Chapter 1

Sterically Overcrowded Alkenes

1.1.1 Introduction

Sterically overcrowded alkenes have attracted considerable interest in view of their unique photochromic and thermodynamic properties. In addition, the beautiful architecture of these structures is as fascinating as their potential applications. When the substituents (R) at the central double bond are bulky (figure 1.1) severe steric hindrance between upper and lower part of the alkene is present. This enforces a distortion from planarity, and in several cases, a helical shape (vide infra) to the entire molecule. As a consequence overcrowded alkenes can exist as stable, optically active stereoisomers (only when substituents R are not identical), although lacking a stereogenic center.

![Figure 1.1 Overcrowded alkene (R = bulky substituent)](image)

1.1.2 Nonplanarity in Overcrowded Alkenes

The bistricyclic aromatic enes of type 1 and bifluorenylidenedes 2 (scheme 1.1a) have received considerable attention in the study of ground state conformations and dynamic stereochemistry of overcrowded alkenes. As early as 1909 Meyer reported thermochromic properties of bianthrone 1c. However, it took until the 1950s before thorough research started of the thermodynamic behavior of bianthrone 1c and its derivatives. First indications were found that bianthrone has no planar structure which was confirmed in short-term in 1954 by X-ray analysis. Soon afterwards, an asymmetric substituted, optically active, bianthrone was isolated proving these structures to be chiral without containing a chiral center (section 1.1.4). Nonplanarity of the ground state conformation of bifluorenylidene 2 was demonstrated by Fenimore in 1948 by X-ray analysis. Thermochromic and photochromic properties of bixanthylidenes 1a and biaclidines 1d were thoroughly examined by Fischer, Muszkat, and Korenstein whereas bixanthylidenes 1a, bianthrone 1c, biaclidines 1d, and bifluorenylidenes 2 were studied by Agranat.
Planarity in the ground state conformations of overcrowded alkenes 1 and 2 is prevented by the very strong non-bonded carbon-carbon and hydrogen-hydrogen interactions in the fjord region (scheme 1.1a) of the molecule. Usually two mechanisms, generally known as twisting and folding, are responsible for the release of strain in overcrowded alkenes. The bistricyclic aromatic enes of type 1 were found to have a folded ground state conformation \(2b,4\) while bifluorenylidenes 2 adopt a twisted conformation. In the schematic drawings, depicted in scheme 1.1b, the structures are viewed along the central \(C^9=C^9'\) bond. The lines represent the peripheral benzene rings of the tricyclic moieties. These schematic projections should not be confused with Newman projections of the double bond! In a folded structure the substituents at the central double bond are folded away from the plane defined by the double bond in a point-symmetric manner. This results in boat conformations in the central rings of the tricyclic moieties.\(^2,^{12}\) The thus induced nonplanarity of the individual tricyclic moieties of folded structures is expressed quantitatively by the folding angles \(A - B\) and \(C - D\) (scheme 1.1a) of the least–squares–planes defined by the carbon atoms of the peripheral benzene rings. Twisted structures are usually found when both halves of the overcrowded alkene are either sterically very demanding\(^1,4\) or planar and rigid.\(^1,5,16\) The latter is due to the presence of substituted cyclopentane rings attached to the central double bond. A twist is enforced over the double bond for the release of steric strain; however, both halves of the molecule remain planar.

The nonplanarity at the central carbon atoms \((C^9\text{ and }C^9',\text{ scheme }1.1a)\) of the double bond of both, twisted and folded, structures is quantified by the pure twist \((\omega)\) of the central double bond \((C^9=C^9')\) and the pyramidalization \((\chi)\) of the individual atoms \(C^9\) and \(C^9'\) of the double bond.
The pure twist is defined as the average of the torsion angles $\tau(C^{9a} - C^{9} - C^{9'} - C^{9a'})$ and $\tau(C^{8a} - C^{9} - C^{9'} - C^{8a'})$:

$$\omega = \frac{1}{2} \left[ \tau(C^{9a} - C^{9} - C^{9'} - C^{9a'}) + \tau(C^{8a} - C^{9} - C^{9'} - C^{8a'}) \right]$$

In addition, the carbon atoms $C^9$ and $C^{9'}$ of the double bond can be pyramidalized. The pure sp$^2$ hybridization is changed toward sp$^3$ hybridization as a result of the out-of-plane deformation which improves the $\pi$-overlap across the adjacent formal single bonds. Pyramidalization of the $C^9$ and $C^{9'}$ atoms can occur in a syn or anti manner (figure 1.2).

**Figure 1.2** Hybridization in syn and anti pyramidalized double bonds.

![Hybridization in syn and anti pyramidalized double bonds.](image)

Throughout the years several measures for pyramidalization have been applied in the literature. In figure 1.3 the pyramidalization angle $\chi(C^9)$ is defined as the improper torsion angle $\tau(C^{9a} - C^{9} - C^{9'} - C^{8a})$ minus 180°. When a double bond is syn pyramidalized, the pyramidalization angles $\chi(C^9)$ and $\chi(C^{9'})$ have identical signs while they have opposite signs in anti pyramidalized double bonds.

**Figure 1.3** Pyramidalization angle ($\chi$) of a double bond carbon atom.

![Pyramidalization angle (\(\chi\)) of a double bond carbon atom.](image)

1.1.3 Types of Conformations

Numerous stable solid state conformations of overcrowded alkenes have been elucidated by X-ray analysis (scheme 1.2). As anticipated, the anti-folded conformation is the most commonly encountered geometry for type 1 bistricyclic enes and folding angles between 40 and 45° are usually found (table 1.1). These structures have pointgroup $C_{2h}$ symmetry. When the four substituents are folded away in the same direction, a syn-folded structure, with pointgroup $C_{2v}$, results with one plane of symmetry oriented perpendicular to the central double bond. Syn-folded structures are rare and bi-$5H$-dibenzo[$a,d$]cyclohepten-5-ylidene 3 represents one of the few examples. Remarkably, for this compound both a syn- and an anti-folded conformation have been characterized by X-ray analysis and NMR solution spectroscopy. In solution, at 200°C, complete isomerization from the syn-folded conformation to the anti-folded conformation was observed. Both conformations have equivalent
folding angles of 55 – 60° (table 1.1). However, differences were found between the pyramidalization angles. A negative value, albeit small, was observed for the anti-folded conformation while a much larger positive angle is attributed to the syn-folded conformation.

![Scheme 1.2](image)

**Scheme 1.2** Ground state conformations, pointgroups and schematic representations of various overcrowded alkenes.

**Table 1.1** Structural data of some overcrowded alkenes.²

<table>
<thead>
<tr>
<th>alkene bridges</th>
<th>X</th>
<th>conformation</th>
<th>twist (°)</th>
<th>folding A – B [°]</th>
<th>C – D [°]</th>
<th>pyr. (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 O</td>
<td>anti-folded</td>
<td>0.0</td>
<td>43.0</td>
<td>43.0</td>
<td>-4.8</td>
<td></td>
</tr>
<tr>
<td>1 S</td>
<td>anti-folded</td>
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<td>43.7</td>
<td>43.7</td>
<td>-2.9</td>
<td></td>
</tr>
<tr>
<td>1 C=O</td>
<td>anti-folded</td>
<td>0.0</td>
<td>40.0</td>
<td>40.0</td>
<td>- c</td>
<td></td>
</tr>
<tr>
<td>2 –</td>
<td>twisted</td>
<td>33.0</td>
<td>5.2</td>
<td>4.2</td>
<td>-2.4</td>
<td></td>
</tr>
<tr>
<td>3 CH=CH</td>
<td>anti-folded</td>
<td>0.0</td>
<td>55.7</td>
<td>55.7</td>
<td>-2.9</td>
<td></td>
</tr>
<tr>
<td>3 CH=CH</td>
<td>syn-folded</td>
<td>1.1</td>
<td>56.6</td>
<td>61.8</td>
<td>10.7</td>
<td></td>
</tr>
</tbody>
</table>

*Data of 2,7'-dimethoxy-bisthioxanthylidene.²³b No experimental data were acquired, therefore values obtained from semiempirical PM3 calculations are given here (see section 1.1.7).²¹ Value not available.

