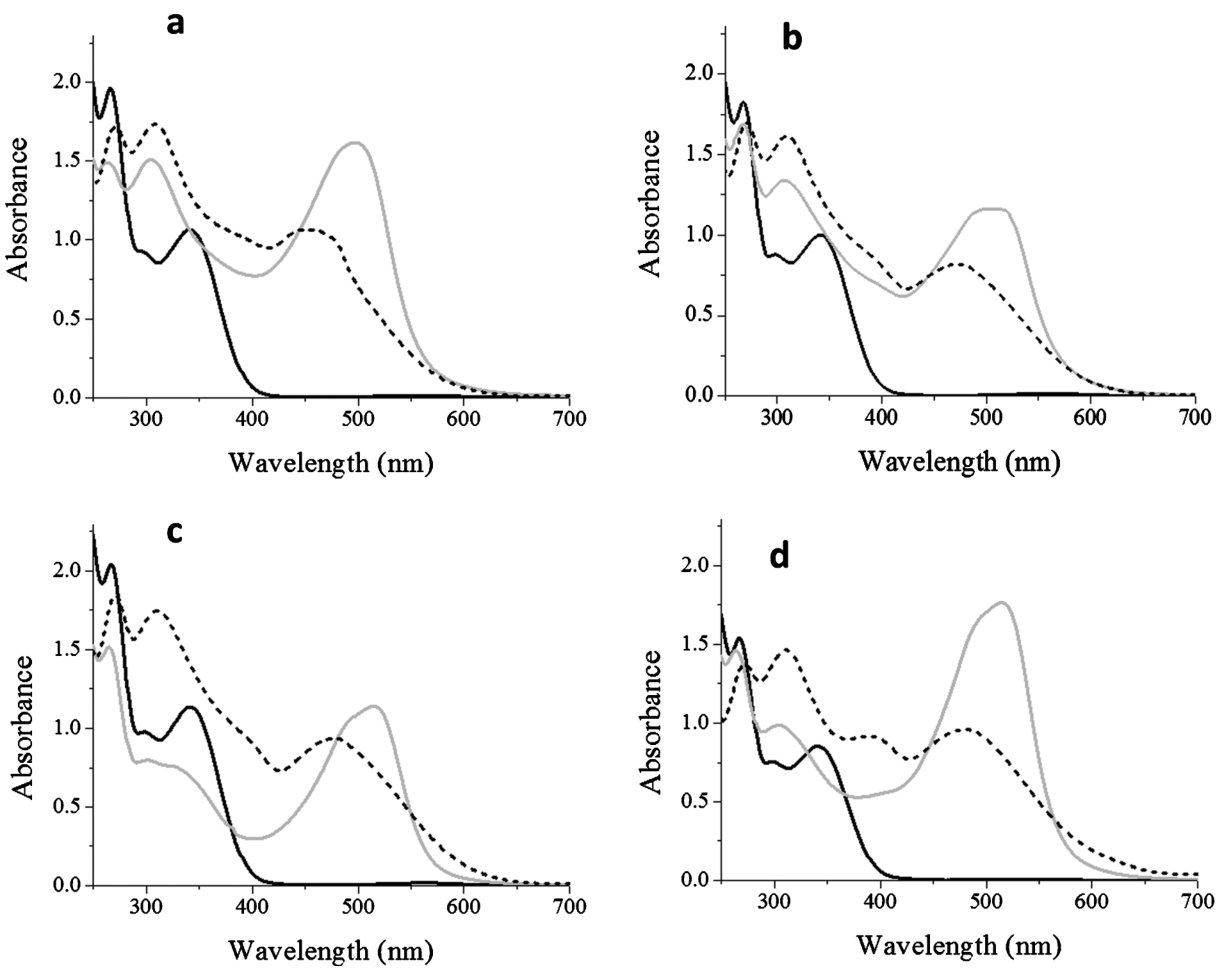


Fig. 3 Absorption spectra of **SP1** (a), **SP2** (b), **SP3**(c), and **SP4** (d) (1.0×10^{-4} M, acetonitrile, 293 K) before (black curves), after the addition of 1 eq of copper perchlorates (grey curves), and irradiation with visible light for 10 min (dotted curves).

dimer was confirmed by its molecular ion peak [**SP3–SP3**]$^+$ at 843 *m*/*z* along with other two peaks at 842 and 844 *m*/*z* smaller in intensity (Fig. 4c), while a peak at 422 *m*/*z* indicated the a single molecule of **SP3**. The carboxylated compound **SP4** formed apparently a dimer as well, whose molecular ion [**SP4–SP4**]$^+$ peak is the one shown in Fig. 4d at 787 *m*/*z*. Two peaks at 786 and 788 *m*/*z* were detected as well. Also in this case a small peak at 393 *m*/*z* revealed the presence of the monomer **SP4**. All these experiments showed the formation of new species that apparently were not complexes.

