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Digital Processing with a Three-State Molecular Switch

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Certain molecular switches respond to input stimulations producing detectable outputs. The interplay of these signals can be exploited to reproduce basic logic operations at the molecular level. The transition from simple logic gates to complex digital circuits requires the design of chemical systems able to process multiple inputs and outputs. We have identified a three-state molecular switch that responds to one chemical and two optical inputs producing two optical outputs. We have encoded binary digits in its inputs and outputs applying positive logic conventions and demonstrated that this chemical system converts three-digit input strings into two-digit output strings. The logic function executed by the three-state molecular switch is equivalent to that of a combinational logic circuit integrating two AND, two NOT, and one OR gate. The three states of the molecular switch are a colorless spiropyran, a purple trans-merocyanine, and its yellow-green protonated form. We have elucidated their structures by X-ray crystallography, ¹H NMR spectroscopy, COSY and NOE experiments, as well as density functional calculations. The three input stimulations controlling the interconversion of the three states of the molecular switch are ultraviolet light, visible light, and H⁺. The two outputs are the absorption bands in the visible region of the two colored states of the molecular switch. We have monitored the switching processes and quantified the associated thermodynamic and kinetic parameters with the aid of ¹H NMR and visible absorption spectroscopies.

Introduction

The rapid progress of information technology continues to stimulate the exploration of innovative materials and architectures for digital processing. Organic molecules appear to be potential candidates for the realization of future data-elaboration, -storage, and -communication devices.¹ Their nanoscale dimensions and the power of chemical synthesis offer access to ultraminiaturized building blocks with tailored structures and properties. These promising features are encouraging the design of practical strategies to integrate molecular components into functioning electronic, optoelectronic, and all-optical devices. Indeed, examples of molecular memories, modulators, rectifiers, switches, transistors, and wires are starting to be developed adapting the operating principles of conventional devices.²

Logic gates convert input signals into output signals according to precise protocols.³ Their processing ability ensures the elaboration of information in present com-

puters, where networks of interconnected gates execute complex logic operations relying on the interplay of electrical inputs and outputs. To reproduce the functions of these devices with organic compounds, strategies to transduce input stimulations into detectable outputs at the molecular level must be developed. Certain molecules switch between two or more states in response to chemical, electrical, or optical signals. Often, the stereoelectronic properties of the various states are sufficiently different to produce distinct spectroscopic or voltammetric responses. It follows that the behavior of these molecular switches^{4,5} is equivalent to that of conventional logic gates. Both can transduce input signals into output signals. Indeed, their analogy has led to the development of chemical systems able to execute the three basic logic

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functions (AND, NOT, OR) and simple combinations of them (EOR, Half-Adder, INH, NOR, XNOR, XOR).6-25

Conventional logic circuits are assembled connecting the input and output terminals of multiple gates.³ The logic operations of the individual components and the interconnection scheme determine the logic function executed by the entire circuit. Thus, designed logic functions can be implemented in combinational circuits by selecting the number, type, and configuration of the individual operators. At the molecular level, however, relatively complex logic functions resulting from the combination of multiple gates can be programmed into a single switch. It is necessary, however, to design chemical systems that can respond to multiple inputs

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producing multiple outputs. In this paper, we demonstrate that a combinational logic function can be implemented with a three-state molecular switch able to transduce one chemical and two optical inputs into two optical outputs. In particular, we have selected for our studies a member of a well-known family of photochromic switches, namely a spiropyran.^{2g,5b,f,26}

Results and Discussion

Synthesis. The spiropyran (R/S)-**SP** (Figure 1) was synthesized in three steps starting from the commercially available compound 2,3,3-trimethyl-3H-indole. Alkylation of 2,3,3-trimethyl-3H-indole with 2-bromoethanol gave the bromide salt 1 in a yield of 69%. Treatment of 1 with KOH afforded the oxazole derivative (R/S)-2 in a yield of 88%. Reaction of (R/S)-2 with 2-hydroxy-5-nitrobenzaldehyde gave the target molecule (R/S)-**SP** in a yield of 79%.

Nuclear Magnetic Resonance Spectroscopy. The chiral spirocenter of (R/S)-SP imposes two different environments (A and B in Table 1) on the methyl protons H^o and H^p. Similarly, it imposes the two environments \mathbf{C} and \mathbf{D} on the methylene protons H^j and H^k and the two environments \mathbf{E} and \mathbf{F} on the methylene protons H^1 and H^m. As a result, two distinct singlets (1.24 and 1.14) ppm) for the methyl protons H^o/H^p and two complex multiplets (3.72-3.47 and 3.38-3.14 ppm) for the two pairs of methylene protons H^j/H^k and H^l/H^m are observed in the ¹H NMR spectrum (Figure 2a). The methylene protons H^j and H^k are coupled to the adjacent hydroxy proton Hⁿ, which resonates as a pseudotriplet at 2.80 ppm. Consistently, the COSY spectrum (Figure S-1, Supporting Information) shows cross-peaks between the pseudotriplet at 2.80 ppm and the multiplet at 3.72-3.47 ppm. The methylene protons H¹ and H^m are close to the aromatic proton H^h. In fact, a positive NOE of the doublet for this proton at 6.65 ppm (Figure 3a) is observed after

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FIGURE 1. Synthesis of the spiropyran derivative (R/S)-SP.

irradiation at 3.26 ppm (Figure S-2a, Supporting Information). The signals for the other three aromatic protons H^c, H^f, and H^d on the indoline fragment were assigned following the coupling pattern in the COSY spectrum. Cross-peaks between (1) the doublet for H^h at 6.65 ppm and the pseudotriplet for H^c at 7.14 ppm, (2) this pseudotriplet and another one for H^f at 6.82 ppm, and (3) the pseudotriplet for H^f and a doublet for H^d at 7.10 ppm can be identified (Figure S-1, Supporting Information). This assignment was confirmed exploiting the proximity of H^d to the methyl protons H^o and H^p. A positive NOE of the doublet for H^d is observed after irradiation at either 1.24 or 1.14 ppm (Figure S-2b,c, Supporting Information). The irradiation at 1.14 ppm also produces a positive NOE of the doublet for Hⁱ at 5.98 ppm. This effect is not observed after irradiation at 1.24 ppm. In fact, only the methyl protons in the environment **B** are sufficiently close to the olefinic proton Hⁱ to induce a NOE. This proton is coupled to the other olefinic proton H^e and, consistently, the COSY spectrum (Figure S-1, Supporting Information) shows cross-peaks between the doublet for Hⁱ at 5.98 ppm and that for H^e at 7.02 ppm. The cis arrangement of the two olefinic protons is confirmed by the positive NOE of the doublet for H^e at 7.02 ppm observed after irradiation at 5.98 ppm (Figure S-2d, Supporting Information). Irradiation at 7.02 ppm produces, in turn, a positive NOE of the doublet for the aromatic proton H^a at 8.06 ppm (Figure S-2e, Supporting Information). The signals for the other two aromatic