Bifluorenyldienes 2 have been found to adopt a twisted conformation with pointgroup D₂ symmetry and the pure twist at the carbon double bond is around 33° (table 1.1). The 2-(thioxanthen-9-ylidene)indane-1,3-diones of type 4 form another intriguing class of overcrowded alkenes. The indane-1,3-dione lower half of the molecule is unable to release steric strain by folding. However, a folded ground state conformation, allowed by the folding abilities of the thioxanthene upper half of the molecule, exhibiting C₁₉ symmetry has been reported.¹⁹ In a higher energy solid state conformation of 4, the folding and twisting mechanisms are combined to give a folded-twisted conformation with C₁ symmetry. Only when one of the halves of the molecule is too rigid to fold, competition between the folded-twisted, the folded, and the twisted conformation takes place.²⁰
1.1.4 Chirality

The nonplanarity in overcrowded alkenes can lead to chirality despite the lack of a stereogenic center. Overcrowded alkenes of which nonplanarity is solely responsible for chirality are denoted inherently dissymmetric alkenes.\textsuperscript{21} The basic structure of type 1 overcrowded alkenes (scheme 1.2) possesses C\textsubscript{2h} symmetry implying achirality. However, substitution at one of the peripheral benzene rings breaks the symmetry and makes the compound chiral (scheme 1.3). The chirality is described by the helicity rules introduced by Cahn, Ingold, and Prelog.\textsuperscript{21b} (\(P\)) stands for plus and denotes a right-handed helix whereas (\(M\)) stands for minus and denotes a left-handed helix. Structures of type 1 always have both a (\(P\))- and an (\(M\))-helix and therefore the helix bearing the substituent of highest priority (IUPAC rules) governs the chirality of these structures. It is noteworthy that symmetric substitution, for example at the 2- and 7-position (see scheme 1.1a), with identical substituents leads to achirality again. An achiral \textit{meso} compound is obtained when identical substituents are present at point symmetric positions (for example at the 2- and 7'-position). Twisted structures of type 2 do not have a plane of symmetry or an inversion point, which implies D\textsubscript{2} symmetry. As a consequence twisted overcrowded alkenes will always be chiral except for the hypothetical case of a twisting angle of exactly 90°. Two (\(P\))- or two (\(M\))-helices are present in these molecules. For \textit{syn}-folded structures 3 the same chirality rules apply as for type 1 structures. The basic geometry of 4 with C\textsubscript{1h} symmetry is achiral (scheme 1.2). But again, a substituent at the upper thioxanthene half or lower indane-1,3-dione half makes 4 chiral. Interestingly, the higher energy folded-twisted conformation of 4 with C\textsubscript{1} symmetry is chiral (scheme 1.2).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{scheme1.3}
\caption{Chirality of folded sterically overcrowded alkenes. The chirality rules are governed by the substituent with highest priority.}
\end{figure}

1.1.5 Dynamic Processes

Separation and isolation of the optical antipodes of inherently dissymmetric alkenes under ambient conditions can only be achieved if they are conformationally stable at room temperature. Two fundamental barriers are responsible for the stability of twisted and folded overcrowded alkenes as well as the extent of twistedness and foldedness. Basically, the potential energy of an overcrowded alkene is the sum of the steric and \(\pi\)-energy. A schematic plot of the potential energy of a twisted overcrowded alkene plotted as a function of the twist angle (\(\omega\)) is depicted in figure 1.4.\textsuperscript{18b} Steric repulsion in the fjord region, as a consequence of the bulky substituents at the upper and lower side of the central double bond, not only causes the twisted or folded shape of the molecule but also hinders
these substituents to move along each other. Since passing this barrier is a \textit{racemization} process, this
is called the racemization barrier (scheme 1.4). The \(\pi\)-energy of the central double bond is responsible
for the second barrier since it prevents free rotation over this bond of the upper and lower part with
respect to each other. A \(180^\circ\) rotation around the double bond implies a \textit{cis-trans isomerization} when
\(Y \neq Z\) and \(A \neq B\) and therefore the second barrier is called the isomerization barrier (scheme 1.4).

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{figure.png}
\caption{Schematic plot of the total sum of steric and \(\pi\)-energy as a function of the twist angle (\(\omega\)). At twist angles of 0° and 180° the steric energy is at its maximum while the \(\pi\)-energy is at its maximum at 90°. The minimum of total energy is found around a twist angle of 35°.}
\end{figure}

\begin{scheme}
\centering
\includegraphics[width=0.5\textwidth]{scheme1.png}
\caption{Racemization and isomerization process of a twisted overcrowded alkene of type 2.}
\end{scheme}

\begin{scheme}
\centering
\includegraphics[width=0.5\textwidth]{scheme2.png}
\caption{Racemization and isomerization process of a folded overcrowded alkene of type 1.}
\end{scheme}
Sterically Overcrowded Alkenes

The same principles apply to folded overcrowded alkenes since the racemization and isomerization barriers (scheme 1.5) also govern stability of these structures. Obviously, the exact shape of overcrowded alkenes (twisted or folded, twist angle, pyramidalization, and folding angle) is determined by the delicate balance between the steric and π-energy.

The racemization and isomerization barriers are quantified by the Gibbs energy of activation ($\Delta G^\ddagger$, kcal mol$^{-1}$). In practice the racemization and isomerization barriers should be at least 20 kcal mol$^{-1}$. A sterically overcrowded alkene with such barriers loses optical activity by a factor of about 2 every 10 minutes at 0°C and every 5 seconds at room temperature. For unstrained alkenes isomerization barriers in the range of 60 – 70 kcal mol$^{-1}$ were found.$^{22}$ In comparison, the barriers of overcrowded alkenes were considerably lower due to destabilization of the double bond by a twist or pyramidalization. This ground state destabilization of overcrowded alkenes led to racemization and isomerization barriers of 10 – 30 kcal mol$^{-1}$ (tables 1.2 and 1.3).

The height of Gibbs energies of activation ($\Delta G^\ddagger$) of racemization and isomerization processes of overcrowded alkenes can be manipulated to a great extent by varying the heteroatoms X and Y in the tricyclic moieties as well as by varying the substituents (R$_1$ and R$_2$) at the peripheral benzene moieties (figure 1.5).$^{23}$

**Figure 1.5** Substituents (X, Y, R$_1$, and R$_2$) that effect the Gibbs energy of activation ($\Delta G^\ddagger$) of the racemization and isomerization barrier of overcrowded alkenes.

The distance d between the carbon atoms 4a’ and 10a’ depends on the size of atom Y and the bond lengths of Y with the adjacent carbon atoms 4a’ and 10a’. The larger distance d the more the peripheral benzene moieties are pushed towards each other which results in more severe steric repulsion in the fjord region of the molecule. This effect is enhanced by the introduction of substituents at the 1- and 2-position. The stronger steric repulsions lead to higher activation energies ($\Delta G^\ddagger$) of the racemization and isomerization processes. Throughout the years massive amounts of data of racemization and isomerization barriers of overcrowded alkenes have been collected and this issue was most recently reviewed by Biedermann et al.$^{2i}$ A summary of interesting data is given in tables 1.2 and 1.3.

Entry series 1 – 5, 6 – 10, and 14 – 16 confirm a significant raise in activation energy ($\Delta G^\ddagger$) when the distance between C$_{4a'}$–C$_{10a'}$ was increased. The general trend derived from table 1.2 is that the distance between C$_{4a'}$–C$_{10a'}$ is increased by atom Y in the following order: Y = – < O < C=O < NCH$_3$ < CH$_2$ <
Chapter 1

CMe₂ < S < CH=CH. The size of substituents at the 2-positions at the peripheral benzene rings does play a role but its influence is less rigorous. When the methyl substituent at the 2-position was replaced by an isopropyl group the Gibbs energy of activation ($\Delta G^\ddagger$) slightly raised (compare entry 4 with 6 and 5 with 9). In contrast, a substituent at the 1-position has a dramatic influence on the Gibbs energy of activation ($\Delta G^\ddagger$) (compare entry 2 with 13, 5 with 11, and see entries 17 – 19).

