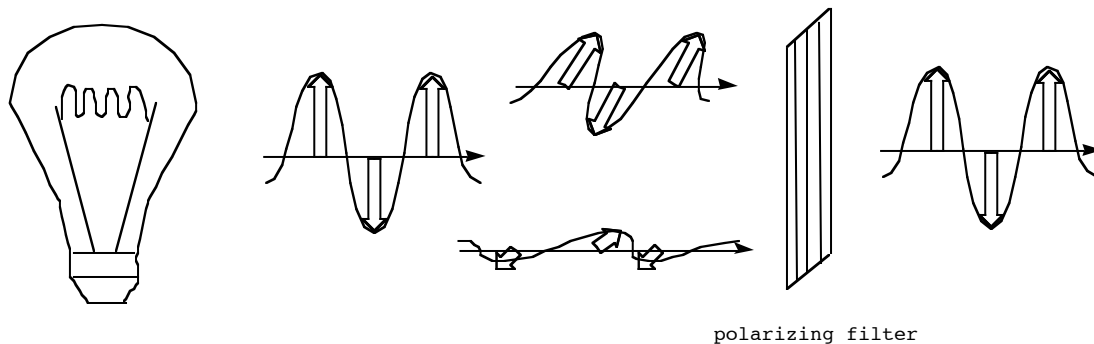


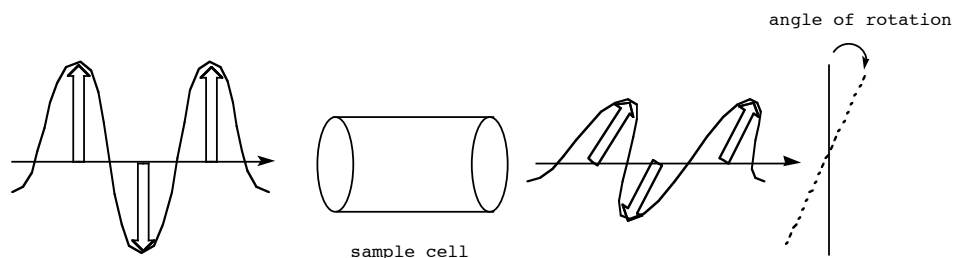
Optical activity

The physical basis of optical activity

A photon is associated with an electric vector and a magnetic vector that oscillate in planes perpendicular to each other and perpendicular to the direction of propagation of that photon, that is, if the photon is moving in the x direction, its electric vector oscillates in the y direction and its magnetic vector oscillates in the z direction. A beam of ordinary light propagating in the x direction consists of many photons whose electric vectors oscillate in planes that are random with respect to each other. The figure below shows photons of ordinary light propagating left to right and their associated oscillating electric vectors: some electric vectors oscillate in the plane of the paper, whereas others at an angle to the plane of the paper. If the light passes through a polarizing filter (e.g., a sheet of Mylar plastic), only those photons whose electric vector oscillates in one specific plane emerge; the filter absorbs all other photons:



The light that emerges from a polarizing filter is called plane-polarized or, simply, polarized light. If the plane of polarized light is rotated upon passing through a solution contained in a sample cell, the sample is said to be optically active:



When the experiment is performed under a set of standard conditions of temperature, solution concentration, sample-cell size, and nature of polarized light, the angle in degrees through which the plane of polarized light is rotated is denoted by the specific rotation $[\alpha]$. Some samples rotate the plane of polarized light in the clockwise direction: such samples are said to be dextrorotary and are denoted by the symbol (+). Some samples rotate the plane of polarized light in the counterclockwise direction: such samples are said to be levorotary and are denoted by the symbol (-).

Only chiral molecules rotate the plane of polarized light. Furthermore, enantiomers rotate the plane of polarized light in equal but opposite directions, that is, enantiomers have equal but opposite specific rotations. For example, (*R*)-2-bromobutane has $[\alpha] = -23^\circ$ and (*S*)-2-bromobutane has $[\alpha] = +23^\circ$. Thus, (*R*)-2-bromobutane is referred to as (-)-2-bromobutane or (-)-(*R*)-2-bromobutane whereas (*S*)-2-bromobutane is referred to as (+)-2-bromobutane or (+)-(*S*)-2-bromobutane.

There is no simple connection between the sign of the specific rotation and the absolute configuration of the molecule. Some (*R*) enantiomers are (+) whereas others are (-); likewise, some (*S*) enantiomers are (+) whereas others are (-).

