

Supporting Information

Spiropyran for light-controlled drug delivery

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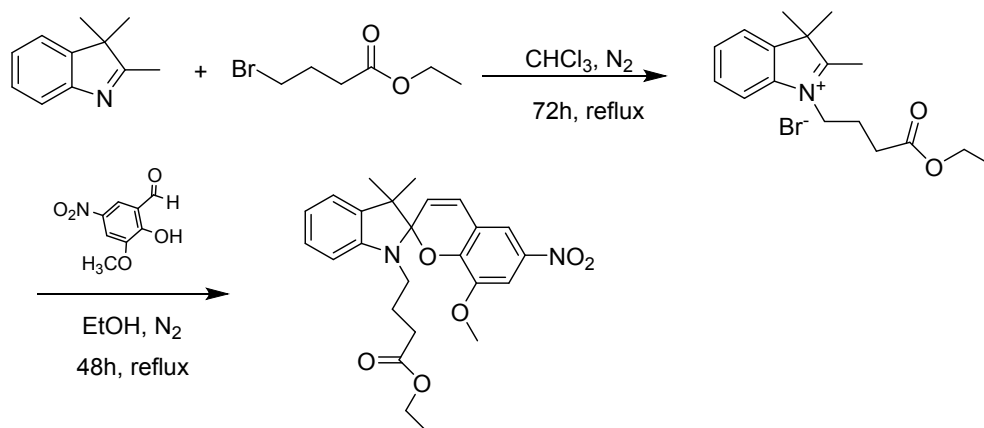
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Synthesis

The desired spiropyran (SP-E) is synthesized accordingly to a reported procedure.¹



¹H NMR (400 MHz, ACETONITRILE-*d*₃) δ ppm 1.16 (s, 3 H) 1.19 (t, *J*=7.15 Hz, 3 H) 1.26 (s, 3 H) 1.79 - 1.94 (m, 2 H) 2.33 (td, *J*=7.15, 2.86 Hz, 2 H) 3.15 - 3.35 (m, 2 H) 3.79 (s, 3 H) 4.06 (q, *J*=7.19 Hz, 2 H) 5.97 (d, *J*=10.56 Hz, 1 H) 6.69 (d, *J*=7.7 0.7 Hz, 1 H) 6.87 (td, *J*=7.37, 0.88 Hz, 1 H) 7.02 (d, *J*=10.56 Hz, 1 H) 7.14 (dd, *J*=7.26, 0.88 Hz, 1 H) 7.19 (td, *J*=7.70, 1.32 Hz, 1 H) 7.69 (d, *J*=2.42 Hz, 1 H) 7.79 (d, *J*=2.64 Hz, 1 H); MS (*m/z*, ESI⁺) calc.: 453.2026, found 453.4.

Additional UV/Vis absorption/Fluorescence emission/MALDI-TOF analyses

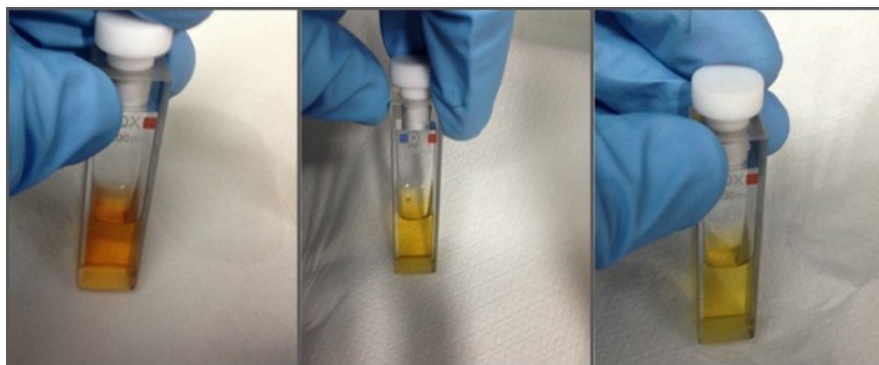


Figure S1. Visible color changes upon addition of increasing amounts of ASA, in details 0-10-30 equivalent of ASA added in titration (ii). The experiment is performed in a 5×10^{-5} M MeCN solution of the titrated compounds (SP-E:Zn²⁺ 1:1) with following additions of the titrant compounds (ASA).