protons H^b and H^g were assigned following the coupling pattern in the COSY spectrum. Cross-peaks between (1) the doublet for H^a at 8.06 ppm and the doublet of doublets for H^b at 7.99 ppm and (2) this doublet of doublets and the doublet for H^g at 6.71 ppm can be identified (Figure S-1, Supporting Information).

The high-field ¹H NMR spectrum of a CD₃CN solution of (R/S)-**SP** equilibrated in the dark shows an additional weak singlet at 1.77 ppm for the six equivalent methyl protons of *trans*-**ME** (Figure 4). The ratio between the two isomers is (26 ± 3) × 10 in favor of (R/S)-**SP** and corresponds to an equilibrium constant (K_1) of (40 ± 5) × 10^{-4} at 298 K (Table 2). After ultraviolet irradiation,²⁷ the singlet at 1.77 ppm increases in intensity (Figure S-3a, Supporting Information), and additional signals can be observed in the ¹H NMR spectrum. In particular, a doublet for one of the olefinic protons of *trans*-**ME** can be identified at 6.50 ppm. Its large coupling constant (16 Hz) confirms the trans configuration of the associated double bond.²⁸

The relatively fast thermal reisomerization of *trans*-**ME** to (R/S)-**SP** prevents an accurate quantification of the photostationary state by ¹H NMR spectroscopy. The ratio between (R/S)-**SP** and *trans*-**ME** appears to be ca. 49, after the delay required to record the spectrum, and changes back to the original value in less than 5 min in the dark. The addition of 1 equiv of CF₃CO₂H immediately after ultraviolet irradiation, however, generates the protonated form *trans*-**MEH** (Figure 4) slowing the formation of (R/S)-**SP**. Consistently, the ¹H NMR spectrum recorded at this point reveals the resonances of (R/S)-**SP** and *trans*-**MEH** in a ratio of ca. 9.

The addition of 1 equiv of CF_3CO_2H to a CD_3CN solution of (R/S)-**SP** maintained in the dark produces significant changes in the ¹H NMR spectrum. The two singlets for the methyl protons H^o and H^p coalesce (Figure 2b), and the two multiplets for the two pairs of methylene protons H^j/H^k and H¹/H^m resolve into two triplets. These changes indicate that, under these conditions, the three sets of protons H^o/H^p, H^j/H^k, and H¹/H^m exchange rapidly on the ¹H NMR time scale between the environments **A/B**, **C/D**, and **E/F** (Table 1), respectively. Their fast exchange is a result of the acid-promoted interconversion between the two enantiomers of (R/S)-**SP**, presumably through the formation of *cis*-**MEH**.

Additional signals appear in the ¹H NMR spectrum (Figures 2c and 3c) if the acidified solution of (R/S)-**SP** is maintained in the dark. Indeed, (R/S)-**SP** switches to *trans*-**MEH** under these conditions (Figure 4). Over the course of ca. 3 d, the ratio between (R/S)-**SP** and *trans*-**MEH** decreases gradually to a stationary value of (25 ± 5) × 10^{-2} , which corresponds to an equilibrium constant (K_2) of (8 ± 3) × 10^2 M⁻¹ at 298 K (Table 2). Upon exposure of the solution to ambient light, *trans*-**MEH** reverts to (R/S)-**SP**. Consistently, the ratio between (R/S)-**SP** and *trans*-**MEH** increases (Figures 2d and 3d). After ca. 4 d, the ¹H NMR spectrum (Figures 2e and 3e) shows almost exclusively the signals of (R/S)-**SP**.

 $[\]left(27\right)$ The solution was irradiated for 5 min with a Mineralight UVGL-25 lamp.

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TABLE 1. ¹H NMR Spectroscopic Data (300 MHz, 298 K, CD₃CN) for (*R/S*)-SP^a and *trans*-MEH^b



(R/S)-SP				trans-MEH					
protons	δ (ppm)	no. of protons	multiplicity	J (Hz)	protons	δ (ppm)	no. of protons	multiplicity	J (Hz)
Ha	8.06	1	d	3	HA	8.78	1	d	3
H^{b}	7.99	1	dd	9 and 3	H^B	8.27	1	dd	9 and 3
Hc	7.14	1	pt	7	$H^{C f}$	7.66 - 7.61	1	m	
$\mathbf{H}^{\mathbf{d}}$	7.10	1	d	7	$\mathrm{H}^{\mathrm{D}g}$	7.74	1	d	7
H^{e}	7.02	1	d	10	$H^{E h}$	8.47	1	d	17
$\mathbf{H}^{\mathbf{f}}$	6.82	1	pt	7	$\mathrm{H}^{\mathrm{F}f}$	7.66 - 7.61	1	m	
$\mathbf{H}^{\mathbf{g}}$	6.71	1	d	9	H^{G}	7.20	1	d	9
H^{h}	6.65	1	d	8	H^{Hg}	7.74	1	d	8
H^i	5.98	1	d	10	$H^{I h}$	7.78	1	d	17
H ^{j c}	3.72 - 3.47	1	m		$H^{J i}$	4.04	1	t	5
$H^{k c}$	3.72 - 3.47	1	m		$H^{K i}$	4.04	1	t	5
$H^{l d}$	3.38 - 3.14	1	m		$\mathrm{H}^{\mathrm{L}j}$	4.66	1	t	5
$H^{m d}$	3.38 - 3.14	1	m		$\mathbf{H}^{\mathbf{M}j}$	4.66	1	t	5
H ⁿ	2.80	1	pt	6	$\mathbf{H}^{N k}$				
Hº/H ^p ^e	1.24	3	s		H ^O	1.80	3	S	
H ^p /H ^o e	1.14	3	S		$H^{P I}$	1.80	3	S	

