Optical activity in absence of chiral carbon (biphenyls)

By
Ambedkar Kumar Verma
Assistant Professor (Guest Faculty)
Dept. Of Chemistry
Araria College Araria

PURNEA UNIVERSITY, Purnia
Course Contents

- Optical activity in absence of chiral carbon (biphenyls)
Introduction to Bi-phenyl

- **Atropisomerism**

Atropisomers can be defined as isomers that can be isolated due to prevention or restriction of rotation about a given single bond, usually between two planar moieties. The term atropisomerism comes from the words α, Greek for not, and τρόπος, Greek for turn.

- If bulky group on ortho position of bi-phenyl or strained ring structural features. Bulky substituents or strained rings may enhance the barrier to rotation between two distinct conformations to such an extent as to allow observation of atropisomers.
Atropisomerism is also called axial chirality and the chirality is not simply a centre or a plane but an axis. As the phenomenon of axial chirality relies on the rotational stability about a single bond, the important preconditions for this stability will be discussed in this Section. Simple biphenyl can easily rotate by C-C bond and it is symmetric so simple biphenyl is achiral (Figure 1). C-C sigma bond is known as pivotal bond.
• Biphenyl substituted on ortho position in molecule 1 (Figure 2), which contains a chiral axis along the biphenyl linkage. The biphenyl rings are perpendicular to each other in order to minimize steric clashes between the four ortho substituents meaning that rotation about the biphenyl bond through pivotal bond is restricted.

• The interconversion between the two isomers is restricted (slow) therefore two isomers are separate entities, and can resolved to its separate enantiomers. The first chirality due to restricted rotation about a single bond was described by Christie and Kenner in 1922, they successfully resolved the enantiomers of 6,6'-dinitrobi phenyl-2,2'-dicarboxylic acid.

Fig. 2. Enantiomers of the 6,6'-dinitrobi phenyl-2,2'-dicarboxylic acid
Atropisomerism is not a phenomenon restricted to biphenyls and other many systems from t-alkyl-tryptycyls to binaphthyls exhibiting atropisomerism. A classic example of an atropisomeric binaphthyl is the ligand BINAP (2), the development of which earned Noyori a share of the Nobel Prize for Chemistry in 2001. Once the atropisomers have been separated, BINAP can be used as a chiral catalyst for the asymmetric hydrogenation of C=C and C=O bonds (Figure 3).
Conditions of Atropisomerism:

1. Two necessary preconditions for axial chirality are:
   • (a) A rotationally stable axis
   • (b) Presence of different substituents on both sides of the axis

2. Atropisomers are recognized as physically separable species when, at a given temperature, they have a half-life of at least 1000 s (16.7 min) [1000 s].

3. The minimum required free energy barriers at different temperature are as below.
   \[ \Delta G_{200K} = 61.6 \text{ kJmol}^{-1} \]
   \[ \Delta G_{300K} = 93.5 \text{ kJmol}^{-1} \]
   \[ \Delta G_{350K} = 109 \text{ kJmol}^{-1} \]
4. The configurational stability of axially chiral biaryl compounds is mainly determined by three following factors:

• i. The combined steric demand of the substituent in the combined steric demand of the substituents in the proximity of the axis.
• ii. The existence, length and rigidity of bridges.
• iii. Atropisomerisation mechanism different from a merely physical rotation about the axis, e.g. photochemically or chemically induced processes.
Biaryl Atropisomers classified into two categories is based upon the basic structure of the biaryl atropisomers

(I) Atropisomerism in Non-bridged Biphenyls

Biphenyl is an aromatic hydrocarbon with a molecular formula \((\text{C}_6\text{H}_5)_2\). It is notable as a starting material for the production of polychlorinated biphenyls (PCBs), which were once widely used as dielectric fluids and heat transfer agents.
Biphenyl is also used as an intermediate for the production of the organic compounds like emulsifiers, optical brighteners, crop protection products, and plastics. Biphenyl is insoluble in water, but soluble in typical organic solvents. Biphenyl is insoluble in water, but soluble in typical organic solvents. The biphenyl molecule consists of two connected phenyl rings. Biphenyl’s ortho positions are substituted with two different bulky groups makes it chiral and resolvable due restricted rotation through pivotal bond.
(II) Stereochemistry of Biphenyls

• Biphenyl does not show geometrical isomerism, it shows conformational isomerism the rotation around the single bond is possible in biphenyls and especially their ortho- substituted derivatives are sterically hindered. For this reason, some substituted biphenyls show atropisomerism that is the individual C2-symmetric-isomers are optically stable.

• Some derivatives, as well as related molecules such as BINAP, find application as ligands in asymmetric synthesis. In the case of unsubstituted biphenyl, the equilibrium torsional angle is 44.4° and the torsional barriers are quite small, 6.0 kJ/mol at 0° and 6.5 kJ/mol at 90°. Adding ortho substituents greatly increases the barrier: in the case of the 2, 2'-dimethyl derivative, the barrier is 17.4 kcal/mol (72.8 kJ/mol).
• The below given compound (3) can resolvable at room temperature

\[ \text{Fig. 4: Adding } ortho \text{ substituents greatly increases the barrier: in the case of the 2, 2'}-\text{dimethyl derivative.} \]
Conditions for biphenyls to be enantiomeric or resolvable:

• 1. The planes of two aryl groups must be non-planar. This can be done by introducing bulky groups in the ortho positions so that the planar conformations are destabilized due to steric repulsion (Figure 5).

\[
\begin{align*}
\text{Fig. 5: Non planarity can be introduced by placing bulky groups in the ortho positions.}
\end{align*}
\]

1. Most of tetra substituted biphenyls (A, B, C, D \( \neq \) H) can be resolved and quite stable to racemization at least two of the groups are fluorine or methoxy.
2. Ortho substituent increases the restricted rotation through pivotal bond (atropisomerism) in non-bridged biaryl compounds by their steric repulsion. If the Van der Walls radiiuses of the substituents are more than hydrogen atom rotation through pivotal bond will be restricted and molecule will show the atropisomerism. The Van der Walls radius I > Br > Cl > NO2 > COOH > OMe > F > H (Figure 6).

![Diagram](image)

**Fig. 6:** Ortho substituent increases the restricted rotation through pivotal bond (atropisomerism) in non-bridged biaryl compounds by their steric repulsion
3. Mono ortho substituted biaryl compounds do not form stable atropisomer at room temperature. This type (4 and 5) of compound show atropisomerism if both substituents are bulky (Figure 7).

(Figure 7).

4. In addition to the bulk of the ortho substituents, the nature and position of other substituents in the ring play some role in configuration stability of the atropisomers. The bulky groups adjacent to the ortho substituents exert a buttressing effect. The buttressing effect of the some of the groups are in the following order: NO2>Br>Cl>Me
Thank you