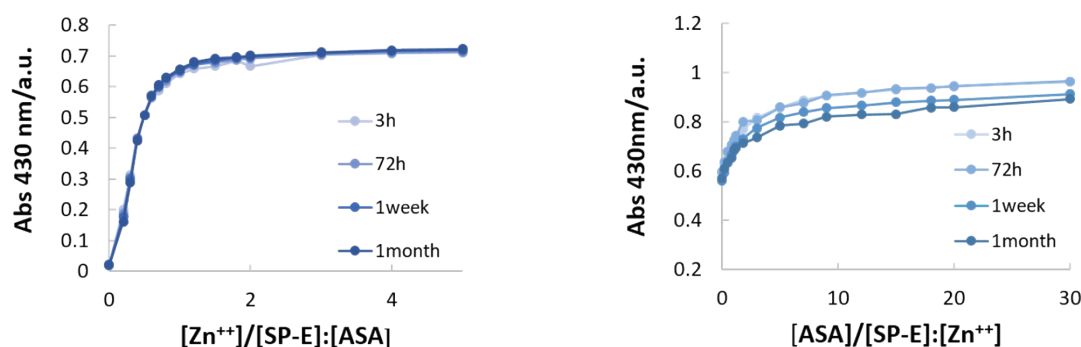


Figure S2. Titration experiments are performed preparing the MeCN solutions containing the necessary components (i.e. SP-E and ASA or SP-E and Zn²⁺), the titrations agents (i.e. Zn²⁺ or ASA) are added to those solutions and the samples are stored in dark condition for 3h to allow the systems' equilibration, then the spectra are recorded. The same samples for the titration Zn²⁺/SP-E:ASA (1:1) and ASA/SP-E:Zn²⁺ (1:1) are kept and monitored in time and they don't show any variation up to one month after the samples' preparation.

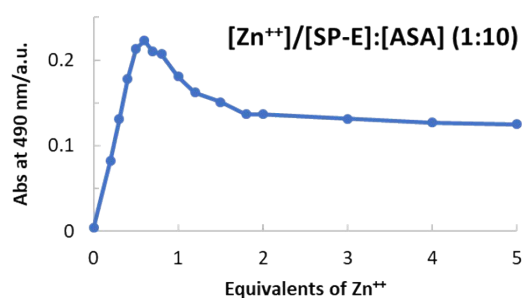


Figure S3. Enlarged version of Figure 5c between 0 and 0.25 a.u. absorption value. The absorbance at 490 nm increase until 0.6 equivalents, then it decreases to a stable value at around 1.8

equivalents, where the plateau region begins. This trend could confirm the evidence that in presence of ASA, zinc is involved also in the formation of the ternary system and is subtracted in the formation of the binary one, as discussed in the main text.

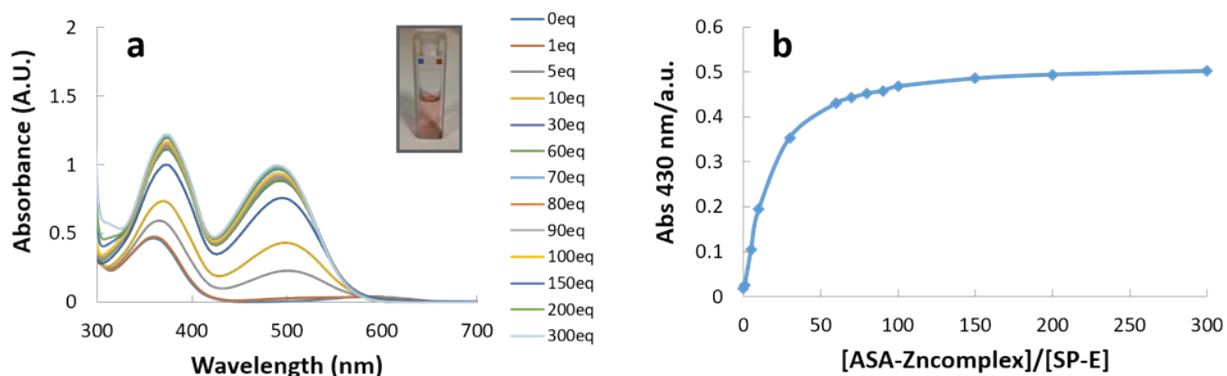


Figure S4. Titration experiments in a 5×10^{-5} M solution of SP-E with equi-molar amounts of ASA-Zn (II) complex. The experiment was conducted up to 300 equivalents, it reached a plateau region at around 120 equivalents. The measurements were performed after 5h from the samples' preparation. The system is not stable over time, after 8h from the samples' preparation, the sample containing 300 eq. of ASA-Zn (II) complex contains some precipitated material, after 24 hours also the samples containing 200-150-100 eq. of ASA-Zn (II) complexes were precipitated, in the consequent 24 hours the samples containing 90 and 80 equivalents showed precipitation. MS analysis performed on this material evidence how the precipitate material is mainly ASA.

