

STEREOCHEMISTRY II

SEM-1, CC-1B

PART-9, PPT-9

Part-9: Configuration-II

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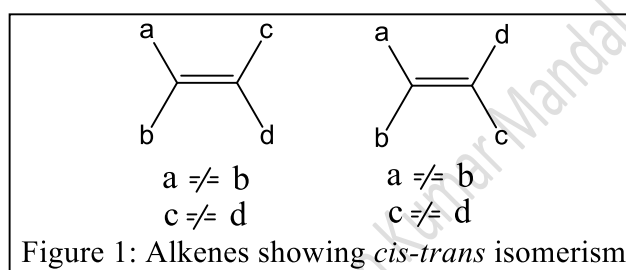
Stereochemistry (PART-9, PPT-9)

Configuration-II

Structure of Alkenes: Nature of *cis-trans* Isomerism

In most alkenes (olefins), the two double-bonded carbon atoms and the four additional ligands attached to them are coplanar (Figure 1). The generally accepted orbital description involves sp^2 hybridized carbon atoms. The carbon atoms are linked to each other and to the attached ligands (a, b and c, d, respectively) by sp^2 hybridized σ bonds, and they are further linked to a π bond formed by lateral overlap of the remaining p orbitals of the two carbon atoms.

The necessary and sufficient condition for *cis-trans* isomers to exist is that one substituent at each end of the double bond must be nonequivalent; referring to Figure 1 this means $a \neq b$ and $c \neq d$.



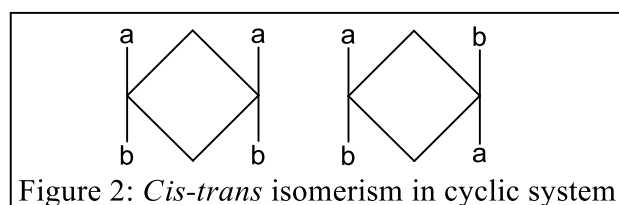
There are no restrictions as to the identity of a, b with c, d; thus $Cab=Cab$ displays *cis-trans* isomerism. The other conditions for *cis-trans* isomerism are implicit. One condition is that the torsion angles $a-C-C-c$, $a-C-C-d$, $b-C-C-c$, and $b-C-C-d$ be near 0° or near 180° (i.e., that the alkene be planar or near-planar) and the second condition is that the barrier for interconversion of the *cis-trans* isomers be high enough for these isomers to be distinguishable entities.

Both of these conditions are generally fulfilled with alkenes. The rotational barriers in alkenes are very much higher than those in alkanes [e.g., $3.6 \text{ kcal mol}^{-1}$ (15.1 kJ mol^{-1}) for the central C-C bond in butane].

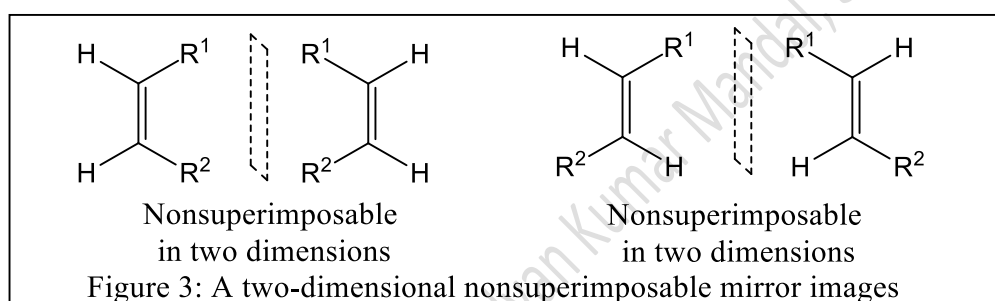
Nature of *cis-trans* Isomerism

Whereas the C-C σ bond energy is about 83 kcal mol^{-1} , the strength of the π bond, with its less favorable lateral overlap, is only 60 kcal mol^{-1} . These two energies add up to the generally accepted total energy of a C=C double bond, $143 \text{ kcal mol}^{-1}$. The activation barrier (E_a) to the thermal isomerization of 2-butene (Figure 1, $Z \rightleftharpoons E$, $a = c = \text{CH}_3$, $b = d = \text{H}$), is $\sim 62 \text{ kcal mol}^{-1}$. In the case of $Cab=Nx$ (for oximes, hydrazones and for semicarbazones), or $Nx=Nx$ (for diazo compounds), the missing substituent is the lone pair of electrons on nitrogen.

Since this isomerism owes its existence to the presence of a π -bond, it has been called π -diastereomerism to distinguish it from σ -diastereomerism exhibited by cyclic compounds (Figure 2).



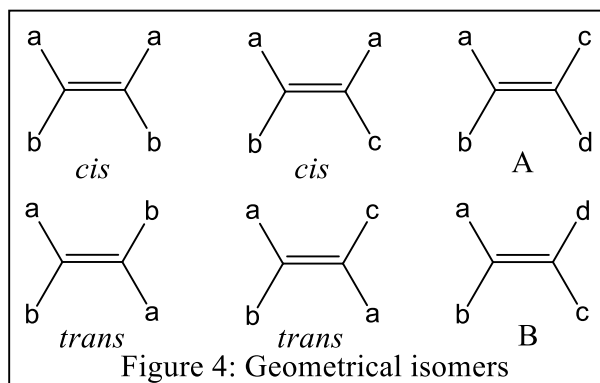
cis-trans Isomerism (sometimes called geometric isomerism) is a type of diastereomerism. The *cis*- and *trans*-isomers are not mirror image stereoisomers (Figure 3). Therefore, they can be considered as two-dimensional enantiomers having a two-dimensional nonsuperimposable mirror images which are produced by reflection, within the plane of the paper, through a straight line which represents a two-dimensional mirror.



