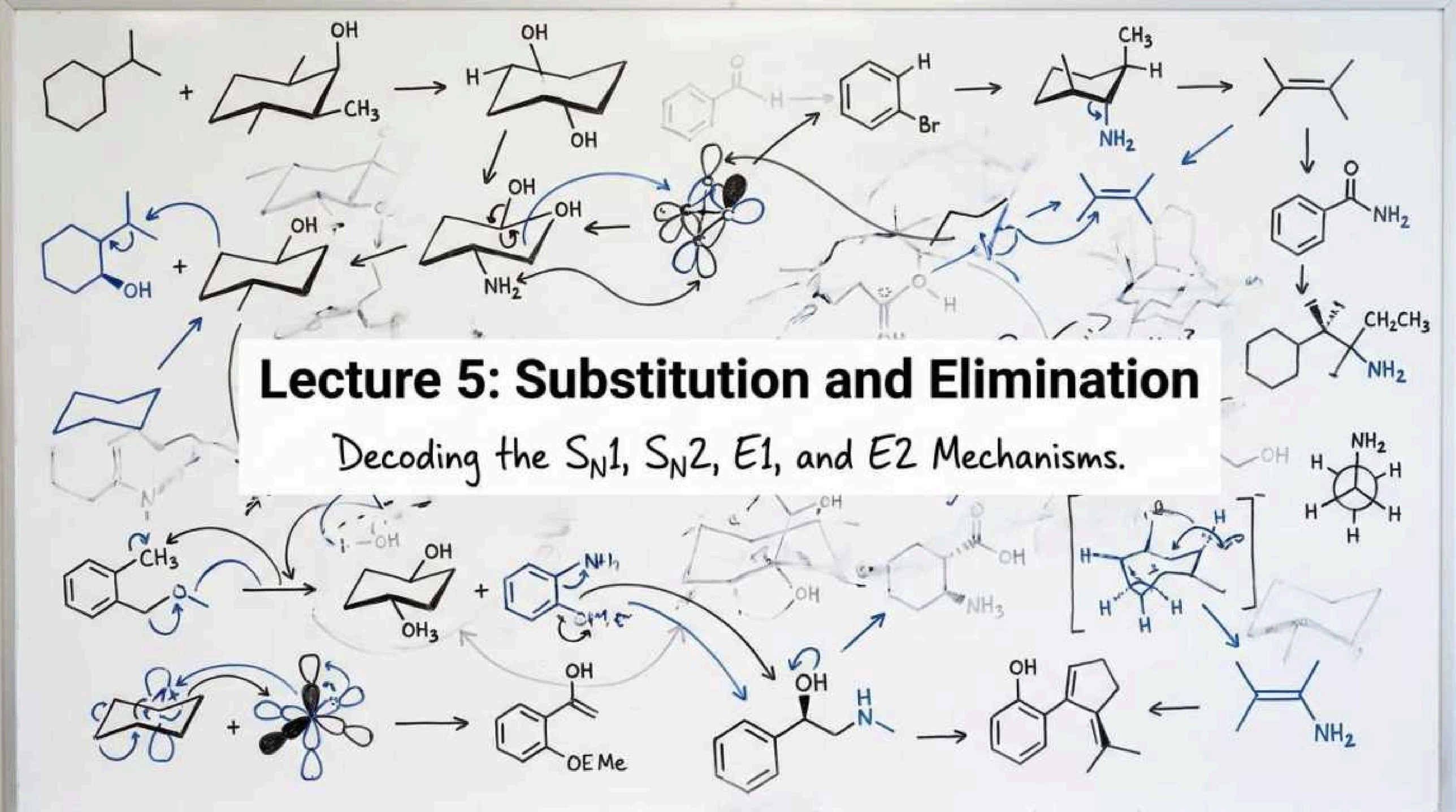
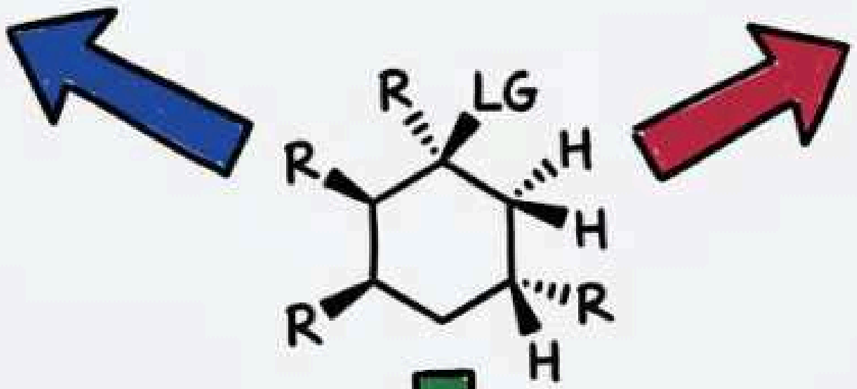