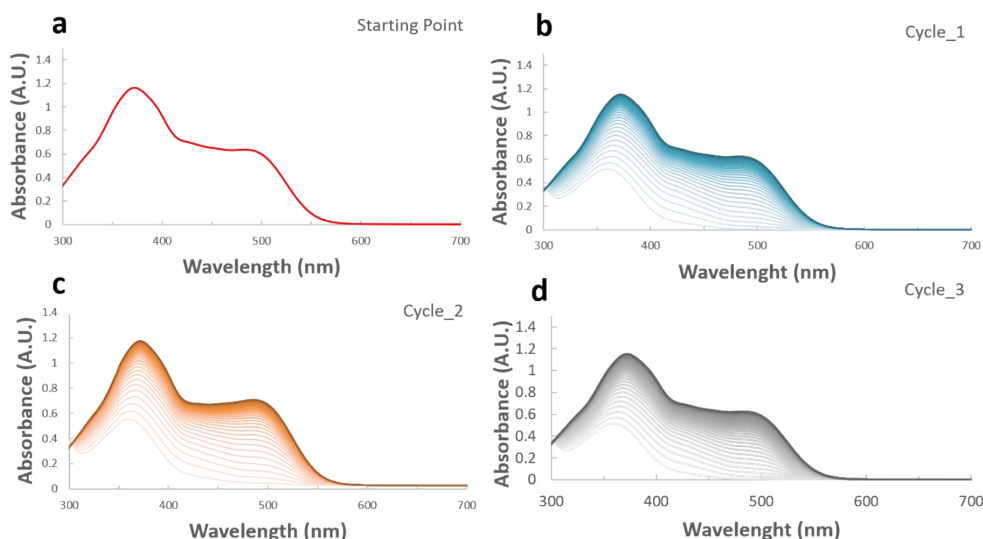


Figure S5_1. The spectra a-b-c-d show the irradiation experiments for 3 sequential cycle for the sample containing SP-ASA-Zn²⁺ (1:1:1.5) as a representative example of the kinetic studies conducted. In details a, the spectrum for the sample after its equilibration overnight; spectra b, c, d show the reformation of the systems monitored for 3h (from clearer to darker color's intensity).

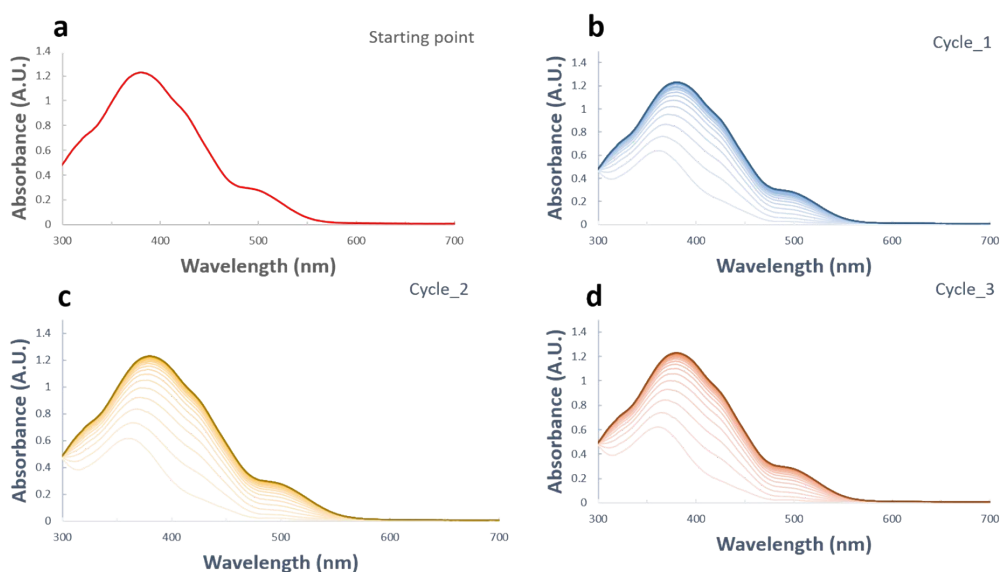


Figure S5_2. The spectra a-b-c-d show the irradiation experiments for 3 sequential cycle for the sample containing SP-E:Zn²⁺:ASA (1:1:15) as a representative example of the kinetic studies conducted. In details a, the spectrum for the sample after its equilibration overnight; spectra b, c, d show the reformation of the systems monitored for 3h (from clearer to darker color's intensity).