Purification and identification of SP-dimers

The MALDI-TOF mass spectra suggested the possible formation of dimers with no trace of copper(II). In order to investigate if copper(II) could be involved in a process different from a chelation, namely a redox reaction, and to characterize the dimers observed *via* mass spectroscopy, we scaled up the process by reacting amounts of the four spiropyrans with equimolar amount of copper perchlorate in the same condition used in the UV-vis experiments. Approximately 10 mmol of each spirochromene were dissolved in 5 ml of acetonitrile and an equimolar amount of copper perchlorate dissolved in 100 ml of deionised water was added to each spiropyran solution which was stirred at room temperature for 24 h. The solvent was evaporated and each crude was redissolved in dichloromethane and washed with an aqueous solution of $NaHCO_3$ containing the 5% of EDTA. The latter is a well known chelating agent that should bind all the copper(II) cations in solution leaving any spiropyran derivative as metal-free compounds. In each solution a red precipitate was observed and filtered off. Each organic phase was collected and the solvent was evaporated under reduced pressure. A first thin layer chromatography analysis of compounds **SP1** and **SP3** reaction mixtures revealed after 24 h the appearance of one new spot each, whose retention factor (0.4 in hexane/ethylacetate 6 : 4) was lower than that of the corresponding spiropyran derivative (0.8 in hexane/ethylacetate 6 : 4). In both cases, these new species were purified *via* flash chromatography on silica gel and successively characterized by means of both mass spectroscopy and ^{1}H-NMR analysis. Reaction yields were calculated to be 46% and 43% for **SP1** and **SP3** respectively. MALDI-TOF MS analysis of the compound purified from the reaction of **SP1** revealed the same peak observed in the previous experiment whose value correspond to a molecular ion of mass equal to 742 Da. Analogously, the purification of the compound obtained during the reaction of **SP3** with copper perchlorate had a mass of 842 Da. In both cases these

