The broad outlines of both polar and radical reactions have been known for more than a century, but our understanding of pericyclic reactions emerged more recently. Prior to the mid-1960s, in fact, they were even referred to on occasion as “no-mechanism reactions” because they seemed so unusual. They occur largely in the laboratory rather than in biological processes, but a knowledge of them is necessary, both for completeness in studying organic chemistry and in understanding those biological pathways where they do occur.

Most organic reactions take place by polar mechanisms, in which a nucleophile donates two electrons to an electrophile in forming a new bond. Other reactions take place by radical mechanisms, in which each of two reactants donates one electron in forming a new bond. Both kinds of reactions occur frequently in the laboratory and in living organisms. Less common, however, is the third major class of organic reactions — pericyclic reactions.

A pericyclic reaction is one that occurs by a concerted process through a cyclic transition state. The word concerted means that all bonding changes occur simultaneously; no intermediates are involved. Rather than try to expand this definition now, we’ll begin by briefly reviewing some of the ideas of molecular orbital theory introduced in Chapters 1 and 9 and then looking individually at the three main classes of pericyclic reactions: electrocyclic reactions, cycloadditions, and sigmatropic rearrangements.

26-1 Molecular Orbitals of Conjugated Pi Systems

A conjugated polyene, as we saw in Section 8-12, is one with alternating double and single bonds. According to molecular orbital (MO) theory, the p orbitals on the sp²-hybridized carbons of a conjugated polyene interact to form a set of orbitals that are extended throughout the entire length of the polyene. These orbitals are called molecular orbitals (MOs).

Chorismate mutase catalyzes a pericyclic reaction that converts chorismate to prephenate, a step in the biosynthesis of the aromatic amino acids phenylalanine and tyrosine.
π molecular orbitals whose energies depend on the number of nodes they have between nuclei. Those molecular orbitals with fewer nodes are lower in energy than the isolated p atomic orbitals and are bonding MOs; those molecular orbitals with more nodes are higher in energy than the isolated p orbitals and are antibonding MOs. Pi molecular orbitals of ethylene and buta-1,3-diene are shown in FIGURE 26.1.

A similar sort of molecular orbital description can be derived for any conjugated π electron system. Hexa-1,3,5-triene, for example, has three double bonds and six π MOs, as shown in FIGURE 26.2. In the ground state, only the three bonding orbitals, \( \psi_1 \), \( \psi_2 \), and \( \psi_3 \), are filled. On irradiation with ultraviolet light, however, an electron is promoted from the highest-energy filled orbital (\( \psi_3 \)) to the lowest-energy unfilled orbital (\( \psi_4^* \)) to give an excited state (Section 10-9), in which \( \psi_3 \) and \( \psi_4^* \) are each half-filled. (An asterisk denotes an antibonding orbital.)

What do molecular orbitals and their nodes have to do with pericyclic reactions? The answer is: everything. According to a series of rules formulated in the mid-1960s by R. B. Woodward and Roald Hoffmann, a pericyclic reaction can take place only if the symmetries of the reactant MOs are the same as the symmetries of the product MOs. In other words, the lobes of reactant MOs must be of the correct algebraic sign for bonding to occur in the transition state leading to product.

If the symmetries of reactant and product orbitals match up, or correlate, the reaction is said to be symmetry-allowed. If the symmetries of reactant and product orbitals don’t correlate, the reaction is symmetry-disallowed. Symmetry-allowed reactions often occur under relatively mild conditions, but symmetry-disallowed reactions can’t occur by concerted paths. Either
they take place by nonconcerted, higher-energy pathways, or they don’t take place at all.

The Woodward–Hoffmann rules for pericyclic reactions require an analysis of all reactant and product molecular orbitals, but Kenichi Fukui at Kyoto Imperial University in Japan introduced a simplified version. According to Fukui, we need to consider only two molecular orbitals, called the frontier orbitals. These frontier orbitals are the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO). In ground-state hexa-1,3,5-triene, for example, $\psi_3$ is the HOMO and $\psi_4^*$ is the LUMO (Figure 26.2). In excited-state hexa-1,3,5-triene, however, $\psi_4^*$ is the HOMO and $\psi_5^*$ is the LUMO.

