A metallo-supramolecular approach to a half-subtractor†‡

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The tetraamine dinucleating ligand L, which bears naphthalene moieties at both ends, behaves as a combinatorial logic circuit for a molecular half-subtractor in the presence of Zn^{II} ions.

Since Nikola Tesla designed the first AND operator in the late nineteenth century,[1] logic gates have become an essential part of our everyday lives. In microelectronics, logic gates are the devices that perform basic Boolean functions and are the core elements of silicon-based computer processors.[2] Based on early ideas to use molecules as logic gates,[3] various chemical systems were developed to mimic Boolean operations (AND, OR, XOR, NAND, NOR, INHIBIT *etc.*).[4] Among these molecular logic devices, those exhibiting a double output channel are currently of particular interest since they are the basis for the construction of molecular logic circuits capable of executing arithmetic operations such as addition or subtraction. However, despite the enormous relevance of this research, molecular-scale arithmetic was only born with the new millennium[5] and therefore literature reports on this subject are scarce.[6,7]

On the other hand, research in coordination chemistry during the last two decades was dominated by the growth of metallo-supramolecular chemistry, which allows the preparation, isolation, and characterization of sophisticated self-assembled polymetallic oligomers.[8] The metallo-supramolecular synthetic approach offers well known advantages over the traditional stepwise synthetic methodologies based on covalent bond formation, and also over the more recent non-covalent supramolecular self-assembly approach, for the construction of predefined chemical systems (directional control and strength of metal–ligand interactions, smaller number of synthetic steps *etc.*). The principles underlying the construction of such assemblies are now reasonably well established, and current effort is focused on the development of practical applications for these metallo-supramolecular systems as functional devices at the molecular level.[4j–9]

Although there are some reports on supramolecular assemblies and bioinspired systems designed as logic circuits that perform molecular-scale calculation functions,[5–7] to the best of our knowledge there are no reports of arithmetic processors based on self-assembled polymetallic architectures. Herein we report for the first time a metallo-supramolecular system capable of performing the subtraction of two binary digits (bits).

The design of ligand **L** (Scheme 1) means that it potentially has a dinucleating character due to its *p*-dibenzyl spacer.[10] **L** contains appended naphthalene fluorophores at the end of the binding units, which display a characteristic monomeric emission band in the 300–360 nm region. This band is implemented as the first fluorescent-emitting channel in our molecular device. It is expected that when **L** is in the presence of metal ions that can be tetrahedrally coordinated, this situation will drive the assembly of a [2 + 2] metallo-supramolecular adduct.[11] Upon coordination, the naphthalene terminal moieties of the **L** molecules present in the adduct will stack together, allowing the formation of intramolecular excimers upon excitation.[12] The excimers display characteristic emission spectra that are structureless and red-shifted with respect to the regular monomeric emission bands.[13] Our purpose is to use the resulting excimer emission band as the second fluorescent-emitting channel of our device. The design of the resulting logic gate, based on a monomer/excimer dual fluorescence output channel, is a robust approach that has already been used in some logic gates and circuits.[14]

The tetraamine **L** was synthesized by a three-step procedure with an overall yield of 80% (see ESI‡). **L** is a white solid that is soluble in water and in most common organic solvents. **L** has an absorption spectrum with a strong band with vibrational structure centered at 281 nm. In water at neutral pH it shows a fluorescence emission band with vibrational structure in the 310–360 nm region (λ_{ex} = 290 nm). As observed in related hybrid naphthalene–polyamine systems, the intensity of the emission fluorescence is maximum at low pH and progressively decreases on increasing the pH, until the emission is eventually completely quenched at pH $\geq$ 8. This behavior is the result of gradual deprotonation of the amines, which act as efficient electron transfer quenchers of the excited naphthalene.[15] Further confirmation of the acid–base dependence of the electronic properties of **L** is the observation that the absorption spectrum of **L** is also pH dependent.