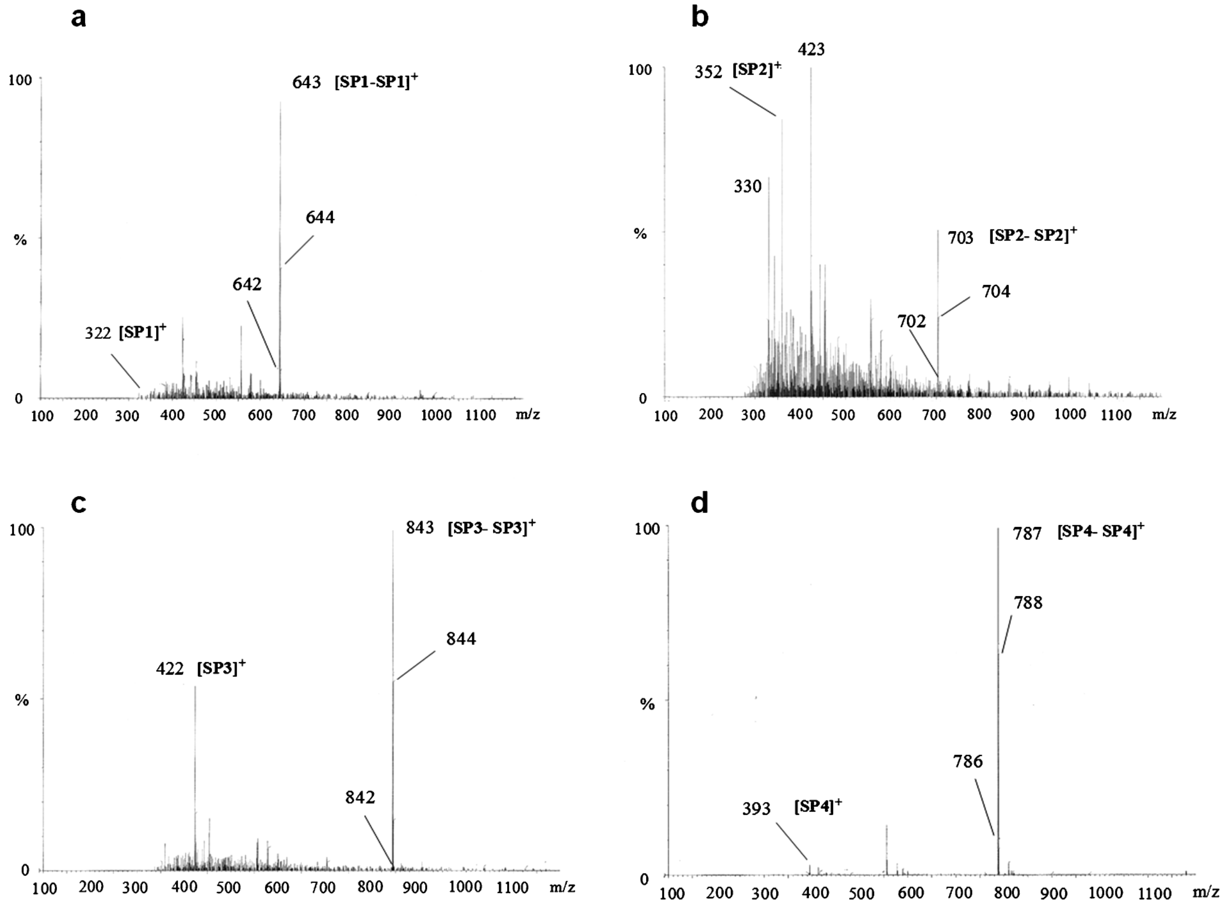


Fig. 4 MALDI-TOF mass spectrum of acetonitrile solutions of **SP1** (a), **SP2** (b), **SP3** (c), and **SP4** (d) containing $[Cu(ClO_4)_2] = [SP] = 1 \times 10^{-3}$ M.

molecular masses are double of the corresponding spiropyrans mass, less two protons each. This implies that two spiropyrans reacted with each other forming probably a C–C bond with the loss of two protons. If this hypothesis was true, the ^{1}H-NMR of each spiropyran should lack of two protons. To confirm this, both mono and bidimensional ^{1}H-NMR analysis were carried out on the two compounds obtained from these purifications. The ^{1}H-NMR spectrum of **SP1–SP1** is shown in Fig. 5a. It is very interesting to observe that this spectrum resembles perfectly that of a single molecule of SP. Seventeen protons are counted in this spectrum while a single molecule of **SP1** has 18 protons. Considering a mass that is equal to the double of that of **SP1** less two protons, the structure of **SP1–SP1** must have a plane of symmetry. Overall, the spectrum found corresponds to molecule **SP1–SP1** (Fig. 5) which is the dimer of two spiropyrans linked to each other through a C–C bond located in 5-position of their indolic system. The typical peaks of the *gem* methyl groups are visible as two singlets that integrate for 6 protons each at 1.25 and 1.36 ppm (*a* in Fig. 5a). These values indicate that the two methyl groups are not magnetically equivalent and the spiropyran is in its closed form. This hypothesis is confirmed by the shift of the indolic methyl groups *j*, which are observed as a singlet that integrates for six protons at 2.79 ppm, and by the coupling constant of the two vinylic protons *b* and *c*, located at 6.02 ppm and 7.14 ppm respectively, that is equal to 10.4 Hz. This value is typical for a *cis* configuration. The aromatic protons *f* are observable as a doublet at 6.82 ppm while protons *e* and *d* are shifted to a lower field at 8.05 (double doublet) and 8.13 (doublet) ppm respectively. The fact that these two signals are not a doublet for *e*, and a singlet for *d*, indicates a long range coupling between the two protons, confirmed by their coupling constant of 2.8 Hz. Protons *g* give a doublet at 6.68 ppm whose coupling constant is equal to 8.0 Hz. The same value is observed for the double doublet located at 7.45 ppm which corresponds to protons *h*. A non-symmetric doublet at 7.42 ppm indicates protons *i*. Also in this case long range coupling between *h* and *i* was observed. The coupling between *d*–*e*–*f* and *h*–*i*–*j* are underlined in the ^{1}H-^{1}H COSY of the compound aromatic region depicted in Fig. 5b. Purification by column flash chromatography of the crude obtained from reacting compound **SP3** with $Cu(ClO_4)_2$ afforded the pure compound **SP3–SP3** whose ^{1}H-NMR and ^{1}H-^{1}H COSY NMR spectra are reported in Fig. S1a and S1b (ESI†), respectively. The presence of a symmetry plane is deduced from its ^{1}H-NMR that shows the proton shifts of one single molecule, minus one aromatic proton. Thus the spectra obtained correspond to a spiropyran dimer like the one depicted in Scheme 3 with two dyes attached to each other through a C–C bond located in *para* position with respect to the indolic nitrogen. Reaction of spiropyran **SP2** with equimolar amount of $Cu(ClO_4)_2$ in larger scale produced several by-products. The purification of these compounds by flash chromatography resulted to be particularly difficult. Several attempts were made changing conditions and eluent polarity but they were all unsuccessful.