Table 1.2 Experimental Gibbs energies of activation ($\Delta G^\ddagger$) of thermal racemization processes of overcrowded alkenes.²¹,²³b

<table>
<thead>
<tr>
<th>entry</th>
<th>alkene type</th>
<th>bridges X, Y</th>
<th>substituents</th>
<th>$\Delta G^\ddagger$ (kcal mol⁻¹)</th>
<th>$C_{4\alpha'-'C_{10\alpha'}}$ distance (Å)</th>
<th>method</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>S, –</td>
<td>2-iPr</td>
<td>12.2</td>
<td>1.44</td>
<td>DNMR</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>S, O</td>
<td>2-iPr</td>
<td>17.1</td>
<td>2.33</td>
<td>DNMR</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>S, C=O</td>
<td>2-iPr</td>
<td>18.5</td>
<td>2.56</td>
<td>DNMR</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>S, NCH₃</td>
<td>2-iPr</td>
<td>21.8</td>
<td>–</td>
<td>DNMR</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>S, S</td>
<td>2-iPr</td>
<td>27.7</td>
<td>2.64</td>
<td>DNMR</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>S, NCH₃</td>
<td>2-Me</td>
<td>21.3</td>
<td>–</td>
<td>HPLC</td>
</tr>
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<td>S, CH₂</td>
<td>2-Me</td>
<td>23.0</td>
<td>2.46</td>
<td>Polarim.</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>S, CMe₂</td>
<td>2-Me</td>
<td>25.1</td>
<td>2.46</td>
<td>Polarim.</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>S, S</td>
<td>2-Me</td>
<td>27.4</td>
<td>2.64</td>
<td>Polarim.</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td>S, CH=CH</td>
<td>2-Me</td>
<td>30.8</td>
<td>3.10</td>
<td>Polarim.</td>
</tr>
<tr>
<td>11</td>
<td>1</td>
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<td>1,2-benzo</td>
<td>28.6</td>
<td>–</td>
<td>Polarim.</td>
</tr>
<tr>
<td>12</td>
<td>1</td>
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<td>1,2-benzo</td>
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<td>–</td>
<td>Polarim.</td>
</tr>
<tr>
<td>13</td>
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<td>S, O</td>
<td>1,2-benzo</td>
<td>25.9</td>
<td>–</td>
<td>Polarim.</td>
</tr>
<tr>
<td>14</td>
<td>1</td>
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<td>2-H</td>
<td>11.8</td>
<td>1.44</td>
<td>DNMR</td>
</tr>
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<td>2-H</td>
<td>18.2</td>
<td>2.33</td>
<td>DNMR</td>
</tr>
<tr>
<td>16</td>
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<td>CMe₂, S</td>
<td>2-H</td>
<td>&gt;24.7</td>
<td>2.64</td>
<td>DNMR</td>
</tr>
<tr>
<td>17</td>
<td>2</td>
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<td>–</td>
<td>DNMR</td>
</tr>
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<td>18</td>
<td>2</td>
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<td>1,1'-di-CO₂-iPr</td>
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<td>DNMR</td>
</tr>
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<td>2,2'-di-iPr</td>
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<td>–</td>
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</tr>
<tr>
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<td>CH₂, CH₂</td>
<td>2,2'-di-Me</td>
<td>23.4</td>
<td>–</td>
<td>DNMR</td>
</tr>
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</table>

Similar trends were observed for the Gibbs energies of activation ($\Delta G^\ddagger$) of isomerization processes (table 1.3). Entry 2 shows an exception and the lower Gibbs energy of activation ($\Delta G^\ddagger$) for the anthrone compared to acridine (entry 3) is most likely due to the sp² hybridization of the C=O bond whereas all other type 1 alkenes presented in table 1.3 have sp³ hybridized X and Y bridges.²³b It should be emphasized that the Gibbs energy (G) of a molecule can be another major factor determining the height of the Gibbs energies of activation ($\Delta G^\ddagger$) of racemization and isomerization processes. Although less steric repulsion is present in bisfluorenylidene 2 than in folded structures 1 it has a remarkable high Gibbs energy of activation ($\Delta G^\ddagger$).
Sterically Overcrowded Alkenes

Table 1.3  Experimental Gibbs energies of activation ($\Delta G^\ddagger$) of thermal isomerizations of overcrowded alkenes.$^{2i}$

<table>
<thead>
<tr>
<th>entry</th>
<th>alkene type</th>
<th>bridges X = Y</th>
<th>substituents</th>
<th>$\Delta G^\ddagger$ (kcal mol$^{-1}$)</th>
<th>$C_{4\alpha}$-$C_{10\alpha}$ distance (Å)</th>
<th>method</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>O</td>
<td>2,2’-di-Me</td>
<td>17.1</td>
<td>2.33</td>
<td>DNMR</td>
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<tr>
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<td>1</td>
<td>C=O</td>
<td>2,2’-di-Me</td>
<td>20.0</td>
<td>2.56</td>
<td>DNMR</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>NCH$_3$</td>
<td>2,2’-di-Me</td>
<td>20.8</td>
<td>–</td>
<td>DNMR</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>CH$_2$</td>
<td>2,2’-di-Me</td>
<td>23.8</td>
<td>2.46</td>
<td>HPLC</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>S</td>
<td>2,2’-di-Me</td>
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</tr>
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<td>2,2’-di-tBu</td>
<td>17.5</td>
<td>2.33</td>
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<tr>
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<td>2,2’-di-MeO</td>
<td>18.0</td>
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<td>8</td>
<td>1</td>
<td>–</td>
<td>2,2’-di-Me</td>
<td>25.0</td>
<td>–</td>
<td>DNMR</td>
</tr>
</tbody>
</table>

1.1.6 Determination of Activation Parameters

As indicated in tables 1.2 and 1.3 several methods have been developed to determine the Gibbs energies of activation ($\Delta G^\ddagger$) of racemization and isomerization processes of sterically overcrowded alkenes. When the activation energies ($\Delta G^\ddagger$) are sufficiently high (exceeding 20 kcal mol$^{-1}$), separation of enantiomers is possible at ambient temperatures and quantitative amounts of optical pure overcrowded alkene can be obtained, for instance, by preparative chiral HPLC. The decay of optical activity in time, under influence of thermal energy, can be monitored by chiral HPLC, polarimetry, or CD spectroscopy. The decay of optical activity as a function of time, at a constant temperature, gives the Gibbs energy of activation ($\Delta G^\ddagger$, kcal mol$^{-1}$) at that temperature through equations 1.1 and 1.2.$^{24}$

$$k = \ln 2/2t_{1/2} \quad (1.1a)$$

$$k = \ln 2/t_{1/2} \quad (1.1b)$$

$$\Delta G^\ddagger = -RT\ln\left(\frac{h}{k_B T}\right) \quad (1.2)$$

$k$ = rate constant of conversion: s$^{-1}$
$t_{1/2}$ = half-life time: s (time required for 50% of the sample to converse)
$k_B$ = Boltzmann constant: $3.301 \times 10^{-22}$ cal K$^{-1}$ ($1.381 \times 10^{-23}$ J K$^{-1}$)
$h$ = Planck’s constant: $1.584 \times 10^{-34}$ cal s ($6.626 \times 10^{-34}$ J s)
$\Delta G^\ddagger$ = Gibbs energy of activation: cal mol$^{-1}$
$R$ = gas constant: 1.987 cal mol$^{-1}$ K$^{-1}$ ($8.314$ J mol$^{-1}$ K$^{-1}$)

* Equation 1.1a applies when the ground state energy difference between ‘A’ and ‘B’ during a process A $\leftrightarrow$ B is zero (racemization) and when the ground state energy difference between ‘A’ and ‘B’ is of such magnitude that the back reaction from ‘B’ to ‘A’ cannot be neglected (most isomerization processes of sterically overcrowded alkenes).
overcrowded alkenes). Equation 1.1b applies when the ground state energy difference between ‘A’ and ‘B’ during a process A ↔ B is of such magnitude that the back reaction from ‘B’ to ‘A’ can be neglected.