^{*a*} The concentration of (*R*/*S*)-**SP** was 3×10^{-2} M. ^{*b*} The data reported for *trans*-MEH were determined recording the ¹H NMR spectrum of a solution prepared from (*R*/*S*)-**SP** (3×10^{-2} M) and 10 equiv of CF₃CO₂H in CD₃CN and maintained in the dark at ambient temperature for 12 d. ^{*c*} The resonances for the protons H^j and H^k overlap and appear as a multiplet at 3.72-3.47 ppm. ^{*d*} The resonances for the protons H^j and H^k overlap and appear as a multiplet at 3.72-3.47 ppm. ^{*d*} The resonances for the protons A and B, respectively. ^{*f*} The resonances for the protons H^C and H^F overlap and appear as a multiplet at 7.66–7.61 ppm. ^{*g*} The resonances for the protons H^D and H^H overlap and appear as a multiplet at 7.76-7.72 ppm. ^{*h*} Structural considerations suggest that the proton H^E should resonate at a chemical shift greater than that of the proton H^I. As a result, we have assigned tentatively the doublet at 8.47 ppm to H^E and that at 7.78 ppm to H^I. ^{*i*} The protons H^J and H^K are equivalent and appear as a triplet at 4.04 ppm. ^{*j*} The protons H^D and H^P are equivalent and appear as a singlet at 1.80 ppm.

The ¹H NMR spectrum (Figures 2f and 3f) of a CD₃CN solution prepared by dissolving (R/S)-**SP** and 10 equiv of CF₃CO₂H and maintained in the dark for ca. 12 d shows almost exclusively the signals of trans-MEH. The loss of the chiral spirocenter simplifies the sets of signals for the methyl and methylene protons of trans-MEH. Only one singlet for the methyl protons H^O/H^P (Table 1) and two triplets for the methylene protons H^J/H^K and H^L/ H^M are observed at 1.80, 4.04, and 4.66 ppm, respectively. The COSY spectrum (Figure S-4, Supporting Information) confirms the coupling of the two pairs of methylene protons showing cross-peaks between the two triplets at 4.66 and 4.04 ppm. The methylene protons H^L and H^M are close to the aromatic proton H^H, and a positive NOE of the doublet for this proton at 7.74 ppm is observed after irradiation at 4.66 ppm (Figure S-5a, Supporting Information). Instead, the methyl protons H^O and H^P are close to the other aromatic proton H^D, and a positive NOE of the doublet for this proton at 7.74 ppm is observed after

irradiation at 1.80 ppm (Figure S-5b, Supporting Information). The two doublets for H^D and H^H overlap and appear in the ¹H NMR spectrum as a multiplet at 7.76– 7.72 ppm. The resonances of the other two aromatic protons H^C and H^F on the indolium fragment were identified from cross-peaks in the COSY spectrum. They overlap and appear as a multiplet at 7.66–7.61 ppm. Cross-peaks in the COSY spectrum allowed also the identification of the signals corresponding to the protons H^A, H^B, and H^G on the *p*-nitrophenol fragment. They resonate at 8.78, 8.27, and 7.20 ppm, respectively.

The COSY spectrum reveals cross-peaks between the remaining two doublets at 8.47 and 7.78 ppm. They correspond to the olefinic protons H^E and $H^{I,29}$ Their large coupling constant of 17 Hz (Table 1) suggests that these

⁽²⁹⁾ Structural considerations suggest that the proton $H^{\rm E}$ should resonate at a chemical shift larger than that of the proton $H^{\rm I}$. As a result, we have assigned tentatively the doublet at 8.47 ppm to $H^{\rm E}$ and that at 7.78 ppm to $H^{\rm I}$.



FIGURE 2. Partial ¹H NMR spectra of (R/S)-**SP** (3 × 10⁻² M, CD₃CN, 298 K, 300 MHz) recorded before (a) and after the addition of 1 equiv of CF₃CO₂H (b), after storing the acidified solution in the dark for 1 d (c), and after the subsequent exposure of the same solution to ambient light for 1 (d) and 4 d (e). ¹H NMR spectrum of *trans*-**MEH** (CD₃CN, 298 K, 300 MHz) prepared by maintaining a solution of (R/S)-**SP** (3 × 10⁻² M) and 10 equiv of CF₃CO₂H in the dark for 12 d (f). The proton labels are assigned in the diagram of Table 1.

two protons are in a trans arrangement relative to the interposed double bond.²⁸ In fact, the coupling constant for the olefinic protons of (R/S)-**SP**, where they are forced in a cis configuration, is only 10 Hz. This interpretation is consistent with the solid-state geometries (vide infra) and with NOE experiments. Indeed, NOEs are observed only between the cis olefinic protons of (R/S)-**SP** (Figures S-2d, Supporting Information).

In the solid-state structure of *trans*-**MEH** (vide infra), the aromatic proton H^A is close to the olefinic proton H^I but far from H^E . Irradiation at 8.47 ppm, however, produces positive NOEs on both H^E and H^I (Figure S-5d, Supporting Information). Similarly, the irradiation of the singlet for the methyl protons H^O and H^P produces positive NOEs on both H^E and H^I (Figure S-5b, Supporting Information). The four observed NOEs indicate that at least two (*I* and *III* or *II* and *IV*) of the four conformations illustrated in Figure 5 coexist in solution. The relative simplicity of the ¹H NMR spectrum (Figures 2f and 3f), however, suggests that the two or more conformers exchange rapidly on the ¹H NMR time scale.