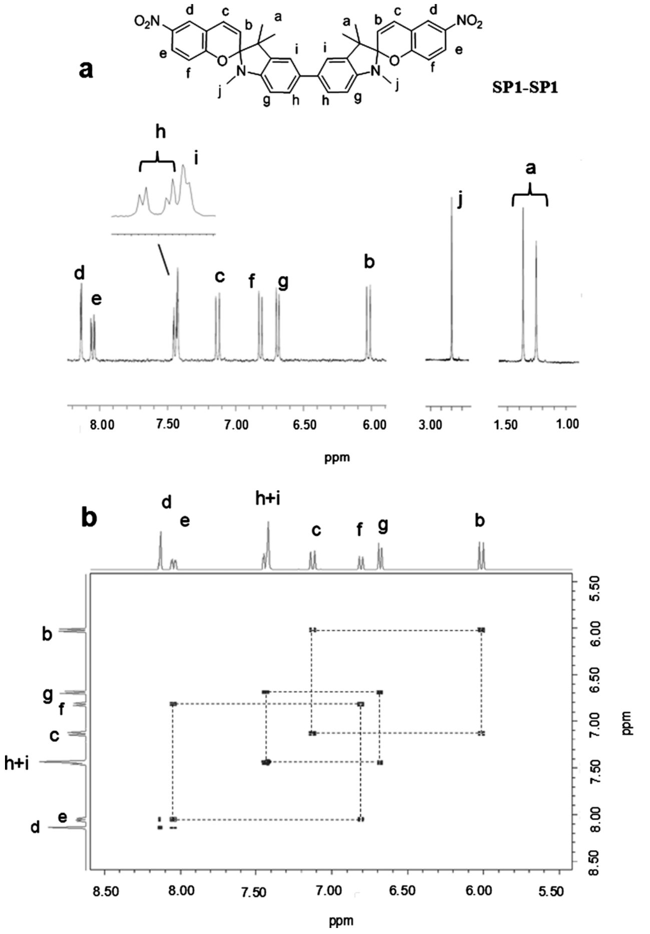
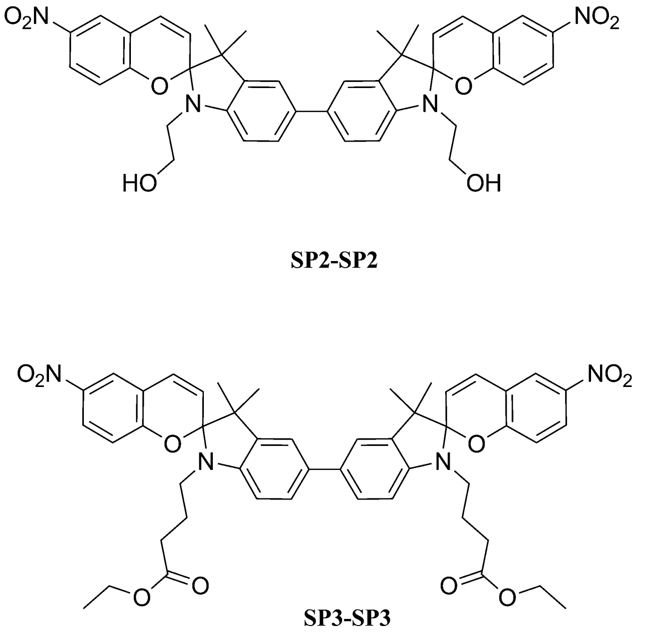


Fig. 5 (a) ^{1}H-NMR and (b) ^{1}H-^{1}H COSY NMR partial spectra of **SP1–SP1** (1×10^{-2} M in acetonitrile, 293 K).