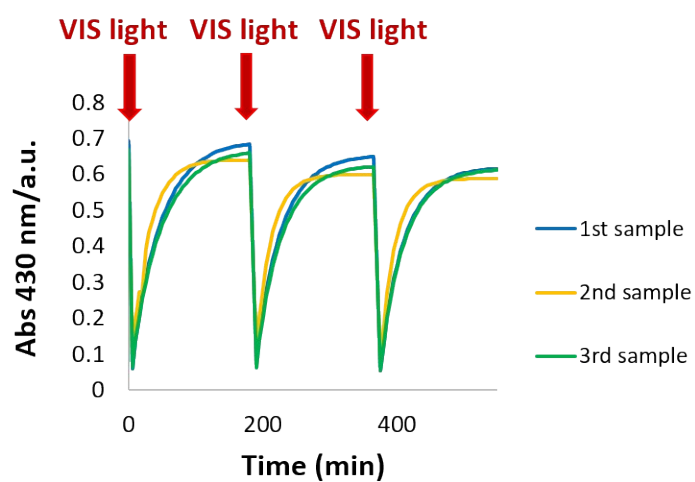


Figure S6. Three different samples of the sample containing SP:ASA:Zn²⁺ (1:1:1.5) are tested to prove the repetitiveness of the formation of the new system over 3 consecutive cycles.

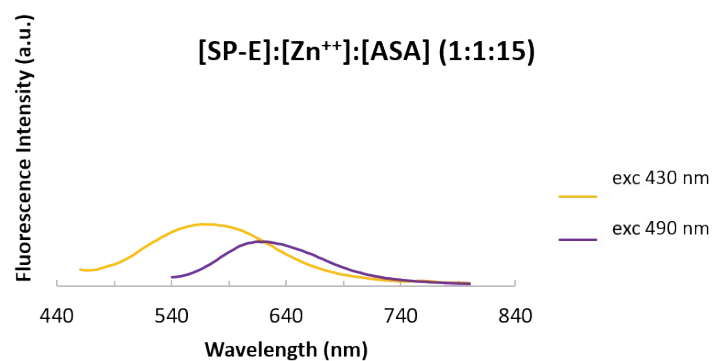


Figure S7. Emission spectra of the sample SP-E:Zn²⁺:ASA (1:1:15), the analyzed sample presents a concentration of 5×10^{-5} M for each component which is analyzed at λ_{exc} 430 nm and λ_{exc} 490 nm, the obtained emission spectra present λ_{max} at 566 nm and 622 nm respectively.