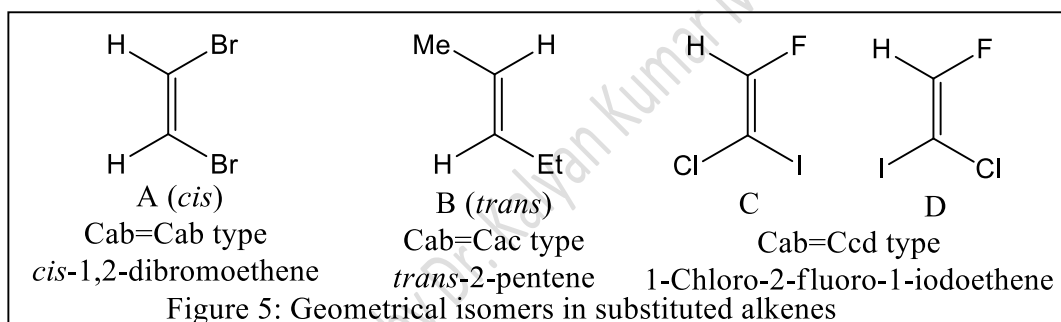
Both the *cis*- and *trans*-isomers of but-2-ene have the same bonding connectivity of atoms but the spatial arrangement around the rigid C=C bond, in each case, is different. They are diastereoisomers. When $R^1 = R^2$, (say, *cis*-but-2-ene) then *cis*-alkene represents a two-dimensional *meso*-compound and *trans*-alkene is two-dimensionally *chiral*. However, in three-dimensions both are *achiral* molecules.

The π -diastereomers are two-dimensional molecules (if one ignores the geometry of the 'a' and 'b' groups), possess a plane of symmetry, and therefore are *achiral*. On the other hand, σ -diastereomers are three-dimensional and may be *chiral*. Since, in general, the plane of the double bond is a plane of symmetry, geometrically isomeric olefins do not usually show optical activity. An exception occurs in compounds that contain asymmetric atoms (or other source of dissymmetry) in addition to the double bond.

For alkenes of the type, Cab=Cab or Cab=Cac, the terms '*cis*' and '*trans*' are adequate and unambiguous. But if three or four of the substituents are different (of the type Cab=Ccd), this nomenclature leads to ambiguity and sometimes to total confusion. In the first two cases (i.e., for alkenes of the types Cab=Cab and Cab=Cac), where at least one group attached to one olefinic carbon is equal to one attached to the other olefinic carbon, the geometrical isomers are distinguished by the prefixes "*cis*" and "*trans*". *cis* being used when the two identical groups are on the same side and *trans* when they are on the opposite sides. The prefixes "*cis*" and "*trans*" are from Latin: "this side of" and "the other side of", respectively.



cis- and *trans*- configurational nomenclature is not applicable to alkenes in which all the four ligands attached to the double bonded carbon atoms are different. For example, 1-chloro-2-fluoro-1-iodoethene has two isomers C and D (Figure 5) but they are difficult to be name as *cis*- and *trans*-isomers. In fact, no suitable general symbolism is developed to name such compounds. When the groups 'a' and 'c' are more alike than 'a' and 'd' or 'b' and 'c' (e.g., if 'a' is methyl, 'c' ethyl, 'b' hydrogen, and 'd' halogen). A (Figure 4) may be called the *cis* isomer and B the *trans* isomer.

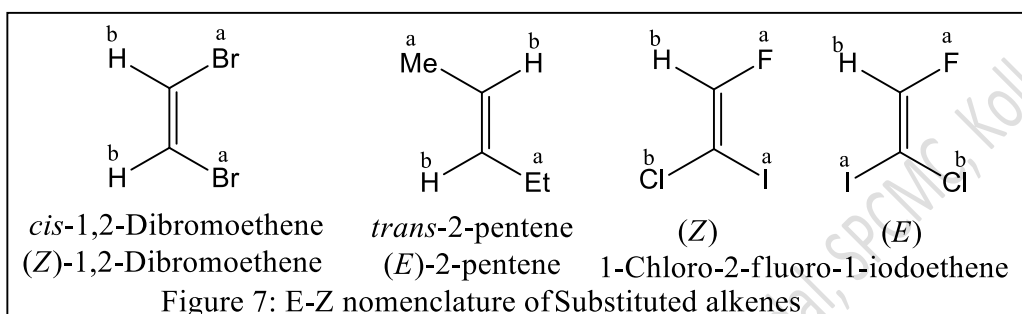
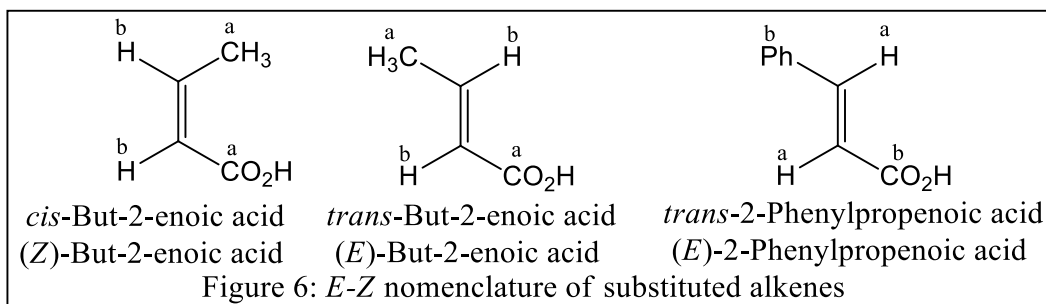