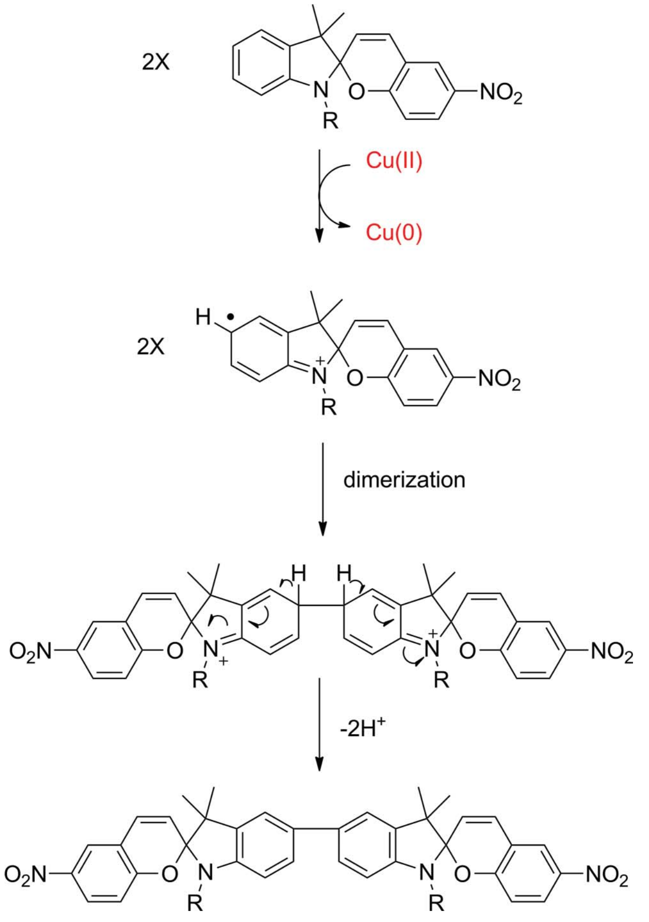
However, a sufficient amount of compound **SP2–SP2**, depicted in Scheme 3, was purified *via* preparative thin layer chromatography by using a mixture 1 : 1 of ethyl acetate and hexane as eluent (R_f 0.4), and eventually characterized. The ^{1}H-NMR spectra of **SP2–SP2** are reported in Fig. S2 (ESI†). Although it was not possible to carry out any UV-visible experiment on this molecule since it was not pure, we identified in its ^{1}H-NMR very similar patterns to those observed for **SP2–SP2** and **SP3–SP3**, and both magnetic resonance and mass spectroscopy analysis suggested that a dimerization took place. Reaction of $Cu(ClO_4)_2$ with **SP4** was carried out but the purification of any side product failed. The MALDI-TOF MS analysis reported above is the only data we have and no speculations are allowed on the hypothetical structures of compounds generated during the reaction.

Possible mechanisms of dimerization

The dimerization observed consists of an aryl carbon-carbon bond formation *via* a regioselective oxidative coupling between two identical molecules. The reaction is likely to be induced by the stoichiometric amount of copper(II) which is probably reduced to copper(0) (the red precipitate we observed) during the process.



Scheme 3



Scheme 4 Mechanism of dimerization *via* radical formation.

We suggest a mechanistic explanation to such a process by following a reaction pathway that involves the formation of radical species (Scheme 4). In this case the Cu(II) is reduced to Cu(0) triggering the formation of two SP radicals. The two radical SPs react with each other forming a symmetric dimer