Experiments in aqueous media in the presence of metal ions suggest that ligand **L** is almost completely removed from the solution upon complexation with 1 equiv. of Zn^{II} ions and precipitation of the resulting metal adduct. The low solubility of

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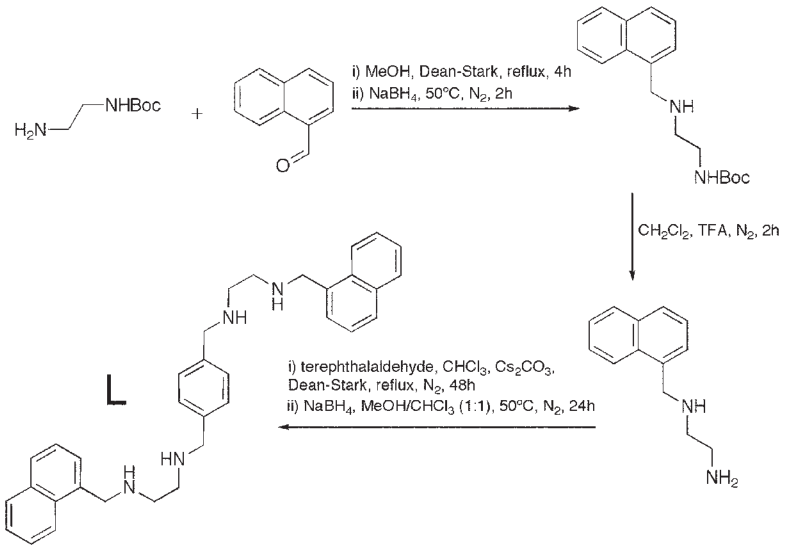
† M. V. L. and C. G.-R. dedicate this work to their newborn and first son, Álvaro.

‡ Electronic supplementary information (ESI) available: Full experimental details for the preparation of **L**, details for the structural characterization of **L** and the Zn:**L** adducts, and ancillary experiments. See DOI: 10.1039/b808888h



Scheme 1 Synthesis of ligand **L**.

this adduct made a detailed spectroscopic analysis of the assembly process impossible. However, elemental analysis of the precipitate confirmed the presence of **L** and Zn^{II} in a 1 : 1 stoichiometry. Moreover, the emission spectrum of the Zn^{II} adduct (λ_{ex} = 290 nm) in the solid state displays a large band occurring at *ca.* 465 nm, with the monomer naphthalene emission band present only as a residual signal in the spectrum (see ESI‡).

In an attempt to avoid the precipitation problems observed in water, we repeated the experiments in organic media. The emission spectrum of **L** (500 nM) in MeCN shows the characteristic monomer band of the naphthalene fluorophore with a maximum at 345 nm. As expected, we observed pH-dependent behavior of the fluorescence emission of **L**: addition of acid (TFA) results in a progressive increase in the intensity of the monomer emission band of the naphthalene fluorophore until it reaches a maximum (~30 equiv.). A very weak excimer emission shoulder is observed at high concentrations of TFA, indicating that **L** slightly aggregates intermolecularly in acidic MeCN media. Subsequent addition of a base (NEt$_3$) gradually decreases the intensity of the fluorescence emission band of the naphthalene monomer until it completely disappears (~60 equiv.). No new emission bands are observed at longer wavelengths in these conditions.

Following the spectroscopic characterization of the ligand in acetonitrile solution, we carried out steady-state fluorescence emission studies on **L** in organic media in the presence of Zn^{II} ions (see ESI‡). Addition of Zn(CF$_3$SO$_3$)$_2$ (7 equiv.) to a solution of **L** in MeCN (500 nM) did not cause any appreciable change in the emission spectrum (Fig. 1, spectrum A and Scheme 2, species A). However, the addition of ~30 equiv. of NEt$_3$ to this solution induced a large fluorescence emission band centered at λ_{max} = 480 nm (Fig. 1, spectrum C and Scheme 2, species C). We believe that this band can be assigned to the naphthalene excimer band resulting from intramolecular interactions between the naphthalene groups of two ligands in the Zn^{II} adduct assembled upon metal coordination. The addition of NEt$_3$ is necessary to allow the association to take place, since the ligand is purified by HPLC and is in fact obtained as the protonated TFA salt; as a result, the equilibrium between **L** and its protonated species in MeCN is not totally displaced towards the unprotonated molecule unless some extra base is added. Subsequent addition of a stoichiometric amount (relative to the previously added amine) of trifluoroacetic acid (TFA) to this solution induces mutual annihilation of acid and base and restores the initial situation (Fig. 1, spectrum D and Scheme 2, species D). Moreover, addition of a further ~30 equiv. of TFA to this solution results in an increase in the intensity of the naphthalene monomer emission band at 345 nm (Fig. 1, spectrum B and Scheme 2, species B). Similar results were obtained on performing these titration experiments at 40 and 60 °C or using a more dilute solution of **L** (5 nM).