The ¹H NMR spectrum of a CD₃CN solution prepared dissolving (R/S)-**SP** and one equivalent of CF₃CO₂H and maintained in the dark for ca. 16 d shows the signals of (R/S)-**SP** and *trans*-**MEH**. The addition of 1 equiv of Et₃N results in the deprotonation of *trans*-**MEH** with the formation of *trans*-**ME** (Figure 4). Consistently, the resonances of *trans*-**MEH** are replaced by those of *trans*-**ME**. In particular, a new singlet for the six equivalent methyl protons of *trans*-**ME** and a new doublet for one of its olefinic protons can be observed at 1.77 and 6.48 ppm respectively (Figure S-3b, Supporting Information). The large coupling constant (16 Hz) of the doublet confirms the trans configuration of the associated double bond.²⁸ Immediately after the addition of the base, the ratio between (R/S)-**SP** and the newly formed *trans*-**ME**



FIGURE 3. Partial ¹H NMR spectra of (R/S)-**SP** (3 × 10⁻² M, CD₃CN, 298 K, 300 MHz) recorded before (a) and after the addition of 1 equiv of CF₃CO₂H (b), after storing the acidified solution in the dark for 1 d (c), and after the subsequent exposure of the same solution to ambient light for 1 (d) and 4 d (e). ¹H NMR spectrum of *trans*-**MEH** (CD₃CN, 298 K, 300 MHz) prepared by maintaining a solution of (R/S)-**SP** (3 × 10⁻² M) and 10 equiv of CF₃CO₂H in the dark for 12 d (f). The proton labels are assigned in the diagram of Table 1.

is ca. 6. Over time, *trans*-**ME** isomerizes to the more stable (R/S)-**SP** (Figure 4) and the ¹H NMR spectrum recorded after ca. 2 h shows almost exclusively the signals of (R/S)-**SP**.

X-ray Crystallography. Single-crystal analysis established unequivocally the spiropyran structure of (R/S)-**SP** (Figure 6), the compound crystallizing in a centrosymmetric space group containing equal numbers of R and S molecules. The geometry of the indoline/benzopyran core is essentially identical to those observed for the methyl,³⁰ *n*-propyl,³¹ and benzyl³² analogues. In all of these structures, the benzopyran unit has the

spirocenter lying slightly out of the plane of its remaining atoms [by 0.07 Å in (*R*/*S*)-**SP**], and the indoline has a ca. 30° fold about the N-C(isopropylidene) vector such that its phenylene ring is folded toward the pyran oxygen atom. In (*R*/*S*)-**SP**, the pyrrole nitrogen atom is pyramidalized and lies 0.24 Å out of the plane of its substituents. The terminal hydroxy group is disordered, and two alternative orientations were identified in the crystals. A feature of the solid-state structure of (R/S)-**SP** not observed in any of the above-mentioned analogues is the formation of a channel structure containing substantial, essentially rectangular, pores of free cross-section ca. 4.5 by 10.0 Å (Figure 7). The inner walls of each of these channels are bounded on two opposite sides by C-H···O and C–H··· π hydrogen-bonded molecules (Figure 8) and on the remaining sides by end-to-end hydrogen-bonded $-CH_2CH_2OH$ chains (O····O 2.82 Å). The channels are filled by diffuse disordered solvent, which has been attributed as comprising a mixture of ethanol and n-

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⁽³¹⁾ Godsi, O.; Peskin, U.; Kapon, M.; Ezra, N. A.; Eichen, Y. *Chem. Commun.* **2001**, 2132–2133.

^{(32) (}a) Karaev, K. Sh.; Belov, N. V. *Kristallografiya* **1983**, *28*, 855–861. (b) Karaev, K. Sh.; Furmanova, N. G. *J. Struct. Chem.* **1984**, *25*, 168–170.



FIGURE 4. Three states (*R*/*S*)-SP, *trans*-ME, and *trans*-MEH of the molecular switch.

TABLE 2. Equilibrium and Rate Constants for the Thermal Interconversion of (R/S)-SP and *trans*-ME and of (R/S)-SP and *trans*-MEH in MeCN at 298 K^a

Ν	probe	λ (nm)	$\epsilon_{\lambda} imes ~ 10^3$ (M $^{-1}$ cm $^{-1}$)	$K_{ m N}$	$k_{ m N}$	k_{-N} (s ⁻¹)
1 2	<i>trans</i> -ME <i>trans</i> -MEH	563 401	$\begin{array}{c} 41\pm5\\ 32\pm1 \end{array}$	$\begin{array}{l} (40\pm5)\times10^{-4} \\ (8\pm3)\times10^2 M^{-1} \end{array}$	$\begin{array}{l}(23\pm1)\times10^{-6}s^{-1}\\(69\pm2)\times10^{-5}M^{-1}s^{-1}\end{array}$	$egin{array}{l} (52\pm2) imes10^{-4}\ (17\pm8) imes10^{-7} \end{array}$

^{*a*} The equilibria (1) and (2) illustrate the thermal processes and the associated rate constants (k_N and k_{-N}). The corresponding equilibrium constants (K_N) were determined by ¹H NMR spectroscopy. The molar extinction coefficients (ϵ_{λ}), k_N and k_{-N} were determined by absorption spectroscopy.

$$(R/S)-SP \xrightarrow{k_1}{k_2} trans-ME$$
(1)

$$(R/S)-\mathbf{SP} + CF_3CO_2H \xrightarrow{\kappa_2}{k_a} trans-\mathbf{MEH}$$
(2)

heptane (see the Experimental Section). An unusual physical feature of these crystals was that, although they were initially colorless, a distinct straw/magenta dichroism developed after a period of X-ray irradiation, with the magenta coloration being at a maximum when viewed along the crystallographic 100 direction. This direction coincides with that of the channels and lies within the planes of the bounding benzopyran ring systems.

A single-crystal X-ray analysis also established the trans-olefinic configuration of MEH (Figure 9) and showed the molecule to have an approximately planar conformation, there being only a ca. 4° torsional twist about the trans-olefinic linkage and a ca. 5° angle between the two ring systems. The cation is fully ordered but the trifluoroacetate anion has 50:50 rotational disorder of its CF₃ group. Analysis of the bond lengths in trans-MEH shows there to be a pattern of conjugation that extends from the *p*-nitrophenol ring, via the C=Cdouble bond, to include the pyrrole nitrogen atom; the indole is planar to within 0.024 Å. Both the bonding and conformation observed here are very similar to those observed in, for example, the related zwitterionic complex 2-(2-(1,5-dinitro-2-oxyphenyl)ethenyl)-1,3,3-trimethyl-3Hindolinium.³³ The molecules are linked to form chains

that extend in the crystallographic $1\overline{11}$ direction. Centrosymmetrically related pairs of molecules are linked by O-H···O hydrogen bonds (*a* and *b* in Figure 10) between (*a*) the phenolic OH group and one of the trifluoroacetate oxygen atoms and (*b*) between the -CH₂-CH₂OH hydroxy and the other trifluoroacetate oxygen atom. These interactions are supplemented by a π ··· π stacking interaction (*c*) between adjacent *p*-nitrophenol rings. These "dimer pairs" are then linked end-to-end by a further π ··· π stacking interaction (*d*) between the indole rings of lattice translated "dimers".