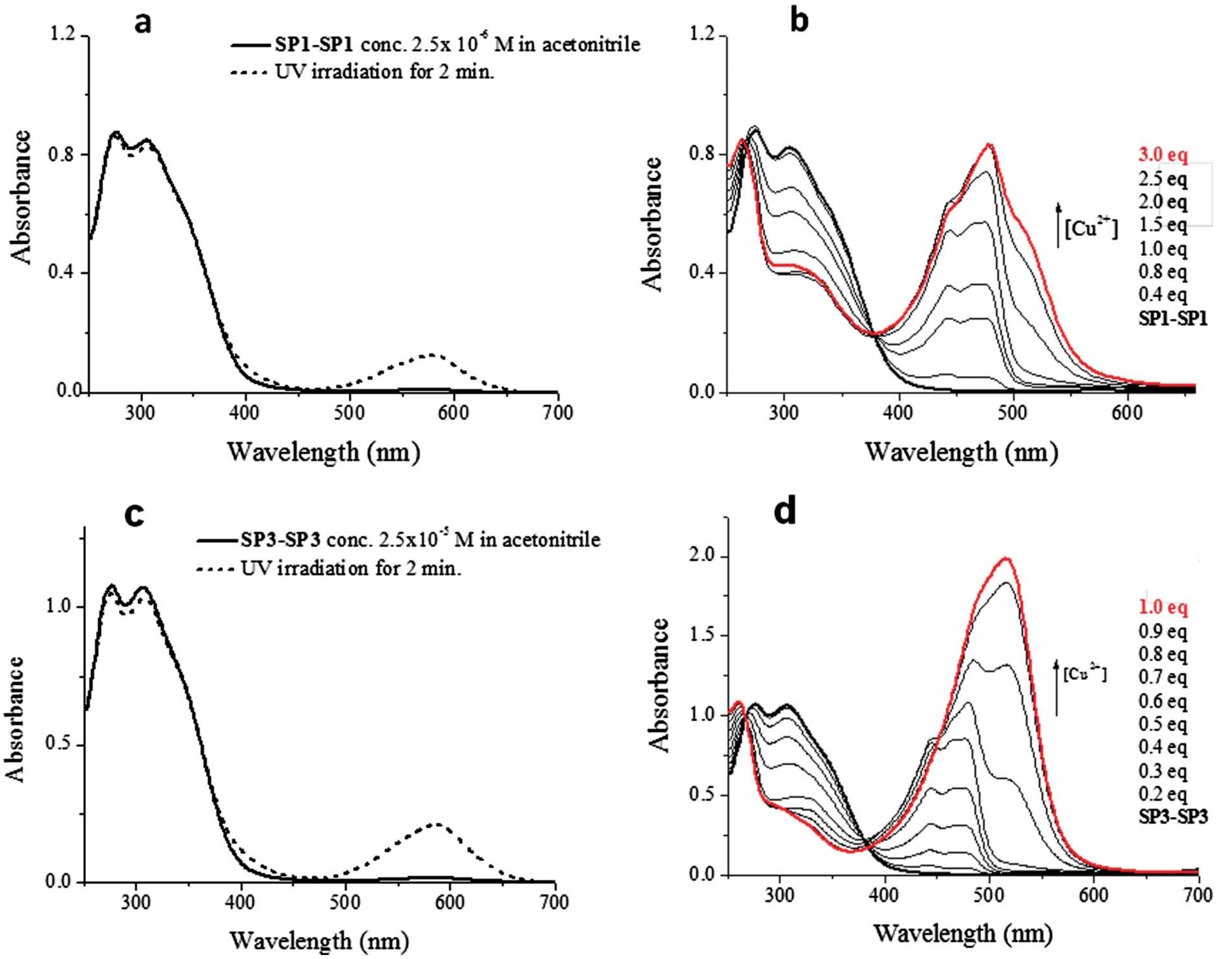


Fig. 6 (a)and (c) UV-vis spectra of a solution of **SP1–SP1** and **SP3–SP3** (2.5×10^{-6} M and 2.5×10^{-5} M in acetonitrile, 293 K) before (black curves) and after (dotted curves) irradiation with UV light; (b) and (d) UV-vis absorption spectra of **SP1–SP1** and **SP3–SP3** (2.5×10^{-6} M and 2.5×10^{-5} M, acetonitrile, 293 K) after increasing the concentration of $Cu(ClO_4)_2$.

with no conjugation between the two halves. Abstraction of two protons from the indolic aromatic regions allows the conjugation to be fully restored and the final dimer to be formed. The ability of copper(II) to trigger radical reactions on similar systems has been reported in the literature.[35] In 1985 Berti and his collaborators reported the dimerization of indoxyls mediated by $FeCl_3$.[36] More recently, Li and co-workers investigated the oxidative homocoupling of naphthylamines mediated by $FeCl_3$ in extremely mild conditions.[37] While Berti claimed the formation of radical intermediates, Li suggested a mechanistic explanation with two plausible routes, involving the formation of either radical or organometallic intermediates. Although the oxidant in these cases is Fe(III) and the substrates are different from our spiropyrans, we believe that an alternative pathway for the homocoupling of our molecules that produces an organometallic intermediate may resemble that suggested by Li. We are currently evaluating this hypothesis.

SP dimers' photoswitchability and response to Cu(II)