Analytical uses of optical activity

Racemic mixtures

Suppose you have a 50–50 mixture of (-)-(*R*)- ($[\alpha] = -23^\circ$) and (+)-(*S*)-2-bromobutane ($[\alpha] = +23^\circ$). Such a mixture, called a racemic mixture or a racemate, exhibits no optical activity because every clockwise rotation of the plane of polarized light caused by a (+)-(*S*)-2-bromobutane molecule is counteracted by an equal counter-clockwise rotation by a (-)-(*R*)-2-bromobutane molecule. A racemic mixture is denoted by the symbol (\pm), for example, (\pm)-2-bromobutane refers to a 50–50 mixture of (+)-(*S*)- and (-)-(*R*)-2-bromobutane.

Enantiomeric excess

Now let's suppose you have a mixture of (-)-(*R*)-2-bromobutane ($[\alpha] = -23^\circ$) and (+)-(*S*)-2-bromobutane ($[\alpha] = +23^\circ$) in which there is more (-)-(*R*)- than (+)-(*S*)-2-bromobutane. Such a mixture exhibits optical activity: the (-)-(*R*)-2-bromobutane molecules rotate the plane of polarized light in the counter-

clockwise direction, but there are not enough (+)-(*S*)-2-bromobutane molecules to counteract the rotation.

This is an important conclusion: in order for a sample to exhibit optical activity, there must be an excess of one enantiomer present in the sample. It follows, then, that a sample consisting of achiral molecules (e.g., benzene) cannot be optically active because an achiral molecule doesn't have an enantiomer: how could there be an excess of something that doesn't exist?

The percentage of one enantiomer in a mixture of two enantiomers is given by the formula

$$\left(1 + \frac{[\alpha]_{mix}}{[\alpha]_{pure}}\right) \times 50\%$$

where $[\alpha]_{mix}$ is the observed rotation of the mixture and $[\alpha]_{pure}$ is the specific rotation of that pure enantiomer. The difference in percent between the two enantiomers is called the enantiomeric excess.

Problem A mixture of (-)-(*R*)- ($[\alpha] = -23^\circ$) and (+)-(*S*)-2-bromobutane ($[\alpha] = +23^\circ$) exhibits a rotation $[\alpha]_{mix}$ of -17° . Calculate the percentage of each enantiomer in the mixture and the enantiomeric excess.

Answer For (+)-(*S*)-2-bromobutane, $[\alpha]_{pure} = +23^\circ$, so

$$\left(1 + \frac{[\alpha]_{mix}}{[\alpha]_{pure}}\right) \times 50\% = \left(1 + \frac{-17^\circ}{+23^\circ}\right) \times 50\% = 13\%$$

For (-)-(*R*)-2-bromobutane, $[\alpha]_{pure} = -23^\circ$, so

$$\left(1 + \frac{[\alpha]_{mix}}{[\alpha]_{pure}}\right) \times 50\% = \left(1 + \frac{-17^\circ}{-23^\circ}\right) \times 50\% = 87\%$$

The enantiomeric excess is $87\% - 13\% = 74\%$ in favor of (-)-(*R*)-2-bromobutane.

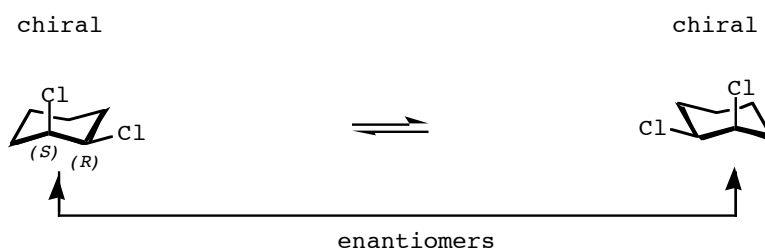
Problem Pure (+)-penicillin has $[\alpha] = +233^\circ$. Calculate the percent of (-)-penicillin in a mixture of (+)- and (-)-penicillin that has $[\alpha]_{mix} = -23.3^\circ$.

