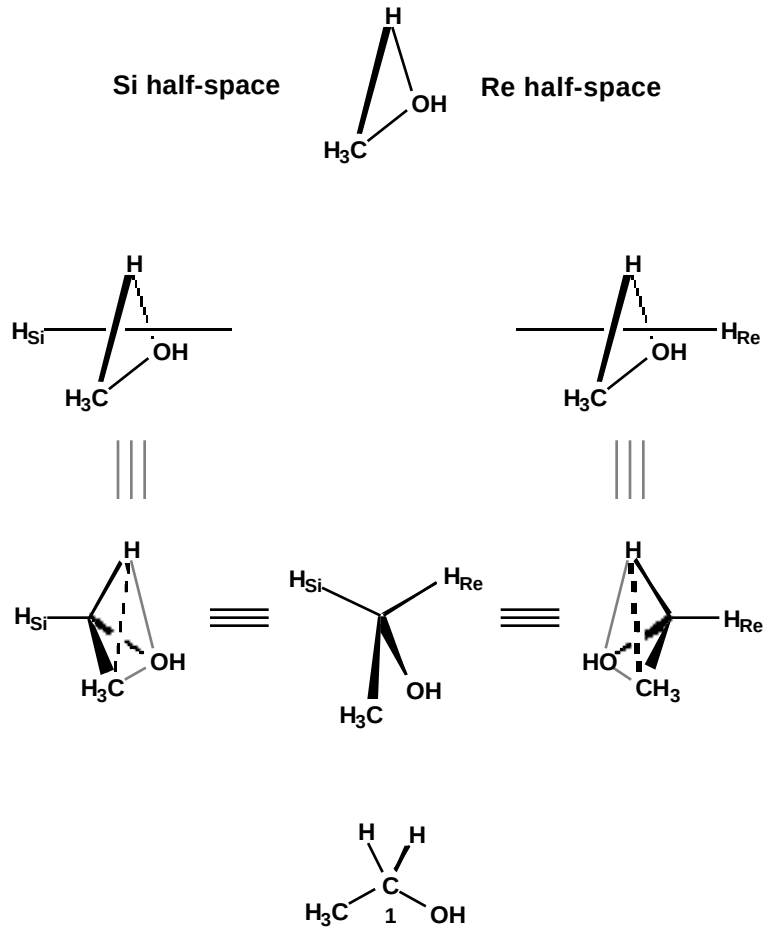
Text Related to Segment 6.07 ©2002 Claude E. Wintner

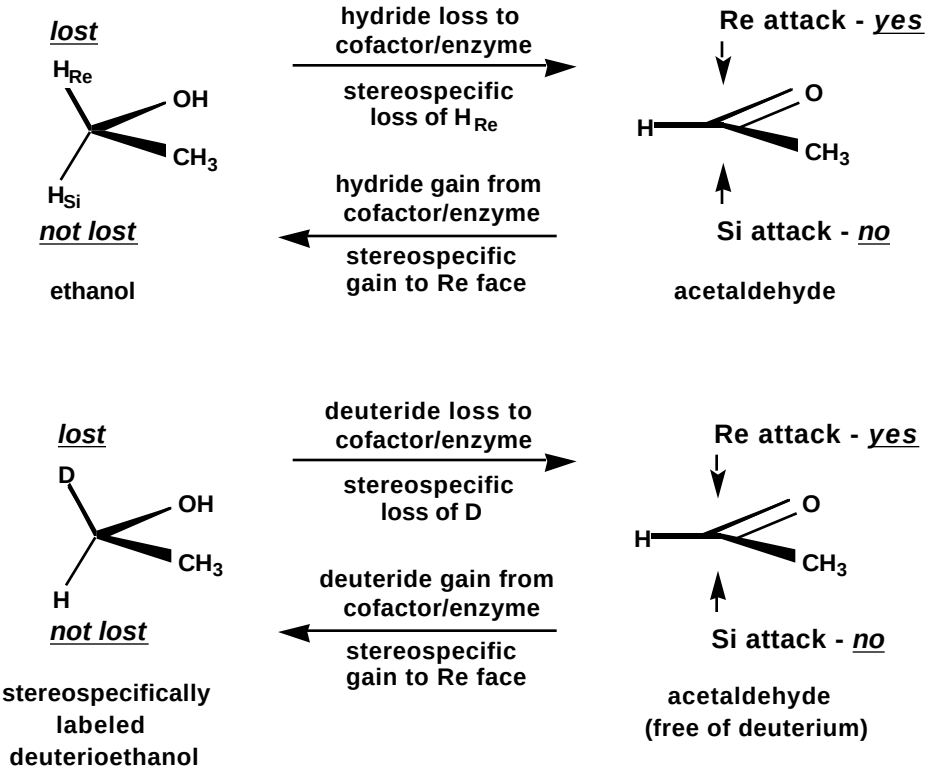
The classical example of a prochiral carbon atom is C-1 in ethanol (the carbon adjacent to the hydroxyl group. The hydrogen atoms at C-1 in ethanol are enantiotopic; the hydrogen residing in the Si half-space is specified as H_{Si}, that in the Re half-space as H_{Re}:



enantiotopic hydrogens H_{Si} and H_{Re} at C-1 in ethanol

In the presence of the enzymes liver alcohol dehydrogenase or yeast alcohol dehydrogenase, H_{Re} of ethanol, *and only H_{Re},* is removed *stereospecifically* and is transferred (as hydride) to the cofactor NAD, leaving acetaldehyde as the product. *H_{Si} is not touched!* Conversely, in the presence of either enzyme, a hydrogen atom

(as hydride) can be transferred by the cofactor NADH *stereospecifically* to the Re face of acetaldehyde, never to the Si face. The transferred hydrogen in the resulting ethanol lies in the Re half-space and is H_{Re}:



the enzymes liver alcohol dehydrogenase and yeast alcohol dehydrogenase mediate hydride (and deuteride) transfer from ethanol, and to acetaldehyde, in a stereospecific manner

That these statements are correct is known from isotopic labeling studies. In the presence of the enzymes, ethanol stereospecifically labeled with deuterium at the Re position on C-1 loses *all* of its deuterium, to yield acetaldehyde free of deuterium. (Ethanol stereospecifically labeled with deuterium at the Si position on C-1 loses *no* deuterium, to yield 1-deuteroacetaldehyde, entirely deuterated at C-1 of acetaldehyde.) Conversely, acetaldehyde gains deuterium stereospecifically, to yield ethanol labeled with deuterium only at the Re position on C-1. (And 1-deuteroacetaldehyde gains hydrogen stereospecifically, to yield ethanol labeled

with deuterium only at the Si position on C-1.) In all of these reactions the (chiral) enzymes, liver alcohol dehydrogenase or yeast alcohol dehydrogenase, "read" the sense of $OH/CH_3/H$ in either ethanol or acetaldehyde, by binding so that only the Re face of acetaldehyde (seen either as starting material or as product) is available for reaction during the course of the hydride transfer. However, in this context it should be noted that the family of dehydrogenase enzymes is large, and that some dehydrogenases are, in fact, stereospecific in the other sense, for H_{Si} in ethanol and for the Si face of acetaldehyde. The important point is that all of the enzymes are stereospecific in their action, responding to the stereotopism of their substrates. (In another nomenclature, which we do not use here, H_{Re} is called pro-R and H_{Si} is called pro-S. Unfortunately, the two systems do not always give equivalent descriptors, in the sense that a pro-R group, as it is defined in the alternate nomenclature, does not necessarily fall in the Re half-space as defined by the triangle of the remaining groups. However, *for enantiotopic or diastereotopic hydrogen atoms,* it turns out that there is no discrepancy between the two systems of nomenclature.)

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