**Problem 26.1**

Look at Figure 26.1, and tell which molecular orbital is the HOMO and which is the LUMO for both ground and excited states of ethylene and buta-1,3-diene.
Electrocyclic Reactions

The best way to understand how orbital symmetry affects pericyclic reactions is to look at some examples. Let’s look first at a group of polyene rearrangements called electrocyclic reactions. An electrocyclic reaction is a pericyclic process that involves the cyclization of a conjugated acyclic polyene. One \( \pi \) bond is broken, the other \( \pi \) bonds change position, a new \( \sigma \) bond is formed, and a cyclic compound results. For example, a conjugated triene can be converted into a cyclohexadiene, and a conjugated diene can be converted into a cyclobutene.

Pericyclic reactions are reversible, and the position of the equilibrium depends on the specific case. In general, the triene \( \Leftrightarrow \) cyclohexadiene equilibrium favors the cyclic product, whereas the diene \( \Leftrightarrow \) cyclobutene equilibrium favors the less strained open-chain product.

The most striking feature of electrocyclic reactions is their stereochemistry. For example, (2\( \text{E} \),4\( \text{Z} \),6\( \text{E} \))-octa-2,4,6-triene yields only cis-5,6-dimethylcyclohexa-1,3-diene when heated, and (2\( \text{E} \),4\( \text{Z} \),6\( \text{Z} \))-octa-2,4,6-triene yields only trans-5,6-dimethylcyclohexa-1,3-diene. Remarkably, however, the stereochemical results change completely when the reactions are carried out under what are called photochemical, rather than thermal, conditions. Irradiation, or photolysis, of (2\( \text{E} \),4\( \text{Z} \),6\( \text{E} \))-octa-2,4,6-triene with ultraviolet light yields trans-5,6-dimethylcyclohexa-1,3-diene (FIGURE 26.3).

A similar result is obtained for the thermal electrocyclic ring-opening of 3,4-dimethylcyclobutene. The trans isomer yields only (2\( \text{E} \),4\( \text{E} \))-hexa-2,4-diene when heated, and the cis isomer yields only (2\( \text{E} \),4\( \text{Z} \))-hexa-2,4-diene. On UV irradiation, however, the results are opposite. Cyclization of the 2\( \text{E} \),4\( \text{E} \) isomer under photochemical conditions yields cis product (FIGURE 26.4).

To account for these results, we need to look at the two outermost lobes of the polyene MOs—the lobes that interact when cyclization occurs. There are two possibilities: the lobes of like sign can be either on the same side or on opposite sides of the molecule.
For a bond to form, the outermost π lobes must rotate so that favorable bonding interaction is achieved—a positive lobe with a positive lobe or a negative lobe with a negative lobe. If two lobes of like sign are on the same side of the molecule, the two orbitals must rotate in opposite directions—one clockwise and one counterclockwise. This kind of motion is referred to as disrotatory.

Conversely, if lobes of like sign are on opposite sides of the molecule, both orbitals must rotate in the same direction, either both clockwise or both counterclockwise. This kind of motion is called conrotatory.
26-3 Stereochemistry of Thermal Electrocyclic Reactions

How can we predict whether conrotatory or disrotatory motion will occur in a given case? According to frontier orbital theory, the stereochemistry of an electrocyclic reaction is determined by the symmetry of the polyene HOMO. The electrons in the HOMO are the highest-energy, most loosely held electrons and are therefore most easily moved during reaction. For thermal reactions, the ground-state electron configuration is used to identify the HOMO; for photochemical reactions, the excited-state electron configuration is used.

Let's look again at the thermal ring-closure of conjugated trienes. According to Figure 26.2, the HOMO of a conjugated triene in its ground state has lobes of like sign on the same side of the molecule, a symmetry that predicts disrotatory ring closure. This disrotatory cyclization is exactly what is observed in the thermal cyclization of octa-2,4,6-triene. The $2E,4Z,6E$ isomer yields cis product, and the $2E,4Z,6Z$ isomer yields trans product (FIGURE 26.5).

![FIGURE 26.5 Thermal cyclizations of octa-2,4,6-trienes. The reactions occur by disrotatory ring closures.](image)

In the same way, the ground-state HOMO of conjugated dienes (Figure 26.1) has a symmetry that predicts conrotatory ring closure. In practice, however, the conjugated diene reaction can be observed only in the reverse direction (cyclobutene $\rightarrow$ diene) because of the position of the equilibrium. We therefore find that the 3,4-dimethylcyclobutene ring opens in a conrotatory fashion. cis-3,4-Dimethylcyclobutene yields $(2E,4Z)$-hexa-2,4-diene, and trans-3,4-dimethylcyclobutene yields $(2E,4E)$-hexa-2,4-diene by conrotatory opening (FIGURE 26.6).