The emission spectra of the system **L** + Zn(II) changed immediately after the addition of acid or base. This suggests that the time required to reach the equilibrium of each species is very short. Although the intent of this work is to demonstrate function, and not to produce a practical device, we have tried to investigate the stability of our system when cycling. After five cycles (meaning the consecutive addition of acid and base to the starting species) the blue and green channels of the logic device remain unaltered or little altered (see ESI‡). These data suggest the reversibility of the assembly processes and therefore of our logic device.

The low-energy emission features of the spectrum are typical of genuine naphthalene-based excimer emission.[16] However, in our system the emission band is red-shifted, an observation that has previously been related with a greater degree of stabilization of the naphthyl-based excited state, which in our case must result from the optimal geometry and microstructure induced by the Zn^{II} ions.[17] As expected, the absorption spectrum of **L** in MeCN in the presence of NEt$_3$ does not change appreciably on addition of Zn^{II}.

We performed molecular modeling studies to ascertain whether the geometric requirements for excimer formation were fulfilled in the hypothetical structure of a [2+2] Zn^{II} complex with ligand **L** (see ESI‡). The resulting structure

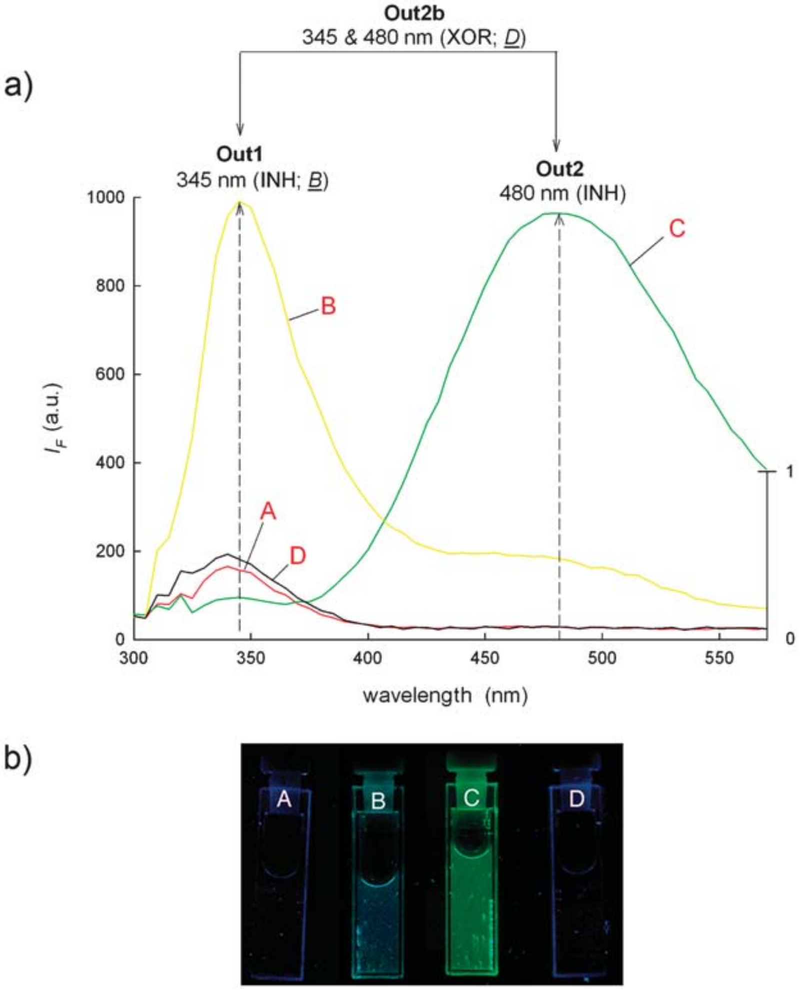
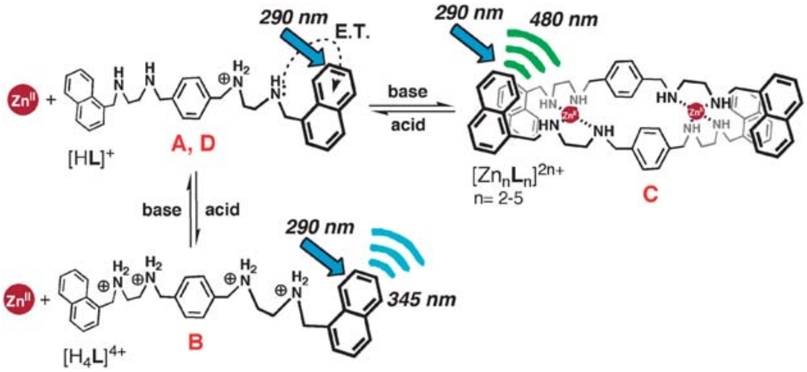