Lecture 5: Substitution and Elimination

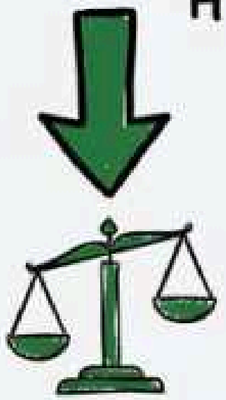
Decoding the S_N1, S_N2, E1, and E2 Mechanisms.

¶ 5.1

Replace a group?
(Substitution)



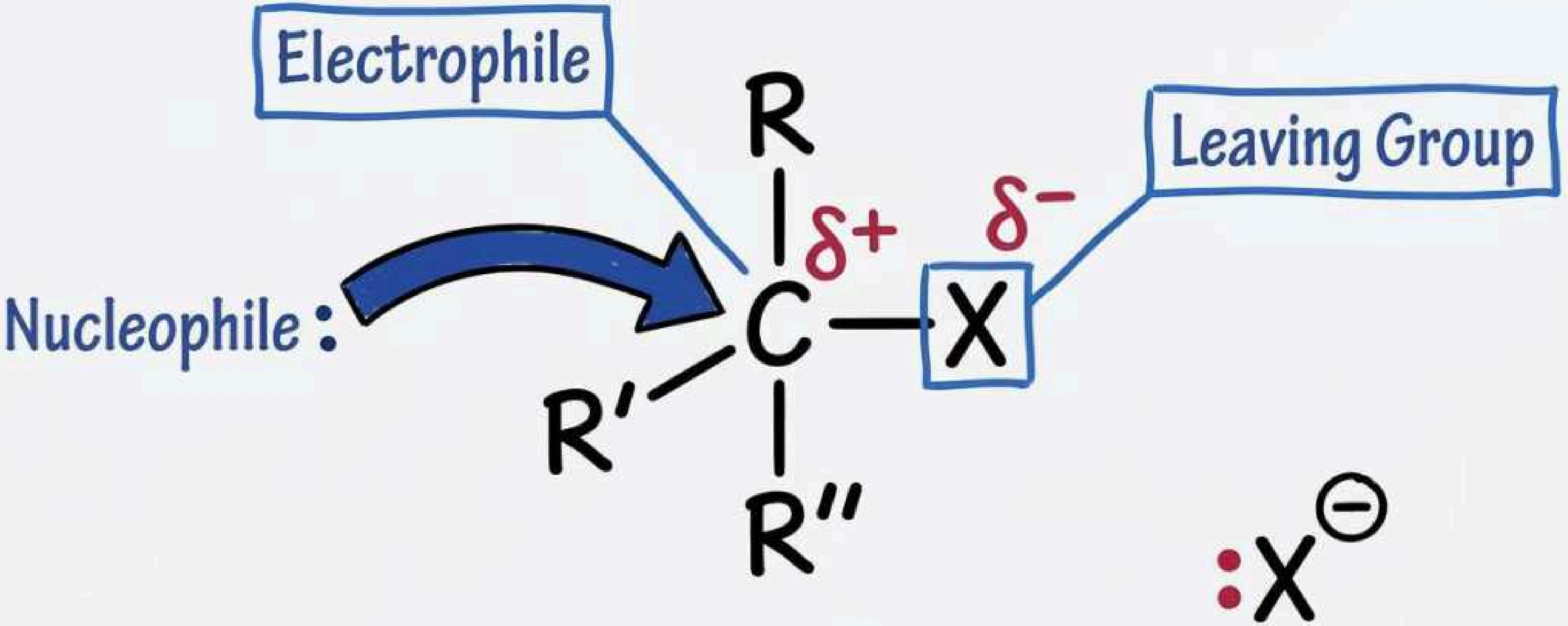
Lose a molecule to form a double bond?
(Elimination)