***E/Z* Configurational Nomenclature**

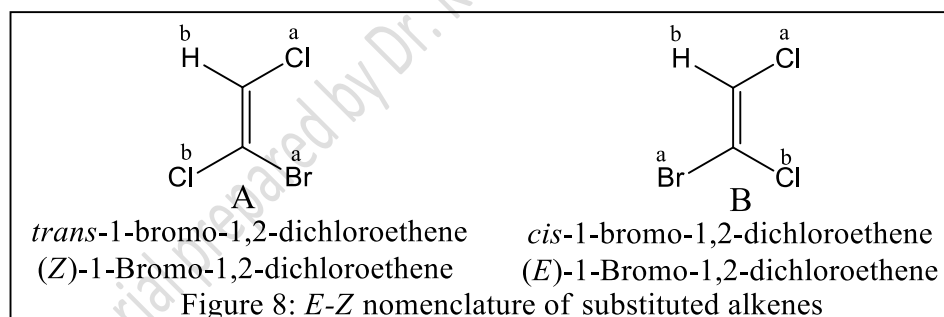
An easy solution to the problem in naming of alkenes with different substituents at the double bond is provided by arranging the pair of ligands at each trigonal carbon in CIP sequence. Then if the groups of higher priority are on the same side, the configuration is *seq-cis* (*sequential-cis*); if they are on the opposite sides, the configuration is *seq-trans* (*sequential-trans*) (CIP 1966).

Later, the system has been modified (Blackwood et al., 1968), the terms being replaced by two shorter symbols '*Z*' (from German *zusammen* meaning 'together') and '*E*' (from German *entgegen* meaning 'opposite'). The two arrangements shown in Figure 6 are called '*Z*' and '*E*' depending on whether the atoms of highest priority in the Cahn-Ingold-Prelog sequence are on the same side or on opposite sides of the double bond.

The descriptors *E* and *Z* are always italicized. When the descriptor (*E* or *Z*) is part of a name, it is placed in parentheses in front of the name followed by a hyphen.



E, *Z* nomenclature is more meaningful than *cis-trans* nomenclature because it is applicable to all cases and is free from ambiguity. It is important to realize that in cases where *cis* and *trans* can be used, *Z* does not always correspond to *cis* and *E* does not necessarily correspond to *trans*. Thus, structures A and B in Figure 8 are called (Z)-1-bromo-1,2-dichloroethene and (E)-1-bromo-1,2-dichloroethene, respectively. Here, atoms of higher priority on each of the olefinic carbons determine the type of descriptors.

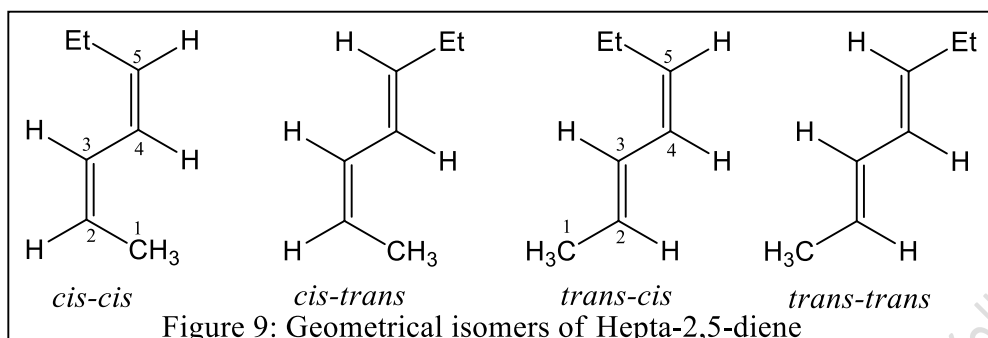


Cis-trans Isomers in Polyenes

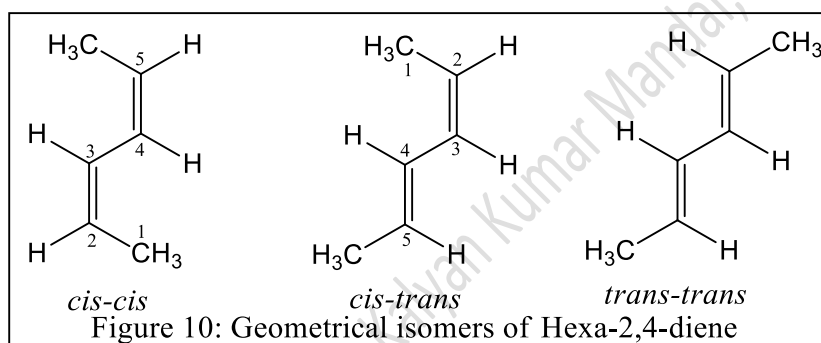
When there is more than one double bond fulfilling the condition for geometrical isomerism in a molecule, the number of geometrical isomers increases by a factor of 2 for each such double bond. Thus, a structure with n different double bonds may exist in 2^n geometrically isomeric forms. This formula is applicable to polyenes (terminal substituents are different) of the type $R^1-(CH=CH)_n-R^2$. Therefore, in case of polyenes capable of showing *cis-trans* isomerism, the number of diastereomers is 2^n , where n is the number of double bonds.

