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Nondestructive Data Processing Based on Chiroptical 1,2-Dithienylethene Photochromes**

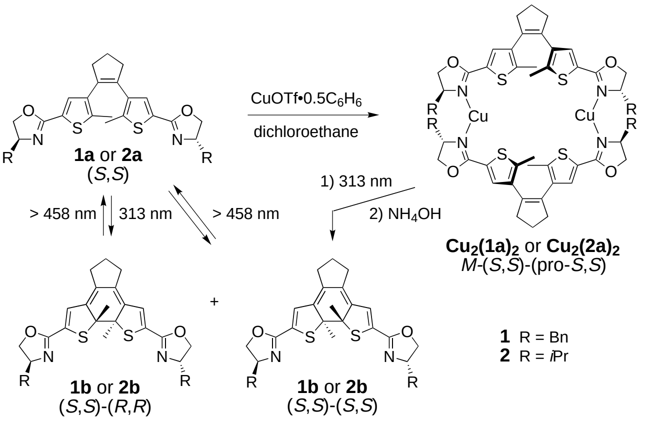
Elisa Murguly, Tyler B. Norsten, and Neil R. Branda*

The viability of photochromic 1,2-dithienylethene derivatives in optical device applications stems from their striking display of advantageous photochromic properties such as thermal irreversibility and fatigue resistance.[1] Their application to erasable memory media requires that both photochromic states be detected in the readout event in a facile and noninvasive manner. Typically, the readout event relies on the use of UV/Vis spectroscopy to record the spectral changes near the absorption bands corresponding to the two photochromic states. However, these are the same absorptions that induce the ring-opening and ring-closing reactions. Thus, sampling near these photoactive absorption bands inevitably causes partial switching of the photochrome and erases the stored information. This problem can be circumvented by developing photochromic systems that employ gated mechanisms[2] or systems that, upon photoisomerization, display variations in their optical properties such as refractive index,[3] luminescence,[4] or optical rotation.[4f, 5] It is the detection of these accompanying changes that may ultimately lead to effective nondestructive information processing systems.

Recording changes in optical rotation is a particularly promising alternative for nondestructive readout, because the detection can often be performed outside the photoactive spectral regions. To enhance the readout signal in order to use this technique, two conditions must be satisfied: 1) the photochromes should exhibit significantly contrasting optical rotating strengths between their two states, and 2) the photochromic reactions should maximize the formation of only one stereoisomer.

The closed forms of 1,2-dithienylethene derivatives are chiral, making them excellent candidates for incorporation into chiroptical devices; however, the ring-closing reactions inevitably yield racemates. The presence of stereogenic centers appended to the thiophene rings can induce stereodifferentiation in the photocyclization reaction,[5d, 6] but the restrictive conditions needed to ensure high stereoselection limit the use of the existing systems.[5d, 6a] Inspired by several recent examples in which remote stereogenic centers guide the creation of metallohelicates in a stereochemically pure form,[7] we began to explore the unique properties of self-assembled helicates in stereoselective photochromic transformations, with the goal of realizing a nondestructive write–read–erase system.

Herein we report the self-assembly of double-stranded stereochemically pure copper(I) helicates from chiral ligands **1** and **2** (Scheme 1). The chiral discrimination event that occurs when the chiral oxazoline auxiliaries on the periphery of the individual strands are brought into close proximity translates through the 1,2-dithienylethene backbone and ultimately dictates the handedness of the helicates. This preorients the thiophene rings with respect to each other so that photocyclization yields a single diastereomer. The dramatic changes in optical rotation that accompany the stereoselective photochromic process can be recorded in a nondestructive manner.



Scheme 1. Formation of ring-closed products **1b** or **2b** from photochromes **1a** or **2a** and their complexes with copper.

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Supporting information for this article is available on the WWW under http://www.angewandte.com or from the author.

Both (*R*,*R*)- and (*S*,*S*)-enantiomers of photochromic bis(oxazolines) **1a** and **2a** were prepared from the known 1,2-bis(5-chloro-2-methyl-3-thienyl)cyclopentene.[8] Copper(I) complexes were prepared by adding an equimolar amount of ligand **1** or **2** in deoxygenated dichloroethane to the benzene complex of copper(I) trifluoromethanesulfonate ($CuOTf \cdot 0.5\,C_6H_6$) under argon. Care was taken when handling the copper(I) reagent to ensure a moisture and oxygen free atmosphere to minimize the oxidation of the metal. With the exception of single crystals grown for X-ray analysis, no attempts were made to isolate the copper(I) complexes.