Note that a conjugated diene and a conjugated triene react with opposite stereochemistry. The diene opens and closes by a conrotatory path, whereas
the triene opens and closes by a disrotatory path. The difference is due to the different symmetries of the diene and triene HOMOs.

It turns out that there is an alternating relationship between the number of electron pairs (double bonds) undergoing bond reorganization and the stereochemistry of ring opening or closure. Polyenes with an even number of electron pairs undergo thermal electrocyclic reactions in a conrotatory sense, whereas polyenes with an odd number of electron pairs undergo the same reactions in a disrotatory sense.

**Problem 26.2**

Draw the products you would expect from conrotatory and disrotatory cyclizations of (2E,4Z,6Z)-octa-2,4,6-triene. Which of the two paths would you expect the thermal reaction to follow?

**Problem 26.3**

trans-3,4-Dimethylcyclobutene can open by two conrotatory paths to give either (2E,4E)-hexa-2,4-diene or (2Z,4Z)-hexa-2,4-diene. Explain why both products are symmetry-allowed, and then account for the fact that only the 2E,4E isomer is obtained in practice.
26-4 **Photochemical Electrocyclic Reactions**

We noted previously that photochemical electrocyclic reactions take a different stereochemical course than their thermal counterparts, and we can now explain this difference. Ultraviolet irradiation of a polyene causes an excitation of one electron from the ground-state HOMO to the ground-state LUMO, thus changing their symmetries. But because electronic excitation changes the symmetries of HOMO and LUMO, it also changes the reaction stereochemistry. 

(2\(E\),4\(E\))-Hexa-2,4-diene, for instance, undergoes photochemical cyclization by a disrotatory path, whereas the thermal reaction is conrotatory. Similarly, (2\(E\),4\(Z\),6\(E\))-octa-2,4,6-triene undergoes photochemical cyclization by a conrotatory path, whereas the thermal reaction is disrotatory *(FIGURE 26.7)*.

**FIGURE 26.7** Photochemical cyclizations of conjugated dienes and trienes. The two processes occur with different stereochemistry because of their different orbital symmetries.

Thermal and photochemical electrocyclic reactions always take place with opposite stereochemistry because the symmetries of the frontier orbitals are always different. *TABLE 26.1* gives some simple rules that make it possible to predict the stereochemistry of electrocyclic reactions.

**TABLE 26.1** Stereochemical Rules for Electrocyclic Reactions

<table>
<thead>
<tr>
<th>Electron pairs (double bonds)</th>
<th>Thermal reaction</th>
<th>Photochemical reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Even number</td>
<td>Conrotatory</td>
<td>Disrotatory</td>
</tr>
<tr>
<td>Odd number</td>
<td>Disrotatory</td>
<td>Conrotatory</td>
</tr>
</tbody>
</table>
What product would you expect to obtain from the photochemical cyclization of (2\textit{E},4\textit{Z},6\textit{E})-octa-2,4,6-triene? Of (2\textit{E},4\textit{Z},6\textit{Z})-octa-2,4,6-triene?

26-5 Cycloaddition Reactions

A cycloaddition reaction is one in which two unsaturated molecules add to one another to yield a cyclic product. As with electrocyclic reactions, cycloadditions are controlled by the orbital symmetry of the reactants. Symmetry-allowed processes often take place readily, but symmetry-disallowed processes take place with difficulty, if at all, and then only by nonconcerted pathways. Let’s look at two examples to see how they differ.

The Diels–Alder cycloaddition reaction (Section 8-14) is a pericyclic process that takes place between a diene (four $\pi$ electrons) and a dienophile (two $\pi$ electrons) to yield a cyclohexene product. Many thousands of examples of Diels–Alder reactions are known. They often take place easily at room temperature or slightly above, and they are stereospecific with respect to substituents. For example, room-temperature reaction between buta-1,3-diene and diethyl maleate (cis) yields exclusively the cis-disubstituted cyclohexene product. A similar reaction between buta-1,3-diene and diethyl fumarate (trans) yields exclusively the trans-disubstituted product.

In contrast to the $[4+2]$-$\pi$-electron Diels–Alder reaction, the $[2+2]$-$\pi$-electron cycloaddition between two alkenes does not occur thermally. The $[2+2]$ cycloaddition takes place only on irradiation, yielding cyclobutane products.
For a successful cycloaddition to take place, the terminal \( \pi \) lobes of the two reactants must have the correct symmetry for bonding to occur. This can happen in either of two ways, called **suprafacial** and **antarafacial**. **Suprafacial** cycloadditions take place when a bonding interaction occurs between lobes on the same face of one reactant and lobes on the same face of the other reactant. **Antarafacial** cycloadditions take place when a bonding interaction occurs between lobes on the same face of one reactant and lobes on opposite faces of the other reactant (Figure 26.8).

