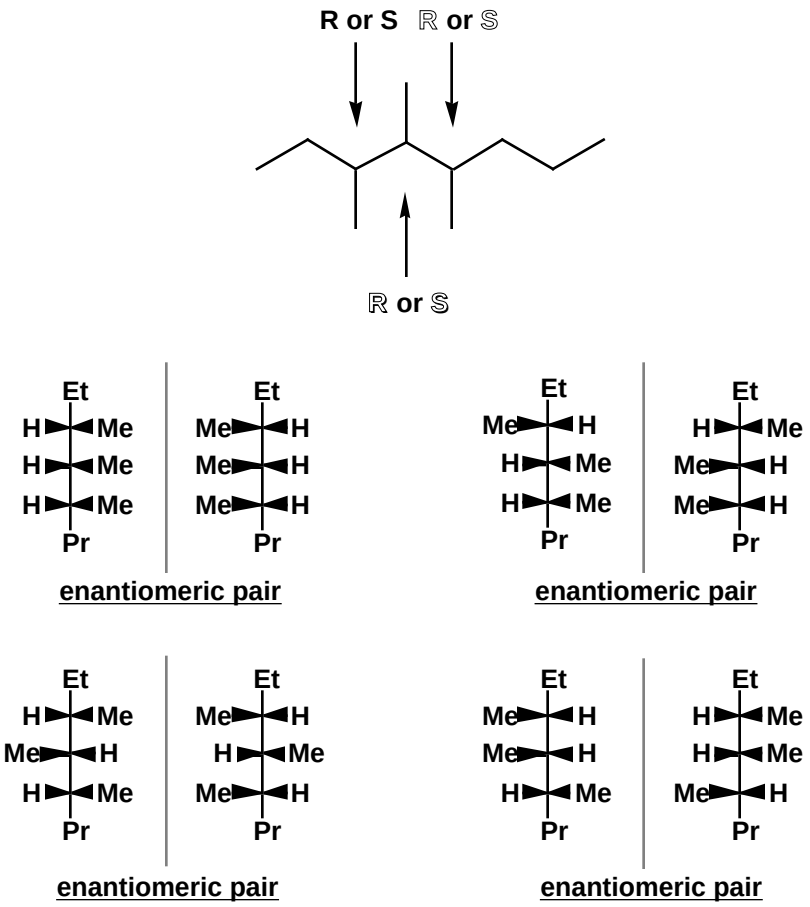
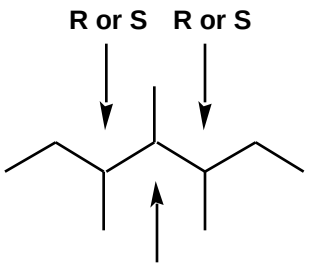
Text Related to Segment 4.06 ©2002 Claude E. Wintner

With these ideas in mind it now is instructive to analyze a final pair of examples. Consider first, as a standard, the case of 3,4,5-trimethyloctane. Molecules having this constitution possess three stereogenic centers, each with ligand substitution constitutionally different from that of the others. Thus, there are eight possible configurational isomers — "eight bottles" — comprising four (diastereoisomeric) enantiomeric pairs, as shown in the figure.

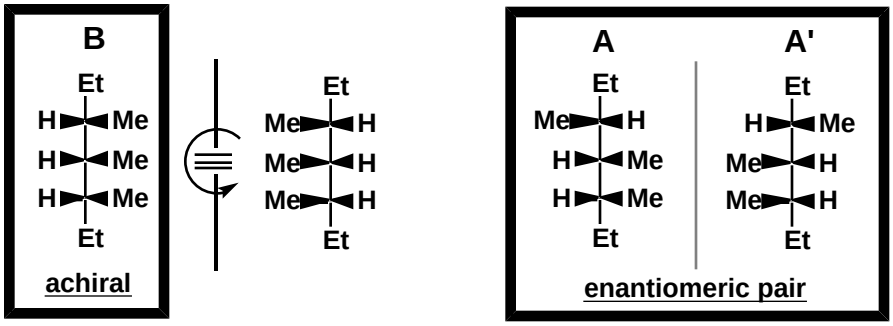


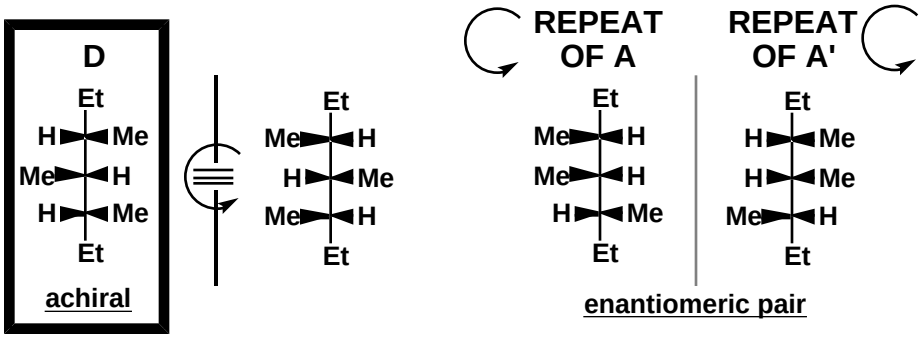
configurational isomers of 3,4,5-trimethyloctane
(four diastereoisomeric enantiomeric pairs)

