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Switching of Chirality by Light

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Optically active photoresponsive molecules are described by which control of chirality is achieved by light. These chiroptical molecular switches are based on inherently dissymmetric overcrowded alkenes and the synthesis, resolution and dynamic stereochemical properties are discussed. Introduction of nitro-acceptor and dimethylamine-donor substituents in a naphto[2,1-b]thiopyran-1'-ylidene-9H-thioxanthene helical shaped alkene resulted in a highly diastereoselective modulation of photostationary states with 70%-M or 90%-P helicity, respectively. The chiroptical switches offer attractive prospects as control elements for (supra)molecular functions and organization. This is demonstrated in dual mode photoswitching of luminescence and photoswitching between liquid crystalline phases.

Keywords: optical switches, chirality control, overcrowded alkenes, helicity, photoresponsive materials, liquid crystals, luminescence

INTRODUCTION

Control of chirality at the molecular and supramolecular level plays a central role in such diverse areas as new drug development, asymmetric synthesis and materials research. It comprises fundamental aspects of chiral recognition [1], the design of enantioselective catalysts [2] or the development of novel (supra)molecular architectures [3].

Molecular chirality offers intriguing possibilities in the design of new photoactive organic materials [4]. Stimulated by the challenge to develop all optical devices, new materials for optical data storage and molecular memory elements photochemically bistable organic molecules have attracted considerable interest in recent years [5]. A variety of photoreversible compounds such as fulgides, diaryl alkenes, spiropyans and azobenzenes have been prepared and the photochromic [6] processes involved are typically cis-trans isomerizations or photocyclization reactions [4–7].

A number of important requirements are inevitable for photobistable organic compounds to be useful as molecular switches: i. no thermal interconversion of the isomers in a large temperature range, ii. ready detectability of both forms, iii. fatigue resistance i.e.: no thermal or photochemical degradation, iv. non-destructive read-out procedures and v. retention of all properties when the photobistable compound is incorporated in a macromolecular material.

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\[
M \xrightarrow{h_\nu (\lambda_1)} P \quad \text{Equation 1}
\]

We devised photoreversible systems based on the interconversion of enantiomers or pseudo enantiomers of inherent dissymmetric molecules (eq. 1). The term pseudo enantiomers is used in this context to indicate the opposite helicity of the inherent dissymmetric molecules.

In this approach the properties of chiral photoresponsive molecules are exploited. Switching occurs between two chiral forms of helical shaped molecules; M indicates a left-handed helix and P a right-handed helix. The P and M helices represent two distinct states in a binary logic element. Read-out procedures in photochromic materials are generally based on UV/VIS spectroscopy often leading to undesired side effects, although changes in other properties accompanying the photochromic event have been explored for non-destructive detection [4,8].

A major advantage of the chiral optical switch, discussed here is the possibility to achieve non-destructive read-out by monitoring the change in optical rotation at wavelengths remote from the switching wavelengths.

If we are successful in the control of chirality in photoresponsive molecules the unique optical- and molecular properties of (pseudo-)enantiomers offer attractive prospects for a variety of applications. The key role for a chiroptical molecular switch is illustrated in Scheme 1.

Essential control elements, ultimately leading to supramolecular photochemical devices, are: function, chirality and organization. These aspects will be discussed as well as the synthesis of the photoreversible chiral molecules.

SCHEME 1
INHERENT DISSYMMETRIC ALKENES

The chiroptical molecular switches are based on inherent dissymmetric sterically overcrowded alkenes and comprise 4 classes of compounds (Scheme 2).

Type 1 alkenes are biphenanthrylidenes incorporating a double helical structure [9], type 2 has a tetrahydrophenanthrene upper half with an anthracene-like lower half [10]. Type 4 alkenes are so-called symmetrically overcrowded alkenes which include the well known bisfluorenylidenes and bisxanthylidenes [11,12]. Type 3 alkenes feature structural elements of the other classes [13]. In order to avoid unfavourable steric interactions the distortion of the molecular framework imparts a helical shape to these molecules. An essential structural feature of these alkenes (except type 1) is furthermore the simultaneous presence of a cis- and a trans stilbene unit in the same molecule.

The key step in the synthesis of the overcrowded alkenes is the formation of the central double bond. The highly strained tetrahydrophenanthrene based type 1 alkenes are synthesized by a McMurry coupling of the corresponding ketones [8]. The other types of olefins consist of different upper and lower parts, therefore an “unsymmetrical” coupling method is required. The diazo-thioketone coupling is the most commonly used procedure in these cases [14].