![Figure 26.8](image)

(a) **Suprafacial**

Like lobes on same face

Like lobes on same face

or

(b) **Antarafacial**

Like lobes on opposite faces

Like lobes on same face

Twist

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Note that both suprafacial and antarafacial cycloadditions are symmetry-allowed. Geometric constraints often make antarafacial reactions difficult, however, because there must be a twisting of the \( \pi \) orbital system in one of the reactants. Thus, suprafacial cycloadditions are much more common for small \( \pi \) systems.

### 26-6 Stereochemistry of Cycloadditions

How can we predict whether a given cycloaddition reaction will occur with suprafacial or with antarafacial geometry? According to frontier orbital theory, a cycloaddition reaction takes place when a bonding interaction occurs between the HOMO of one reactant and the LUMO of the other. An intuitive
explanation of this rule is to imagine that one reactant donates electrons to the other. As with electrocyclic reactions, it’s the electrons in the HOMO of the first reactant that are least tightly held and most likely to be donated. But of course when the second reactant accepts those electrons, they must go into a vacant, unoccupied orbital—the LUMO.

For a [4 + 2] cycloaddition (Diels–Alder reaction), let’s arbitrarily select the diene LUMO and the alkene HOMO. The symmetries of the two ground-state orbitals are such that bonding of the terminal lobes can occur with suprafacial geometry (FIGURE 26.9), so the Diels–Alder reaction takes place readily under thermal conditions. Note that, as with electrocyclic reactions, we need be concerned only with the terminal lobes. For purposes of prediction, interactions among the interior lobes need not be considered.

In contrast with the thermal [4 + 2] Diels–Alder reaction, the [2 + 2] cycloaddition of two alkenes to yield a cyclobutane can only be observed photochemically. The explanation follows from orbital-symmetry arguments. Looking at the ground-state HOMO of one alkene and the LUMO of the second alkene, it’s apparent that a thermal [2 + 2] cycloaddition must take place by an antarafacial pathway (FIGURE 26.10a). Geometric constraints make the antarafacial transition state difficult, however, and so concerted thermal [2 + 2] cycloadditions are not observed. Photochemical [2 + 2] cycloadditions, however, are observed. Irradiation of an alkene with UV light excites an electron from \( \psi_1 \), the ground-state HOMO, to \( \psi_2^* \), which becomes the excited-state HOMO. Interaction between the excited-state HOMO of one alkene and the LUMO of the second alkene allows a photochemical [2 + 2] cycloaddition reaction to occur by a suprafacial pathway (FIGURE 26.10b).

The photochemical [2 + 2] cycloaddition reaction occurs smoothly, particularly with \( \alpha,\beta \)-unsaturated carbonyl compounds, and represents one of the best methods known for synthesizing cyclobutane rings. For example:

\[
\begin{align*}
\text{Cyclohex-2-enone} & \quad + \quad \text{2-Methylpropene} \\
& \quad \xrightarrow{hv} \\
& \quad \text{Cyclobutane ring}
\end{align*}
\]
Thermal and photochemical cycloaddition reactions always take place with opposite stereochemistry. As with electrocyclic reactions, we can categorize cycloadditions according to the total number of electron pairs (double bonds) involved in the rearrangement. Thus, a thermal \([4 + 2]\) Diels–Alder reaction between a diene and a dienophile involves an odd number (three) of electron pairs and takes place by a suprafacial pathway. A thermal \([2 + 2]\) reaction between two alkenes involves an even number (two) of electron pairs and must take place by an antarafacial pathway. For photochemical cyclizations, these selectivities are reversed. The general rules are given in \textbf{TABLE 26.2}.

<table>
<thead>
<tr>
<th>Electron pairs (double bonds)</th>
<th>Thermal reaction</th>
<th>Photochemical reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Even number</td>
<td>Antarafacial</td>
<td>Suprafacial</td>
</tr>
<tr>
<td>Odd number</td>
<td>Suprafacial</td>
<td>Antarafacial</td>
</tr>
</tbody>
</table>

\textbf{PROBLEM 26.5}

What stereochemistry would you expect for the product of the Diels–Alder reaction between \((2E,4E)\)-hexa-2,4-diene and ethylene? What stereochemistry would you expect if \((2E,4Z)\)-hexa-2,4-diene were used instead?
**Problem 26.6**

Cyclopenta-1,3-diene reacts with cycloheptatrienone to give the product shown. Tell what kind of reaction is involved, and explain the observed result. Is the reaction suprafacial or antarafacial?