The binding capability of the spiropyran dimers obtained by addition of $Cu(ClO_4)_2$ and their corresponding monomers were investigated by UV-vis absorption spectroscopy. Spectra of colourless acetonitrile solutions containing **SP1–SP1** and **SP3–SP3** are shown in Fig. 6. Spiropyran **SP1–SP1** absorbs in the UV region with two distinctive bands with maxima at 275 nm and 303 nm. It is interesting to observe that its molar absorption coefficient of 3.5×10^5 M^{-1} cm^{-1} is an order of magnitude higher than 1.1×10^4 M^{-1} cm^{-1} observed for the corresponding monomer **SP1**. This increased capability of absorbing light of compound **SP1–SP1** is probably due to its extended conjugation between the two indolic moieties. Irradiation with UV light at 254 nm caused the appearance of a new band in the visible region at 579 nm (Fig. 6a) accompanied by blue coloration of the solution. This band indicates more likely the photoisomerization of the spiropyran units in their corresponding merocyanines. At this stage it is not clear if one or both units are involved in the photoisomerization. The band in the visible region disappeared after 10 min of storage in the dark and the spiropyran spectrum was fully recovered. Addition from 0.4 to 3 equivalent of $Cu(ClO_4)_2$ to the same spiropyran solution produced the appearance of new bands in the visible region with the highest intensity peak at 475 nm that reached its maximum value after the addition of 3 equivalent of salt. Concomitantly, the two absorption maxima in the UV region decreased asymmetrically and two isosbestic points were noticed at 264 nm and 368 nm (Fig. 6b). No response was observed with concentrations of salt below 0.4 equivalents and the fact that 3 equivalents of $Cu(ClO_4)_2$ were needed to produce the maximum effect may reflect a low association constant between the dimer and the salt. The appearance of the new bands is probably due to ring opening of both spiropyran units and the following formation of a copper complex where the metal is trapped between the two phenolates. Compound **SP3–SP3** responded to photostimulation with UV light as well. Its spectra before and after irradiation are shown in Fig. 6c. Analogously to compound **SP1–SP1**, an acetonitrile solution of **SP3–SP3** is colourless and absorbs in the UV region with maxima at 275 nm and 308 nm. Its molar absorption coefficient of 4.2×10^4 M^{-1} cm^{-1} four times higher than 1.0×10^4 M^{-1} cm^{-1} observed for the corresponding monomer **SP3**. Irradiation with UV light triggers the photoisomerization of the spiropyran subunits to the open merocyanines accompanied by the appearance of a visible band with maximum intensity at 586 nm. This new absorption band disappeared shortly after storage in the dark. The addition of $Cu(ClO_4)_2$ caused dramatic changes in the molecule absorption profile, similar to those observed for **SP1–SP1**. The absorption maximum at 275 nm blueshifted to 261 nm while that at 308 nm decreased in intensity (Fig. 6d). A strong intensity band evolved in the visible region reaching its maximum absorption intensity at 515 nm after the addition of 1 equivalent of Cu(II). This band indicates probably the formation of a complex with a copper ion coordinated by the phenolate units of an isomer with two merocyanines. The two tethers present on each SP subunits can participate at the chelation as well; this offers alternative coordination geometries that still need more comprehensive investigations. However, we exclude the possibility of formation of only one type of complex where the metal is coordinated by the two tethers with the SP units being in their closed form as the conjugation through the two spiropyrans would remain unaltered. Thus no absorption would be expected in the visible region. By comparing the UV-vis spectra of compounds **SP1**, **SP3**, and their corresponding dimers **SP1–SP1** and **SP3–SP3** (Fig. 1 and Fig. 6) at their ground state in absence of Cu(II), it is noticed that all SPs show negligible absorptions in the visible region. Addition of Cu(II) to the dimers' solutions causes the appearance of absorption bands in the visible region that are comparable to those observed when Cu(II) is added to the monomer solutions. If the dimerization mechanism involving the formation of an organometallic intermediate is correct, the absorption bands in the visible region observed after the addition of Cu(II) to **SP1** and **SP3** solutions (Fig. 1) may be due by the contribution of more than one species. It is plausible to expect a first Cu^{2+} cation to trigger the formation of a transient merocyanine-metal complex (the first species absorbing in the visible region) with the cation coordinated by the phenolate. This open form, for the reasons mentioned in the mechanistic explanation, would be susceptible to homocoupling with an analogous species that would lead to a dimer formation. The same dimer would not be able to react any further but could coordinate Cu^{2+} cations thus forming a complex with absorption in the visible region.

The response of both dimers to the presence of mono and bivalent metal cations was also evaluated. The same cations used before with the monomers were utilized also in this instance. None of the metal cations produced any changes in the dimers UV-vis absorption spectra (Fig. S3, ESI†). We are currently evaluating if this apparent selectivity towards copper(II) is retained also in the presence of different counter ions.