When the rate constant of conversion (k) is measured over a wide range of temperatures the enthalpy of activation ($\Delta H^\ddagger$) and entropy of activation ($\Delta S^\ddagger$) can be determined by applying the Eyring equation (1.3, which is rewritten from eq. 1.2 by the relation $\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger$).

$$\ln(k/T) = \ln(k_B/h) + \Delta S^\ddagger/R - \Delta H^\ddagger/RT \quad (1.3)$$

$\Delta H^\ddagger = \text{enthalpy of activation: cal mol}^{-1}$

$\Delta S^\ddagger = \text{entropy of activation: cal K}^{-1}\text{ mol}^{-1}$

A plot of $\ln(k/T)$ versus $1/T$ gives a straight line (when the process is first-order), the slope of which yields the enthalpy of activation ($\Delta H^\ddagger$). From the intercept at $1/T = 0$ the entropy of activation ($\Delta S^\ddagger$) can be calculated. From the Arrhenius equation (1.4) the activation energy ($E_a$) and the pre-exponential factor ($A$) can be obtained. A plot of $\ln k$ versus $1/T$ gives a straight line (when the process is first-order), the slope of which yields the activation energy ($E_a$). The intercept at $1/T = 0$ gives the value of $\ln A$.

$$\ln k = \ln A - E_a/RT \quad (1.4)$$

$A = \text{pre-exponential factor: s}^{-1} \text{ (for first-order processes)}$

$E_a = \text{activation energy: cal mol}^{-1}$

The activation energy ($E_a$) is merely a correlation between the change in temperature ($\Delta T$) and the change in the rate of conversion ($\Delta k$). In other words, a high activation energy ($E_a$) means that the rate of conversion changes rapidly with temperature.

Accurate values of Gibbs energies of activation ($\Delta G^\ddagger$), enthalpies of activation ($\Delta H^\ddagger$), and activation energies ($E_a$) between 20 kcal mol$^{-1}$ and 30 kcal mol$^{-1}$ are obtained when the measurements are performed at temperature not lower than $-10^\circ$C and not exceeding $100^\circ$C.

Especially when barriers are below 20 kcal mol$^{-1}$, dynamic $^1$H NMR and $^{13}$C NMR spectroscopy (DNMR) are convenient methods for determining the Gibbs energies of activation ($\Delta G^\ddagger$) of racemization and isomerization of sterically overcrowded alkenes.$^{10,11b,25}$ Activation energies ($\Delta G^\ddagger$) between 12.0 and 27.7 kcal mol$^{-1}$ have been ascertained with these techniques.$^{23b,26}$ Employment of DNMR for determining activation energies ($\Delta G^\ddagger$) of racemization processes requires a pair of nonequivalent nuclei A and B that interchange during a thermally induced conformational change. Prochiral isopropyl groups are particularly suitable since their methyl protons and methyl carbons give rise to two distinct NMR signals when they are attached to a folded overcrowded alkene. The isopropyl group(s) can be substituted at the peripheral benzene rings (see table 1.2: entries 1 – 5, 17,
Sterically Overcrowded Alkenes

18 (t-Bu groups), 19, and 20) or can be part of the central ring of one of the bistricyclic ring systems (see table 1.2: entries 14 – 16 and 21 where two methylene groups were employed of which the protons show two distinct absorptions at NMR spectra). Upon heating, the separated signals of the methyl groups (nuclei A and B) are averaging at the coalescence temperature $T_c$ and the Gibbs energy of activation of racemization ($\Delta G^\ddagger$) can be obtained from equation (1.5).

$$\Delta G^\ddagger = -RT_c \cdot \ln RT_c \sqrt{2/\pi N_A h (\nu_a - \nu_b)} \quad (1.5)$$

$T_c$  = coalescence temperature
$N_A$  = Avogadro’s constant: $6.02205 \times 10^{23}$ mol$^{-1}$
$\nu_a$  = frequency at which absorption occurs of nucleus A
$\nu_b$  = frequency at which absorption occurs of nucleus B

Thus in case of chiral compounds no optical resolution is needed to determine energy barriers (table 1.2: entries 1 – 5) and, moreover, barriers of achiral compounds can be determined. This information can also be used to predict racemization barriers of their chiral analogues (table 1.2: entries 14 – 16).

Both techniques, monitoring the decay of optical activity and DNMR, can also be applied for determining activation energies of isomerization processes (table 1.3). Prochiral substituents are not necessary for DNMR studies since a clear distinction between cis and trans isomers is observed.

1.1.7 Experimental versus Computational Data

**Table 1.4** Comparison of experimentally and computationally (PM3) obtained structural data of overcrowded alkenes 1 – 3.$^{2b,i}$

<table>
<thead>
<tr>
<th>entry</th>
<th>alkene bridges (X)</th>
<th>method</th>
<th>conformation</th>
<th>twist $\omega$$^\circ$</th>
<th>folding A – B$^\circ$</th>
<th>C – D$^\circ$</th>
<th>C$^9$ – C$^9'$ (Å)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 O</td>
<td>Exp.</td>
<td>anti-folded</td>
<td>0.0</td>
<td>43.0</td>
<td>43.0</td>
<td>1.369</td>
</tr>
<tr>
<td>1</td>
<td>1 O</td>
<td>PM3</td>
<td>anti-folded</td>
<td>0.0</td>
<td>40.4</td>
<td>40.4</td>
<td>1.354</td>
</tr>
<tr>
<td>2</td>
<td>1 S</td>
<td>Exp.$^a$</td>
<td>anti-folded</td>
<td>0.5</td>
<td>43.7</td>
<td>43.7</td>
<td>1.351</td>
</tr>
<tr>
<td>1</td>
<td>1 S</td>
<td>PM3</td>
<td>anti-folded</td>
<td>0.0</td>
<td>46.8</td>
<td>46.8</td>
<td>1.353</td>
</tr>
<tr>
<td>3</td>
<td>1 C=O</td>
<td>Exp.</td>
<td>anti-folded</td>
<td>0.0</td>
<td>40.0</td>
<td>40.0</td>
<td>1.364</td>
</tr>
<tr>
<td>1</td>
<td>1 C=O</td>
<td>PM3</td>
<td>anti-folded</td>
<td>0.0</td>
<td>46.6</td>
<td>46.6</td>
<td>1.353</td>
</tr>
<tr>
<td>4</td>
<td>2 –</td>
<td>Exp.</td>
<td>twisted</td>
<td>33.0</td>
<td>5.2</td>
<td>4.2</td>
<td>1.364</td>
</tr>
<tr>
<td>2</td>
<td>2 –</td>
<td>PM3</td>
<td>twisted</td>
<td>30.2</td>
<td>2.5</td>
<td>2.5</td>
<td>1.368</td>
</tr>
<tr>
<td>5</td>
<td>3 CH=CH</td>
<td>Exp.</td>
<td>anti-folded</td>
<td>0.0</td>
<td>55.7</td>
<td>55.7</td>
<td>1.348</td>
</tr>
<tr>
<td>3</td>
<td>3 CH=CH</td>
<td>PM3</td>
<td>anti-folded</td>
<td>0.0</td>
<td>61.6</td>
<td>61.6</td>
<td>1.347</td>
</tr>
<tr>
<td>6</td>
<td>3 CH=CH</td>
<td>Exp.</td>
<td>syn-folded</td>
<td>1.1</td>
<td>56.6</td>
<td>61.8</td>
<td>1.341</td>
</tr>
<tr>
<td>3</td>
<td>3 CH=CH</td>
<td>PM3</td>
<td>syn-folded</td>
<td>0.0</td>
<td>64.7</td>
<td>64.7</td>
<td>1.347</td>
</tr>
</tbody>
</table>

$^a$Data of 2,7’-dimethoxy-bisthioxanthylidene.$^{2b}$
Not surprisingly, the fascinating architecture of overcrowded alkenes, as well as their numerous dynamic processes, have been reasons to subject these structures to elaborate computational studies. Biedermann et al. successfully performed semiempirical PM3 calculations to gather structural data such as bond length of the central double bond, folding angle, and twist ($\omega$). In table 1.4 experimental and computational data of overcrowded alkenes 1 – 3 are collected. The bond length of the central ethylene bond $C^9=C^9'$ was predicted very accurately by the (PM3) calculations. The calculated twisting ($\omega$) and folding angles differ no more than $8^\circ$ from the experimental.

1.2 Molecular Switches

1.2.1 Introduction

Communication is playing a vital role in our present-day society and the demand for high-speed computers with enormous data storage capacities has dramatically increased. As a consequence the extension of storage capacity and the possibility to process larger amounts of data at higher speeds is a major challenge. Thus, a continuous search for materials and techniques to store as much data on as least amounts of surface is ongoing. The ultimate goal is to achieve storage as well as manipulation of data at the molecular level in which each single molecule functions as a separate storage device. The design of molecular switches and trigger elements, able to execute the action of storage and manipulation, offers a formidable challenge toward the desired miniaturization in future technology. The employment of individual molecules is highly attractive since a molecule is the smallest logic elements available. Moreover, molecular design gives the opportunity to build in various characteristics. The main disadvantage, however, is the lack of order and one of the most difficult aspects will be the controlled coordination of all single molecular devices in larger macroscopic structures such as polymer matrices or liquid crystals. Supramolecular chemistry and nanotechnology can possibly provide solutions for these problems. Supramolecular chemistry deals with the development of a range of techniques for synthesis and characterization of large molecular assemblies, held together by noncovalent interactions. Nanotechnology involves the synthesis, characterization, and application of structures of nanosize dimensions (1 – 100 nm). The incorporation of individual molecular devices in separate building blocks offers a ‘bottom up’ approach to create complex nanosize structures in which precise positioning is achieved by controlled assembly.