Fig. 1 (a) Fluorescence spectra of **L** + 7 equiv. of Zn^{II} (λ_{ex} = 290 nm) in the absence and presence of acid (trifluoroacetic acid, ~30 equiv., In1) and base (triethylamine, ~30 equiv., In2), in MeCN solution (500 nM) at 298 K. *Spectrum A*: [**L** + Zn^{II}]; *spectrum B*: [**L** + Zn^{II} + acid]; *spectrum C*: [**L** + Zn^{II} + base]; *spectrum D*: [**L** + Zn^{II} + acid + base] and (b) their corresponding visual features (λ_{ex} = 360 nm).

displays a helical arrangement of the ligands around the axis defined by the two metal ions, and the naphthalene units are clearly stacked in the minimized structure. On the basis of these minimization calculations we suggest that the helical arrangement is favored in the metal adduct assembled. As expected, the ESI mass spectrum of the Zn^{II} adduct with **L** shows a series of peaks that can be assigned to the [2 + 2] adduct with different numbers of anions. However, there are also other peaks that can be attributed to higher 1 : 1 oligomers ($[Zn_nL_n]^{2n+}$; n = 3–5). These data suggest the coexistence of the [2 + 2] adduct with other assemblies in MeCN solution (see ESI‡).



Scheme 2 Representation of the Zn^{II}:**L** species present in solution in MeCN under different conditions, and the corresponding maximum emission wavelength in the fluorescence spectra. A, B, C and D correspond with the fluorescence spectra shown in Fig. 1. Species A, D are partly protonated, likely in exchange through multiple equilibria involving all the basic amines.

Logic circuits capable of performing arithmetic operations are currently implemented in semiconductor technology by combining several logic gates in parallel.[18] A half-adder, which requires two binary inputs and two binary outputs to work, can carry out elementary addition of two bits utilizing a XOR gate to generate the sum digit (S), and an AND gate to produce the carry (C). On the other hand, a half-subtractor is a combinatorial circuit that subtracts two bits and outputs their difference. A half-subtractor, like a half-adder, needs two outputs: one generates the difference (D) and the second generates the borrow (B). These outputs are generated through XOR and INHIBIT gates, respectively.

The acid–base behavior in MeCN of the system [$\mathbf{L}+\mathrm{Zn^{II}}$] can be interpreted in binary logic (Fig. 2). The tetraamine **L** acts, in MeCN solution and in the presence of $\mathrm{Zn^{II}}$, as a molecular logic circuit operated by two chemical inputs [acid (TFA) and base (NEt_3)] and with a dual fluorescent-emitting channel: 345 nm (blue emission) and 480 nm (green emission). The truth table for this system shows that operation of [$\mathbf{L}+\mathrm{Zn^{II}}$] by acid and base expresses two INHIBIT logic functions working in parallel when the outputs are read separately at 345 (Out1) and 480 nm (Out2). An XOR gate is obtained when the two fluorescent-emitting channels are read simultaneously. In digital logic this would be equivalent to applying an OR operator to Out1 and Out2 to give a new output: Out2b. Consequently, by an appropriate choice of the detection wavelengths, the system [$\mathbf{L}+\mathrm{Zn^{II}}$] can be used to generate simultaneously borrow (B; INHIBIT function; Out1) and difference (D; XOR function; Out2b) bits of 0–0, 1–0, 0–1 and 1–1, that is, to function as half-subtractor. This approach to achieve an XOR gate by summing up the outputs of two complementary INH functions has been previously reported by M. N. Stojanovic *et al.* in their DNA logic gates[19] and subsequently by others.[20] This method is completely acceptable but, in our opinion, it has a conceptual weakness because a molecular arithmetic operation (subtraction) happens following a manual arithmetic operation (addition), and the real need is for molecules to intrinsically perform arithmetic operations.

