

CHEM 221 section 01

LECTURE #25

Tues., Nov.29, 2005

ASSIGNED READINGS:

TODAY'S CLASS: Continue Ch.11 up to 11.8

Think about date for problem session during exams
Dec. 13th? 14th? 15th? 19th?

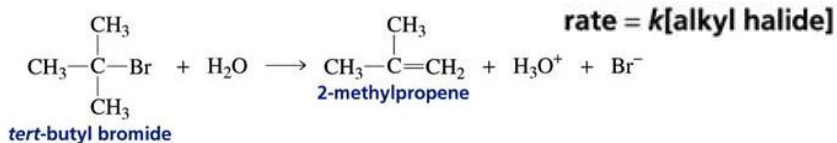
Problem sets due next class!

NEXT LECTURE: Finish Ch.11

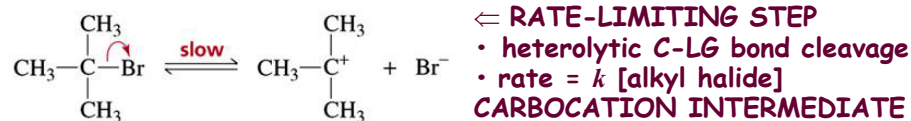
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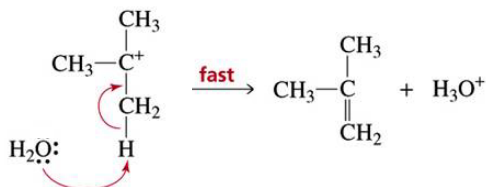
11.3 The E1 reaction: unimolecular RLS



mechanism of the E1 reaction



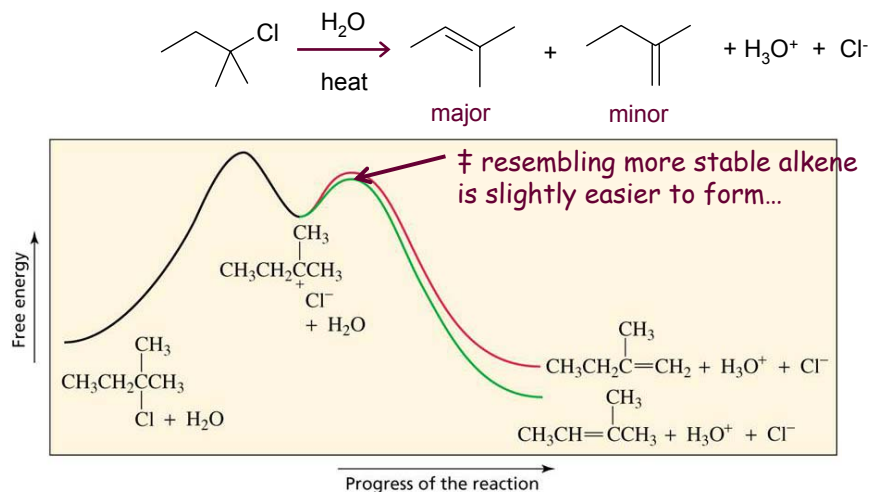
Carbocation intermediate gets deprotonated by base at the β -position (more acidic than typical C-H, because adjacent to C^+ centre... like a powerful EWG!)



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When carbocation has 2 different β -H's:
two possible products (MAJOR = more stable alkene)
Zaitsev's rule applies...

Rxn coordinate diagram for E1 rxn of 2-chloro-2-methylbutane



Increase rate of E1 rxn by improving C-LG cleavage step...