1.2.2 Switches

In recent years, considerate effort has been put into development of switching molecules based on organic materials. In the desired situation, reversible, complete, and fast switching between two different stable states ‘A’ and ‘B’, induced by external stimuli, is accomplished (scheme 1.6).
Scheme 1.6 Molecular switch. ‘A’ and ‘B’ represent the two different stable states whereas S₁ and S₂ refer to different external stimuli which effect the controlled reversible switching behavior.

A number of sources can serve as external stimuli such as temperature, pH, magnetic fields, electric fields, and light. Especially the last stimulus is playing a key role in the ongoing search for organic materials suitable for data storage. Photoreversible compounds in which the reversible switching is controlled by light are promising since photochemical conversions are fast which is an essential factor for efficient data processing. Besides technical, economical, and environmental restrictions, the system should meet a number of other criteria:

- Selective and efficient photochemical switching between the two stable states with high quantum yields should be achieved. Degradation of the materials must not take place.
- Besides the photochemical switching, no thermal conversions should occur over a large range of temperatures (–20° to 80°C).
- Both stable states ‘A’ and ‘B’ must be clearly detectable and a non-destructive read-out procedure which does not interfere with, or erase, the written data must be available.
- Retention of all properties of the individual switching molecules is necessary upon incorporation the molecules into macromolecular materials and nanosize assemblies.
- Writing and erasing must be possible without degradation

In view of the criteria outlined above, photochemical cis-trans isomerizations have attracted considerable interest and this topic will be surveyed shortly in the next section. The subject of photochemical switches has been reviewed recently.33d

1.2.3 Cis-trans Isomerizations

Cis-trans isomerizations are rotations of about 180° around a carbon-carbon double bond (see section 1.5). One of the basic processes of vision is a photochemically induced cis-trans isomerization.36 In the eyes of vertebrates, and thus humans, an image of the external world is focussed on a single layer of photoreceptor cells on the back of the retina. Here the absorption of a light quantum leads to the cis-trans isomerization of an 11-cis-retinal moiety (scheme 1.7).

Upon absorption of a photon, the 11-cis-retinal moiety of structure 5a (λ_max = 498 nm), having a bent form, is converted into a rod-like 11-trans-retinal moiety (structure 5b) (λ_max = 380 nm). The retinal
moiety is covalently bound to the protein opsin, via an imine bond with the amino acid lysine, together forming the protein rhodopsin. The structural change of the retinal moiety leads to a conformational change in the entire protein. The conformational change initiates a cascade of reactions during which 11-trans-retinal moiety is released form the protein. A nerve pulse to the brain is generated creating an image thus giving a sense of vision. After release, 11-trans-retinal is reduced enzymatically to trans-retinol (vitamin A) and transformed to 11-cis-retinal to recombine with free opsin to form 5a. With an extreme high quantum yield ($\Phi = 0.67$) and high reversibility ($>10^6$ cycles)\textsuperscript{37} the cis-trans isomerization process of retinal, giving vertebrates the ability to see, is certainly one of the most fascinating examples of the superb systems created by nature. It has inspired chemists to mimic the cis-trans isomerization of retinal and to search for possible applications of retinal derivatives for reversible data storage. And indeed, biological switches based on bacteriorhodopsin, with retinal as photoreceptive element, were applied for holographic data storage.\textsuperscript{38} This issue has been recently reviewed by Hampp et al.\textsuperscript{39}

![Scheme 1.7](image)

**Scheme 1.7** Cis-trans isomerization of retinal.

Three important classes of synthetic molecular switches of which bistability is established by light induced cis-trans isomerizations, have been developed: stilbenes (section 1.2.4), azobenzenes (section 1.2.5), and sterically overcrowded alkenes in which a switching process is accompanied by a change in chirality (section 1.2.6).

### 1.2.4 Stilbenes

![Scheme 1.8](image)

**Scheme 1.8** Photochemistry of stilbenes 6.

The photochemistry of stilbenes 6 has been studied thoroughly and reversible light induced cis-trans isomerization was observed (scheme 1.8).\textsuperscript{40} However, the scope of stilbenes 6 for reversible
photoswitching is limited because of undesired side reactions. Irradiation of cis-stilbene 6a gave rise to ring closure and subsequent oxidation yielded phenanthrene 7 while trans-stilbene 6b was converted into substituted cyclobutanes 8 by [2 + 2] cycloaddition reactions. Supramolecular control of the photochemistry of trans-stilbenes 6b was achieved by Wenz et al. Host-guest chemistry with different cyclodextrines (host) provided selective isomerization toward cis-stilbene 6a or selective formation of the cycloaddition product 8.

1.2.5 Azobenzenes

Two stable states for azobenzene 9 have been found (scheme 1.9). The trans isomer was converted into the cis isomer by UV light irradiation. The reverse reaction was initiated upon irradiation with visible light. A serious drawback of this system is the possible thermal cis to trans isomerization due to a low Gibbs energy of activation ($\Delta G^\ddagger$) for this process.

Different substitution patterns strongly influence the Gibbs energy of activation ($\Delta G^\ddagger$) which resulted in half-life times of the cis isomer 9b ranging from minutes to several days at room temperature. The isomERIC rate of trans and cis azobenzene 9 could be detected by UV/VIS spectroscopy, although this is not a non-destructive read-out method.

\[
\begin{align*}
&\text{trans-azobenzene } 9a & \text{cis-azobenzene } 9b
\end{align*}
\]

Scheme 1.9 Cis-trans isomerization of azobenzene 9.

Despite aforementioned limitations, azobenzenes 9 were abundantly employed to generate major structural changes in supramolecular assemblies or photochromic polymers such as polypeptides. It appeared that the thermal decay of the cis isomer 9b was reduced significantly when azobenzenes were incorporated in polymers, liquid crystalline material, or monolayers. Furthermore, non-destructive read-out methods, such as changes in conductivity, transmittance, or chirality, can be applied without interfering with the photoisomerization processes.

The ability of azobenzenes to induce phase transitions of liquid crystalline materials has attracted considerable interest. The rod-like trans configuration of azobenzene tends to stabilize nematic crystalline phases, whereas the bent cis isomer has a destabilization effect on nematic phases resulting in transition to the isotropic phase. Since the nematic phase shows transmittance and the isotropic state does not, the photochemically driven nematic-isotropic (N-I) phase transition was conveniently followed by monitoring the transmittance of light passing through the sample. N-I phase transitions with response times down to 200 $\mu$s have been reported. When irradiation was ceased, the nematic phase was recovered rapidly and especially 4,4’-donor-acceptor substituted azobenzenes gave fast
recovery times of at best 8 ms at 146°C. These features have been used in research toward applications in optical switching, optical imaging, optical data storage, and optical display.

Other applications of azobenzenes include: (1) photoresponsive dendrimers containing azobenzene units, (2) functionalization of Langmuir-Blodgett (LB) films, (3) azobenzene dimers based on proline peptides suitable for holographic data storage, (4) azobenzene charge transfer trimers based on liquid crystalline donor-acceptor systems.

1.2.6 Chiroptical Molecular Switches

Chiroptical molecular switches 10 represent an intriguing class of sterically overcrowded alkenes (scheme 1.10). They are strongly related to the bistricyclic ene systems 1 (sections 1.1.2 – 1.1.5) with respect to architecture, helicity, chirality, and possible dynamic processes. However, distinct differences give chiroptical molecular switches their unique photochromic and thermodynamic properties which make them suitable for optical data storage.

![Scheme 1.10 Dynamic processes of chiroptical molecular switch 10. Atom numbering scheme according to IUPAC nomenclature.](image)

Chiroptical molecular switches 10 consist of a different upper and lower part. The lower part is a xanthene moiety while the upper part is a phenanthrene moiety. They are connected by a central double bond and the size of upper and lower part causes an anti-folded, helical shape to the entire molecule. The helicity makes these compounds chiral (section 1.1.4) and the chirality is defined at the naphthalene chromophore side of the molecule by an (M) (Minus, left-handed helix) or a (P) (Plus, right-handed helix).