Molecular Modeling. The spirocenter of (R/S)-SP locks the olefinic fragment in a cis configuration. In **ME** and **MEH**, four different conformations with a trans configuration (Figure 5) plus four with a cis geometry are possible. To assess their relative stabilities, model structures with a methyl group in place of the 2-hydroxyethyl appendage of (R/S)-SP, ME, and MEH were optimized at the B3LYP/6-31G(d) level. The density functional calculations identified minima on the potential energy surfaces for all four trans geometries of the merocyanine

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FIGURE 5. Four possible conformations of *trans*-**MEH** and the NOEs observed experimentally.



FIGURE 6. Molecular structure of (*R*)-**SP** in the solid state.

forms and for two of their four cis structures. In the case of **ME** (Figures 11a and S-7 (Supporting Information)), the trans forms I-IV are at least 3.7 kcal mol⁻¹ lower in energy than the cis forms V and VI, but at least 5.1 kcal mol⁻¹ higher in energy than (R/S)-**SP**. This trend is consistent with the nuclear magnetic resonance spectroscopic analyses, which revealed (1) only trans isomers for **ME** and (2) (R/S)-**SP** to be the predominant species in the dark. In the case of **MEH** (Figures 11b and S-8 (Supporting Information)), the difference in energy be-

FIGURE 7. Ball and stick (a) and space-filling (b) representations of the channel structure formed by (R/S)-**SP** in the solid state.

FIGURE 8. Pattern of C–H···O and C–H··· π hydrogenbonding interactions between molecules of (*R*/*S*)-**SP** that bind to the sides of the channels in the crystal. The C–H···O hydrogen bonds have [C···O], [H···O] (Å), and [C–H···O] (deg): (*a*) 3.37, 2.45, 163; (*b*) 3.37, 2.43, 170. The C–H··· π interactions have [H··· π] (Å) and [C–H··· π] (deg): (*c*) 3.02, 140; (*d*) 2.98, 150.

tween the trans and cis forms is larger and exceeds 8.8 kcal mol⁻¹. Furthermore, the energies of the trans forms

FIGURE 9. Molecular structure of *trans*-**MEH** in the solid state. Selected bond lengths (Å): (*a*) 1.440(3), (*b*) 1.343(3), (*c*) 1.424(3), (*d*) 1.322(3).

FIGURE 10. Part of one of the chains of molecules present in the crystal of *trans*-**MEH**. The hydrogen bonds have [O··· O], [H···O] (Å), and [O–H···O] (deg): (a) 2.58, 1.69, 169; (b) 2.72, 1.83, 171. The π ··· π stacking interactions have centroid ··centroid and mean interplanar separations (Å) of (c) 3.55, 3.44; (d) 4.06, 3.53. The figure also shows the disorder in the CF₃ groups of the trifluoroacetate anions.

I–*IV* lie within 2.1 kcal mol⁻¹. Both observations are in agreement, once again, with the nuclear magnetic resonance spectroscopic analyses, which (1) did not detect cis isomers for **MEH** and (2) suggested the coexistence of several trans forms in solution (Figure 5).

For both merocyanine forms, the trans structures **I** and **II** are slightly lower in energy than **III** and **IV** (Figure 11). The examination of the corresponding geometries (Figures S-7 and S-8) reveals that steric interactions between the alkyl group on the indolium nitrogen atom and the adjacent olefinic fragment force **III** and **IV** to deviate from planarity. Interestingly, **I** appears to be more stable than **II** for *trans*-**ME**, while **II** is the lowest energy structure for *trans*-**MEH** and happens to be the one observed in the solid state (Figure 9).

The calculated bond lengths for (R/S)-**SP** are in good agreement with the experimental values. The largest difference is observed for the double bond of the olefinic bridge (calcd = 1.340 Å, expt = 1.320 Å). A similar trend emerges from the comparison of the calculated bond lengths for **II** of *trans*-**MEH** and the experimental values. Once again, the largest difference is observed for the olefinic bridge (calcd = 1.360 Å, expt = 1.340 Å). This

FIGURE 11. Zero-point corrected B3LYP/6-31G(d) energies of the trans and cis geometries of **ME** (a) and **MEH** (b). The energies are reported relative to that of (R/S)-**SP** (a) and **II** (b). The geometries are illustrated in Figures S-6, S-7, and S-8 (Supporting Information).

bond appears to be significantly longer in *trans-***ME** (calcd = 1.400 Å). In fact, the three bonds linking the indolium and *p*-nitrophenolate fragments of *trans-***ME** are almost equal in length,³⁴ suggesting a pronounced electronic delocalization between them.

Absorption Spectroscopy. The absorption spectrum of a relatively concentrated MeCN solution of (R/S)-**SP** reveals a band at 563 nm corresponding to the purple isomer *trans*-**ME**. The absorbance at this wavelength decreases linearly with the total concentration of the two isomers (Figure 12a). From this correlation and the equilibrium constant (K_1) determined by ¹H NMR spectroscopy, the molar extinction coefficient of *trans*-**ME** can be estimated to be (41 ± 5) × 10³ M⁻¹ cm⁻¹ (Table 2).

At a total concentration of ca. 1 \times 10^{-4} M, the absorption band for trans-ME cannot be detected. After ultraviolet irradiation,³⁵ however, (R/S)-**SP** isomerizes to trans-ME (Figure 4) and the absorbance at 563 nm increases dramatically. Its value at the photostationary state suggests that the ratio between (R/S)-SP and *trans*-**ME** is 27 ± 4 . The reisomerization of the purple *trans*-**ME** to the colorless (R/S)-**SP** occurs in the dark (Figure 4). Consistently, the band at 563 nm fades over the course of 20 min (Figure 12b,c). The time dependence of the absorbance indicates that the rate constant (k_1) for the thermal interconversion of (R/S)-**SP** into *trans*-**ME** and that (k_{-1}) for the opposite process are (23 ± 1) imes 10⁻⁶ and (52 \pm 2) imes 10⁻⁴ s⁻¹, respectively, at 298 K (Table 2). The reisomerization of *trans*-**ME** to (R/S)-**SP** can be accelerated by irradiating the sample with visible light. Complete decoloration occurs in ca. 5 min under constant irradiation at ca. 562 nm.³⁶

⁽³⁴⁾ It is important to note that the lack of diffuse functions in the basis set employed might have resulted in an underestimation of the zwitterionic character of *trans*-**ME**.