Faster E1 reaction if...:

1. More stable carbocation (resonance stabilized / alkyl substituted)

relative reactivities of alkyl halides in an E1 reaction = relative stabilities of carbocations

3° benzylic \approx 3° allylic > 2° benzylic \approx 2° allylic \approx 3° > 1° benzylic \approx 1° allylic \approx 2° > 1° > vinyl

most stable

least stable

2. Better leaving group (weaker base!)

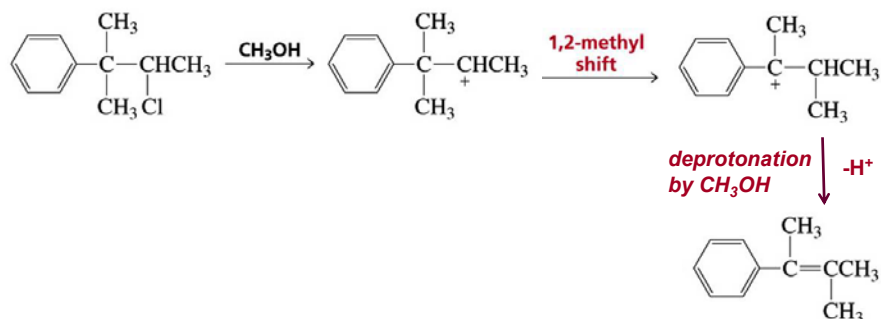
relative reactivities of alkyl halides in an E1 reaction

most reactive \leftarrow RI > RBr > RCl > RF \leftarrow least reactive

← increasing reactivity

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E1 involves carbocation intermediate: rearrangements...



Remember: *the more stable carbocation will dominate*
 Carbocations can rearrange via:
 1,2-methyl shifts
 1,2-hydride shifts

- it sometimes results in ring expansion
- & it tends NOT to disrupt aromatic rings

(5)

11.4 Competition Between E2 and E1 Reactions

Table 11.3 Summary of the Reactivity of Alkyl Halides in Elimination Reactions

Primary alkyl halide	E2 only
Secondary alkyl halide	E1 and E2
Tertiary alkyl halide	E1 and E2

Same rules learned for substitutions:

- bimolecular rxn: favoured by high conc. of strong base
E2 in an aprotic polar solvent

- unimolecular rxn: favoured by weak base & protic solvent!
E1

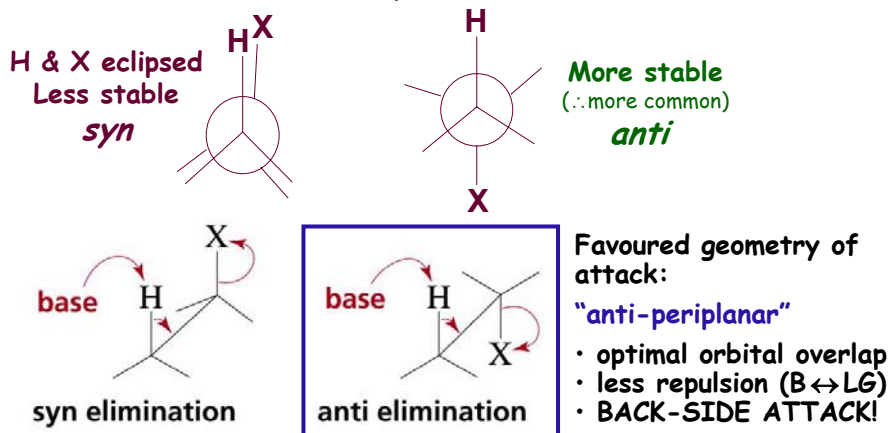
E2 offers better control of products, since rxn is concerted
E1 offers less control, since rxn involves C⁺ intermediate

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11.5 Stereochemistry of Elimination reactions

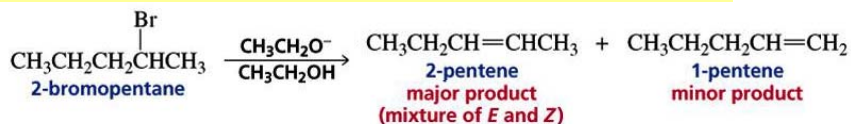
Stereochemistry of E2:

The bonds to the eliminated groups (H & X) must be coplanar in order to achieve correct overlap of p-orbitals in product
 → **THUS: need either "syn" or "anti" conformation:**



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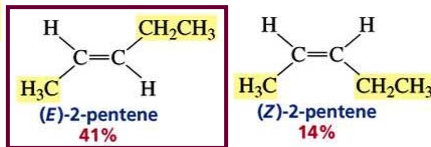
Consider the regioselectivity of the E2 reaction



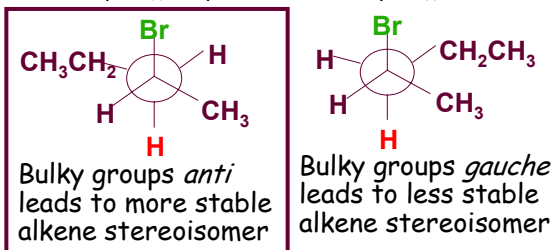
What about stereoselectivity?

The alkene with the bulkiest groups **TRANS** to each other will be formed in greater yield, because:

- it starts from conformation with bulky groups **ANTI** (less steric strain)
- means: less strain in ‡ ⇒ easier to form ⇒ faster rxn to form alkene with bulkiest groups trans



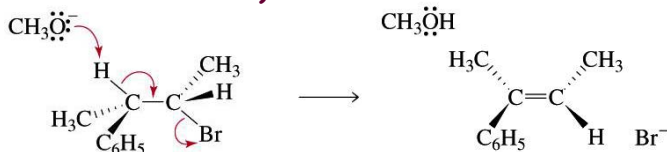
NOTE: always have 2 "H-X-anti" conformers to choose from when the β-C has 2H's on it



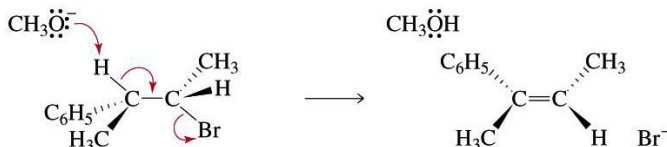
(8)

For E2 elimination from any substrate with only 1H on the β -C (note: often = chiral substrate): only 1 H-X-anti conformer...
 ⇒ One stereoisomer formed preferentially

This compound yields the (E) isomer:



Its diastereomer below (opposite config. at left C) yields (Z) isomer:



NOTE: EACH ONLY YIELDS ONE STEREOISOMER PRODUCT...
 only 1 H-X-anti conformer per compd here, since β -C has only 1 H on it!
 Also: only considering major product here...other β -C yields minor product

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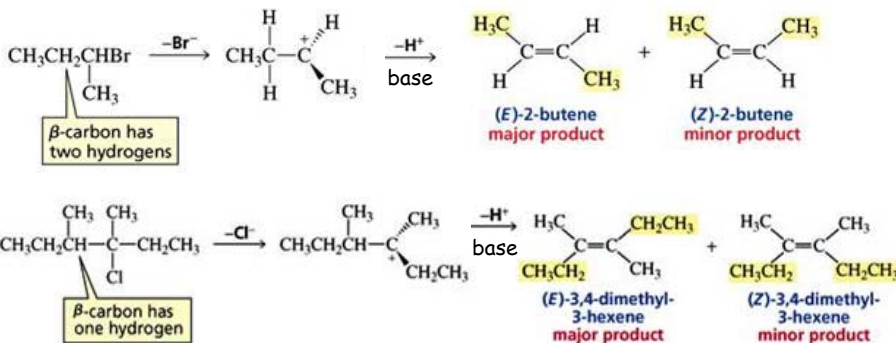
Stereochemistry of the E1 Reaction

Planar carbocation intermediate: makes reaction **non-stereospecific**

WHY?

(again, like S_N1 ...)