The electrospray mass spectra of dichloromethane solutions of freshly prepared mixtures of ligand **1a** and $CuOTf \cdot 0.5\,C_6H_6$ shows peaks at *m*/*z* 579.1 and 641.1, which correspond to free ligand **1a** and a mixture of the coordination compounds $\mathbf{Cu_2(1a)_2}$ and **Cu(1a)**, respectively. The isotopic abundance of the peak at *m*/*z* 641.1 shows the typical half-peak separation of a doubly charged species, which confirms the presence of the binuclear complex $\mathbf{Cu_2(1a)_2}$. The isotopic distribution pattern verifies the presence of $\mathbf{Cu_2(1a)_2}$ along with mononuclear **Cu(1a)**. The ratio of $\mathbf{Cu_2(1a)_2}$ to **Cu(1a)** increases when the solutions are concentrated. This observation clearly emphasizes the need to control the concentration when generating the coordination compounds, a condition that's importance will be illustrated in further studies.

Single crystals of both (*R*,*R*)- and (*S*,*S*)-enantiomers of $\mathbf{Cu_2(1a)_2} \cdot (OTf)_2$ that were suitable for X-ray crystallographic analysis were obtained by layering hexane upon freshly prepared dichloromethane solutions of the copper(I) complexes. The crystal structure (Figure 1) highlights the role of the metal centers in the self-assembly process. The resulting solid-state architecture is the anticipated stereochemically pure binuclear double helix. The bis(monodentate) oxazoline ligands coordinate to the metal centers. The two chiral auxiliaries are brought close together and can thus influence the stereochemistry of the helicate. In all cases, (*S*,*S*)-**1a** generated solely the *M* helix and (*R*,*R*)-**1a** generated solely the *P* helix. The helical handedness, in turn, biases the relative orientation of the methyl groups on the thiophene heterocycles (C10, C10′, C20, and C20′) and sets the carbon atoms involved in forming the new single bond in the photoinduced ring closure (C11, C11′, C21, and C21′) as pro-(*S*,*S*) for the *M* helix and pro-(*R*,*R*) for the *P* helix.

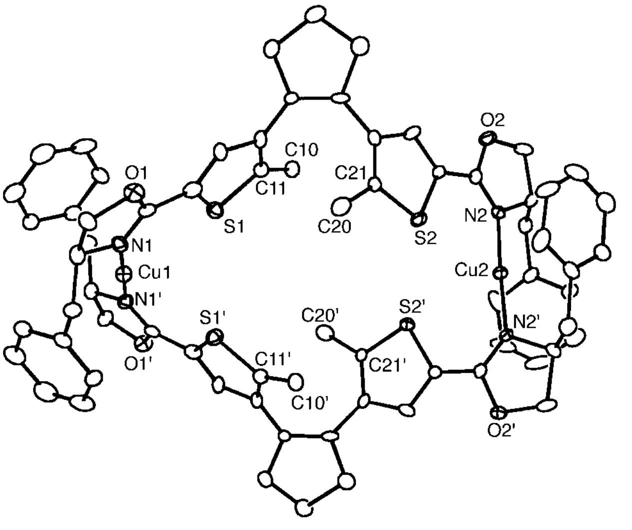

Figure 1. The structure of the copper(I) complex (*S*,*S*)-$\mathbf{Cu_2(1a)_2}$ in the crystal. All nonheteroatomic hydrogen atoms and counterions have been removed for clarity. The thermal ellipsoids are drawn at the 20% probability level. The structure of the (*R*,*R*)-enantiomer is a perfect mirror image.

