Lecture 2

Conformational Analysis of Acyclic Alkenes

Learning outcomes: by the end of this lecture after answering the associated problems, you will be able to:

1. draw low-energy conformations of acyclic alkenes;
2. appreciate that the relative energy of these conformations is a balance between 1,2- and 1,3-interactions;
3. recognise and use the term $A^{1,3}$-strain;
4. draw the mechanism of the hydroboration reaction;
5. rationalise the regio- and stereoselectivity of this reaction.

Propene

Propene can exist in different conformers generated by rotation about the $\mathbf{C}H_3–\mathbf{C}H=CH_2$ bond; obviously rotation about the C=C bond is impossible without breaking the π-bond.

We can identify two low-energy conformations, namely the *eclipsing* conformer, in which an allylic C–H eclipses the C=C bond, and the *bisecting* conformer, in which an allylic C–H eclipses the internal vinylic C–H bond, leaving the remaining two allylic C–Hs to bisect the plane containing the C=C bond.

In the case of C–H bonds eclipsing a C=C bond, a 1,2-interaction is clearly worse than a 1,3-interaction

But-1-ene

In this case there are two possible eclipsing conformers (an allylic C–H or C–CH_3 bond can eclipse the C=C bond). The conformer in which the C–H bond eclipses the C=C bond is generally agreed (depends on the method of calculation) to be the more stable, although the energy difference between these two conformers is small (≤ 0.5 kcal mol^{-1}). There are also two possible bisecting conformers (allylic C–H or C–CH_3 bond eclipsing the internal vinylic C–H). The bisecting conformer in which the C–CH_3 is *anti* to the C=C bond and eclipses the internal vinylic C–H, is the high-energy conformer ΔE(low-energy eclipsing - high-energy bisecting) ~ 1.74 kcal mol^{-1}. Again we have to maintain a balance between 1,2- and 1,3-interactions.

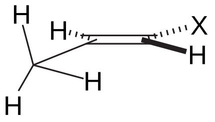
eclipsing conformers

high-energy bisecting conformer

Substituted Propenes (CH_3-CH=CHX)

In these systems, the stereochemistry of the olefin is very important. If X = Me or Cl, the energy barrier to rotation in the (*Z*)-stereoisomer is *reduced* relative to that observed in propene (X = H). This is most probably a result of destabilisation of the low-energy eclipsing conformation resulting from increased $A^{1,3}$-strain.

In the (*E*)-stereoisomer the energy barrier to rotation is similar to that for propene (~ 2.0 kcal mol^{-1}) since the vinylic substituent is always remote from the allylic group.



low energy eclipsing conformer

2-Methylbut-1-ene

There is an increased barrier to rotation about the C–C bond compared with but-1-ene owing to severe 1,2-interactions in the high-energy bisecting conformer.

Hydroboration

The chemistry of olefins is not restricted to electrophilic addition reactions. For example, hydroboration of a C=C bond proceeds *via* a completely different mechanism. It is an important reaction that can be used to hydrate an olefin in an anti-Markovnikov fashion. You can read more about this reaction and its synthetic utility in Maitland Jones, 2nd edition, Chapter 8, pp 335-346; 1st edition, Chapter 9, pp 363-374.

Overall transformation

In the next lecture we will see how we can use conformational analysis to predict the stereochemical outcome of hydroboration reactions on olefins containing proximal stereogenic centres. However, before we do this, we need to understand the reaction mechanism.

Mechanism of Hydroboration

M*echanism of oxidative work-up*

The mechanism of hydroboration / oxidative cleavage can be understood by assuming the B and H atoms are delivered in a *syn* fashion to the olefin, and the C–B bond is oxidatively cleaved in a *stereospecific* fashion in which the migrating bond proceeds with *retention of configuration*.

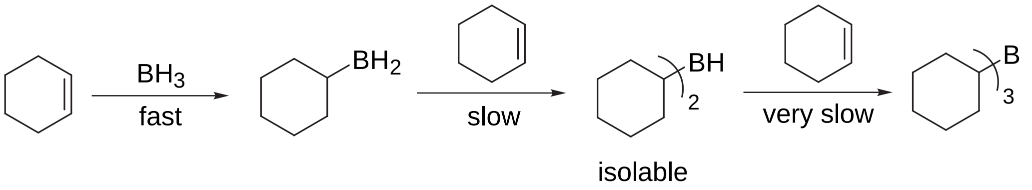
Bearing the mechanism in mind, it is easy to predict the stereochemical outcome of a hydroboration / oxidation sequence.

Regioselectivity of Hydroboration

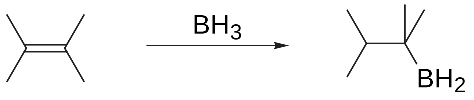
Hydroboration of unsymmetrically substituted olefins is highly regioselective with the boron atom invariably adding to the less hindered carbon. The reasons for this are primarily steric in origin. However, assuming an asynchronous transfer of the "B" and H to the olefin, polarisation of the olefin will result in the more substituted end of the olefin acquiring a positive charge. Since Boron is metallic the hydrogen substituents on a borane are hydridic in character, and on electronic grounds, would be expected to transfer preferentially to the more electron-deficient carbon atom, which in this case, in the T.S., is the more substituted carbon atom.

Rate of Reaction

The rate of hydroboration of olefins is dependent on the substituents already attached to the boron atom as well as those appended to the reacting olefin. For example, when BH_3 reacts with cyclohexene, the first hydroboration, to produce (cyclohexyl)BH_2, is fast. The presence of the cyclohexyl group in (cyclohexyl)BH_2, however, renders a second hydroboration slow, and a third even slower. In this way it is possible to isolate (cyclohexyl)$_2$BH.



When more-substituted olefins, such as 2,3-dimethylbut-2-ene, are hydroborated, it is possible to stop the reaction after a single hydroboration step.

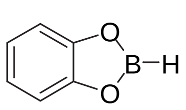


thexyl borane

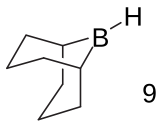
thexyl borane is isolable and can be used to hydroborate one other olefin. Transfer of the second H is too slow for it to be synthetically useful

Commercially Available Boranes

A range of boranes are commercially available. These include catechol borane and 9-BBN, both of which can react with one olefin (they only have one B–H bond). Borane itself is also available as a Lewis acid-Lewis base complex with THF and Me_2S.



catechol borane



9-BBN

Summary

In this lecture we have examined the various low-energy conformations of acyclic molecules containing olefins. We find that the low-energy conformations arise from allylic substituents eclipsing either the C=C group or the internal vinylic group. The relative energies of these low-energy conformations depend on a balance between 1,2-interactions and 1,3-interactions.

The reaction of olefins with electrophiles is typified by an electrophilic addition mechanism, which can be highly stereoselective (*e.g.* bromination). Hydroboration is another important reaction of olefins and provides an excellent method for hydrating olefins in an anti-Markovnikov fashion. The stereoselectivity and regioselectivity of the reaction can be understood by assuming an asynchronous *syn*-delivery of the hydrogen and boron substituents to the olefin, followed by a stereospecific oxidative cleavage of the C–B bond in the work-up that proceeds with retention of configuration at the migrating centre.