We have explained above that the ESI-MS data and molecular modeling studies suggest the coexistence of a [2 + 2] complex with other higher 1 : 1 assemblies in MeCN solution, along with their possible helical microarchitectures. Fortunately, the design of the present logic circuit is such that the exact stoichiometry of the mixture of metallo-supramolecular adducts present in solution, and their helical or non-helical arrangement, are irrelevant for the signal processing function. We believe that this constitutes an added virtue of the approach presented here.

In summary, a metallo-supramolecular approach to molecular arithmetic has been proposed for the first time. We have demonstrated that a simple tetraamine molecule, **L**, in the presence of $\mathrm{Zn^{II}}$ ions and in MeCN solution, mimics a half-subtractor with distinct INHIBIT and XOR logic gates working in parallel. The mechanism of this device is based on the assembly of $[\mathrm{Zn}_n\mathbf{L}_n]^{2n+}$ (n = 2–5) metallo-supramolecular adducts with fluorescence excimer emission properties. We strongly believe that the approach reported herein will open new and interesting opportunities for the development of highly functional metallo-supramolecular devices capable of performing increasingly sophisticated arithmetic/logic operations.

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					HALF-SUBTRACTOR	
spectra	In1 (acid)	In2 (base)	Out1 (345 nm) INH	Out2 (480 nm) INH	Out1 (345 nm) INH (*B*)	Out2b (345 & 480 nm) XOR (*D*)
A	0	0	0 (156.3; low)	0 (28.8; low)	0 (156.3; low)	0 (156.3 & 28.8; low)
B	1	0	1 (991.3; high)	0 (183.0; low)	1 (991.3; high)	1 (991.3 & 183.0; high)
C	0	1	0 (94.4; low)	1 (963.5; high)	0 (94.4; low)	1 (94.4 & 963.5: high)
D	1	1	0 (181.3; low)	0 (27.8; low)	0 (181.3; low)	0 (181.3 & 27.8; low)

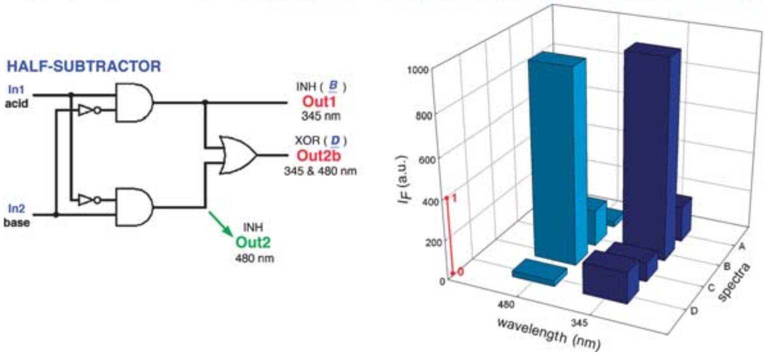

Fig. 2 Truth table, logic scheme and experimental outputs (λ_{ex} = 290 nm) for the INHIBIT/XOR (half-subtractor) logic pattern. The output signals of the molecular logic circuit are the emission bands at 345 nm (INHIBIT gate, Out1) and simultaneously at 345 and 480 nm (XOR gate, Out2b). It should be noted that the maximum naphthalene excimer emission (480 nm, green) is very strong, with more than 97% of the maximum emission of the monomer (345 nm, blue).

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