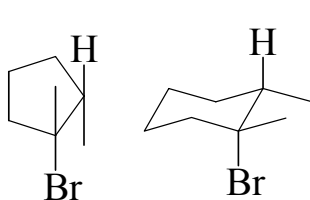
- free rotation about β C-C⁺ bond in carbocation
- means e⁻ pair from departing H⁺ can attack from either side
 → same result as if both syn & anti elimination could occur
 → both the (E) & (Z) isomers will form (E favoured due to stability...)
 AND same whether β -C has 1H or 2H bonded to it!



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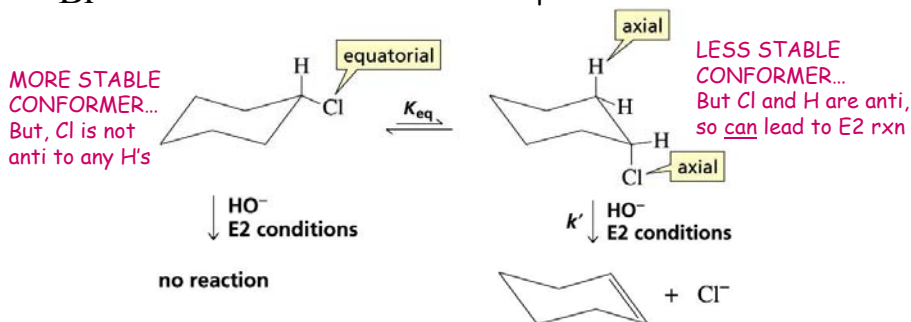
11.6 Elimination from cyclic compounds

- **E2 reaction:** requires anti-periplanar geometry
 \Rightarrow H and LG must be **TRANS** to each other on a ring!



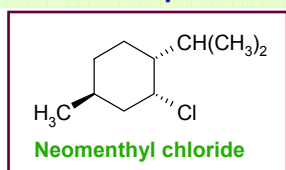
For cyclohexanes: need 1,2-diaxial H & LG
 IMPLIES: E2 rxn rate depends on conc'n of "H-LG-diaxial" conformer

- Relative stabilities of conformers matters!
- If reacting conformer is less stable, less of it is present \Rightarrow slower E2 rxn.

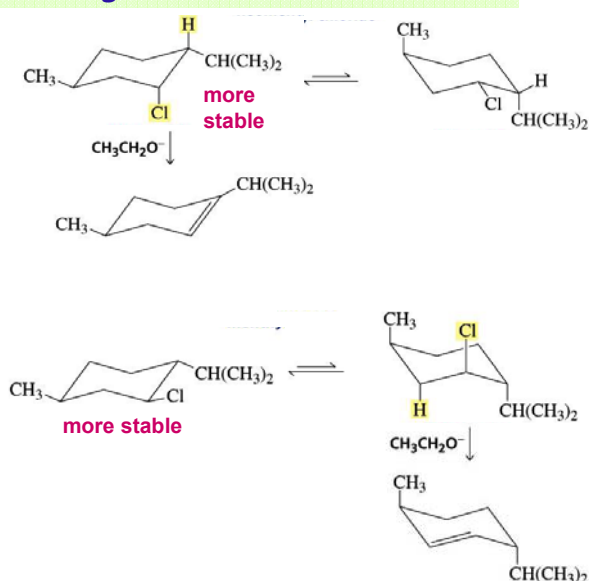
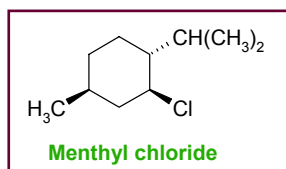


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Which compound will undergo faster E2 elimination?



