



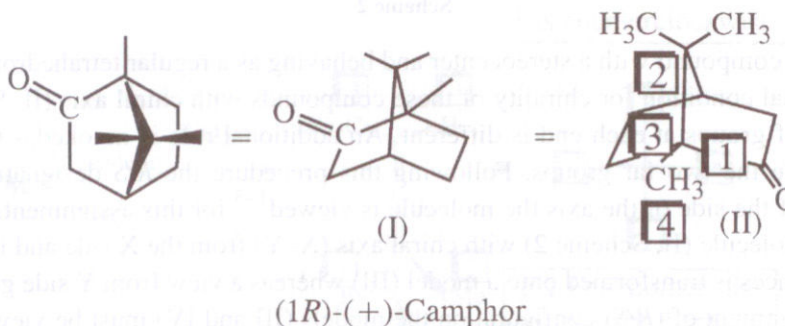
CHEMICAL EDUCATION
A SIMPLE MENTAL EXERCISE FOR ASSIGNING
CONFIGURATIONAL DESCRIPTORS (*R/S*) TO MOLECULES
WITH A STEREOAXIS (CHIRAL-AXIS)

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INTRODUCTION

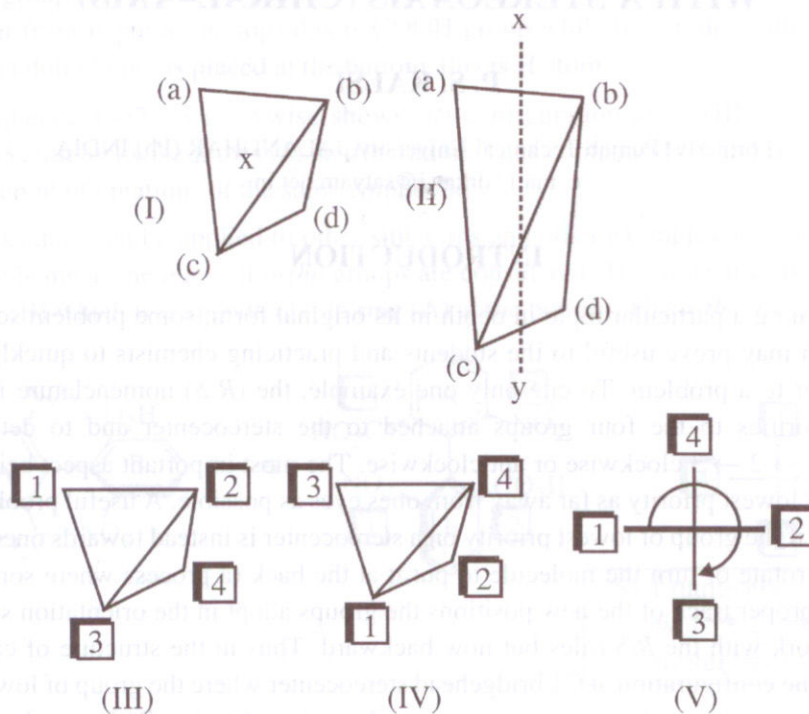
After learning a particular topic in depth in its original form, some problem solving hints emerge which may prove useful to the students and practicing chemists to quickly reach the correct answer to a problem. To cite only one example, the (*R S*) nomenclature is based on assigning priorities to the four groups attached to the stereocenter and to determine the progression 1 → 2 → 3 clockwise or anticlockwise. The most important aspect being to place the group 4 of lowest priority as far away from one's eyes as possible. A useful problem solving hint emerges, if the group of lowest priority on a stereocenter is instead towards one's eyes there is no need to rotate or turn the molecule to put it at the back (a process where some students don't keep a proper track of the new positions the groups adopt in the orientation so obtained) but simply work with the *R/S* rules but now backward. Thus in the structure of camphor (II, Scheme-I). The configuration at C1 bridgehead stereocenter where the group of lowest priority 4 (methyl group) is towards one's eyes is correctly assigned to be (*R*) by working with *R/S*



Scheme 1

system backwards. Similarly in the other equivalent orientation (I Scheme – I) of the same molecule at the second bridge head carbon the group of lowest priority 4 is H and the same procedure again gives the same descriptor.