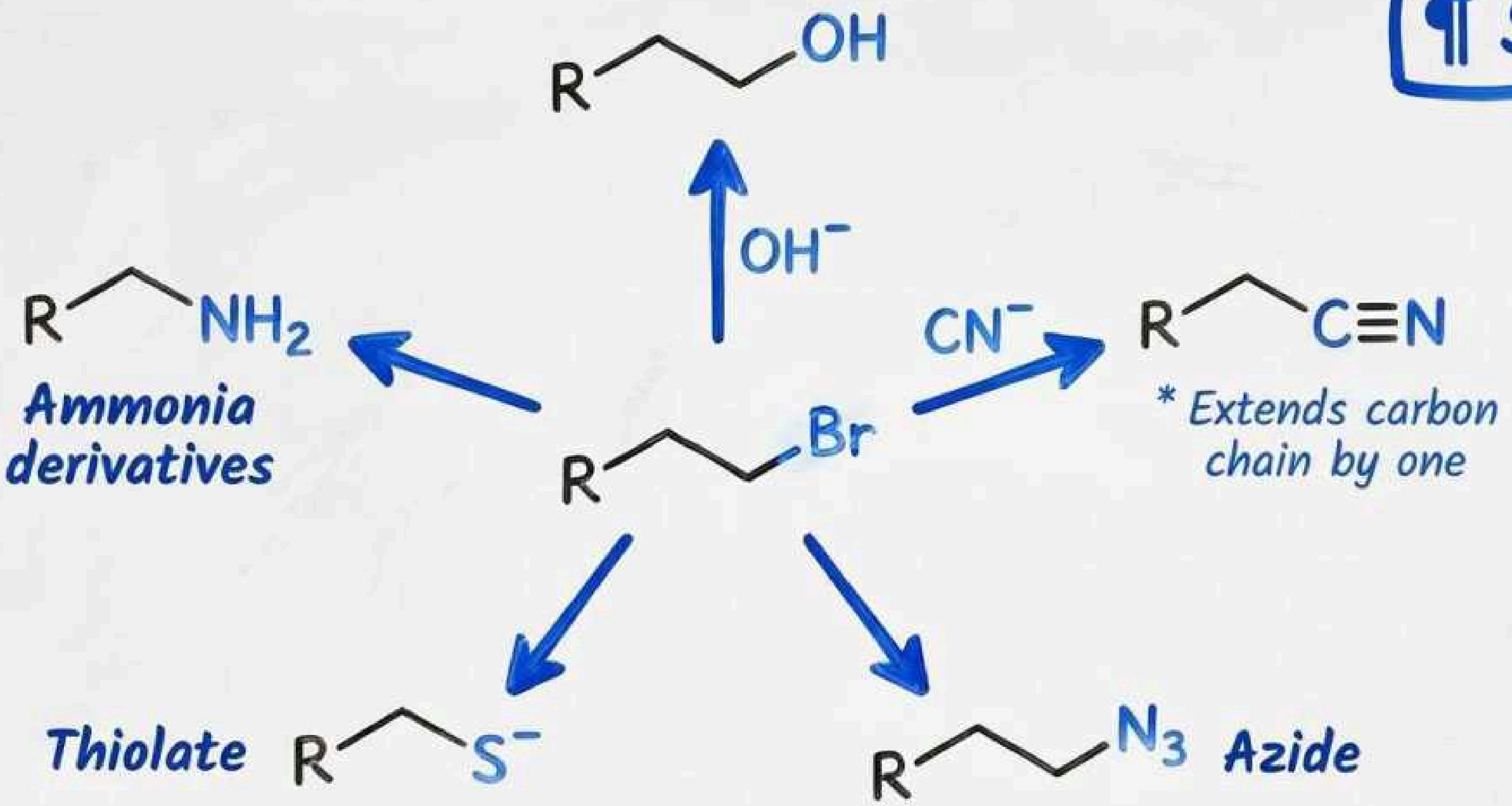
Which path wins?