If the general formula of the polyene is $R-(CH=CH)_n-R$ (terminal substituents are identical), then the number of geometrical isomers is $(2^{n-1} + 2^{p-1})$, where $p = n/2$ when n is even, and $p = (n + 1)/2$ when n is odd. Dienes of the type $R^1-CH=CH-CH=CH-R^2$, with terminal

substituents different exist in $2^2 (= 4)$ geometrically isomeric forms. Figure 9 shows all the diastereomers of hepta-2,5-diene.

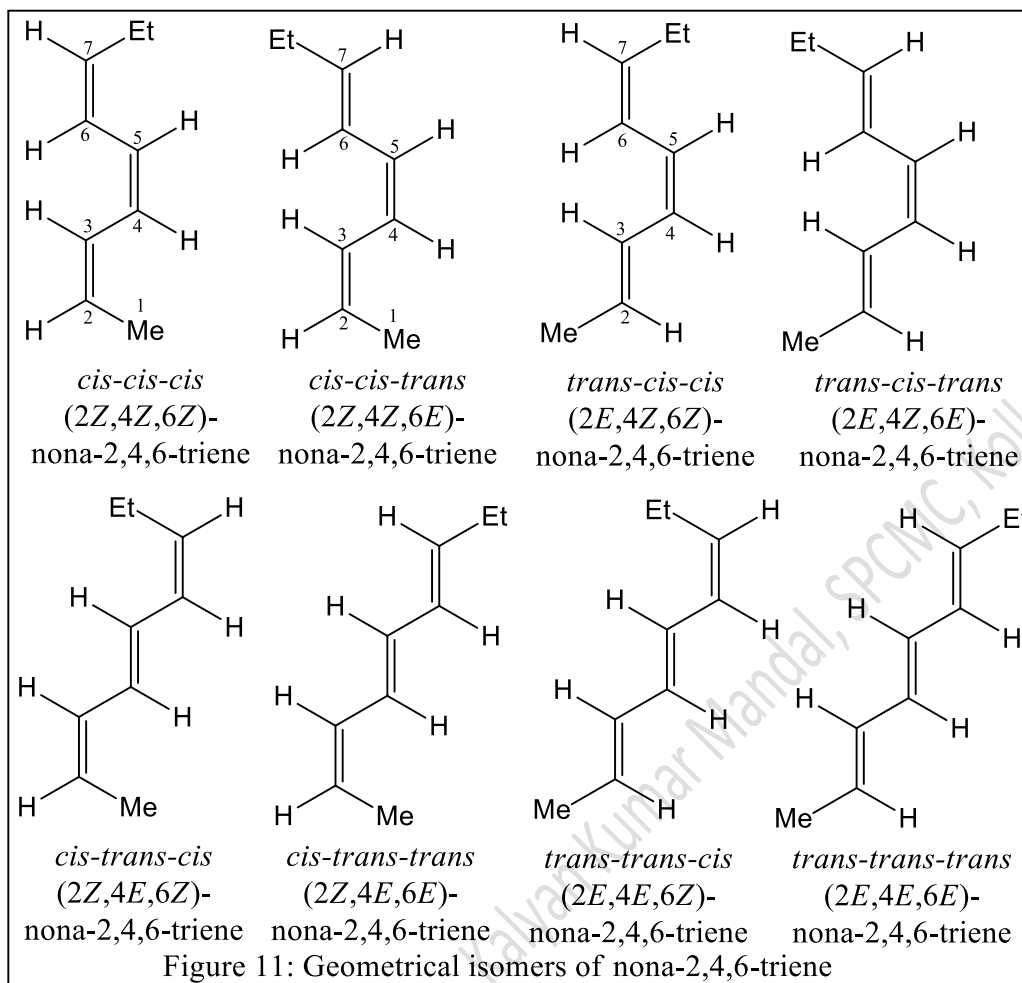


On the other hand, dienes of the type $R-CH=CH-CH=CH-R$, with terminal substituents identical exist in $3 (= 2^{2-1} + 2^{2/2-1} = 2 + 1)$ geometrically isomeric forms. Figure 10 shows all the diastereomers of hexa-2,4-diene.



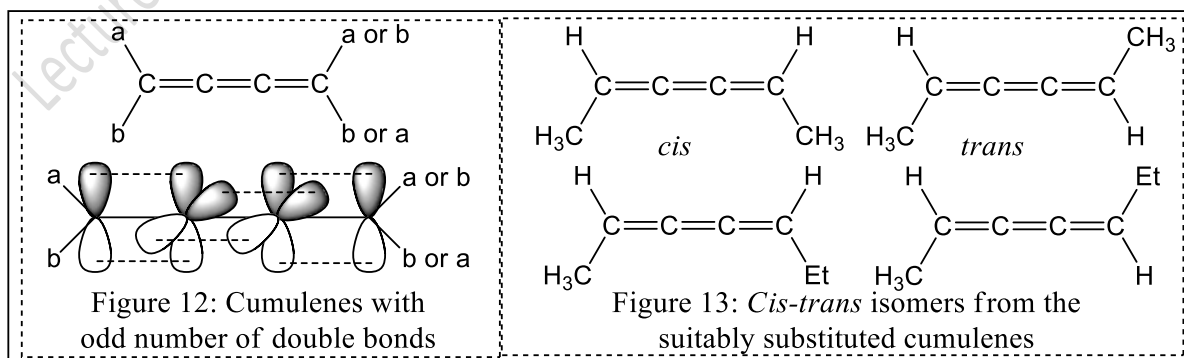
- For trienes $H_3C-CH=CH-CH=CH-CH=CH-C_2H_5$, number of geometrical isomers $= 2^3 = 8$. Figure 11 shows all the diastereomers of nona-2,4,6-triene.
- For trienes $H_3C-CH=CH-CH=CH-CH=CH-CH_3$, number of geometrical isomers $= 2^{3-1} + 2^{\{(3+1)/2\}-1} = 4 + 2 = 6$.