In the experience of author as a teacher, the students face lot of difficulties in assigning configuration to compounds with chiral axes, e.g., allenes, spiranes, adamantanes, biphenyls, binaphthyls etc. In these molecules no stereocenter exists, the molecule is observed as an elongated tetrahedron (Scheme-2) when the conditions for chirality become less stringent



Scheme 2

compared to a compound with a stereocenter and behaving as a regular tetrahedron (I, Scheme 2). The minimal condition for chirality of these compounds with chiral axis (II, Scheme 2) is that the pair of groups at each end is different. An additional rule is invoked – the two near groups precede the two far groups. Following this procedure the *R/S* designation becomes independent of the side of the axis the molecule is viewed¹⁻⁵ for this assignment. Thus e.g. if one views a molecule (II, Scheme 2) with chiral axis (X–Y) from the X side and if $a > b$ and $c > d$ this sequence is transformed onto a model (III) whereas a view from Y side gives a model (IV). For assignment of (*R/S*) configuration the models (III and IV) must be viewed from the side opposite the least priority group. The path $1 \rightarrow 2 \rightarrow 3$ in both the models (III = IV) is the same and gives R configuration.

A second different way is to translate the groups on (II, Scheme 2) on to a cross (V Scheme 2) placing the two near groups horizontally and the two far groups vertically. The horizontal and vertical lines represents the two relevant edges of the tetrahedron and these lines join each pair.

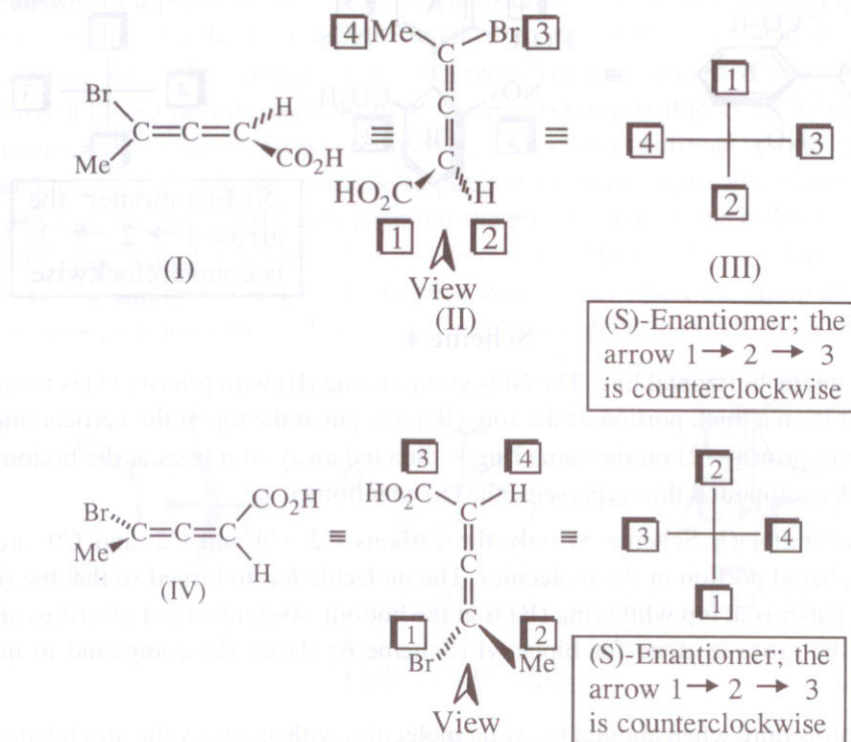
In the present case under discussion the arrangement (V) is obtained in which the path $1 \rightarrow 2 \rightarrow 3$ is again suggestive of (*R*) configuration.

It is here that most students make an error to properly transform the groups on to a model (III or IV Scheme 2) and face a difficulty in viewing the model keeping the priority group 4 at the rear and same is the case with model V. In order to circumvent these difficulties the author has devised a very simple and easy model⁶ to assign stereochemical descriptors to molecules with chiral axes.

THE NEW MODEL

The following simple model is proposed to assign configuration to compounds with chiral axis⁶.