Governed by electron flow, stability, and shape.

¶5.2

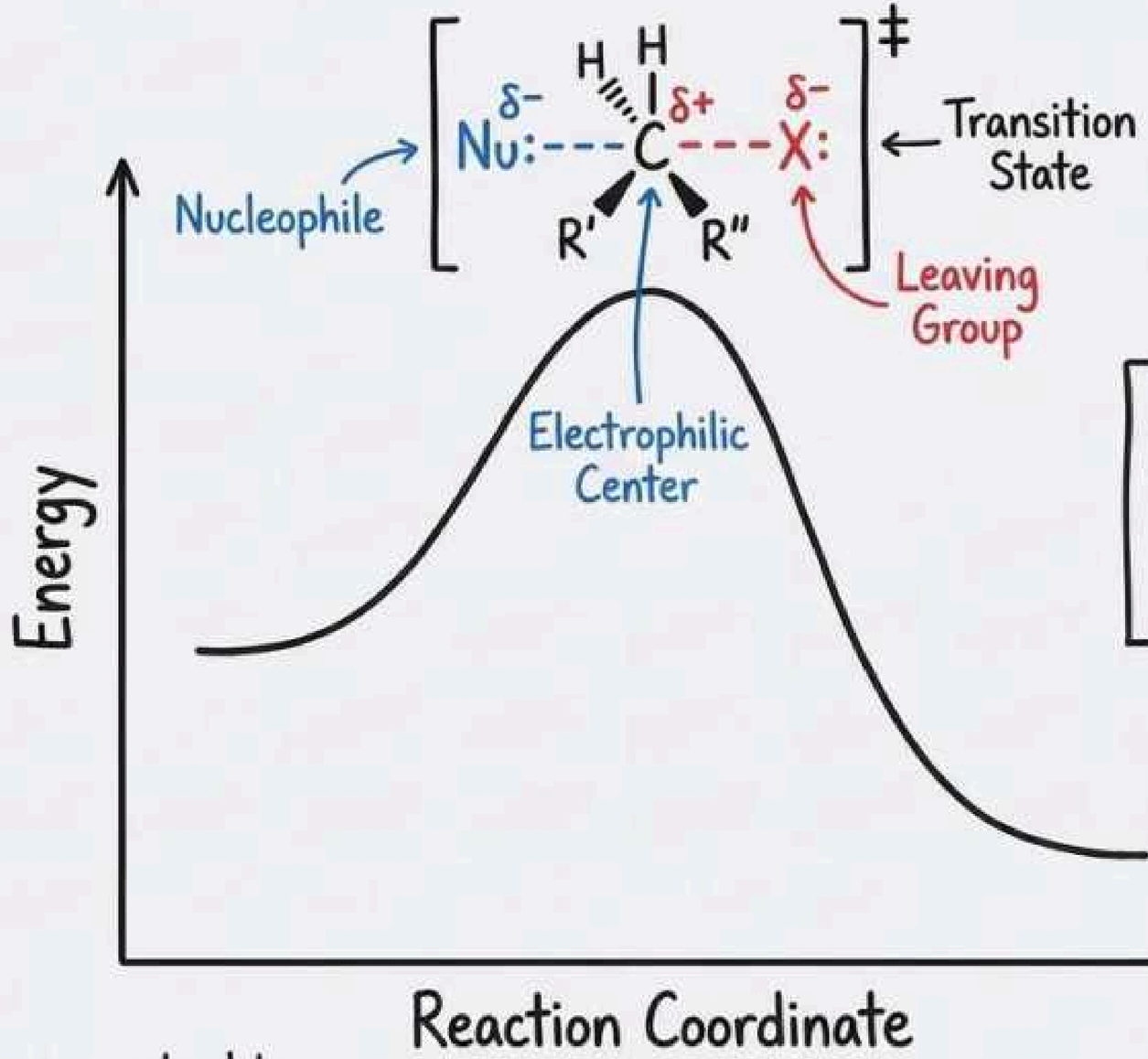


¶ 5.3



One of the most versatile ways to convert functional groups.

¶ 5.4



$$\text{Rate} = k[\text{Substrate}][\text{Nucleophile}]$$

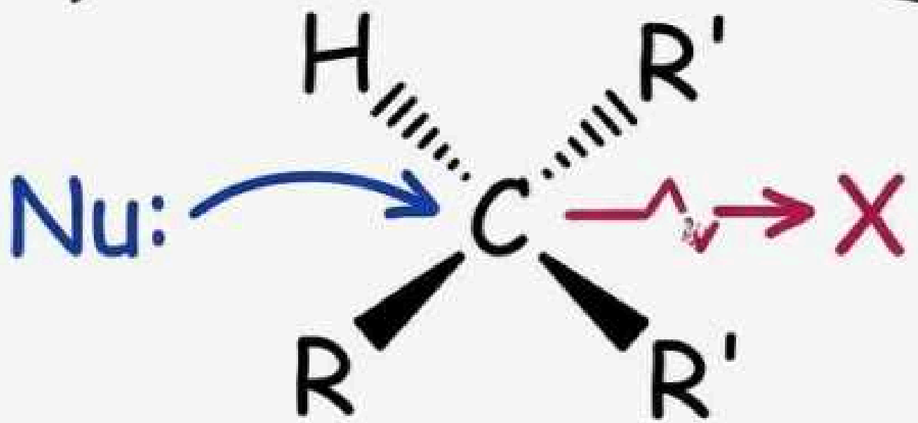
(Second Order / Bimolecular)

Mechanism solved by Hughes & Ingold, 1930s.