Answer If (+)-penicillin has $[\alpha] = +233^\circ$, then (-)-penicillin has $[\alpha] = -233^\circ$. Substituting values gives

$$\begin{aligned}
 \% (-)\text{-penicillin} &= \left(1 + \frac{[\alpha]_{mix}}{[\alpha]_{pure}} \right) \times 50\% \\
 &= \left(1 + \frac{-23.3^\circ}{-233^\circ} \right) \times 50\% \\
 &= 55\%
 \end{aligned}$$

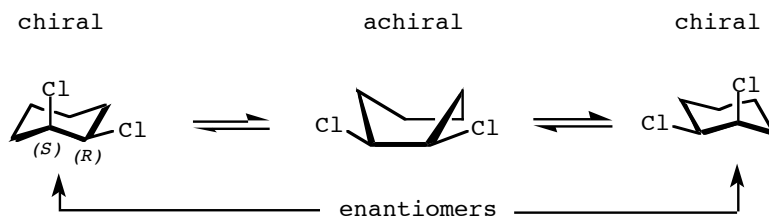
Meso compounds

(1*R*,2*S*)-1,2-Dichlorocyclohexane exists as a pair of chair conformations:

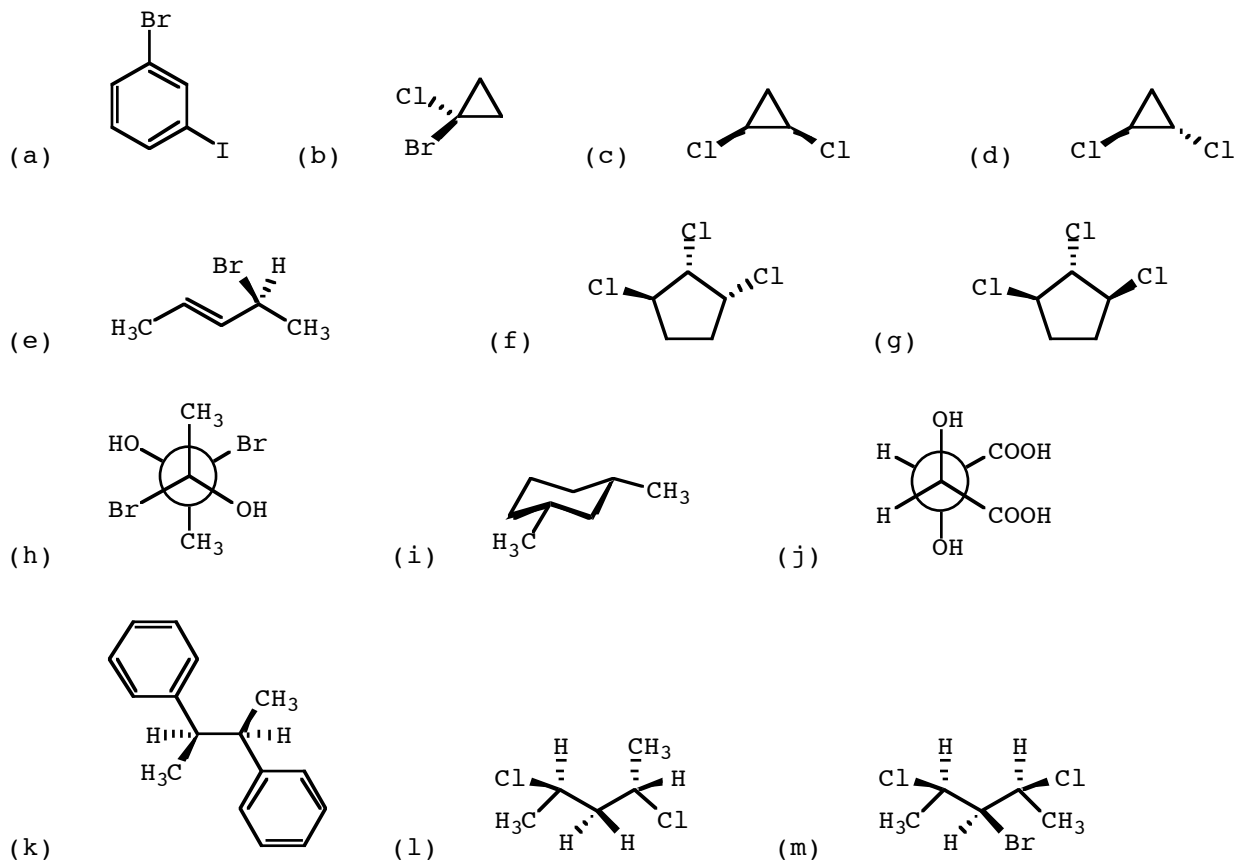


Both (1*R*,2*S*)-1,2-dichlorocyclohexane chairs are chiral: neither has a center of symmetry or a plane of symmetry. However, as we hope that you perceive from the drawing above, the two chairs are also enantiomers of each other. In order for a sample to exhibit optical activity, there must be an excess of one enantiomer present in that sample, but this is not the case with a sample of (1*R*,2*S*)-1,2-dichlorocyclohexane. If we were to go through a conformational analysis of each chair, we would find that they have the same value of *Estrain*: both have two Cl-H 1,3-diaxial interactions and one Cl-Cl *gauche* interaction. Because the energy of both chairs is the same, there will be equal numbers of both chairs. Thus, there is no excess of one enantiomer and the sample is not optically active.