The reversibility of copper complexation was investigated by irradiating with visible light the spiropyran solutions **SP1–SP1** and **SP3–SP3** containing the metal. Interestingly, the phenomena observed were very similar to those observed after shining visible light on the solutions containing spiropyrans **SP1** and **SP3** in the presence of copper(II). In both cases the bands in the visible region of their spectra decreased in intensity and blueshifted but the spectra of the spirochromenes in the absence of copper(II) was not recovered (Fig. 7a and 7b). This indicates probably just a partial release of the metal cation from the photochromic system. Additionally these changes were not reversible; neither storage in the dark nor irradiation with UV light recovered the spectra observed before irradiation with visible light. These unexpected results need to be further investigated.

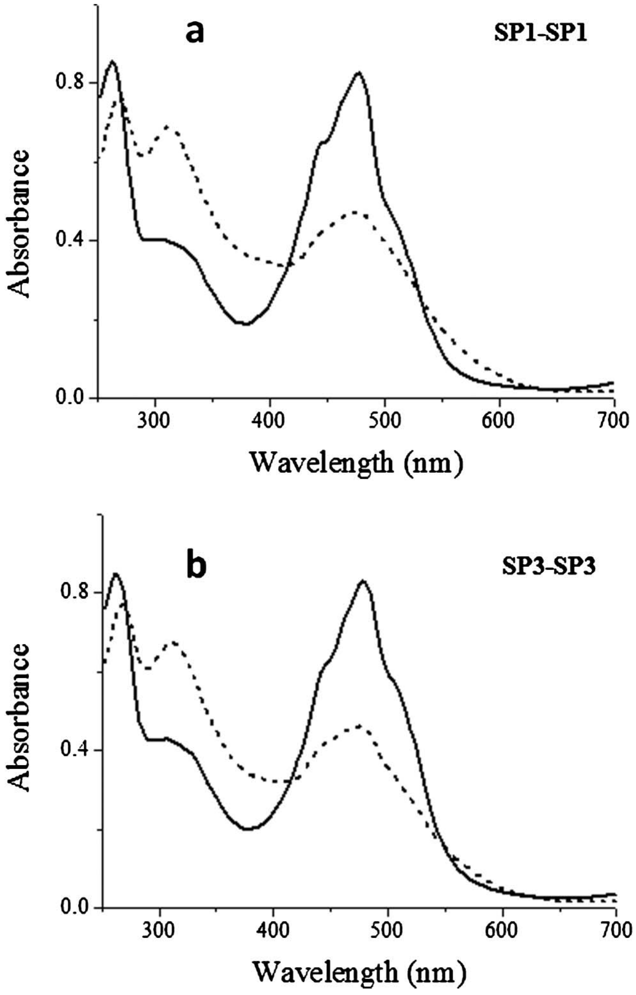


Fig. 7 (a) UV-vis spectra of a solution of **SP1–SP1** (2.5×10^{-6} M in acetonitrile, 293 K) in the presence of 3 equivalents of $Cu(ClO_4)_2$ before (black curve) and after (dotted curve) irradiation with visible light; (b) UV-vis spectra of a solution of **SP3–SP3** (2.5×10^{-5} M in acetonitrile, 293 K) in the presence of 1 equivalent of $Cu(ClO_4)_2$ before (black curve) and after (dotted curve) irradiation with visible light.

Conclusions

This group of spiropyrans bearing different substituents only on the indolic part of their skeleton showed selective responses only to the presence of copper(II) ions. However the interaction with copper(II) appeared to be only partially reversible as irradiation with visible light was not capable of producing the complete release of the metal cation. By deepening our studies on these unusual interactions with copper(II) we discovered that the binding of this metal is accompanied by a dimerization of our molecules. Indeed, we purified two compounds, namely **SP1–SP1** and **SP3–SP3**, that are the products of a regioselective oxidative cross-coupling mediated by copper(II). A third compound, **SP2–SP2**, was identified *via* MALDI-TOF MS and mono- and bidimensional ^{1}H-NMR spectroscopies, however any purification attempt failed. The pure dimers **SP1–SP1** and **SP3–SP3** retained their capability of chelating copper(II) ions but irradiation of the formed complexes with visible light produced irreversible changes that are currently under investigation. It is interesting to observe that compounds **SP1–SP1** and **SP3–SP3** were produced in very mild conditions with yields ranging around 45%. To the best of our knowledge this is the first example of cross-coupling mediated by copper(II) in such mild conditions causing the symmetric dimerization of spiropyran dyes. Since homocoupling was investigated only in the presence of Cu(II) perchlorate, we are currently investigating the effect of different counter ions and verifying if the scope of this reaction can be broadened. Additionally, since the two purified dimers respond only to the presence of copper(II), we are currently evaluating the possibility of using these molecules as sensitive and selective sensors for this metal.

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