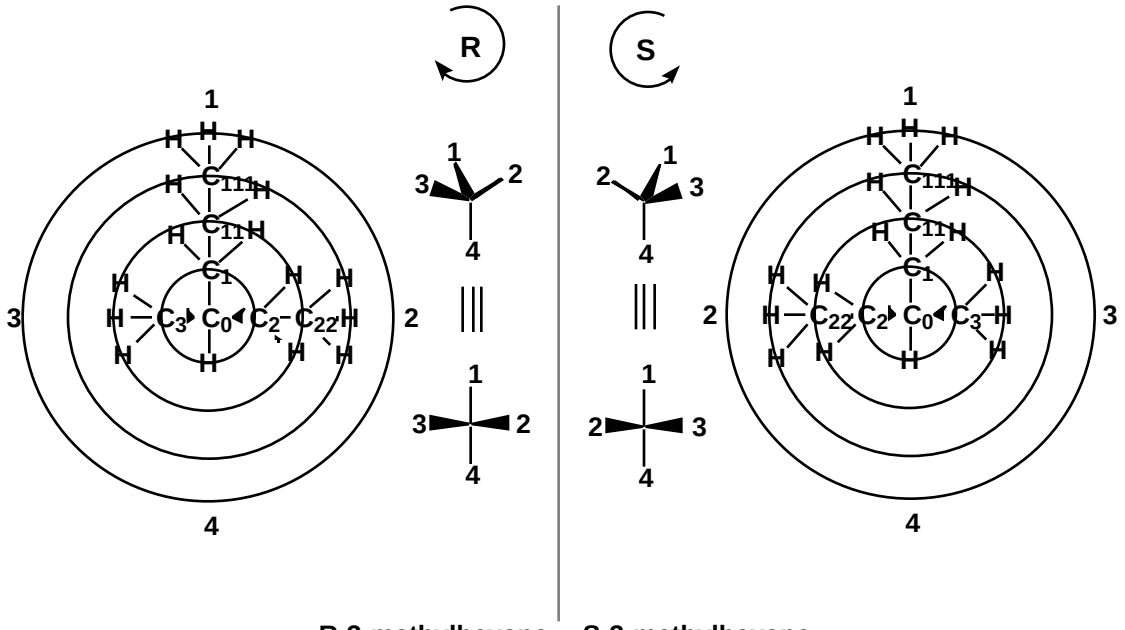
Text Related to Segment 4.03 ©2002 Claude E. Wintner

It remains to outline the method by which the sequence 1, 2, 3, 4 is determined for the four different ligands of the stereogenic carbon atom. Formally, one begins by writing out a two-dimensional map. The maps for the two enantiomers of 3-methylhexane are presented in the figure. To aid the discussion, each carbon atom is given a subscript, the stereogenic carbon atom to be described being C_0. For the present purpose we need only consider the first two "sequence rules" (of several in the complete C-I-P system). These rules are:

(1) Consider atoms near C_0 before considering farther ones, always comparing only those atoms which are the same number of bonds removed (that is, in the figure, those which appear on the same circle).

(2) High atomic number "precedes" low.



determination of the sequence of ligands for 3-methylhexane according to the Cahn-Ingold-Prelog system, followed by assignment of a descriptor to each enantiomer

Concentrating initially on the first circle of atoms, we find that H clearly is the "loser," and thus #4 in the sequence; but the three carbon atoms C_1, C_2, and C_3 are "tied" for first place. We proceed, in sequence, to the next nearest atoms — those in the second circle. Looking at the highest (in atomic number) atom on each branch, we find C_{11} "tied" with C_{22}, with both "beating" any of the hydrogens connected to C_3; the latter branch is, therefore, #3. There remains only the task of making a differentiation between the first two branches, but this is not possible in the second circle. Extending the game one circle farther brings an end; C_{111} "beats" any H attached to C_{22}, and we thus can sequence the ligands as follows (certainly the outcome one would hope for in this simple case!):

Propyl#1

Ethyl #2

Methyl	#3
Hydrogen	#4

When, as already described, the four ligands are modeled three-dimensionally and in sequence, according to the "steering wheel" convention, an unambiguous descriptor must result for any case in which all four ligands do, in fact, differ in their constitutions. Minimal practice makes this procedure, so cumbersome to describe in detail in words, an easy and rapid one to carry out. *Note that the sequence rule must not be misinterpreted to be an additive one where the "weight" on a branch is added up.* One proceeds in *sequence*, and the first time a high atomic number "beats" a low one, the game is over, no matter what may be hanging on to the molecule farther out on the "losing" branch. It also bears repeating that there is no clear relationship between the absolute configuration, as specified by the descriptors R or S, and the observed sign of rotation of polarized light, (+) or (-). As mentioned above, in this particular case R-3-methylhexane is R-(-)-3-methylhexane and S-3-methylhexane is S-(+)-3-methylhexane. Finally, it certainly should be stated here that although hydrocarbons afford a simple and instructive entree to these ideas, they by no means provide the examples of greatest interest to us! Most of the molecules of nature are chiral, and exist naturally (or in any single organism) as only one enantiomer, the prototypical cases being those of the naturally occurring amino acids, for which the absolute configuration in higher organisms is quite generally S. (The amino acid cysteine provides an exception only because of the way in which the sequence rule must be applied to the sulfur atom in that case.)