- The molecule with a stereoaxis e.g. an allene is rotated (turned) so that the groups in the plane of paper (shown by continuous lines) are at the top while the pair of groups which are perpendicular are at the bottom (II Scheme 3).

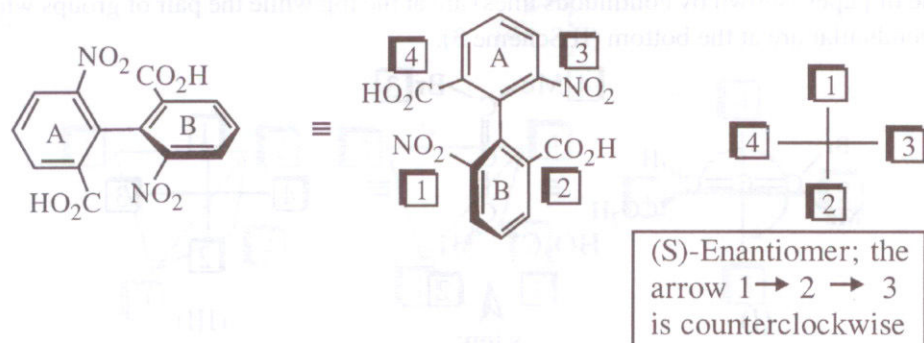


Scheme 3

- Always view the molecule from bottom, the groups at bottom precede over the other pair and thus assign the priorities to all the groups.

- Draw a cross with a vertical line and a horizontal line (III Scheme 3). Put the groups on the top of the molecule as you see them on the horizontal line [Br (3) is on the right hand while CH₃ (4) is on the left hand]
- Put the groups of the bottom pair on the vertical line. The group on the thick wedge (i.e. the group at front is put at the top) this is COOH group while the group at the back (i.e. the group on dotted line) is placed at the bottom, this is H atom.
- The sequence 1→2→3 clockwise shows (*R*) configuration as in (III, Scheme 3) while 1→2→3 anticlockwise shows (*S*) configuration. Thus compounds (I and II, Scheme 3) are the different orientations of the same compound.

The procedure can be applied to other situations and other examples are presented. In the biphenyl (Scheme 4) the relevant *ortho* groups are considered. The molecule is first turned to put the ring (B) which is perpendicular to ring (A) at the bottom. The *ortho* groups on ring (A)