⁽³⁵⁾ The solution was irradiated with a liquid light guide coupled to a 150 W Xe arc lamp and a 341 \pm 10 nm interference filter. A photostationary state was reached in ca. 5 min.

⁽³⁶⁾ A 562 \pm 10 nm interference filter, coupled to the illumination system described in ref 35, was employed to irradiate the solution.

FIGURE 12. Concentration dependence of the absorbance at 563 nm of a MeCN solution of (*R*/*S*)-**SP** and *trans*-**ME** equilibrated in the dark at 298 K (a). Evolution of the absorption spectrum (b) and time dependence of the absorbance at 563 nm (c) of a solution (1×10^{-4} M, MeCN, 298 K) of (*R*/*S*)-**SP** and *trans*-**ME** in the dark after irradiation at ca. 341 nm for 15 min.

The absorption spectrum of an acidified solution of (R/S)-**SP** maintained in the dark changes over the course of ca. 1 d (Figure 13a). The gradual formation of the protonated merocyanine *trans*-**MEH** (Figure 4) produces an increase in absorbance at 401 nm. The time dependence of this absorption band (Figure 13b) reveals that the molar extinction coefficient of *trans*-**MEH** is (41 ± 1) × 10³ M⁻¹ cm⁻¹ (Table 2). From the same analysis, the rate constant (k_2) for the transformation of (R/S)-**SP** into *trans*-**MEH** and that (k_{-2}) for the opposite process can be estimated to be (54 ± 2) × 10⁻⁵ M⁻¹ s⁻¹ and (5 ± 2) × 10⁻⁶ s⁻¹, respectively, at 298 K.

The protonated form *trans*-**MEH** switches back to (R/S)-**SP** under visible irradiation (Figure 4). Complete decoloration occurs in less than 5 min, if the sample is irradiated at ca. 413 nm.³⁷ Instead, the addition of Et₃N results in the deprotonation of *trans*-**MEH** to produce *trans*-**ME** (Figure 4).³⁷ Consistently, the characteristic absorption band of *trans*-**ME** can be observed at 563 nm immediately after the addition of Et₃N. However, *trans*-**ME** isomerizes to (R/S)-**SP** in the dark and only the absorption bands of (R/S)-**SP** can be detected after ca. 2 h from the addition of Et₃N.

FIGURE 13. Evolution of the absorption spectrum (a) and time dependence of the absorbance at 401 nm (b) of a solution $(1 \times 10^{-4} \text{ M}, \text{ MeCN}, 298 \text{ K})$ of (R/S)-**SP** and CF₃CO₂H $(1 \times 10^{-2} \text{ M})$ in the dark.

Binary Logic Analysis. The spectroscopic analyses revealed that the interconversion of (R/S)-SP, trans-ME, and trans-MEH can be controlled with external stimulations (Figure 4). Ultraviolet irradiation induces the transformation of the colorless (R/S)-**SP** into the purple *trans*-ME. At a total concentration of ca. 1×10^{-4} M, complete decoloration occurs either if the ultraviolet source is turned off or if the sample is irradiated with visible light. The addition of CF₃CO₂H either before or after ultraviolet irradiation promotes the formation of the yellow-green trans-MEH. Complete decoloration occurs after either the addition of Et₃N or visible irradiation. In summary, three input stimulations (ultraviolet light, visible light, and H⁺) control the proportions of the three states of the molecular switch and determine the absorbance at the two wavelengths (401 and 563 nm) corresponding to the yellow-green and purple colors.

The ultraviolet light (**11**), visible light (**12**), and H⁺ (**13**) inputs can be either off or on. Binary digits can be encoded in them applying positive logic conventions (off = 0, on = 1). The absorbance at 401 nm (**01**) and that at 563 nm (**02**) are below 0.02, when (R/S)-**SP** is the dominant species in solution. They are above this threshold when the concentrations of *trans*-**MEH** or *trans*-**ME**, respectively, are significant. Binary digits can be encoded in them applying, once again, positive logic conventions (low = 0, high = 1). Thus, this chemical system responds to an input string of three binary digits (**11 12 13**) producing an output string of two binary digits (**01 02**).

⁽³⁷⁾ A MeCN solution of (R/S)-**SP** (1 × 10⁻⁴ M) and CF₃CO₂H (1 × 10⁻² M) was maintained in the dark for 15 h. After this time, the absorption spectrum (Figure 13a) revealed the band for *trans*-**MEH** at 401 nm. Part of the solution (0.5 mL) was irradiated with the illumination system described in ref 35 using a 413 ± 10 nm interference filter. After 5 min of continuous irradiation, the absorption band at 401 nm could not be detected. Another aliquot of the same solution (0.5 mL) was treated with Et₃N (2 × 10⁻² M). Complete decoloration occurred in ca. 2 h.

TABLE 3. Truth Table of the Three-State MolecularSwitch a

	input data ^{b}		output data ^c		
<i>I</i> 1	I 2	<i>I</i> 3	01	02	
0	0	0	0	0	
0	0	1	1	0	
0	1	0	0	0	
1	0	0	0	1	
0	1	1	0	0	
1	0	1	1	0	
1	1	0	0	1	
1	1	1	1	0	

FIGURE 14. Combinational logic circuit equivalent to the three-state molecular switch.

For example, the input string $0 \ 0 \ 0$ indicates that all three input stimulations are off. Under these conditions, the colorless (R/S)-**SP** is the dominant species and the absorbance in the visible region is low. The output string is 0 0. Instead, an input string 1 0 1 indicates that the ultraviolet and H⁺ inputs are on. Under these conditions, the yellow-green trans-MEH is the dominant species. The absorbance at 401 nm is high while that at 563 nm is low. The output string is 1 0. Following similar considerations, the eight output strings corresponding to the eight possible combinations of input strings can be determined (Table 3). It is interesting to note that the output string 1 1 is excluded by the molecular processors. In fact, it would correspond to a condition that cannot be satisfied experimentally, namely the simultaneous presence of relatively large amounts of trans-MEH and *trans*-**ME** in solution.