When (M)-cis-10 is irradiated with light of appropriate wavelength λ₁, cis-trans isomerization takes place giving (P)-trans-10. The reverse isomerization will be induced upon irradiation with light of wavelength λ₂. An important feature of the cis-trans isomerizations of chiroptical molecular switches 10 is the concomitant helix inversion from (M) to (P) or vice versa. The (M)-cis-10 and (P)-trans-10 isomer have opposite helicity but they are not enantiomers due to the presence of substituent R. Because of that they are called pseudoenantiomers. Pseudoenantiomers are almost mirror images of each other and therefore their circular dichroism (CD) spectra show opposite signs, but almost identical values, of optical rotation (ORD). These properties imply that the two bistable states, (M)-
cis-10 and (P)-trans-10, can be identified, utilizing CD, or ORD, at wavelengths far from the switching wavelengths. The latter method provides an excellent non-destructive read-out method. Racemization (scheme 1.10) of (M)-cis-10 to (P)-cis-10 [or (P)-trans-10 to (M)-trans-10, not visualized in scheme 1.10] obviously is a highly unwanted side reaction since the loss of optical activity makes CD and ORD unusable as read-out methods. It should be emphasized that optically active material is required for applying CD and ORD. Separation of enantiomers is usually performed by preparative chiral HPLC.23b,e,f,32,33c,51

When a definite photoequilibrium of cis and trans isomers is obtained during irradiation, the photostationary state (PSS) is reached and the ratio of cis and trans isomers is largely governed by two factors reflected by equation 1.6. The isomeric composition is determined by 1) the ratio of extinction coefficients ($\varepsilon$) of the isomers at the irradiation wavelength and 2) the ratio of the quantum yields ($\Phi$) for $cis \rightarrow trans$ and $trans \rightarrow cis$ isomerizations. These two factors relate to parameters such as temperature at which irradiation takes place and polarity of the solvent.

$$\frac{cis}{trans} = \frac{\varepsilon_{trans} \Phi_{trans \rightarrow cis}}{\varepsilon_{cis} \Phi_{cis \rightarrow trans}}$$

(1.6)

In order to achieve high selectivities it is of utmost importance that the differences between UV/VIS spectra of cis and trans isomers are large at specific wavelengths. Differences in UV/VIS spectra can, among other things, be realized by introducing electron withdrawing and/or electron donating substituents at various positions of the switch (scheme 1.11 and table 1.5). Different through space interactions are at work when the naphthyl moiety of the upper half is in proximity of an electron withdrawing group or an electron donating group attached to the lower part of the switch. Various differently substituted chiroptical switches have been synthesized and examined on their photochemical behavior (scheme 1.11).1,23f,32b,33,51 Typical results are summarized in table 1.5.

![Scheme 1.11](image)

Scheme 1.11 Photochemical cis-trans isomerizations of various differently substituted chiroptical molecular switches 11 – 13.

De Lange and Jager introduced the first chiroptical molecular switch based on inherently dissymmetric alkenes.23a,b,51 Irradiation with 300 nm light gave a photoequilibrium composed of 64% (M)-11 and 36% (P)-11. Irradiation with 250 nm light yielded a mixture of 68% (M)-11 and 32% (P)-11. Although the difference between the (M)/(P) ratios at the two photostationary states is rather small, i.e. 4%, this was the first example of a light-driven chiroptical molecular switch. Unfortunately,
the undesired thermal process of racemization could not be suppressed at room temperature and after 20 minutes of alternating irradiation at 250 and 300 nm 10% of the switch appeared to have racemized ($\Delta G^\ddagger_{\text{rac.}} = 26.5$ kcal mol$^{-1}$).

Table 1.5 Composition of switches 11 – 13. Wavelengths $\lambda_1$ and $\lambda_2$ are given with the $(M)/(P)$ ratio at the photostationary state (PSS).

<table>
<thead>
<tr>
<th>entry</th>
<th>switch</th>
<th>X</th>
<th>Y</th>
<th>R$_1$</th>
<th>R$_2$</th>
<th>R$_3$</th>
<th>$\lambda_1$ (nm)$^a$</th>
<th>PSS $(M)/(P)$</th>
<th>$\lambda_2$ (nm)$^a$</th>
<th>PSS $(M)/(P)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1$^{23a,b,51}$</td>
<td>11</td>
<td>CH$_2$</td>
<td>S</td>
<td>OMe</td>
<td>H</td>
<td>Me</td>
<td>300</td>
<td>64/36</td>
<td>250</td>
<td>68/32</td>
</tr>
<tr>
<td>2$^{23a,b,f,33c}$</td>
<td>12</td>
<td>S</td>
<td>S</td>
<td>NMe$_2$</td>
<td>NO$_2$</td>
<td>H</td>
<td>435</td>
<td>10/90</td>
<td>365</td>
<td>70/30</td>
</tr>
<tr>
<td>3$^{32b}$</td>
<td>13</td>
<td>S</td>
<td>S</td>
<td>H</td>
<td>NO$_2$</td>
<td>NMe$_2$</td>
<td>313</td>
<td>45/55</td>
<td>435</td>
<td>99/1</td>
</tr>
</tbody>
</table>

$^a$Band width of applied filters $\approx$ 10 nm

Scheme 1.12 Switching behavior of overcrowded alkene 12.

Spectacular improvement was observed when an electron withdrawing nitro group and an electron donating dimethylamino group were introduced at either side of the lower part of the switch.$^{23a,b,f,33c}$ A photostationary state, composed of 10% $(M)$-12 and 90% $(P)$-12 was observed upon irradiation with 435 nm light whereas irradiation with 365 nm light gave a photostationary state of 70% $(M)$-12 and 30% $(P)$-12 (scheme 1.12).

The high diastereomeric excesses of 80 and –40% can be largely attributed to the clear differences in UV/VIS spectra of both isomers. In addition, the thermal stability of this switch was sufficient ($\Delta G^\ddagger_{\text{rac.}} = 29.2$ kcal mol$^{-1}$) and no racemization was observed at room temperature. Since the ultimate goal is to accomplish complete selective switching, during which diastereomeric ratios of 100% in both directions are achieved, attempts were undertaken to further manipulate the electronic behavior of switches. Therefore, switch 13, with an electron donating substituent at the upper part and a withdrawing group at the lower part was synthesized.$^{32b}$ Disappointingly, this endeavor by Schoevaars was not rewarded with more selective switching behavior. Switch 13 showed improved selectivity in one direction only. Irradiation for 2 min with 435 nm light gave an almost perfect photostationary state of 99% $(M)$-13 and 1% $(P)$-13 but a maximum diastereomeric excess of only 10% (45% $(M)$-13 and 55% $(P)$-13) into the other direction was obtained (irradiation time of 2 min with 313 nm light). The search for optimization of these systems is still ongoing.$^{52}$
Scheme 1.13 Racemization process of chiroptical molecular switch 10. (The IUPAC numbering scheme for thio- and oxo-phenanthrylidenes is used in scheme 1.13 and table 1.6. However, phenanthrylidenes (X = CH2) on one hand and thio- (X = S) and oxo-phenanthrylidenes (X = O) on the other adopt different atom numbering schemes according to IUPAC rules. For the sake of clarity we have used the same system for numbering phenanthrylidenes in scheme 1.13 and table 1.6. See chapter 6 for further specification.)