¶ 5.5



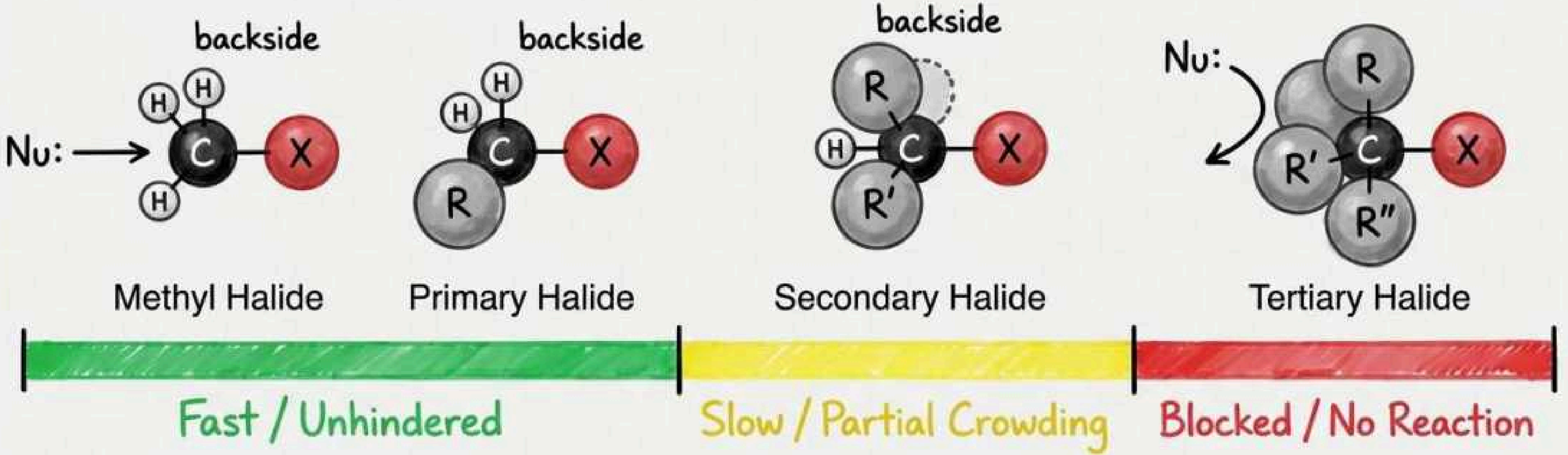
R configuration ⟶ S configuration



First observed by Paul Walden in 1896.