(1*R*,2*S*)-1,2-Dichlorocyclohexane is an example of a *meso* compound. To qualify as a *meso* compound, a molecule must have more than one chirality center and must be able to adopt at least one achiral conformation. In the case of (1*R*,2*S*)-1,2-dichlorocyclohexane, that achiral conformation is the boat, which has a plane of symmetry:



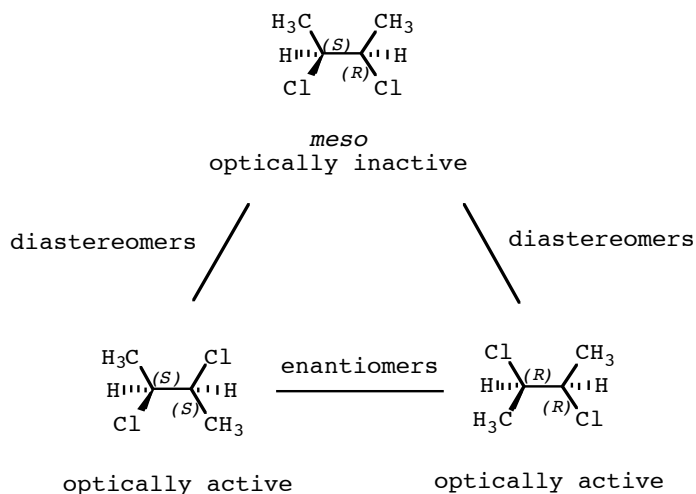
Problem Identify the *meso* compounds.



Answer (c), (g), (h), (i), (l), (m)

Problem (a) Draw the structure of *meso*-2,3-dichlorobutane; clearly show stereochemistry using dashing and wedging. Determine the absolute configuration of all chirality centers in the molecule. (b) *meso*-2,3-Dichlorobutane has two optically active stereoisomers: draw their structures, clearly showing stereochemistry using dashing and wedging. (c) Determine how each stereoisomer is related to the other two.

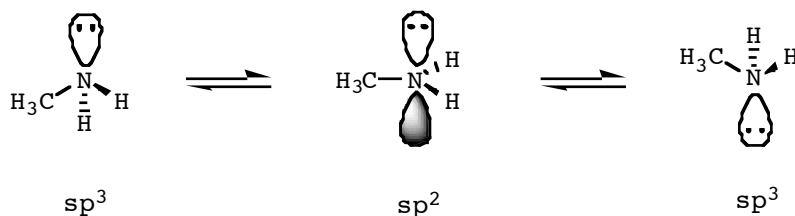
Answer



The Walden inversion of amine nitrogens

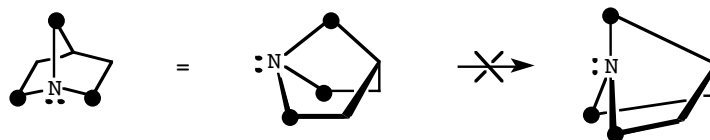
Some amine nitrogen atoms undergo a curious flip called the Walden inversion ("Walden" is the anglicized name of the Latvian chemist Pauls Valdens who discovered the process in 1896). In order for an amine nitrogen to undergo the Walden inversion, that amine nitrogen must (1) be sp^3 hybridized, (2) bear an unshared electron pair, and (3) be able to become coplanar with the three atoms to which it is bonded.

Consider the nitrogen atom in 1-methanamine (CH_3NH_2). The nitrogen is sp^3 hybridized, it has an unshared electron pair, and there is no steric impediment preventing it from becoming coplanar with the three atoms to which it is bonded. As the nitrogen atom undergoes the Walden inversion, it becomes sp^2 hybridized for about 10^{-14} s, and then assumes its original sp^3 hybridization once again:

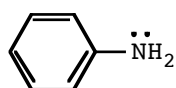


The activation energy barrier to the process is only about 10 kJ/mol. Thus, the Walden inversion is unimaginably fast at room temperature: methanamine undergoes about 10^{11} inversion per second. Even at 77 K, methanamine inverts about 10^6 times per second.