Home-work: Draw all the diastereomers of octa-2,4,6-triene and designate them as *cis-trans* and *E-Z* isomers.



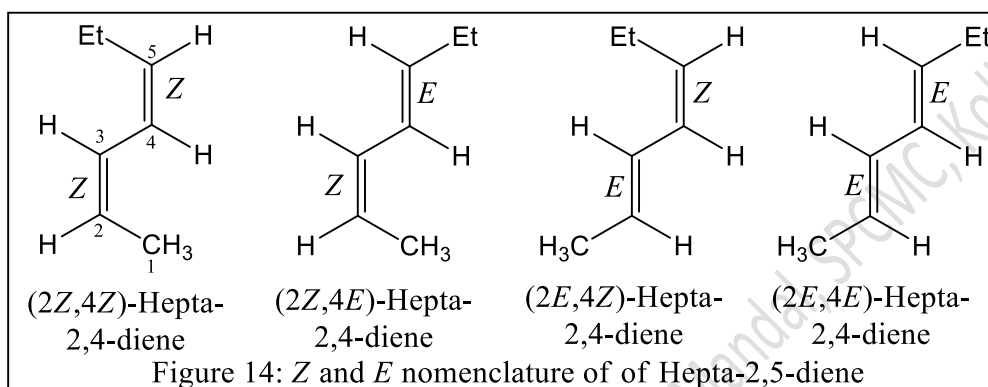
Cis-trans Isomers in Cumulenes

Cumulenes having odd number of adjacent double bonds also exhibit *cis-trans* isomerism when the terminal carbons contain different substituents. This is because of the fact that in cumulenes with odd number of double bonds, the terminal carbon atoms along with their substituents lie in the same plane (Figure 12) and such cumulenes have always σ planes irrespective of the nature of the substituents. However, the number of geometrical isomers is always 2 (two) irrespective of the number of double bonds (3, 5, 7...). An example is shown in Figure 13.

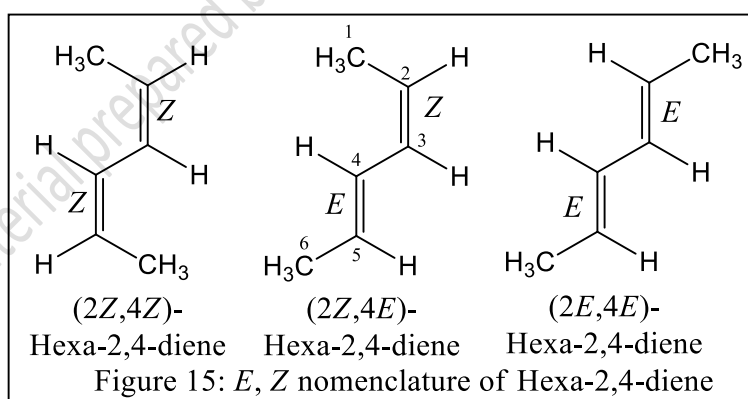


E/Z Configurational Nomenclature in Polyenes

When *cis-trans* isomers contain two or more double bonds, nomenclature using *E* and *Z* descriptors (the same CIP sequence rule is applied in all these cases) is done specifying the configuration of each double bond. For example, hepta-2,4-diene can have following configurational isomers (Figure 14), each written in a *s-transoid* (describing an *antiperiplanar* spatial arrangement of two conjugated double bonds about the intervening single bond; *s-trans*) form.



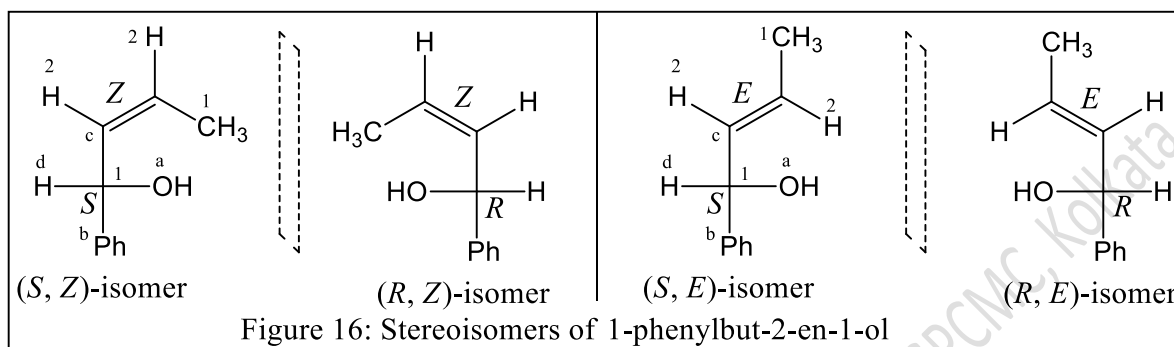
When an unsymmetrical polyene compound such as hepta-2,4-diene (Figure 14) is considered then IUPAC rules gets preference in numbering the carbon atoms and not the *Z* or *E* descriptors. When there is a choice in counting the carbon atoms in a molecule having both *Z* and *E* descriptors, *Z* gets preference over *E*. Hexa-2,4-diene can have following configurational isomers (Figure 15), each written in a *s-transoid* (*s-trans*) form. Hexa-2,4-diene can have three diastereomers. The reduction in the total number of diastereomers (as obtained from 2^n) is due to the fact that the terminal substituents are identical.



