Chemistry II (Organic): Introduction to Stereoelectronics

Stereochemistry and Regiochemistry of Elimination Reactions

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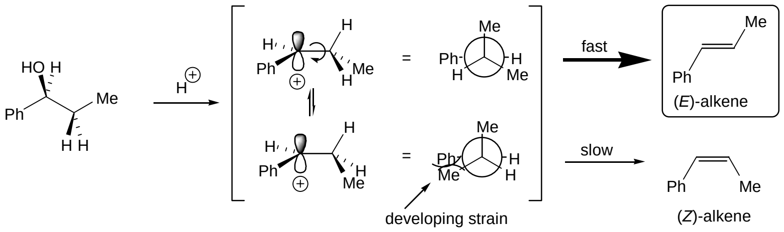
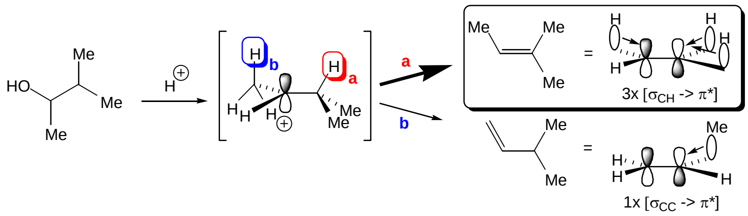
E1 Eliminations:

Stereochemistry: E1 elimination to form an alkene is a common fate of a carbocation if there are α-protons available. The stereochemistry [(*E*) or (*Z*)] of the resulting double bond is determined at the moment the α-proton is lost. The new π bond can only form when the p_{vac} orbital and the $\sigma_{C\text{-}H}$ bond are co-planar (i.e. to facilitate the *stereoelectronic* $\sigma_{C\text{-}H} \rightarrow p_{vac}$ interaction). If there are two α-protons on the same carbon, and the system enjoys free rotation (i.e. it is not part of a ring system), then both $\sigma_{C\text{-}H}$ bonds can usually become co-planar. The proton that is lost is generally that leading to the E-alkene because (*E*)-alkenes [and transition states (TSs) leading to (*E*)-alkenes] are generally of lower energy for *steric* reasons.

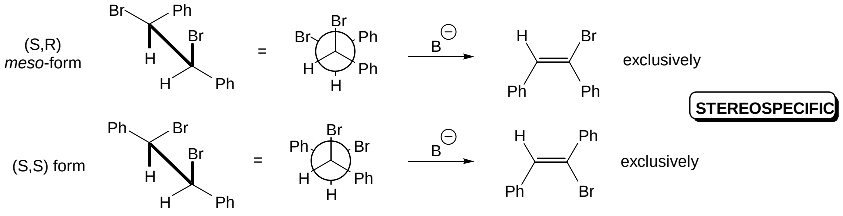


Regiochemistry: When a carbocation can eliminate to give more than one regioisomeric alkene then the major product is generally the most substituted alkene. This is because more substituted alkenes (and TSs leading to more substituted alkenes) are generally of lower energy as the result of multiple *stereoelectronic*, hyperconjugative $\sigma_{C\text{-}H}$ or $\sigma_{C\text{-}C} \rightarrow \pi^*$ stabilising interactions (see 'structural phenomena attributable to hyperconjugation' handout).



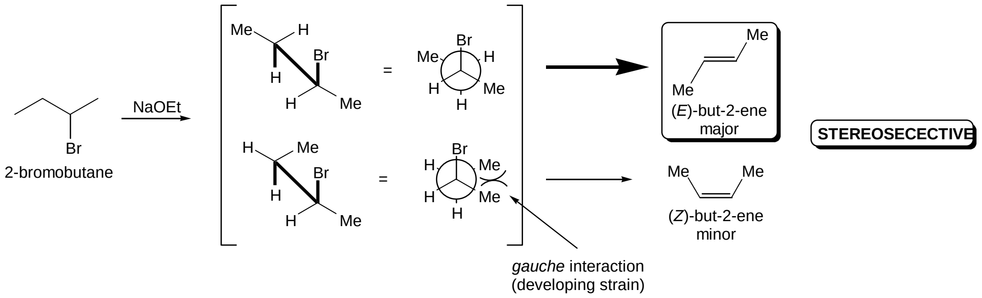
E2 Eliminations:

Stereochemistry: In an E2 elimination, the new π bond is formed by overlap of the $\sigma_{C\text{-}H}$ bond with the $\sigma^*_{C\text{-}X}$ antibonding orbital. The orbitals need to be anti-periplanar. Hence the contrasting outcomes of the E2 eliminations of the diastereomeric dibromides shown below.