- \Rightarrow this compound will react faster via E2.
- \rightarrow its preferred conformation has the required geometry



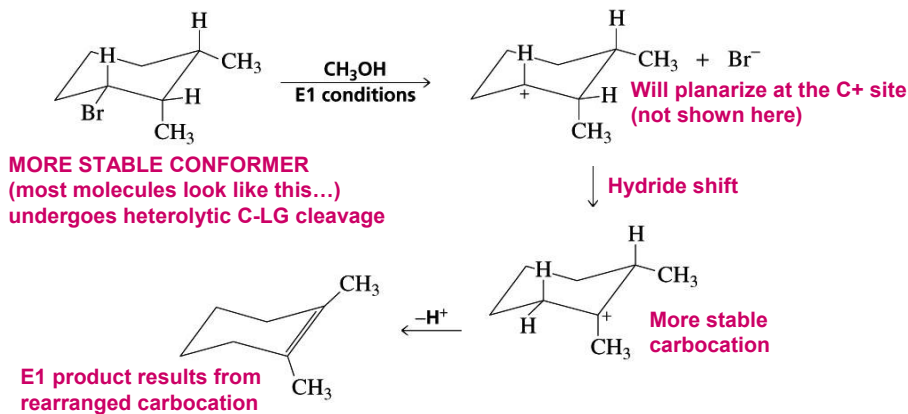
(12)

• **E1 reaction:** not concerted \therefore no conformational requirements

NO NEED TO WORRY ABOUT PREFERRED CONFORMATION.

Just worry about:

1. Figuring out which H would be attacked by base (Zaitsev's rule...)
2. Possibility of carbocation rearrangements



(13)

Summary of stereochemistry of rxns of alkyl halides (& other compounds with LGs)...

Table 11.4 Stereochemistry of Substitution and Elimination Reactions

Mechanism	Products
S_N1	Both stereoisomers (<i>R</i> and <i>S</i>) are formed (more inverted than retained).
E1	Both <i>E</i> and <i>Z</i> stereoisomers are formed (more of the stereoisomer with the bulkiest groups on opposite sides of the double bond).
S_N2	Only the inverted product is formed.
E2	Both <i>E</i> and <i>Z</i> stereoisomers are formed (more of the stereoisomer with the bulkiest groups on opposite sides of the double bond is formed) unless the β -carbon of the reactant is bonded to only one hydrogen, in which case only one stereoisomer is formed, with a configuration that depends on the configuration of the reactant.

(14)

11.8 Competition between substitution & elimination

How can we tell which rxn should dominate? S_N2 , S_N1 , E2, E1 ?

- 1) Decide if **substrate** is likely to undergo heterolytic cleavage
 → leaving group: weaker base = better L.G.
 → stability of carbocation: resonance stabilized > 3° > 2° > 1° ...

Table 11.5

In an S_N2 reaction: $1^\circ > 2^\circ > 3^\circ$

In an S_N1 reaction: $3^\circ > 2^\circ > 1^\circ$

In an E2 reaction: $3^\circ > 2^\circ > 1^\circ$

In an E1 reaction: $3^\circ > 2^\circ > 1^\circ$

- 2) Decide whether rxn **conditions** favour S_N2 /E2 or S_N1 /E1
i.e., will we have to wait for the LG to fall off, or not?

- S_N2 /E2 rxns are favoured by a high concentration of good nucleophile / strong base in aprotic solvents
- S_N1 /E1 rxns are favoured by poor Nu / weak base in polar, protic solvents

- 3) Decide which dominates: **substitution vs. elimination**

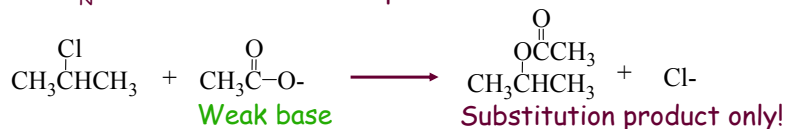
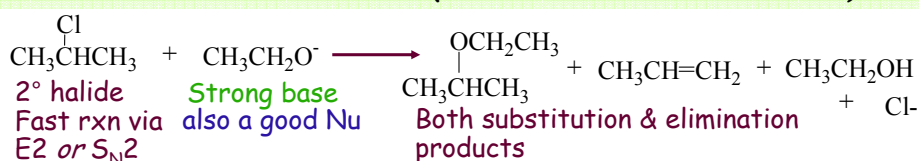
- bulkiness of substrate has opposite effect for S_N2 vs. E2...
- a base won't be a good nucleophile if it's very bulky...
- elimination rxns are favoured by elevated temperatures!