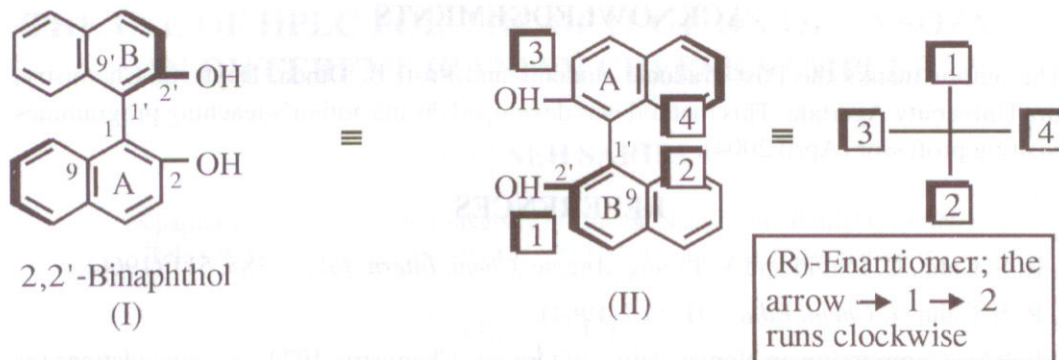


Scheme 4

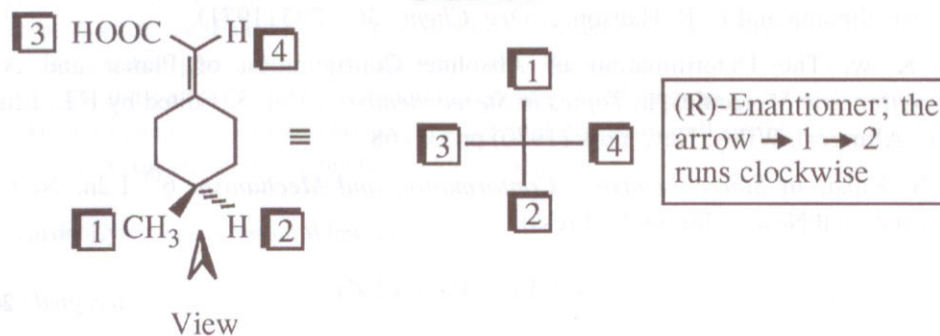
are transferred on the horizontal line. The NO₂ group in ring (B) with priority (1) is towards the viewer [since it is on a thick portion of the ring (B)] it is put at the top of the vertical line while the COOH group priority (2) on the same ring is directed away so it goes at the bottom of the vertical line. The compound thus represents the (*S*) enantiomer.

In 2,2'-binaphthol (I, Scheme 5) only the carbons C₂, C₉ and C_{2'} and C_{9'} are to be considered (biphenyl portion of the molecule). The molecule has to be turned so that the ring (A) in the plane of paper is at top while ring (B) is at the bottom. Assignment of priorities and their placement on the cross as done for biphenyl (Scheme 6) shows the compound to have (*R*) configuration.

A similar procedure when applied to cyclic molecules with an exocyclic alkylidene moiety (Scheme 6) gives the correct descriptor. Note the molecule is already drawn in suitable fashion and has not to be rotated. One may note that cyclohexyl "arms" are in the plane of *pi* bond and H and COOH groups along with the cyclohexyl arms are in the plane of paper. The CH₃ and H at C₄ of the cyclohexane ring are in a different plane.

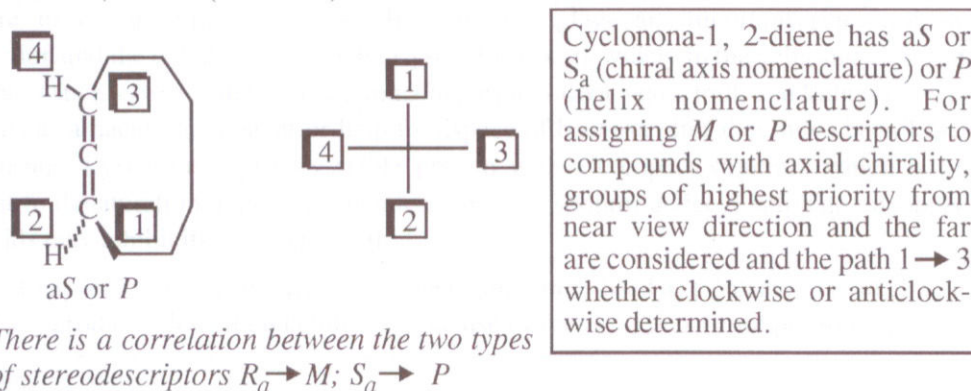


Scheme 5



Scheme 6

The present method further shows that cyclonona-1,2-diene can be assigned proper configurational descriptor (Scheme 7). From this very model one can relate the chiral axis nomenclature (a *S*) or (a *R*) for axial chirality to *M* or *P* helix nomenclature as shown for cyclonona-1,2-diene (Scheme 7).



Scheme 7

ACKNOWLEDGEMENTS

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REFERENCES

1. R. S. Cahn, C. Ingold and V. Prelog, *Angew. Chem. Intern. Ed.*, **5**, 385, 511 (1966).
2. R. S. Cahn, *J. Chem. Educ.*, **41**, 116 (1964).
3. IUPAC Commission on Nomenclature of Organic Chemistry, 1974 recommendations for Section E, Fundamental Stereochemistry, *Pure Appl. Chem.* **45**, 11(1976).
4. H. Hirschmann and K. R. Hanson, *J. Org. Chem.*, **36**, 3293 (1971).
5. G. Krow, The Determination of Absolute Configuration of Planar and Axially Dissymmetric Molecules, in *Topics in Stereochemistry*, Vol. 5 (Edited by E.L. Eliel and N.L. Allinger), Wiley, New York (1970) pp. 31–68.
6. P. S. Kalsi, in *Stereochemistry, Conformation and Mechanism* 6th Edn. New Age, International New Delhi (under Press).

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