The UV/Vis spectra of the open (**1a**) and closed (**1b**) isomers of the benzyl-substituted photochrome, and the corresponding copper(I) complexes that are generated in situ are shown in Figure 2, with the wavelengths of maximum absorption (λ_{max}) labeled for comparison. The ring-closed isomer was produced by irradiating a dichloroethane solution of an equimolar mixture of **1a** and $CuOTf \cdot 0.5\,C_6H_6$ with a hand-held (313 nm)[9] lamp. After irradiating for two minutes, the photostationary state was formed, which showed 90% conversion to the closed isomer by ^1H NMR spectroscopic analysis. Subsequent irradiation of the closed isomer at wavelengths greater than 458 nm[9] restored the spectrum to its original trace by regenerating the open isomer quantitatively. As expected, the spectral characteristics of both (*R*,*R*)- and (*S*,*S*)-enantiomers were identical.

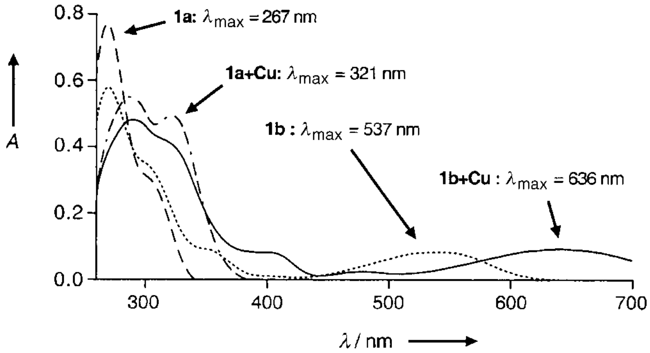

Figure 2. UV/Vis absorption spectra of photochromes **1a** and **1b** with and without $CuOTf \cdot 0.5\,C_6H_6$ (1 equiv). All spectra were measured in dry deoxygenated dichloroethane (3.5×10^{-5} M).

Irradiation of the open isomer (*S*,*S*)-**1a** at 313 nm also produced characteristic shifts of the signals in the ^1H NMR spectrum. Of particular importance is the resonance assigned to the C-H protons on the thiophene rings, which appears as a singlet at $\delta = 7.65$ in **1a** and as two singlets of nearly equal intensity at $\delta = 6.47$ and 6.48 for the corresponding ring-closed product **1b**. These two singlets (Figure 3) are clearly a result of the formation of the two diastereomers in the conrotatory ring-closing reaction of the 1,2-diarylethene photochrome (i.e. (*S*,*S*)-(*R*,*R*) and (*S*,*S*)-(*S*,*S*)). The relative integrations of the two singlets indicate that both diastereomeric products are formed to nearly the same extent in the photocyclization reaction. When the photocyclization reaction of **1a** was repeated in the presence of copper(I), a major stereoisomeric product was formed with a diasteroselectivity of 86%, as shown by the nonequivalent signals in the ^1H NMR spectrum (Figure 3). This stereoselectivity can be best justified by the existence of the helical binuclear complex $\mathbf{Cu_2(1a)_2}$ in solution.

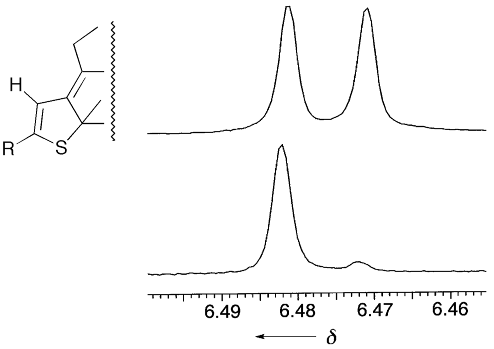

Figure 3. ^1H NMR (500 MHz, CD_2Cl_2) spectra of the C-H protons in **1b** generated from **1a** without $CuOTf\cdot 0.5\,C_6H_6$ (top trace) and **1b** generated from **1a** with $CuOTf\cdot 0.5\,C_6H_6$ after washing with NH_4OH to remove the metal (bottom trace).

The results of the stereoselective ring-closing reactions are shown in Table 1. We attribute the increase in diastereoselectivity as the concentration was increased (entries 1–3) to the predominance of the binuclear complex $\mathbf{Cu_2(1a)_2}$ at higher concentrations.[10] The high degree of diastereoselectivity at 10^{-3} M is accompanied, however, by a coinciding increase in the amount of photochemical degradation. The diastereoselectivities were also lower when the photocyclization reactions were repeated with the isopropyl ligand **2a** (entries 5 and 6). We attribute this to the formation of a less robust coordination compound. Whether this difference in stability is a result of steric and/or electronic factors is currently under investigation.