Table 1.6 Racemization barriers of various chiroptical molecular switches 10 with different atoms X and Y.23a,b

<table>
<thead>
<tr>
<th>entry</th>
<th>X</th>
<th>Y</th>
<th>R1</th>
<th>R2</th>
<th>R3</th>
<th>rac. barrier</th>
<th>C3' – C10a' (Å)</th>
<th>C4a – C10a (Å)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>O</td>
<td>O</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>24.9</td>
<td>2.34</td>
<td>2.33</td>
</tr>
<tr>
<td>2</td>
<td>CH2a</td>
<td>O</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>27.4</td>
<td>2.48</td>
<td>2.33</td>
</tr>
<tr>
<td>3</td>
<td>CH2a</td>
<td>O</td>
<td>H</td>
<td>H</td>
<td>Me</td>
<td>27.2</td>
<td>2.48</td>
<td>2.33</td>
</tr>
<tr>
<td>4</td>
<td>S</td>
<td>O</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>28.0</td>
<td>2.75</td>
<td>2.33</td>
</tr>
<tr>
<td>5</td>
<td>O</td>
<td>S</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>21.8</td>
<td>2.34</td>
<td>2.64</td>
</tr>
<tr>
<td>6</td>
<td>CH2a</td>
<td>S</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>25.5</td>
<td>2.48</td>
<td>2.64</td>
</tr>
<tr>
<td>7</td>
<td>CH3a</td>
<td>OMe</td>
<td>H</td>
<td>Me</td>
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<td>26.5</td>
<td>2.48</td>
<td>2.64</td>
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<td>S</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>28.9</td>
<td>2.75</td>
<td>2.64</td>
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<tr>
<td>9</td>
<td>S</td>
<td>CMe2</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>28.9</td>
<td>2.75</td>
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<td>10</td>
<td>O</td>
<td>CH=CH</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>23.8</td>
<td>2.38</td>
<td>3.10</td>
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<td>11</td>
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<td>H</td>
<td>H</td>
<td>H</td>
<td>29.0</td>
<td>2.48</td>
<td>3.10</td>
</tr>
</tbody>
</table>

*aSee remark at scheme 1.13.

Similar to bistricyclic ene systems, discussed in section 1.1.5, the Gibbs energy of activation ($\Delta G^\ddagger$) of the racemization process of unsymmetrical alkenes of type 10 (and 11 – 13) can be manipulated by varying the identity of atoms X and Y (scheme 1.13).23a,b Compounds of class 10 (and 11 – 13) have never been observed to perform thermal cis-trans isomerizations but as indicated previously for alkene 11, thermal racemization can take place all the more.23b

A summary of Gibbs energies of activation of racemization ($\Delta G^\ddagger$) of unsymmetrical alkenes is presented in table 1.6.23b Increasing the distance between carbon atoms adjacent to atoms X and Y (C3' – C10a' and C4a – C10a) causes more steric hindrance in the fjord region of the switch (see section 1.1.5)
which in turn brings about higher Gibbs energies of activation ($\Delta G^\ddagger$) of racemization. This general tendency is clearly confirmed by entries 1 – 4 and 5 – 8. Remarkably, substitution at the upper phenanthrene part of the molecule slightly lowers the racemization barrier (entries 2 and 3). The normal trend of a moderate elevation of activation energy by introducing substituents is resumed in entries 6 and 7. A stunning low racemization barrier is found in entry 5. When compared with entries 1 and 4 one realizes that distances $C_3' - C_{10a}'$ and $C_{4a} - C_{10a}$ are not the sole parameters affecting the height of racemization barriers.

### 1.2.7 Switching between Enantiomers

![Scheme 1.14 Chiroptical switch 15 interconverted by circular polarized light (CPL switch).](image)

The research on chiroptical molecular switches is mainly focused on photochemical switching between two pseudoenantiomers with the ultimate goal to achieve complete selectivities in both directions (section 1.2.6). In the mean time attempts were undertaken to develop a molecular switch of which the two enantiomers could be interconverted by circular polarized light (CPL). Indeed, switch 15 was successfully applied for this purpose and by employing left and right circular polarized light ($l$-CPL and $r$-CPL) switching between the ($P$)- and ($M$)-enantiomers was observed with enantiomeric excesses of 0.07 and $-0.07\%$, respectively (scheme 1.14).$^{23b,53}$

### 1.2.8 Applications of Chiroptical Molecular Switches

It is a well-known phenomenon that small amounts of optically active dopant (guest) may induce transition from a nematic phase to a cholesteric phase of liquid crystalline host material.$^{54}$ Moreover, subtle chemical modifications of a chiral guest molecule can heavily influence the helical pitch in a twisted nematic phase. In view of the intended application in information technology (section 1.2.1) chiroptical molecular switches were doped into liquid crystalline material.$^{32a,55}$ Optically active molecular switch 12 (1 wt %), giving the highest difference in diastereomeric excesses upon irradiation in solution (section 1.2.7), was added to liquid crystalline 4'- (pentyloxy)-4-biphenylcarbonitrile (liquid crystalline phase). Irradiation of the sample with 313 nm light resulted in a nematic phase while irradiation with 435 nm light induced a cholesteric I phase (scheme 1.15). Furthermore, irradiation of the cholesteric I phase with 365 nm light gave a cholesteric II phase while
Sterically Overcrowded Alkenes

the reverse transition was established by irradiation with 435 nm light. The size of the pitch alternated from 12.29 µm (cholesteric I) to 5.31 µm (cholesteric II).

```
<table>
<thead>
<tr>
<th>LC phase</th>
<th>nematic</th>
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<th>cholesteric II</th>
</tr>
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<tr>
<td>dopant (M)-trans-12</td>
<td>435 nm</td>
<td>365 nm</td>
<td>313 nm</td>
</tr>
<tr>
<td>50% (M)-trans-12</td>
<td>excess (P)-cis-12</td>
<td>excess (M)-trans-12</td>
<td></td>
</tr>
<tr>
<td>50% (P)-cis-12</td>
<td></td>
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</tr>
</tbody>
</table>
```

**Scheme 1.15** Photochemical switching processes of LC-phase (4′-(pentyloxy)-4-biphenylcarbonitrile) and chiral dopants (M)-trans-12 and (P)-cis-12.

The phase transition as well as the pitch modulation were performed reversibly and repetitive. With these qualities the system meets some of the criteria required for possible application in data storage. The same switch 12 was integrated in a chiro-optic device by Demus et al. 56 A cholesteric mixture, containing 12, was put into a hybrid cell and two stable states, a dark state and a bright state, were observed repetitively when alternately irradiated by 435 and 365 nm light. With this basic design a holographic recording system was developed.

CPL switch 15 exhibited similar abilities with respect to phase transition within liquid crystalline material. 53 In this case irradiation with CPL of liquid crystalline material, doped with 20 wt % 15, afforded a chiral mesoscopic phase. By modulation of the polarization of the light reversible switching between cholesteric (CPL) and nematic (LPL) phases was achieved.

As considered in section 1.2.1 the controlled assembly is one of the most prominent aspects of applying molecular switches as memory elements. Incorporation of switches into polymer films is a promising opportunity to achieve this goal. Switching units covalently attached, via a spacer, to a polymer backbone or thin polymer films doped with switches are two approaches that were followed. 32b Chiroptical switch 11 was coupled to a polymer (polymethyl methacrylate) by an alkyl spacer. 58 Excellent film forming properties were found for the functionalized polymers, bearing 4.0 – 4.7% of optical pure switch 11. Unfortunately, no repetitive reversible switching was observed upon alternating irradiation by two different wavelengths. Therefore these studies were maintained by focussing on thin polymer films doped with chiroptical switches. For this purpose the feasible use of
switch 12 is a major advantage because of its high selective switching behavior. Switch 12 was not suitable for covalent binding to polymers due to solubility problems. The highest difference in diastereomeric excesses of optical active switch 12 was observed when doped in polystyrene. \((P)/(M)\) ratios of 30/70 and 23/77 were detected at 435 and 365 nm, respectively, reflecting diastereomeric excesses of 40 and 54%. These values are significantly lower than the initial stereoselectivities obtained in solution (table 1.5, scheme 1.12), however, for efficient read-out, a difference in diastereomeric excesses of >2% is sufficient, which is fulfilled by this system.

### 1.3 Controlled Dynamic Behavior of Molecular Systems

#### 1.3.1 Introduction

Dynamic biological processes are intriguing and have inspired scientists immensely (see also section 1.2.3). In particular systems such as ATP-synthase\(^5^9\) and skeletal muscles\(^6^0\), in which energy is converted into controlled motion, play essential roles in vertebrates. Attempts to mimic these processes by synthetic design have lead to many fascinating molecular systems whose dynamic behavior can be controlled by regulated energy consumption.\(^1^,6^1^,6^2^,6^3^,6^4^,6^5\)

#### 1.3.2 Catenanes and Rotaxanes

Catenanes (interlocking rings) and rotaxanes (stringlike components) comprise a set of compounds which could possibly serve as building blocks of molecular machines.\(^6^2\) One of the most recent findings in this field was reported by Sauvage et al. and comprehends the contraction and stretching of a linear rotaxane dimer resembling a natural muscle at work (scheme 1.16).\(^6^3\) Analogous to real muscles a molecular assembly was designed in which two filaments glide along one another. In this fashion the process taking place in the sarcomere, in which the thick and thin filament are able to move along each other, was imitated.
As visualized in scheme 1.16, the assembly is capable of binding two metal ions. When Cu (I) is present two four-coordinated centers, with each copper ion bound to two phenanthroline moieties, are formed leading to an extended geometry. When Cu (I) is replaced by Zn (II) two five-coordinated centers, each created by one phenanthroline and one terpyridine moiety, are formed giving the contracted situation. Both motions proceeded quantitatively and reversibly giving this process a repetitive nature.