The logic behavior of the three-state molecular switch corresponds to that of a combinational logic circuit integrating two AND, two NOT, and one OR gate (Figure 14). One portion of the logic circuit combines the three inputs **I**1, **I**2, and **I**3 through NOT, OR, and AND operations producing the output **O**1. The other combines the two inputs **I**1 and **I**3 through NOT and AND operations producing the output **O**2. Comparison of the two independent parts of the logic circuit reveals that the input **I**2 has no influence on the output **O**2.

Conclusions

A spiropyran was synthesized in three steps, and its structure was confirmed unequivocally by X-ray crystallography. Nuclear magnetic resonance and visible absorption spectroscopies revealed that this compound is in equilibrium with a purple *trans*-merocyanine in MeCN.

The ratio between the colorless and colored isomers is ca. 260 at equilibrium in the dark. Consistently, molecular modeling indicated that the spiropyran state is at least 5.1 kcal mol⁻¹ lower in energy than the merocyanine isomer. Upon ultraviolet irradiation, the ratio decreases to a photostationary value of ca. 27. The colored form reisomerizes to the colorless species in the dark or under visible irradiation. At a total concentration of ca. 1×10^{-4} M, complete decoloration occurs in less than 20 min. In this concentration range, the addition of acid produces a yellow-green protonated merocyanine over the course of ca. 15 h in the dark. In the presence of at least 1 equiv of acid, the protonated form becomes the predominant species at equilibrium. However, visible light irradiation or the addition of a base regenerates quantitatively the spiropyran state in ca. 5 min or 2 h, respectively. X-ray crystallography revealed that the olefinic bridge linking the indolium and *p*-nitrophenol fragments of the yellowgreen form has a trans configuration. Nuclear magnetic resonance spectroscopy, however, indicated that at least two trans isomers exchange rapidly on the ¹H NMR time scale in solution. Density functional calculations confirmed that the four trans geometries possible for both merocyanines lie within 3.1 kcal mol^{-1} but are up to 12.6 kcal mol⁻¹ lower in energy that the cis forms.

In summary, the interconversion between a colorless spiropyran, a purple merocyanine and its yellow-green protonated form, can be (1) induced addressing the system with ultraviolet light, visible light, and/or H⁺ and (2) monitored measuring the absorbance of the two colored forms in the visible region. The interplay of the three input stimulations and the two optical outputs can be exploited to implement logic operations at the molecular level. Indeed, the logic function executed by this particular molecular switch is equivalent to that of a combinational logic circuit incorporating two AND, two NOT, and one OR gate. Similar logic conventions can be employed to encode binary digits in the inputs and outputs of any multistable chemical or biochemical system. In principle, it should be possible to program a specific logic function into an ensemble of interconverting molecules by imposing the required number of inputs and outputs and designing their transduction protocol. This approach can lead to the development of a wealth of chemical systems for digital processing. At this stage, it is certainly unclear if practical applications in information technology can emerge for these chemical processors. It is worth noting, however, that our central nervous system relies on the ability of molecular components to transduce input stimulations into specific outputs.³⁸ We do not have sophisticated semiconductor-based transistors in our brain, but we are capable of much more than present computers.³⁹ Perhaps, future data-processing, -storage, and -communication devices might share the "chemical" operating principles of neurotransmission rather than continuing to rely on silicon and electronics.

Experimental Section

General Methods. MeCN was distilled over CaH_2 . Aluminum plates coated with silica gel 60 F_{254} were used for thin-

⁽³⁸⁾ Wasserman, P. D. *Neural Computing: Theory and Practice*, Van Nostrand Reinhold: New York, 1989.

⁽³⁹⁾ Nolte, D. D. *Mind at Light Speed: A New Kind of Intelligence*, Free Press: New York, 2001.

layer chromatography (TLC). Melting points (mp) were determined with an Electrothermal 9100. Fast atom bombardment mass spectra (FABMS) were recorded with a VG Mass Lab Trio-2 using a 3-nitrobenzyl alcohol matrix.

1-(2-Hydroxyethyl)-2,3,3-trimethyl-3*H***-indolium Bromide 1.** A solution of 2,3,3-trimethyl-3*H*-indole (2.61 g, 16 mmol) and 2-bromoethanol (2.46 g, 20 mmol) in MeCN (20 mL) was maintained under N₂ and heated under reflux for 1 d. After the mixture was cooled to ambient temperature, the solvent was distilled off under reduced pressure. The residue was suspended in hexane (25 mL), and the mixture was sonicated and filtered. The resulting solid was crystallized from CHCl₃ (35 mL) to afford **1** (2.95 g, 69%) as a pink solid: mp = 195 °C; FABMS *m*/*z* 204 [M - Br]⁺; ¹H NMR (CD₃CN) δ 7.83–7.75 (1H, m), 7.72–7.65 (1H, m), 7.64–7.54 (2H, m), 4.71 (1H, t, *J* = 6 Hz), 4.54 (2H, t, *J* = 5 Hz), 4.02–3.94 (2H, m), 2.81 (3H, s), 1.57 (6H, s); ¹³C NMR (CD₃CN) δ 198.84, 142.95, 142.42, 130.69, 130.00, 124.29, 116.50, 58.79, 55.63, 51.79, 22.89, 15.54.

(*R/S*)-9,9,9a-Trimethyl-2,3,9,9a-tetrahydrooxazolo[3,2a]indole (*R/S*)-2. A solution of 1 (2.93 g, 10 mmol) and KOH (0.92 g, 16 mmol) in H₂O (50 mL) was stirred at ambient temperature for 10 min. Then, it was extracted with Et₂O (3 × 20 mL). The organic phase was dried (MgSO₄), filtered, and concentrated under reduced pressure to afford (*R/S*)-2 (1.84 g, 88%) as a yellow oil: FABMS *m/z* 204 [M + H]⁺; ¹H NMR (CD₃CN) δ 7.14–7.03 (2H, m), 6.90–6.82 (1H, m), 6.76 (1H, d, *J* = 8 Hz), 3.81–3.65 (2H, m), 3.57–3.45 (1H, m), 3.40– 3.30 (1H, m), 1.35 (3H, s), 1.31 (3H, s), 1.11 (3H, s); ¹³C NMR (CD₃CN) δ 152.11, 140.97, 128.35, 123.24, 122.21, 112.76, 109.61, 63.50, 50.37, 47.51, 28.17, 20.92, 17.47.