![Chemical Structures]

**26-7 Sigmatropic Rearrangements**

A **sigmatropic rearrangement**, the third general kind of pericyclic reaction, is a process in which a $\sigma$-bonded substituent atom or group migrates across a $\pi$ electron system from one position to another. A $\sigma$ bond is broken in the reactant, the $\pi$ bonds move, and a new $\sigma$ bond is formed in the product. The $\sigma$-bonded group can be either at the end or in the middle of the $\pi$ system, as the following [1,5] and [3,3] rearrangements illustrate:

**A [1,5] sigmatropic rearrangement**

![Diagram]

**A [3,3] sigmatropic rearrangement**

![Diagram]

The notations [1,5] and [3,3] describe the kind of rearrangement that is occurring. The numbers refer to the two groups connected by the $\sigma$ bond in
the reactant and designate the positions in those groups to which migration occurs. For example, in the [1,5] sigmatropic rearrangement of a 1,3-diene, the two groups connected by the \( \sigma \) bond are a hydrogen atom and a pentadienyl group. Migration occurs to position 1 of the H group (the only possibility) and to position 5 of the pentadienyl group. In the [3,3] Claisen rearrangement of an allylic vinylic ether, the two groups connected by the \( \sigma \) bond are an allylic group and a vinylic ether group. Migration occurs to position 3 of the allylic group and also to position 3 of the vinylic ether.

Like electrocyclic reactions and cycloadditions, sigmatropic rearrangements are controlled by orbital symmetries. There are two possible modes of reaction: migration of a group across the same face of the \( \pi \) system is suprafacial, and migration of a group from one face of the \( \pi \) system to the other face is antarafacial (FIGURE 26.11).

Both suprafacial and antarafacial sigmatropic rearrangements are symmetry-allowed, but suprafacial rearrangements are often easier for geometric reasons. The rules for sigmatropic rearrangements are identical to those for cycloaddition reactions (TABLE 26.3).

<table>
<thead>
<tr>
<th>Electron pairs (double bonds)</th>
<th>Thermal reaction</th>
<th>Photochemical reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Even number</td>
<td>Antarafacial</td>
<td>Suprafacial</td>
</tr>
<tr>
<td>Odd number</td>
<td>Suprafacial</td>
<td>Antarafacial</td>
</tr>
</tbody>
</table>

TABLE 26.3 Stereochemical Rules for Sigmatropic Rearrangements
PROBLEM 26.7

Classify the following sigmatropic reaction by order \([x,y]\), and tell whether it will proceed with suprafacial or antarafacial stereochemistry:

\[
\begin{array}{c}
\text{H} \\
\text{H}
\end{array}
\quad \xrightarrow{25^\circ C} \quad \begin{array}{c}
\text{H} \\
\text{H}
\end{array}
\]

26-8 Some Examples of Sigmatropic Rearrangements

Because a [1,5] sigmatropic rearrangement involves three electron pairs (two \(\pi\) bonds and one \(\sigma\) bond), the orbital-symmetry rules in Table 26.3 predict a suprafacial reaction. In fact, the [1,5] suprafacial shift of a hydrogen atom across two double bonds of a \(\pi\) system is one of the most commonly observed of all sigmatropic rearrangements. For example, 5-methylcyclopenta-1,3-diene rapidly rearranges at room temperature to yield a mixture of 1-methyl-, 2-methyl-, and 5-methyl-substituted products.

As another example, heating 5,5,5-trideutério-(3\(Z\))-penta-1,3-diene causes scrambling of deuterium between positions 1 and 5.

Both these [1,5] hydrogen shifts occur by a symmetry-allowed suprafacial pathway, as illustrated in FIGURE 26.12. In contrast with these thermal [1,5] sigmatropic hydrogen shifts, however, thermal [1,3] hydrogen shifts are unknown. Were they to occur, they would have to proceed by a strained antarafacial reaction pathway.

Two other important sigmatropic reactions are the Cope rearrangement of a hexa-1,5-diene and the Claisen rearrangement of an aryl allyl ether or a vinyl allyl ether (Section 13-10). These two, along with the Diels–Alder reaction, are the most useful pericyclic reactions for organic synthesis; many thousands of examples of all three are known.