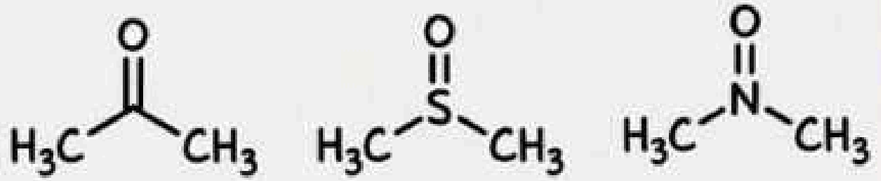
Steric Hindrance Spectrum

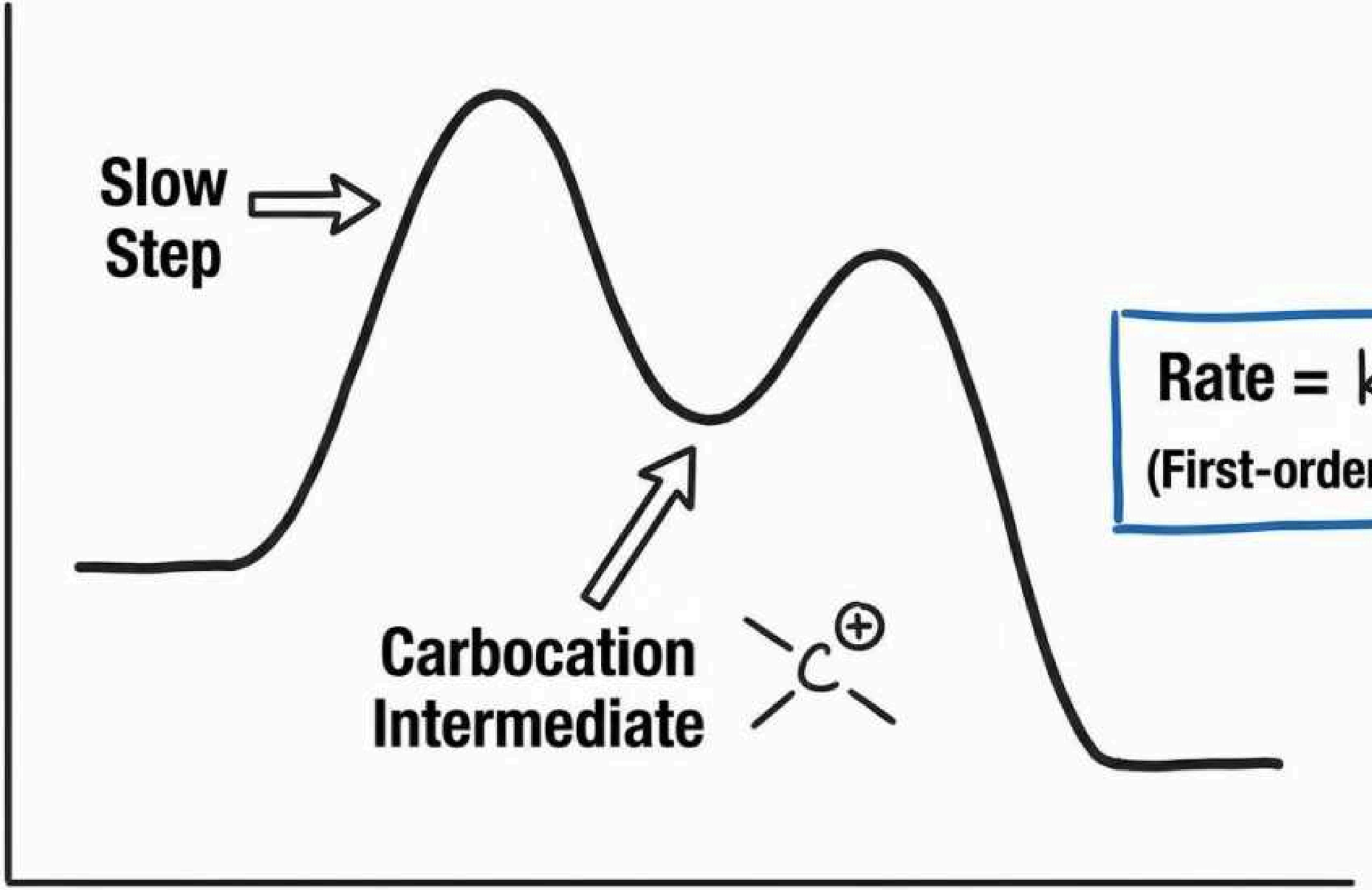
¶ 5.6



Ideal Setup

Strong Nucleophile + Good Leaving Group