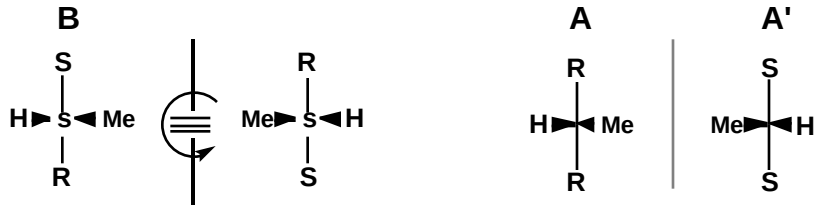
On the other hand, in the related case of 3,4,5-trimethylheptane (next figure), in which the terminal propyl group of 3,4,5-trimethyloctane is replaced



This carbon atom MAY OR MAY NOT be stereogenic!

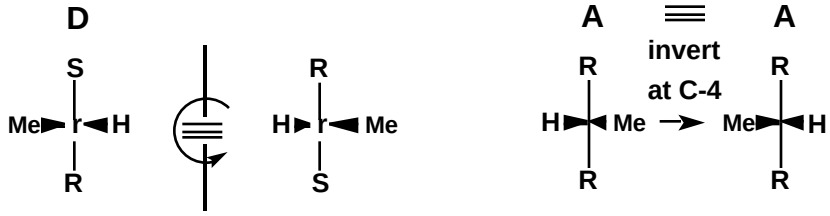






In both B and D the central carbon atom IS stereogenic, but in each case the descriptor must be reflection INVARIANT.

In A and A' the central carbon atom IS NOT stereogenic. It cannot have a descriptor.



configurational isomers of 3,4,5-trimethylheptane
(an enantiomeric pair and its two achiral diastereoisomers)

by an ethyl group, the increased symmetry alters the result dramatically, to just a single enantiomeric pair and two achiral diastereoisomers, as indicated by the formulae framed by boxes. The proper dissection of this situation requires some care. In all configurationally stereoisomeric molecules having the constitution 3,4,5-trimethylheptane, the carbon atoms at positions 3 and 5 have four ligands, each differing in constitution from the other three. Hence, the carbon atoms at positions 3 and 5 must be stereogenic in all cases. On the other hand, while in all cases the carbon atom at position 4 is substituted by two groups which are identical in constitution, these groups *may or may not* differ in configuration. Thus, it must be understood that, for molecules having the constitution 3,4,5-trimethylheptane, the carbon atom at position 4 *may or may not* be stereogenic. *The constitutional formula does not, in itself, give enough information for this to be determined. Each individual configurational stereoisomer must be examined separately.* Suppose that the absolute configuration at both C-3 and C-5 is R, as in formula **A** in the figure. Then the carbon atom at position 4 *is not* stereogenic, since it bears two substituents that are identical in all respects — in configuration as well as in constitution. This statement perhaps is most easily tested and apprehended if we attempt to invert the configuration at position 4 in formula **A**, by exchanging Me and H. If a carbon atom is stereogenic, such an exchange operation must generate a new molecule. Instead, we *regenerate* **A**. (In particular, it should be emphasized, the enantiomer **A'** is *not* generated in this manner!) Note that, not being stereogenic, with two identical ligands, carbon atom 4 in **A** does not deserve (and cannot be given!) a configurational descriptor. Exactly the same situation holds for the enantiomer **A'**, where both substituents are S. Finally, note how the descriptors — R, R at positions 3 and 5 in **A** and S, S at positions 3 and 5 in **A'** — are *reflection variant:* they *change* across the mirror plane.

Now suppose instead that one substituent has the R configuration, and the other the S, as in formulae **B** and **D** in the figure. In the molecules corresponding to these formulae the carbon atom at position 4 *is* stereogenic, since the two substituents differ in their configuration; C-4 now is substituted by four *different* ligands, two of them differing as do a right and a left hand. Note that when we apply to **B** and to **D** the unambiguous test of stereogenicity — Can we invert the configuration at position 4 in these molecules by exchanging Me and H? — then, in fact, we generate **D** from **B** and **B** from **D.** Molecules **B** and **D** each are achiral: each can be made congruent with its own mirror image. It will be seen immediately that they are diastereoisomers of one another — *not* enantiomers — and also diastereoisomers of the enantiomeric pair **A**, **A'**.

To decide the sequence of the ligands at stereogenic carbon atoms such as those in **B** and **D**, which bear constitutionally identical groups differing only in their chirality, the rule is that the R substituent is given precedence over the S substituent. Descriptors determined by this rule must be *reflection invariant* (that is, *unchanging* across the mirror plane: see the figure), as opposed to the reflection variant descriptors R and S. It would be contradictory to have the possibility of two different descriptors for the same carbon atom (4) in the same molecule, as would have to be the case if the reflection variant R and S were used (and as, again it needs emphasizing, they *must* be at carbon atoms 3 and 5). Indeed, it then would be true that *both* **B** *and* **D** could be described as *either* 3(R)—4(R)—5(S) *or* 3(R)—4(S)—5(S), a situation which certainly would result in a most unhappy state of the nomenclature for these molecules! Thus, in this special circumstance the lower case descriptors r and s, *defined* as reflection invariant, are used to specify the configuration at position 4.