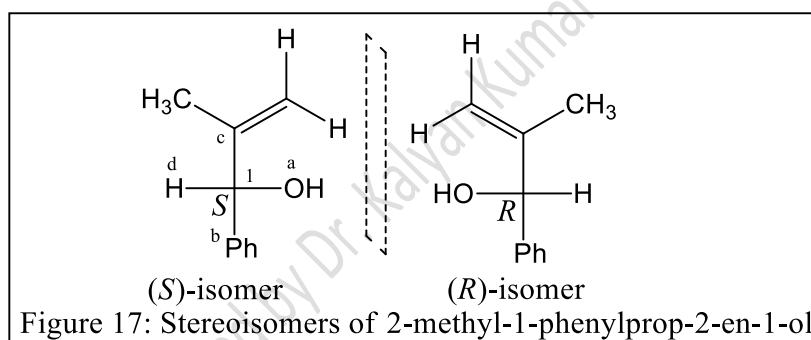
Combination of *R*, *S* and *E*, *Z* Isomerism

It is to be noted that *cis-trans* isomers, in true sense, are not optically active but if they develop molecular chirality (with *chiral* centre or without *chiral* centre), then they also exhibit optical isomerism. In such cases, both *E*, *Z*- and *R*, *S*-stereodescriptors should be used to indicate both diastereomeric and enantiomeric configurations of the stereoisomers.

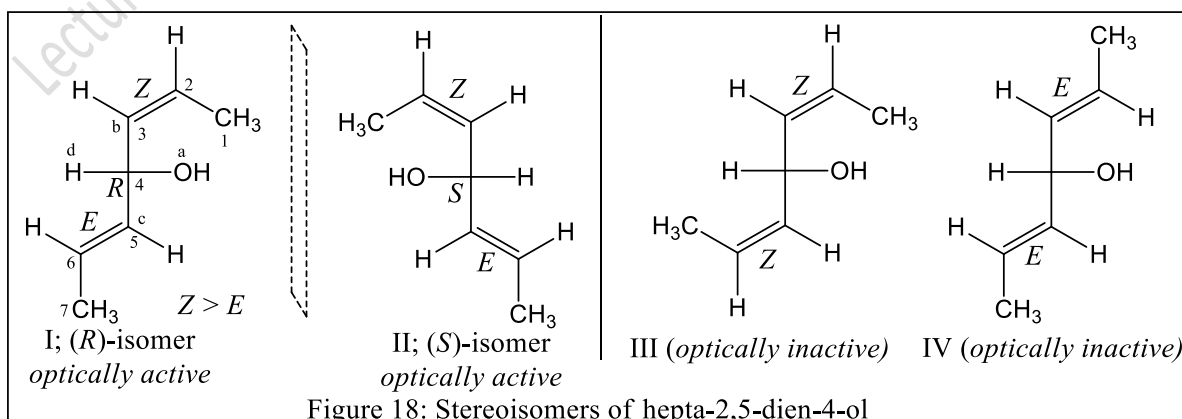
If a molecule contains both *chiral* centre and an appropriately substituted olefinic bond to give *E,Z*-isomers, then four stereoisomers are possible. According to CIP system they may be specified as *(R,E)*, *(R,Z)*, *(S,E)* and *(S,Z)*. For example, $\text{PhCH}^*(\text{OH})\text{CH}=\text{CHCH}_3$ contains a *chiral* centre (starred atom) and a suitably substituted double bond capable of giving *E,Z*-isomers. Its four possible configurations are shown in Figure 16.



The same molecular formula can give another constitutional isomer [$\text{PhCH}^*(\text{OH})\text{C}(\text{CH}_3)=\text{CH}_2$]. This compound has no *cis-trans* isomers because the alkene has the general structure of the type $\text{Ccd}=\text{Ca}_2$. The molecule contains one *chiral* centre.

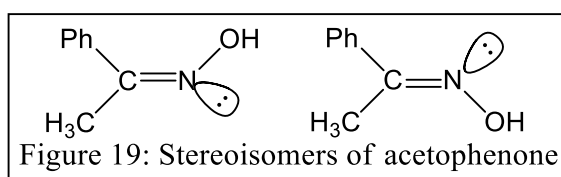


Therefore, total number of stereoisomers this structure contain will be 2. They are optical isomers. Figure 17 will show these isomers. In [$\text{CH}_3\text{CH}=\text{CHCH}(\text{OH})\text{CH}=\text{CHCH}_3$], two constitutional identical alkenyl groups ($-\text{CH}=\text{CHCH}_3$) are present. The C-4 carbon atom is *achiral* when both the $-\text{CH}=\text{CHCH}_3$ groups have *Z* or *E* configurations. But the C-4 centre is *chiral* when one of them is *Z* and the other is *E*. Four stereoisomers are possible with this structure. They are shown in Figure 18.