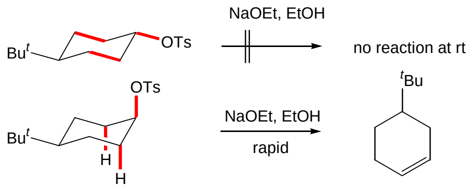


Pfeiffer *Z. Phys. Chem.* **1904**, *48*, 40

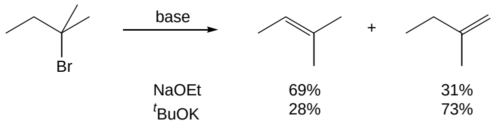
If there are two α-protons on the same carbon, and the system enjoys free rotation (i.e. it is not part of a ring system), then both $\sigma_{C\text{-}H}$ bonds can usually adopt an anti-periplanar conformation. The one that eliminates fastest is generally from the conformation that has the lowest energy (i.e. that which has least serious *gauche*, steric interactions) because this conformation will be the most populated of the two.



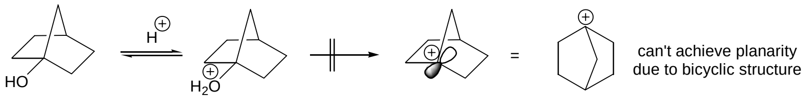
For E2 eliminations in cyclohexanes, the $\sigma_{C\text{-}H}$ and $\sigma^*_{C\text{-}X}$ orbitals must be *trans*-diaxial. This requirement accounts for the often greatly differing behaviour between epimeric substrates of this type. For example:



Regiochemistry: In the elimination of 2-bromobutane (shown above), but-1-ene is also formed as a minor product (~19%) along with the two stereoisomeric but-2-enes (~81%). In general, E2 reactions like this, involving uncharged leaving groups (e.g. Br, OTs etc.), furnish predominantly the more substituted products because they proceed *via* 'late' (product-like) TSs. This is sometimes referred to as ***Zaitsev's rule*** and is a consequence of *stereoelectronic*, hyperconjugative $\sigma_{C\text{-}H}$ or $\sigma_{C\text{-}C} \rightarrow \pi^*$ stabilising interactions lowering the energy of the TSs leading to these products. However, this preference for more substituted products can be reversed (***Hofmann's rule***) when the base used is very hindered and/or when the nucleofuge is charged (e.g. NR_3^+). These reactions proceed *via* 'early' (substrate-like) TSs in which two factors favour removal of the protons leading to the less substituted alkenes: Firstly, the protons leading to less substituted products are less hindered and more easily accessible; and secondly, these protons are more acidic (the conjugate base: carbanions are destabilised by inductively electron releasing akyl groups).



Lastly, elimination towards a bridgehead is never observed (***Bredt's rule***). This is because bridgehead double bonds would be of very high in energy due to the strain inherent in achieving a planar (sp^2) bridgehead carbon. This strain is felt in the preceding TS, raising its energy. For example, the norbornane alcohol shown below will not undergo elimination. The E2 pathway is precluded because there is no anti-periplanar C-H bond and the E1 pathway is precluded because although the resulting cation would be tertiary it would not be planar. Norbornane-based carbocations, do however undergo a number of interesting Wagner-Meerwein rearrangements (see Chapter 37 of of '*Organic Chemistry*', Clayden, Greeves, Warren, and Wothers, Oxford, 2001).



For an excellent overview of elimination reactions see Chapter 19 of '*Organic Chemistry*', Clayden, Greeves, Warren, and Wothers, Oxford, 2001. See also '*Advanced Organic Chemistry*', March, 4th Ed, 1992, pp998.

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