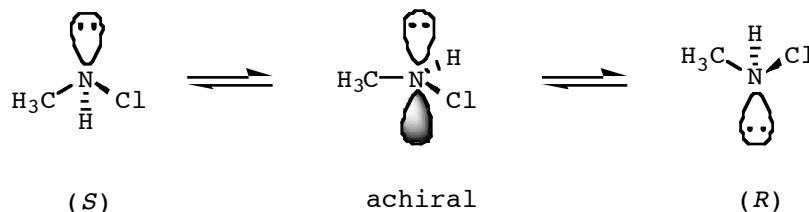
The nitrogen atom in the molecule shown below does not undergo the Walden inversion because the three carbon atoms bonded to the nitrogen are locked rigidly in place and cannot ever lie in the same plane as the amine nitrogen:



Still another example of a nitrogen atom that does not undergo the Walden inversion is the nitrogen atom in 1-benzenamine (nickname "aniline") because it is sp^2 hybridized to take advantage of resonance with the benzene ring:

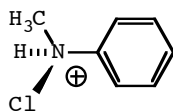


When an amine nitrogen that can undergo the Walden inversion is a chirality center, as in *N*-chloro-1-methanamine, the Walden inversion results in the inversion of the absolute configuration at that nitrogen:



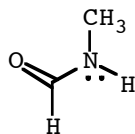
Thus, a sample of *N*-chloromethanamine does not exhibit optical activity because such a sample consists of equal amounts of two enantiomers.

Problem Is a sample of the compound below optically active?



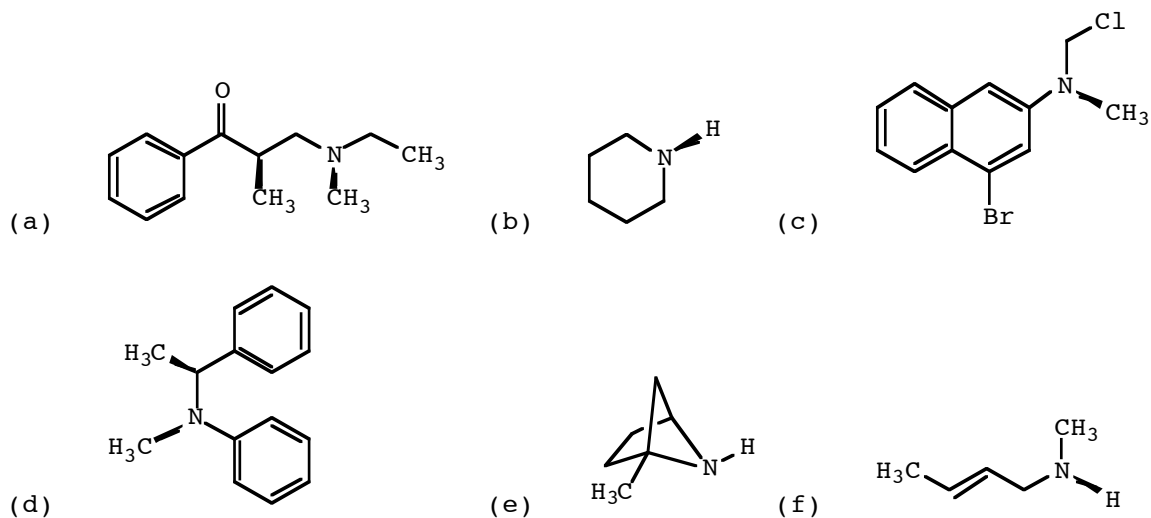
Answer Yes. The molecule is chiral (it has one and only one chirality center) and its sp^3 hybridized nitrogen atom doesn't have an unshared electron pair, so the Walden inversion cannot happen. A sample of the compound is optically active because that sample does not consist of a mixture of two enantiomers.

Problem Is a sample of the compound below optically active?



Answer No. The nitrogen atom is an amide nitrogen and is sp^2 hybridized because it is enjoying resonance with the neighboring carbon–oxygen double bond, so the Walden inversion doesn't happen.

Problem Identify the compounds that exhibit optical activity.



Answer (a), (d), (e)