Depending on the type of alkene a “diazo upper half” and a “thioketone lower half” can be coupled or the reverse building blocks can be used. A typical example is given in Scheme 3. The hydrazone 1 is oxidized to the corresponding diazo-compound 2 and subsequent 1,3-dipolar cycloaddition with thioketone 3 results in a thiadiazolidine as an intermediate, which readily loses nitrogen by a thermal extrusion process to form episulfide 4. The episulfide is desulphurised by reduction with copper powder to the alkene which is obtained as a cis-trans mixture. When this method does not succeed, which is often the case with more hindered molecules like the episulfide precursors for type 3 olefins, LiAlH₄ or PPh₃ are used for desulfurization. The Peterson olefination [15] is another

![Scheme 2](image-url)
useful method to synthesize unsymmetrical alkenes. The trimethylsilyl derivative of the lower part is deprotonated with n-BuLi and coupled with the ketone of the upper part resulting in the desired olefin. However, this procedure is not appropriate for synthesis of alkenes of type 1 and 2, since it does not allow the use of ketones with α-hydrogen atoms, which can be abstracted under basic conditions. The geminal dichloride coupling, originally developed by Schönberg and Nickel, proved to be suitable for molecules of type 4 consisting of the same subunits in the upper and lower part. In this synthetic procedure the ketone is first converted to the corresponding geminal dichloride and subsequently brought into reaction with copper to yield the symmetrical overcrowded alkene.

A common structural feature of type 2, 3 and 4 alkenes is a strongly folded geometry. The molecular structures based on X-ray analyses, shown in figure 1a and 1c, illustrate typical examples. Type 4 alkene 9-(2'-methyl-9'H-thioxanthene-9'-ylidene)-9H-xanthene (6) has an anti-folded structure. The folding is best illustrated by the angles between the mean planes through the phenyl rings in each tricyclic unit being 36° for the xanthene and 51° for the thioxanthene part, respectively. The central double bond show a slight torsion as illustrated by the Newman projection (figure 1b), with a twist angle of 4.8°.

For the donor-acceptor substituted molecule 7 (a type 2 alkene) again an anti-folded structure is seen, in which the top and bottom halves are tilted up and down, respectively, relative to the plane of the central double bond to avoid severe non-bonded interactions and to generate a helical shape. The arrangement about the central alkene bond is nearly planar (dihedral angle 0.4–5.4°) and a normal value of 1.35 Å is found for the Cα-Cβ bond.

The racemic alkenes were resolved by chiral high performance liquid chromatography (HPLC) with (+)-poly(triphenylmethylmethacrylate) as a chiral stationary phase. This method was successful for the separation of all four types of overcrowded alkenes synthesized so far (X = CH₂, O, S; Y = O, S, –). The only restriction is that the racemization barrier (ΔGrac) has to be sufficiently high to avoid (partly) racemization at room temperature (>87.9 kJ mol⁻¹).

An attractive feature in the structural design of the chiral overcrowded alkenes, discussed here, is the possibility to tune the racemization
bars by modification of the bridging unit in the lower half of the alkenes [12a]. For instance a surprisingly high thermal racemization barrier of 114.6 kJ mol⁻¹ was found for 2-methyl-9H-thioxanthene-9-(9H-thioxanthen-9-ylidene) 8, a value exceeding the barrier for bixanthylidenes [17] (75.3 kJ mol⁻¹) by 39.3 kJ mol⁻¹.

Systematic modification of the atom X, bridging the aryl-moieties in the lower half of alkenes 8-11 allowed a comparison of the racemization barriers and the aryl-X bond lengths. The data in Table I clearly indicate a remarkable correlation: a large increase in racemization barrier is found when the aryl-X bond is lengthened. This “remote bond length effect” can be explained by the fact that a longer aryl-X bond will force the aromatic halves of the lower part of the molecule into the direction of the upper thioxanthene moiety. Since during racemization two peri H-peri H (H1-H1’; Hσ-Hσ’) passages have to take place, the smaller aryl-aryl distance between the lower and upper halves will clearly enhance the steric barrier for this process.

Circular dichroism (CD) spectroscopy was extensively used for all alkenes for determination of the absolute configuration and to assess quantitatively the changes in helicity upon irradiation [12,18].