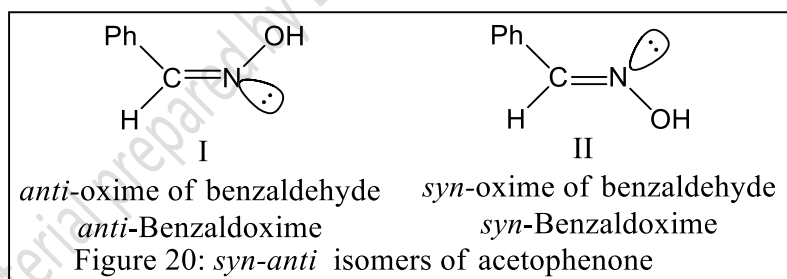
cis-trans Isomerism of Compounds with C=N and N=N

Oxime, hydrazones and semicarbazones of unsymmetrical carbonyl compounds can exhibit *cis-trans* isomerism due to the presence of rigid -C=N- moiety. Diazo compounds with rigid -N=N- moiety also exhibit *cis-trans* isomerism. Both the carbon and nitrogen atoms of C=N group in oximes are sp^2 hybridized. This is analogous to the hybridization of the carbon atoms in ethylene. Therefore, the C=N double bond consists of one sigma (σ) and one pi (π) bond, the third sp^2 orbital of nitrogen is occupied by a lone pair of electrons. Thus, oximes (Figure 19) are coplanar about the C=N bond and can exhibit *cis-trans* isomerism. Similar is the case with hydrazones and semicarbazones.

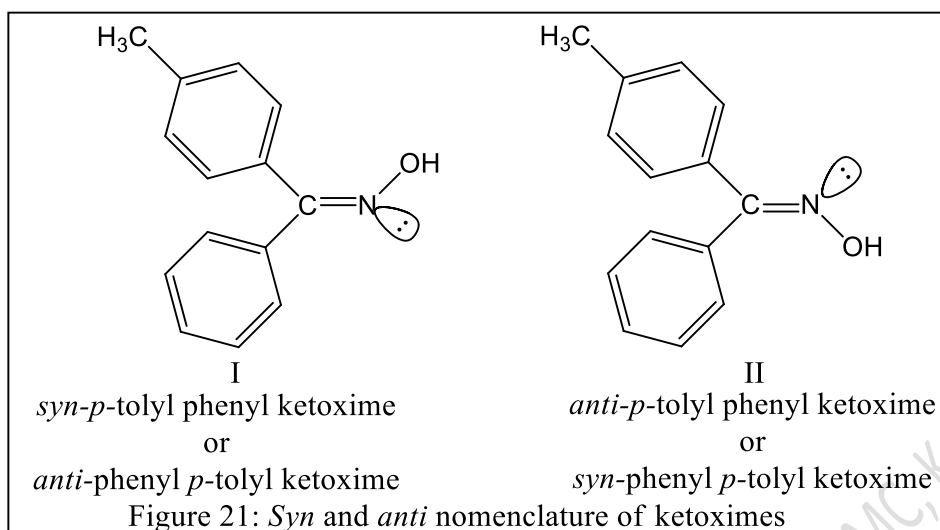


Stereochemical Nomenclature of Oximes

The configuration of stereoisomeric oximes is usually denoted by the prefixes *syn* and *anti* instead of *cis* and *trans* respectively. In case of oximes of aldehydes (aldoximes), carbon atom of C=N group contains one hydrogen atom. In an aldoxime, therefore, the *syn* form is one in which the hydrogen atom and the hydroxyl group (on N atom) are on the same side of the double bond. When H and OH groups are on the opposite sides of the double bond, the configuration is *anti*. The *syn* and *anti*-isomer of benzaldoxime are shown in Figure 20.

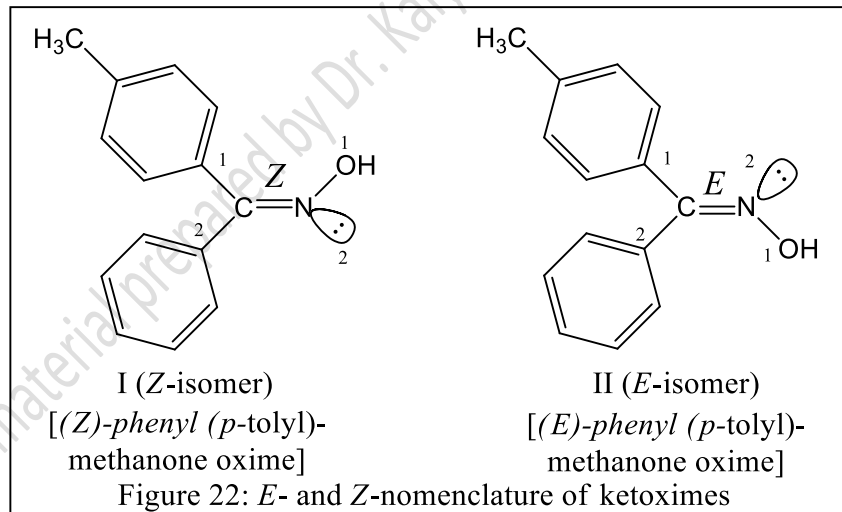


In a ketoxime, it is necessary to specify the group with respect to which the oxime OH group is *syn*. The nomenclature is illustrated in Figure 21. The prefix *syn* or *anti* indicates the configurational relationship between the first group named and the hydroxyl group.