(R/S)-2-(3',3'-Dimethyl-6-nitro-3'H-spiro[chromene-2,2'indol]-1'-yl)ethanol (R/S)-SP. A solution of 2-hydroxy-5nitrobenzaldehyde (1.05 g, 6 mmol) and (R/S)-2 (0.87 g, 4 mmol) in EtOH (10 mL) was maintained under N₂ and heated under reflux for 3 h. After being cooled to ambient temperature, the mixture was filtered. The resulting purple solid was washed with EtOH (2 mL) and purified by semipreparative HPLC to afford (R/S)-**SP** (1.18 g, 79%): HPLC (analytical) $t_{\rm R}$ = 9.4 min, PA = 3.0, APP = 239.4 ± 0.1 nm; mp = 171 °C; FABMS m/z 353 [M + H]⁺; ¹H NMR (CD₃CN) δ 8.06 (1H, d, J = 3 Hz), 7.99 (1H, dd, J_1 = 9 Hz, J_2 = 3 Hz), 7.14 (1H, pt, J = 7 Hz), 7.10 (1H, d, J = 7 Hz), 7.02 (1H, d, J = 10 Hz), 6.82 (1H, pt, J = 7 Hz), 6.71 (1H, d, J = 9 Hz), 6.65 (1H, d, J = 8 Hz), 5.98 (1H, d, J = 10 Hz), 3.72-3.47 (2H, m), 3.38-3.14(2H, m), 2.80 (1H, pt, J = 6 Hz), 1.24 (3H, s), 1.14 (3H, s); ¹³C NMR (CD₃CN) δ 160.43, 148.35, 142.10, 136.97, 128.80, 128.66, 126.56, 123.70, 123.25, 122.70, 120.36, 120.04, 116.24, 108.03, 107.77, 60.89, 53.49, 46.90, 26.15, 20.07.

High-Performance Liquid Chromatography. A Varian ProStar high-performance liquid chromatography (HPLC) system, equipped with a ProStar 330 photodiode array detector, was used to purify (R/S)-**SP**. Analytical (column dimensions = 4.6 × 250 mm, flow rate = 1.0 mL min⁻¹, injection volume = 20 μ L, sample concentration = 1 × 10⁻³ M) and semipreparative (column dimensions = 21.4 × 250 mm, flow rate = 10.0 mL min⁻¹, injection volume = 1.0 mL, sample concentration = 2 × 10⁻² M) Varian Microsorb BDS columns were employed. The mobile phase was MeCN. The retention time ($t_{\rm R}$) and the peak asymmetry (PA) reported were determined at a wavelength of 253.6 nm. The average purity parameter (APP) reported was calculated for the peak heart in the wavelength range 200–700 nm.

Nuclear Magnetic Resonance Spectroscopy. A Bruker DPX 300 (300 MHz) was used to record ¹H- and ¹³C-nuclear magnetic resonance (NMR) spectra and to perform correlated spectroscopy (COSY) and nuclear Overhauser enhancement (NOE) experiments. Bruker Avance 400 (400 MHz) and 500 (500 MHz) were employed to study the photoisomerization of (R/S)-**SP** to *trans*-**ME** by difference ¹H NMR spectroscopy. Quartz NMR tubes were employed for these experiments. The samples were irradiated for 5 min with a Mineralight UVGL-25 lamp.

X-ray Crystallography. Crystal data for (*R*/*S*)-SP: C₂₀H₂₀N₂O₄·0.5EtOH·0.5C₇H₁₆, M = 425.5, monoclinic, *I*2/*a* (no. 15), a = 11.379(1) Å, b = 14.139(1) Å, c = 28.767(1) Å, $\beta = 93.66(1)^{\circ}$, V = 4618.8(3) Å³, Z = 8, $D_c = 1.224$ g cm⁻³, μ (Cu K α) = 0.68 mm⁻¹, T = 183 K, colorless/straw-magenta dichroic plate-like needles; 3433 independent measured reflections, F^2 refinement, $R_1 = 0.052$, w $R_2 = 0.138$, 2248 independent observed reflections [$|F_0| > 4\sigma(|F_0|)$, $2\theta \le 120^{\circ}$], 244 parameters. CCDC 206822.

Crystal data for *trans***·MEH:** $[C_{20}H_{21}N_2O_4](CF_3CO_2)$, M = 466.4, triclinic, $P\overline{1}$ (no. 2), a = 8.778(1) Å, b = 11.494(2) Å, c = 11.637(1) Å, $\alpha = 77.59(1)^\circ$, $\beta = 71.22(1)^\circ$, $\gamma = 82.62(1)^\circ$, V = 1083.4(2) Å³, Z = 2, $D_c = 1.430$ g cm⁻³, μ (Mo K α) = 0.12 mm⁻¹, T = 293 K, orange diamond plates; 3807 independent measured reflections, F^2 refinement, $R_1 = 0.048$, w $R_2 = 0.120$, 2888 independent observed reflections $[|F_0| > 4\sigma(|F_0|), 2\theta \le 50^\circ]$, 334 parameters. CCDC 206823.

Molecular Modeling. A methyl group was used in place of the 2-hydroxyethyl appendage of (R/S)-**SP**, **ME**, and **MEH**. Four coplanar geometries with trans configurations and four with cis were generated for the merocyanine forms. All structures were optimized at the B3LYP/6-31(d) level using Gaussian 98.⁴⁰ The configuration of two of the four cis geometries changed to trans upon optimization. Frequency calculations on the stationary points found did not reveal imaginary frequencies confirming that the optimized geometries of Figures S-6–S-8 (Supporting Information) correspond to minima on the potential energy surface. The resulting zeropoint energies and a scaling factor⁴¹ of 1.0119 were applied to compute the energy differences of Figure 11.

Absorption Spectroscopy. Absorption spectra were recorded with a Varian Cary 100 Bio. The samples were irradiated with a Thermo Oriel liquid light guide coupled to a Spectral Energy LH 150/1 light source equipped with a Spectral Energy 150 W Xe arc lamp and Thermo Oriel 341, 413 or 562 ± 10 nm interference filters.

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Supporting Information Available: COSY, NOE, and ¹H NMR difference spectra; thermal ellipsoid plots, CIF files; calculated structures; determination of molar extinction coefficients and rate constants. This material is available free of charge via the Internet at http://pubs.acs.org.

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