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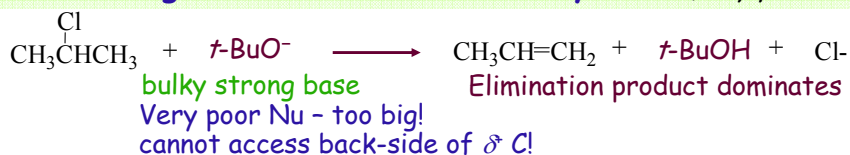
If looks like S_N2 / E2 are the most likely pathways...

To encourage substitution: use a weak base

(weak bases can still act as Nu's...)



To encourage elimination: use a bulky base (very poor Nu...)



(16)

If looks like S_N1 / $E1$ are the most likely pathways...

Reactions both occur via carbocation intermediate

IMPLIES: no way to select for substitution vs. elimination

- same order of reactivity for S_N1 & $E1$ rxns: $3^\circ > 2^\circ \gg 1^\circ$
- same rate determining step
 - no difference in rate if change base/Nu strength

ALWAYS GET BOTH S_N1 & $E1$ PRODUCTS TOGETHER!

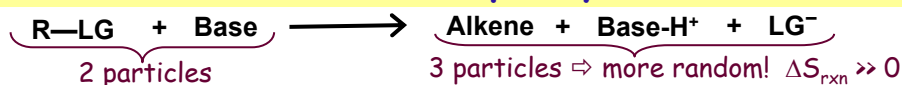
Summary of all situations:

Class of alkyl halide	S_N2 versus $E2$	S_N1 versus $E1$
Primary alkyl halide	Primarily substitution, unless there is steric hindrance in the alkyl halide or nucleophile, in which case elimination is favored	Cannot undergo $S_N1/E1$ reactions
Secondary alkyl halide	Both substitution and elimination; the stronger and bulkier the base, the greater is the percentage of elimination	Both substitution and elimination
Tertiary alkyl halide	Only elimination	Both substitution and elimination

But: 1 last rxn condition we can control: TEMPERATURE
(not mentioned in your textbook, but chemists routinely take advantage of this!)

(17)

Elimination rxns are entropically favourable...



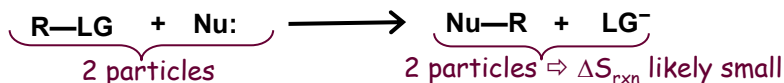
How much driving force?

$$\Delta G_{\text{rxn}} = \Delta H_{\text{rxn}} - T\Delta S_{\text{rxn}} \quad \text{Entropy term } (-T\Delta S) \text{ is larger at higher } T \Rightarrow \text{makes } \Delta G \text{ more negative...}$$

Thus: elimination rxns are more thermodynamically favoured at $\uparrow T$!

- increases ΔG^\ddagger for reverse rxn (*recall like E_a but includes entropy*)
- means $k_{\text{fwd}} \gg k_{\text{rev}} \Rightarrow$ rxn is more product favoured (larger eqm constant, K)!

...but substitutions are not



Substitution rxns have similar thermo. driving force at high & low T ...
i.e., see only kinetic effect if $\uparrow T$ (rxn will be faster, but ΔG^\ddagger is same)

If you want elimination: heat up the rxn mixture!
 indicate heat by using symbol Δ above or below the rxn arrow

(18)

ASSIGNED READINGS

BEFORE NEXT LECTURE:

Read: Ch.11 up to 11.8

Practice: predicting products & stereochemistry