Both Cope and Claisen rearrangements involve reorganization of an odd number of electron pairs (two π bonds and one σ bond), and both react by suprafacial pathways (FIGURE 26.13).

As noted in Section 13-10, biological examples of pericyclic reactions are relatively rare, although one much-studied example occurs during our body’s synthesis of vitamin D. That process is discussed in the Something Extra at the end of this chapter.

**Problem 26.8**

Propose a mechanism to account for the fact that heating 1-deuterioindene scrambles the isotope label to all three positions on the five-membered ring.

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PROBLEM 26.9

When a 2,6-disubstituted allyl phenyl ether is heated in an attempted Claisen rearrangement, migration occurs to give the \( p \)-allyl product as the result of two sequential pericyclic reactions. Explain.

**A Summary of Rules for Pericyclic Reactions**

How can you keep straight all the rules about pericyclic reactions? The summary information in Tables 26.1 to 26.3 can be distilled into one mnemonic phrase that provides an easy way to predict the stereochemical outcome of any pericyclic reaction:

The Electrons Circle Around (TECA)

Thermal reactions with an Even number of electron pairs are Conrotatory or Antarafacial.
A change either from thermal to photochemical or from an even to an odd number of electron pairs changes the outcome from conrotatory/antarafacial to disrotatory/suprafacial. A change from both thermal and even to photochemical and odd causes no change because two negatives make a positive.

These selection rules are summarized in TABLE 26.4; knowing them gives you the ability to predict the stereochemistry of literally thousands of pericyclic reactions.

**TABLE 26.4 Stereochemical Rules for Pericyclic Reactions**

<table>
<thead>
<tr>
<th>Electronic state</th>
<th>Electron pairs</th>
<th>Stereochemistry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ground state (thermal)</td>
<td>Even number</td>
<td>Antara–con</td>
</tr>
<tr>
<td></td>
<td>Odd number</td>
<td>Supra–dis</td>
</tr>
<tr>
<td>Excited state (photochemical)</td>
<td>Even number</td>
<td>Supra–dis</td>
</tr>
<tr>
<td></td>
<td>Odd number</td>
<td>Antara–con</td>
</tr>
</tbody>
</table>

**PROBLEM 26.10**

Predict the stereochemistry of the following pericyclic reactions:
(a) The thermal cyclization of a conjugated tetraene
(b) The photochemical cyclization of a conjugated tetraene
(c) A photochemical [4 + 4] cycloaddition
(d) A thermal [2 + 6] cycloaddition
(e) A photochemical [3,5] sigmatropic rearrangement

**SOMETHING EXTRA**

**Vitamin D, the Sunshine Vitamin**

Vitamin D, discovered in 1918, is a general name for two related compounds, cholecalciferol (vitamin D₃) and ergocalciferol (vitamin D₂). Both are derived from steroids (Section 23-9) and differ only in the nature of the hydrocarbon side chain attached to the five-membered ring. Cholecalciferol comes primarily from dairy products and fish; ergocalciferol comes from some vegetables.
The function of vitamin D in the body is to control the calcification of bones by increasing intestinal absorption of calcium. When sufficient vitamin D is present, approximately 30% of ingested calcium is absorbed, but in the absence of vitamin D, calcium absorption falls to about 10%. A deficiency of vitamin D thus leads to poor bone growth and to the diseases rickets in children and osteoporosis in adults.

Actually, neither vitamin D2 nor D3 is present in foods. Rather, foods contain the precursor molecules 7-dehydrocholesterol and ergosterol. In the presence of sunlight, both precursors are converted in the outer, epidermal layer of skin to the active vitamins, hence the nickname for vitamin D, the “sunshine vitamin.”

Pericyclic reactions are unusual in living organisms, and the photochemical synthesis of vitamin D is one of only a few well-studied examples. The reaction takes place in two steps, an electrocyclic ring-opening of a cyclohexadiene to yield an open-chain hexatriene, followed by a sigmatropic [1,7] H shift to yield an isomeric hexatriene. Only the initial, electrocyclic ring-opening requires irradiation, with so-called UVB light of 295 to 300 nm wavelength required. The subsequent sigmatropic [1,7] H shift occurs spontaneously by a thermal isomerization.

Following synthesis under the skin, further metabolic processing of cholecalciferol and ergocalciferol in the liver and kidney introduces two additional –OH groups to give the active forms of the vitamin, calcitriol and ergocalcitriol.

A pericyclic reaction takes place in a single step through a cyclic transition state without intermediates. There are three major classes of pericyclic processes: electrocyclic reactions, cycloaddition reactions, and sigmatropic rearrangements. The stereochemistry of these reactions is controlled by the symmetry of the orbitals involved in bond reorganization.