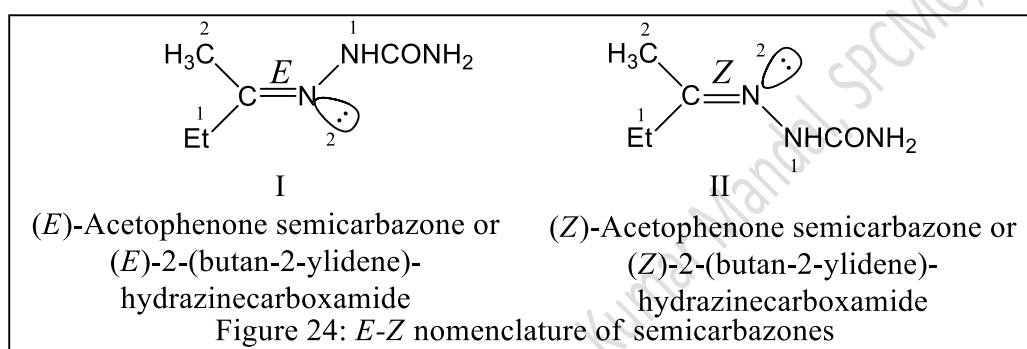
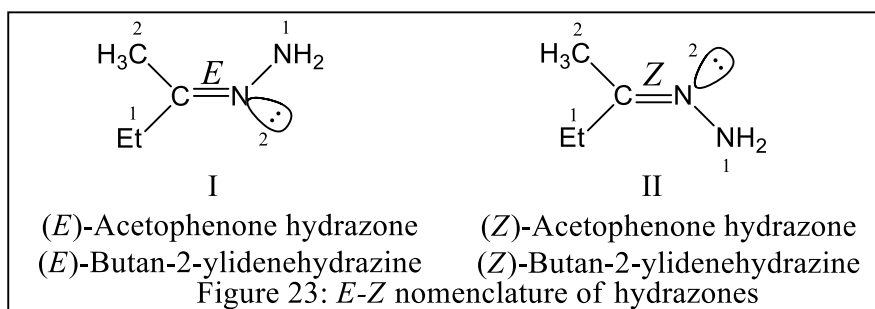
***E/Z* Stereochemical Nomenclature of Oximes**

The *E-Z* system (CIP) can also be used to specify the configurations of oximes. For example, *syn-p-tolyl ketoxime* is (*Z*)-phenyl-*p*-tolyl ketoxime because *p*-tolyl group has priority over phenyl and hydroxyl group has priority over the lone pair of electrons. *Syn* and *anti*-nomenclature are now abandoned for specifying the configurations of oximes. The nomenclature is illustrated in Figure 22.



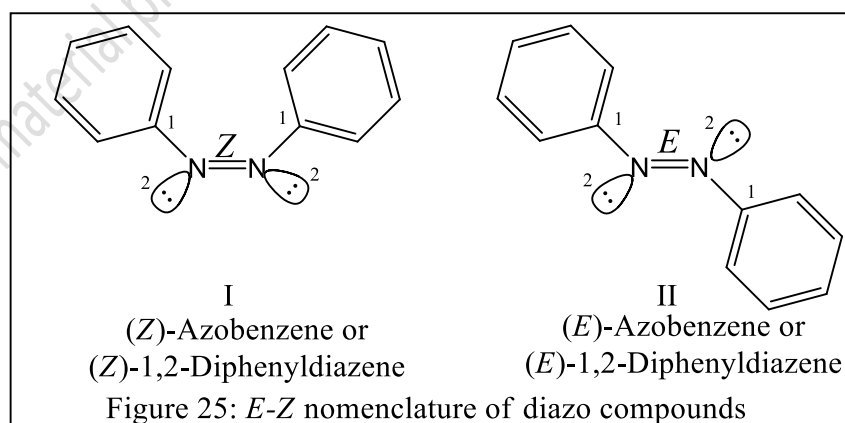
Stereochemical Nomenclature of Hydrazones and Semicarbazones

Semicarbazones and hydrazones of aldehydes (except HCHO) and unsymmetrical ketones ($R-CO-R^1$) also exhibit *cis-trans* isomerism. Examples are given below.



Stereochemical Nomenclature Diazo Compounds

A doubly bonded nitrogen may play the same part in geometrical isomerism as a doubly bonded carbon. Azobenzenes having rigid $-N=N-$ bond can also give rise to *cis-trans* isomerism. For example, azobenzene ($Ph-N=N-Ph$) can give *E*- and *Z*-isomers as shown in Figure 25.



Syn/anti Nomenclatures for Aldols

“Aldol” is an abbreviation of aldehyde and alcohol. When the enolate of an aldehyde or a ketone reacts at the α -carbon with the carbonyl of another molecule under basic or acidic conditions to obtain β -hydroxy aldehyde or ketone, this reaction is called Aldol Reaction.

When R^3 is -H, it is a β -hydroxy aldehyde,
otherwise it is a β -hydroxy ketone.

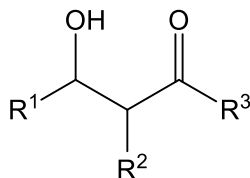


Figure 26: Generalized structure
of the aldol moiety

A simple system of nomenclature especially adaptable to aldol-type compounds containing multiple *chiral* centres is the use of *syn* and *anti*-descriptors. The type of aldols ($R^1/R^2 \neq H$) shown in Figure 26 contains two *chiral* centres and it is of the AB type of molecule. The number of optical isomers this type of structures possess are four. All the optical isomers are shown in Figure 27.