An extensive discussion of CD effects is beyond the scope of this article [12,18,19]. Typical UV and CD spectra of type 2 alkene i.e. M-cis 12 and P-trans 13, are shown in figure 2. Strong UV absorption around 230 nm and medium intense absorptions at 310 and 330 nm are accompanied
by strong CD absorptions in particular in the short wavelength region ($\Delta e$ typically 15–200). UV spectra for cis-12 and trans-13 are nearly identical although small but distinct differences are observed in extinction coefficients.

The CD spectra for M-cis-12 and P-trans-13 are mirror images in the short wavelength region, below 250 nm, while at longer wavelengths these spectra are clearly different. This remarkable feature is due to the fact that, although 12 and 13 are diastereomers the overall helicity shows a mirror image relationship (e.g. pseudo enantiomers) and determines the major CD effects.

### TABLE I  Racemization barriers of overcrowded ethylenes

<table>
<thead>
<tr>
<th>compound</th>
<th>X</th>
<th>Aryl-X bond length $\AA$</th>
<th>Racemization barrier $\text{kJ mol}^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>S</td>
<td>1.77</td>
<td>114.6 ± 0.8</td>
</tr>
<tr>
<td>9</td>
<td>C(CH$_3$)$_2$</td>
<td>1.52</td>
<td>105.0 ± 1.3</td>
</tr>
<tr>
<td>10</td>
<td>NCH$_3$</td>
<td>1.42</td>
<td>89.1 ± 2.1</td>
</tr>
<tr>
<td>11</td>
<td>O</td>
<td>1.38</td>
<td>&lt;83.7</td>
</tr>
</tbody>
</table>

Investigations concerning the thermal and photochemical behaviour, have revealed the occurrence of cis-trans isomerization ($\text{M-cis } \rightleftharpoons \text{P-trans}$) and conformational inversion simultaneously. The photochemically induced interconversion of P and M helices can be detected by monitoring the change in optical activity using CD or ORD spectroscopy at wavelengths remote from those used to effect cis-trans isomerization. This implies that “non-destructive” read-out is feasible.

The first successful cis-trans chiroptical switch developed in our group was a methoxy substituted alkene of type 2, 4-[(9’-2′-methoxythioxanthylidene)-7-methyl-1,2,3,4-tetrahydrophenanthrene (12/13)$^{10}$. Irradiation of M-12 (cis) in n-hexane at 300 nm yielded a mixture of 64% M-12 and 36% P-13 whereas similar irradiation at 250 nm yielded a photostationary state with 68% M-12 and 32% P-13. Successive irradiations during 30 sec at these two wavelengths resulted in modulation of the photostationary states with d.e.’s of 28% and 36%, respectively.

A remarkable improvement in the selectivity of the chiroptical switch was found by introducing strong donor- and acceptor substituents in the lower thioxanthene half (Scheme 5) $^{20}$. The UV/VIS spectra of 14 (cis-nitro) and 15 (trans-nitro) are clearly distinguishable and show a large bathochromic shift allowing the switching pro-
FIGURE 2  UV spectrum of cis-12 in n-hexane and the CD spectra of M-12 (cis) and P-13 (trans) in hexane/isopropanol 9:1.

From the UV spectrum, it is clear that the absorption maxima are around 232 nm for cis-12, indicating that this is the dominant form in solution. The CD spectra show a strong CD signal around 222 nm for cis-12, which is characteristic of a CD-active chiral molecule. The CD spectra also show a smaller signal around 278 nm for trans-13, indicating that the trans isomer is present in smaller amounts.

The CD spectrum of M-12 shows a positive signal around 222 nm, indicating that the M-12 molecule is chiral with a right-handed helix. The CD spectrum of P-13 shows a negative signal around 222 nm, indicating that the P-13 molecule is chiral with a left-handed helix.

The switching process in the M-12/P-13 system is monitored by CD, and the CD spectra show a gradual change from the cis to the trans form. The CD signal around 222 nm decreases as the trans form is formed, indicating that the CD-active chiral center is lost.

In summary, the CD spectra provide valuable information about the chiral properties of the M-12/P-13 system and can be used to monitor the switching process. The UV/CD spectra are useful tools for studying the conformational properties of these molecules in solution.
which either of the pseudo enantiomers M-14 or P-15 is present in large excess makes the switch relatively insensitive towards racemization.

The donor-acceptor based switch allows photochemical control of the chirality with a notable selectivity, an increased stability and a switching process to be executed in the visible.