Electroyclic reactions involve the cyclization of conjugated acyclic polyenes. For example, hexa-1,3,5-triene cyclizes to cyclohexa-1,3-diene on heating. Electroyclic reactions can occur by either conrotatory or disrotatory pathways, depending on the symmetry of the terminal lobes of the π system. Conrotatory cyclization requires that both lobes rotate in the same direction, whereas disrotatory cyclization requires that the lobes rotate in opposite directions. The reaction course in a specific case can be found by looking at the symmetry of the highest occupied molecular orbital (HOMO).
Cycloaddition reactions are those in which two unsaturated molecules add together to yield a cyclic product. For example, Diels–Alder reaction between a diene (four \( \pi \) electrons) and a dienophile (two \( \pi \) electrons) yields a cyclohexene. Cycloadditions can take place either by suprafacial or antarafacial pathways. Suprafacial cycloaddition involves interaction between lobes on the same face of one component and on the same face of the second component. Antarafacial cycloaddition involves interaction between lobes on the same face of one component and on opposite faces of the other component. The reaction course in a specific case can be found by looking at the symmetry of the HOMO of one component and the lowest unoccupied molecular orbital (LUMO) of the other component.

Sigmatropic rearrangements involve the migration of a \( \sigma \)-bonded group across a \( \pi \) electron system. For example, Claisen rearrangement of an allylic vinylcyl ether yields an unsaturated carbonyl compound, and Cope rearrangement of a hexa-1,5-diene yields an isomeric hexa-1,5-diene. Sigmatropic rearrangements can occur with either suprafacial or antarafacial stereochemistry; the selection rules for a given case are the same as those for cycloaddition reactions.

The stereochemistry of any pericyclic reaction can be predicted by counting the total number of electron pairs (bonds) involved in bond reorganization and then applying the mnemonic “The Electrons Circle Around.” That is, thermal (ground-state) reactions involving an even number of electron pairs occur with either conrotatory or antarafacial stereochemistry. Exactly the opposite rules apply to photochemical (excited-state) reactions.

**EXERCISES**

**VISUALIZING CHEMISTRY**

(Problems 26.1–26.10 appear within the chapter.)

26.11 Predict the product obtained when the following substance is heated:

![Cycloaddition Reaction](image)

26.12 The \(^{13}\text{C}\) NMR spectrum of homotropilidene taken at room temperature shows only three peaks. Explain.

![NMR Spectrum](image)
26.13 Have the following electrocyclic reactions taken place in a conrotatory or disrotatory manner? Under what conditions, thermal or photochemical, would you carry out each reaction?

(a)

(b)

26.14 The following thermal isomerization occurs under relatively mild conditions. Identify the pericyclic reactions involved, and show how the rearrangement occurs.

26.15 Would you expect the following reaction to proceed in a conrotatory or disrotatory manner? Show the stereochemistry of the cyclobutene product, and explain your answer.

26.16 Heating (1Z,3Z,5Z)-cyclonona-1,3,5-triene to 100 °C causes cyclization and formation of a bicyclic product. Is the reaction conrotatory or disrotatory? What is the stereochemical relationship of the two hydrogens at the ring junctions, cis or trans?

(1Z,3Z,5Z)-Cyclonona-1,3,5-triene
26.17 (2E,4Z,6Z,8E)-Deca-2,4,6,8-tetraene has been cyclized to give 7,8-dimethyl-
cycloocta-1,3,5-triene. Predict the manner of ring closure—conrotatory or
disrotatory—for both thermal and photochemical reactions, and predict the
stereochemistry of the product in each case.

26.18 Answer Problem 26.17 for the thermal and photochemical cyclizations
of (2E,4Z,6Z,8Z)-deca-2,4,6,8-tetraene.

26.19 The cyclohexadecaoctaene shown isomerizes to two different isomers,
depending on reaction conditions. Explain the observed results, and
indicate whether each reaction is conrotatory or disrotatory.

Cycloaddition Reactions

26.20 Which of the following reactions is more likely to occur? Explain.

26.21 The following reaction takes place in two steps, one of which is a cyclo-
addition and the other of which is a reverse cycloaddition. Identify the
two pericyclic reactions, and show how they occur.