Table 1. Conversions and diastereoselectivities in the photochromic processes.[a]

Entry	Photochrome	Concentration [M]	Conversion [%][b]	*de* [%]
1	(*S,S*)-**1a** + Cu(I)	0.001	95	98
2		0.0001	94	86
3		0.00001	85	14
4	(*R,R*)-**1a** + Cu(I)	0.0001	92	89
5	(*S,S*)-**2a** + Cu(I)	0.0001	70	55
6	(*R,R*)-**2a** + Cu(I)	0.0001	79	49

[a] In a typical reaction, the ligand and $CuOTf\cdot 0.5\,C_6H_6$ were mixed in deoxygenated dichloroethane and exposed to 313-nm light for 20 minutes. After washing with excess NH_4OH to remove the metal, the conversions and *de* values of the products were measured by ^1H NMR spectroscopy in CD_2Cl_2. [b] Based on the disappearance of the open isomers.

The optical rotary dispersion (ORD) spectra of the photochromic reactions are shown in Figure 4. In the presence of copper(I), both the open and closed isomers **1a** and **1b** strongly rotate light throughout the UV/Vis spectrum. There are several spectral regions where the differences in rotation between copper(I) complexes of **1a** and **1b** are dramatic and provide potential nondestructive regions for read-out. For example, the angles of optical rotation at 450 nm and 475 nm can be regulated by toggling between the copper(I) complex of **1a** and the corresponding complex of **1b** by alternate irradiation at 313 nm and at wavelengths greater than 458 nm (Figure 5), which demonstrates the utility of this system for reversible data processing. This detection method is noninvasive as illustrated by the lack of variation in the UV/Vis spectrum upon extended irradiation at 475 nm.[11]

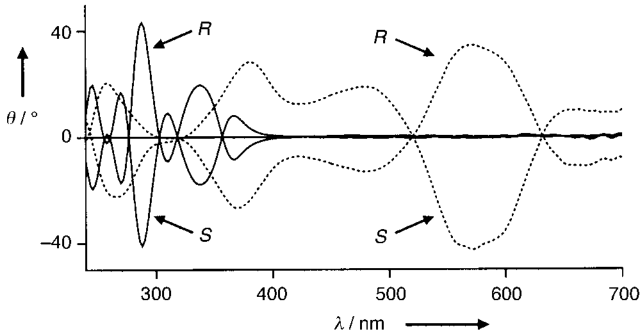

Figure 4. ORD spectra of **1a** with $CuOTf\cdot 0.5\,C_6H_6$ (——) and **1b** with $CuOTf\cdot 0.5\,C_6H_6$ (••••). All spectra were measured in dry deoxygenated dichloroethane (2.8×10^{-4} M).

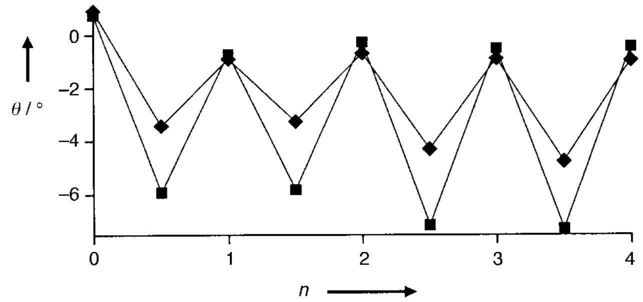

Figure 5. Modulated optical rotation at 450 nm (◆) and 475 nm (■) of a dichloroethane solution of **1a** with $CuOTf\cdot 0.5\,C_6H_6$ (2.8×10^{-4} M) during alternating irradiation at 313 nm at wavelengths greater than 458 nm (n = number of cycles).

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[8] The photochromic bis-oxazolines **1** and **2** were synthesized from the known 1,2-bis-(5-chloro-2-methyl-3-thienyl)cyclopentene, see: L. N. Lucus, J. van Esch, R. M. Kellogg, B. L. Feringa, *Chem. Commun.* **1998**, 2313. See Supporting Information for details.