**GATED RESPONSE SYSTEMS**

A highly desirable property of photochromic systems is gated response, meaning that photoresponsive effects are blocked upon irradiation unless another external stimulus, either physical or chemical, is applied. Recently, Lehn and co-workers demonstrated electrochemical gated photochromism with a dual-mode molecular switching device in which photochromism could be reversibly blocked by an electrochemical reaction [8,21].

In order to achieve gated response in the chiroptical switches we chose two different approaches, one of them based on reversible protonation and the other on reversible complexation of alkali metal ions with a covalently bound crown ether host. An elegant example of an aza-crown ether photoswitchable host-guest system was developed by Shinkai and co-workers [22]. It can be imagined that the photoresponsive properties of the chiroptical switch can reversibly be locked by complexation at a crown ether unit attached to the switch. The synthetic accessibility of crown ether bound chiroptical switches and their ion complexation was investigated with new bisthioxanthylidene crown ethers (Scheme 6) [23].

Another approach is focused on reversible protonation of the dimethylamino donor functionality in the donor-acceptor switch M-14, P-15 (Scheme 7).

It was shown that the switching process can be blocked by protonation of the donor unit. The high effectiveness of the donor-acceptor system

**SCHEME 5** Chiroptical molecular switching process.

**SCHEME 6** Chiral switchable crown-ethers.
is now lost due to a non-effective acceptor-acceptor unit in the chiroptical switch. P-15 and M-14 are also fluorescent compounds and distinct differences (ΔΦ = 0.016) are seen in fluorescence intensities. Fluorescence emission is totally quenched after complete protonation. After deprotonation fluorescence intensities are completely recovered and the photochemical switching between P- and M- helices is fully restored. The key features of the “dual mode photo-switching of luminescence” [24] described here are the proton-dependent photomodulation of fluorescence and chirality and the ability to interconvert between three distinctive states, namely dimmed, on and off, as shown in Scheme 7. In the on mode, P-15 and M-14 show at the maxima different intensities in their fluorescence emission. Visualized, this means a molecular device which can be dimmed or lighted photochemically. After amine protonation the fluorescence is quenched and both the switching process and the emission are in the off mode. This constitutes a locking device for information storage. Deprotonation reestablishes the molecular switching behaviour as well as the fluorescence (on mode).

LIQUID CRYSTALLINE (LC) SWITCH

For possible applications in optical data storage systems, the switching process should be executed in an organized matrix. The chiroptical molecular switch was therefore incorporated as a guest in a liquid crystalline host material.

The modulation of the mesophases and physical properties of LC materials by reversible photochemical reactions is a major challenge for information technology. We designed a host-guest system consisting of P-15 and a nematic liquid crystalline material 4′-(pentyloxy)-4-biphenylcarbonitrile 16 for the development of new LC optical devices. It is well known that small
amounts of optically active guest molecules added to a nematic host induce a cholesteric phase. By doping 1 wt% of enantiomerically pure P-15 to the nematic host 16 the nematic phase converts to a cholesteric phase. By irradiation with light of the proper wavelength the cholesteric phase can be converted to a nematic phase or, alternatively the cholesteric phase can be modulated [25]. Both the helicity and the pitch of the cholesteric phase change upon changing the chirality of the dopant P-15 by irradiation. All these processes are fully controlled by light and fully reversible. The complete switching cycle is illustrated in Scheme 8.

These findings make it possible to modify liquid crystalline phases by means of light and also to control the optical properties of liquid crystalline phases by optical means.

**CONCLUSIONS AND PROSPECTS**

Chiral photoresponsive molecules were designed based on helical shaped inherent dissymmetric alkenes incorporating a stilbene type chromophore in their molecular structures. High stereoselectivity was achieved in the photochemical switching of the helicity. The change in chiroptical properties can be exploited as a mean of non-destructive read-out in a binary logic memory element incorporating these chiral photochromic materials. Additional characteristics, which are attractive for potential data storage systems, are the possibility to perform a writing, reading and erasing cycle by a single physical method and the feasibility to achieve gated response. Furthermore it was demonstrated that amplification of the photochemically induced change in helicity of the photoresponsive molecules to changes in mesoscopic organization can be achieved.

The control of helicity both at the molecular- and mesoscopic level by light holds promise for the photochemical control of chirality in a variety of supramolecular materials. Having realized chiroptical molecular switches these systems might be incorporated, as light addressable units, in multicompound devices. Chirality is an essential element in recognition, catalysis and assembly processes in living nature and the possibility to control molecular chirality by light of-
fers a bright stage for an molecular designer to address bioprocesses.

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