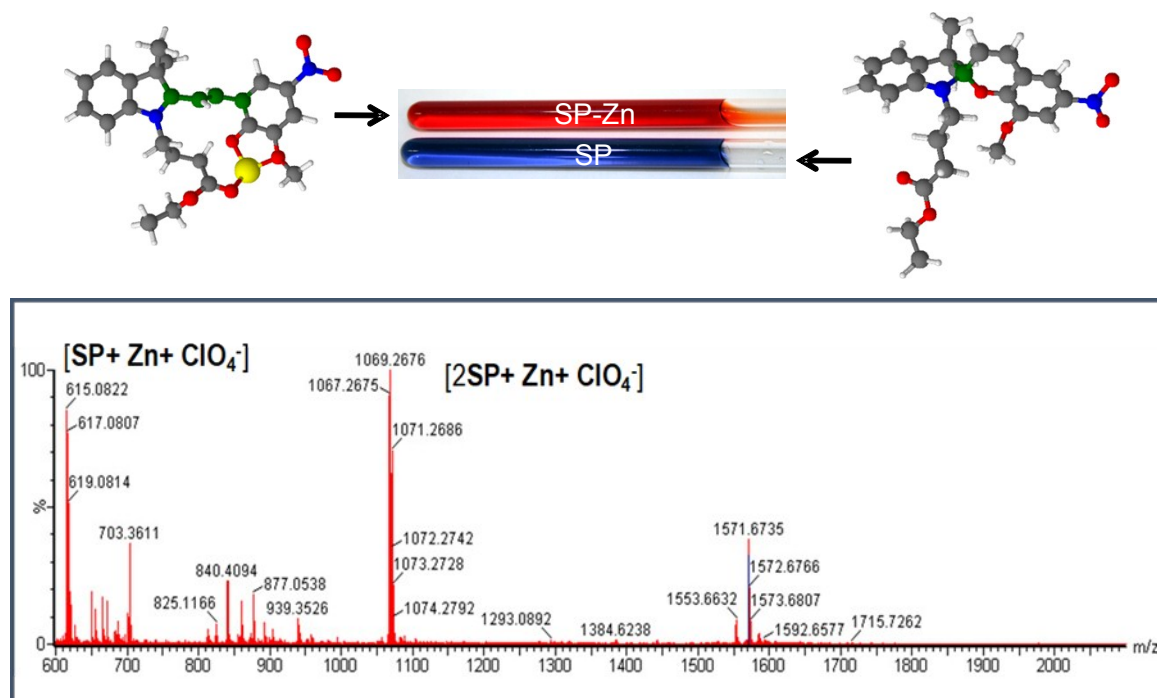


Figure S8. Top) NMR tubes containing SP before and after the addition of zinc. Bottom) High resolution mass spectrum of the sample containing MC-Zn²⁺ complex in MeCN. In this MALDI-TOF spectrum the m/z peaks belonging to the MC-Zn²⁺ systems are highlighted. It is useful to compare this spectrum with the one reported in the main text, to evidence the formation of the ternary system in presence of ASA.

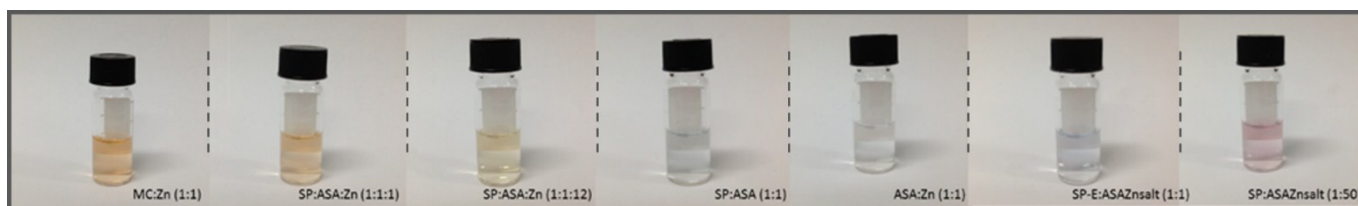


Figure S9. Representative solutions of different combinations of the three analyzed components with 5×10^{-5} M concentration.

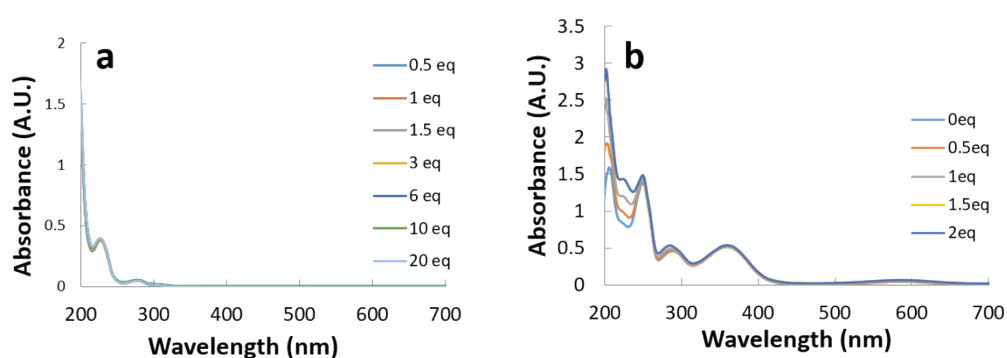


Figure S10. Control experiments. a) titration in a 5×10^{-5} M solution of ASA with equi-molar amounts of $\text{Zn}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$ up to 20 equivalents b) titration in a 5×10^{-5} M solution of SP-E with equi-molar amounts of ASA up to 2 equivalents. In both cases no species characterized by absorbance at 430 nm are detected.

References

[S1] M. Baldrighi, G Locatelli, J. Desper, C.B. Aakeroy, S. Giordani, Chemistry-A European Journal 2016, **22**, 13976.