[9] Standard lamps used for visualizing TLC plates (Spectroline E-series, 470 $\mu W cm^{-2}$) were used to carry out the ring-closing reaction of **1a** to **1b** and **2a** to **2b** with and without copper(I). The ring-opening reactions were carried out by irradiation with a 150-W tungsten source, which was equipped with a 458 nm cutoff filter to eliminate higher energy light.

[10] This was already suggested by the results of the ESMS studies.

[11] The monochromator of a fluorescence spectrophotometer (1-mm slit) was employed (65-W Xenon lamp).

Synthesis and Stability of Phosphatidylcholines Bearing Polyenoic Acid Hydroperoxides at the *sn*-2 Position[**]

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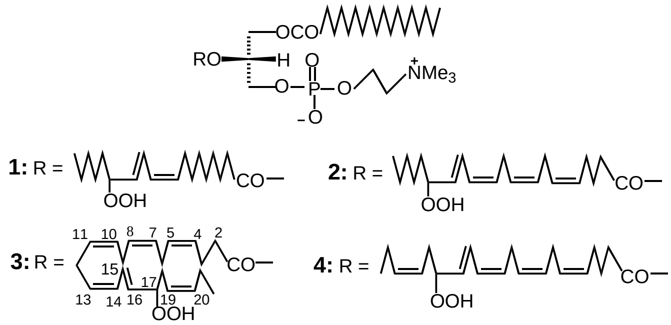
Lipid peroxides, including phospholipid hydroperoxides, have been known to exist in mammalian blood in very low concentrations, which increase during some physiological dysfunctions and aging. Although they are generally considered to have detrimental effects, some reports have described possible beneficial actions of them both in vivo and in vitro.[1] Gonzalez et al. found that administration of a fish oil (menhaden) diet to mice with transplanted human breast cancer significantly reduced the size of the tumors, and showed the involvement of lipid peroxidation products.[1a] Such a diet also significantly protected mice against a strain of the malaria parasite that is resistant to the antimalarial drug chloroquin.[1b] Unfortunately, the nature of the lipid peroxidation products that are responsible for such beneficial effects remains largely unknown. Pure, well-defined lipid peroxides for the necessary biological studies can best be obtained by synthesis. We previously synthesized two phospholipids bearing hydroperoxides of linoleic and arachidonic acids at the *sn*-2 position (PC-LA-OOH (**1**) and PC-AA-OOH (**2**) in Scheme 1, respectively),[2] where PC refers to phosphatidylcholine, and LA-OOH and AA-OOH denote linoleic and arachidonic acid hydroperoxides, and studied their inducement of cell death in normal and cancer cells.



Scheme 1. Phosphatidylcholine hydroperoxides.

The major polyunsaturated fatty acid components in fish oil are docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). However, there has been no report on the synthesis of phospholipids bearing DHA or EPA hydroperoxides. These $\omega-3$ fatty acids are known to be very unstable due to their high degree of unsaturation with all-*cis* unconjugated double bonds, and it was considered that the synthesis of their corresponding phospholipid hydroperoxides PC-DHA-OOH (**3**) and PC-EPA-OOH (**4**) by the method we established for **1** might be very difficult. However, with only slight modification, we have now found that it is possible. Typically, the synthesis of **3** (Scheme 2) was achieved by dicyclohexylcarbodiimide(DCC)-mediated esterification of lysophosphatidylcholine **8** with peracetal acid **7**, followed by deprotection of the hydroperoxy group. Compound **8** with *R* configuration was prepared as described previously,[2a] and **7** was synthesized according to Scheme 2.

Docosahexaenoic acid was converted by soybean lipoxygenase to an optically active hydroperoxide, which for easier purification by column chromatography was converted to methyl ester **6** ($[\alpha]_D^{20}=-3$, $c=1.67$ in $CHCl_3$)[3] followed by protection of the labile hydroperoxy group to give a peracetal methyl ester, which was hydrolyzed by lipase PS (Amano) to give the desired peracetal acid **7**. In the new experimental procedure, omitting the azeotropic removal of residual water from **7** was important for maintaining its structural integrity, while the use of excess DCC facilitated the esterification to give the desired phospholipid **9**. Hydrolytic removal of the

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