### 1.3.3 Unidirectional Rotary Motion

While the movement of muscles can be classified as linear, unidirectional rotary motion was observed in the ATP-synthase protein.\(^{59}\) The unidirectional rotation of the actin filament with respect to the static \(\alpha\beta_3\) lower part was proven by Noji et al. (figure 1.6).\(^{59a}\)

![Figure 1.6 Unidirectional rotation in the ATP-synthase protein.](image)

In recent nanotechnological terms a molecular motor is described as a device that can convert any form of energy into controlled motion.\(^{52b}\) Eventually this controlled motion should be translated into any kind of work. The first synthetic approaches toward molecular motors, performing unidirectional rotary motion, were put forward in 1999 by Kelly et al.\(^{65}\) and our group.\(^{66}\) Kelly’s motor 16 exists of a helicene stator which was connected to a three-bladed triptycene rotor by a single bond (scheme 1.17).\(^{65}\) The Gibbs energy of activation (\(\Delta G^\ddagger\)) for a 120° rotation, during which the rotor moiety passes the helicene stator, lies around 25 kcal mol\(^{-1}\).

This barrier was significantly lowered by activation of the rotor by addition of phosgene. The amine was transformed into isocyanate 17 and random ‘Brownian’ motion within 17 brought the isocyanate moiety in close proximity of the alcohol functionality of the helicene (intermediate 18) resulting in ring closure giving urethane 19. The ring closure was only facilitated by a clockwise rotation of the helicene moiety. A counter clockwise rotation did not bring the alcohol and isocyanate functionality in sufficient proximity for ring closure. This observation was the actual prove for unidirectional rotation. The steric repulsion between rotor and helicene moiety was considerably higher in 19 than in starting structures 16 and 17. However, reverse rotation to geometries akin to 16 and 17 was
prevented by the urethane bond. The thus induced reduction of the Gibbs energy of activation (\(\Delta G^\ddagger\)) enabled a 120° unidirectional rotation of the triptycene rotor at ambient temperature yielding 20. Finally, the urethane bond of 20 was cleaved which simultaneously completed the chemically driven rotation of 16 to 21.

Scheme 1.17 Chemically driven, unidirectional, 120° rotation of the triptycene motor.

The architecture of the molecular motor developed in our group is based on helical shaped overcrowded alkenes (scheme 1.18). Two phenanthrene moieties were connected by a central double bond while at the upper and lower part of the motor a stereogenic center was created by a methyl substituent. Irradiation of \((P,P)\)-trans-22 with \(\geq 280\) nm light induced a trans-cis isomerization giving \((M,M)\)-cis-23 in a 5/95 ratio. Irradiation was carried out at \(-55^\circ C\) since heating to \(20^\circ C\) immediately resulted in quantitative thermal isomerization to \((P,P)\)-cis-24. Photochemical isomerization of \((P,P)\)-cis-24 gave \((M,M)\)-trans-25 in a 90/10 ratio. Finally, starting compound \((P,P)\)-trans-22 was formed by a second quantitative thermal step (60°C). This sequence of events proved that two photochemical trans-cis isomerizations, each followed by a thermal conversion, effected a four-step cycle, completing a full unidirectional 360° rotation of the upper part with respect to the lower part. It should be emphasized that, regarding structures 22 – 25, the axial orientation of the methyl substituent is favored over the equatorial orientation. Therefore, the two photochemical steps were energetically uphill processes whereas the thermal steps were energy relaxing. The four individual steps were, among other techniques, monitored by CD spectroscopy since each step involved a helix inversion ((\(P\) to \(M\) or vice versa, see section 1.1.4). The direction of rotation was governed by the two stereogenic centers. The four-step cycle, completing the full 360° rotation, was repeated thrice.
Sterically Overcrowded Alkenes

without degradation of the olefins demonstrating the repetitive nature of the rotation process performed by this motor.

\[ \text{(P,P)-trans-22} \quad \xrightarrow{\text{ratio 5/95}} \quad \text{Me}_{\text{ax}} \]
\[ \text{Me}_{\text{eq}} \quad \xrightarrow{\text{≥ 280 nm}} \quad \geq 380 \text{ nm} \quad \xrightarrow{\text{≤ -55°C}} \quad \text{(M,M)-cis-23} \]

\[ \text{(M,M)-trans-25} \quad \xrightarrow{\text{≥ 380 nm}} \quad \geq 280 \text{ nm} \quad \xrightarrow{\text{ratio 90/10}} \quad \text{RT} \]
\[ \text{(P,P)-cis-24} \quad \xrightarrow{\text{20°C}} \]

Scheme 1.18 Photochemically and thermally driven unidirectional 360° rotation of the biphenanthrylidene motor.

1.4 Aim of this Thesis and Overview of Contents

This thesis presents developments in the field of optically active bis(thio)xanthylidenes (chapters 2 through 4) and the evolution of chiroptical molecular switches into the second generation of light-driven molecular motors (chapters 5 through 7).

Chapter 2 describes the development of a synthetic route toward enantiomerically pure bisthioxanthylidene. In this procedure, (S,S)-Threitol-ditosylate and optically active binaphthol served as chiral templates. Thus, transfer of axial single bond chirality to axial double bond chirality was achieved. Moreover, the determination of the absolute configuration of enantiomerically pure bisthioxanthylidene was accomplished.

This concept was extended to the synthesis of optically active bisxanthylidenes. Thermochemical properties were expected and attempts were undertaken to develop the first thermochromic molecular switch. These studies are dealt with in chapter 3.

A remarkable feature of bistricyclic ene systems, as a consequence of their folded shape (section 1.1.2 and 1.1.3), is the presence of two helices of opposite sign ((P) and (M), see section 1.1.4). In order to
exploit this feature, both sides of bisthioxanthylidene were functionalized with differently sized crown ethers. The different substituents created a chiral compound. It is a well documented fact that crown ethers have a distinct preference for complexation with metal cations which exactly fit into their ring size. With this knowledge in hand we envisioned activation of either the (P)- or (M)-helix, by addition of the appropriate metal cation, for asymmetric catalysis. Synthesis of bircrown bisthioxanthylidenes and their structural properties are reported in chapter 4.

The realization of the second generation of molecular motors is surveyed in chapter 5. Extending the initial machinery, described in section 1.3.3, we started construction of molecular motors with distinct upper and lower parts. They are reminiscent of the chiroptical molecular switches, discussed in section 1.2.6, which have been examined thoroughly on their photochemical and thermodynamic behavior. The introduction of a methyl substituent at the upper part of the molecule created a stereogenic center. Anticipated key features of this second generation molecular motors are the control of unidirectional rotation by a single stereogenic center and the ability to tune the speed of rotation which is governed by the two thermal steps of the 4–step cycle. The architecture of the new class of motors allowed structural modification enabling adjustment of speed of rotation. This latter aspect is dealt with in chapter 6. The synthesis of seven new motors accompanied with detailed quantitative data of the thermodynamics of the thermal steps are given there. Furthermore, stunning high selectivities at photoequilibria are reported.

Whereas chapters 5 and 6 describe motors with a phenanthrene upper part, chapter 7 focuses on motors with a methyl substituted naphthalene upper part. The naphthalene upper part was supposed to decrease the steric repulsion in the fjord region (section 1.1.5) which in turn was expected to further speed up the rate of rotation. Some remarkable results were found which are certainly an addition to our knowledge about the parameters governing the behavior of molecular motors.

1.5. References

1 This chapter is partly based on the following review: B. L. Feringa, R. A. van Delden, N. Koumura, E. M. Geertsema, Chem. Rev. 2000, 100, 1789.


Sterically Overcrowded Alkenes