26.22 Two sequential pericyclic reactions are involved in the following furan
synthesis. Identify them, and propose a mechanism for the trans-
formation.
**Sigmatropic Rearrangements**

26.23 Predict the product of the following pericyclic reaction. Is this [5,5] shift a suprafacial or an antarafacial process?

\[
\begin{align*}
\text{[5,5]} & \text{Heat} \\
\end{align*}
\]

26.24 Propose a pericyclic mechanism to account for the following transformation:

\[
\text{Heat} \quad \begin{align*}
\end{align*}
\]

26.25 Vinyl-substituted cyclopropanes undergo thermal rearrangement to yield cyclopentenes. Propose a mechanism for the reaction, and identify the pericyclic process involved.

\[
\text{Vinylcyclopropane} \quad \text{Cyclopentene}
\]

26.26 The following synthesis of dienones occurs readily. Propose a mechanism to account for the results, and identify the kind of pericyclic reaction involved.

\[
\text{Heat} \quad \text{Acid catalyst}
\]

26.27 Karahanaenone, a terpenoid isolated from oil of hops, has been synthesized by the thermal reaction shown. Identify the kind of pericyclic reaction, and explain how karahanaenone is formed.

\[
\text{Karahanaenone}
\]

**General Problems**

26.28 What stereochemistry—antarafacial or suprafacial—would you expect to observe in the following reactions?

(a) A photochemical [1,5] sigmatropic rearrangement

(b) A thermal [4 + 6] cycloaddition

(c) A thermal [1,7] sigmatropic rearrangement

(d) A photochemical [2 + 6] cycloaddition
26.29 The following thermal rearrangement involves two pericyclic reactions in sequence. Identify them, and propose a mechanism to account for the observed result.

\[
\begin{align*}
\text{H}_2\text{C} & \quad \text{H}_2\text{C} \\
\text{CD}_2 & \quad \text{D} \\
\text{CD}_2 & \quad \text{D} \\
\end{align*}
\]

275 °C

26.30 Bicyclohexadiene, also known as Dewar benzene, is extremely stable despite the fact that its rearrangement to benzene is energetically favored. Explain why the rearrangement is so slow.

\[
\text{Bicyclohexadiene} \xrightarrow{\text{Heat (slow)}} \text{Dewar benzene} \rightarrow \text{Benzene}
\]

26.31 Ring-opening of the trans-cyclobutene isomer shown takes place at much lower temperature than a similar ring-opening of the cis-cyclobutene isomer. Explain the temperature effect, and identify the stereochemistry of each reaction as either conrotatory or disrotatory.

26.32 Photolysis of the cis-cyclobutene isomer in Problem 26.31 yields cis-cyclododecaen-7-yne, but photolysis of the trans isomer yields trans-cyclododecaen-7-yne. Explain these results, and identify the type and stereochemistry of the pericyclic reaction.

26.33 The \(^1\)H NMR spectrum of bullvalene at 100 °C consists only of a single peak at 4.22 δ. Explain.
26.34 The following rearrangement was devised and carried out to prove the stereochemistry of [1,5] sigmatropic hydrogen shifts. Explain how the observed result confirms the predictions of orbital symmetry.

26.35 The following reaction is an example of a [2,3] sigmatropic rearrangement. Would you expect the reaction to be suprafacial or antarafacial? Explain.

26.36 When the compound having a cyclobutene fused to a five-membered ring is heated, (1Z,3Z)-cyclohepta-1,3-diene is formed. When the related compound having a cyclobutene fused to an eight-membered ring is heated, however, (1E,3Z)-cyclodeca-1,3-diene is formed. Explain these results, and suggest a reason why opening of the eight-membered ring occurs at a lower temperature.

26.37 In light of your answer to Problem 26.36, explain why a mixture of products occurs in the following reaction:

26.38 The sex hormone estrone has been synthesized by a route that involves the following step. Identify the pericyclic reactions involved, and propose a mechanism.
26.39 Coronafacic acid, a bacterial toxin, was synthesized using a key step that involves three sequential pericyclic reactions. Identify them, and propose a mechanism for the overall transformation. How would you complete the synthesis?

26.40 The following rearrangement of \( N\)-allyl-\( N\),\( N\)-dimethylanilinium ion \( \text{has been observed. Propose a mechanism.} \)

26.41 Plastic photochromic sunglasses are based on the following reversible rearrangement of a dye inside the lenses that occurs when the lenses are exposed to sunlight. The original dye absorbs UV light but not visible light and is thus colorless, while the rearrangement product absorbs visible light and is thus darkened.

(a) Show the mechanism of the rearrangement.
(b) Why does the rearrangement product absorb at a longer wavelength (visible light) than the original dye (UV)?