+ Polar Aprotic Solvent

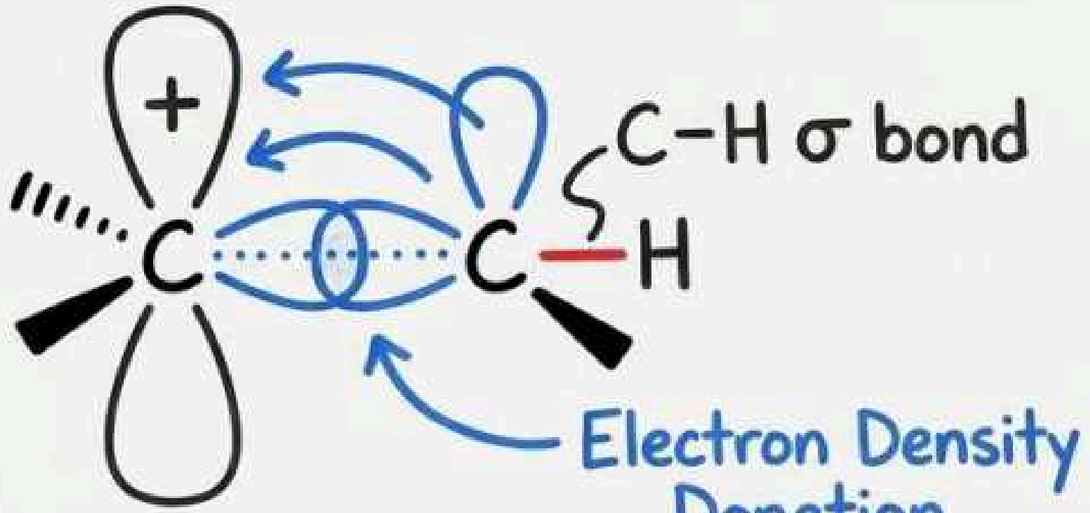




Rate = k[Substrate]

(First-order / Unimolecular)

¶ 5.8



Hyperconjugation

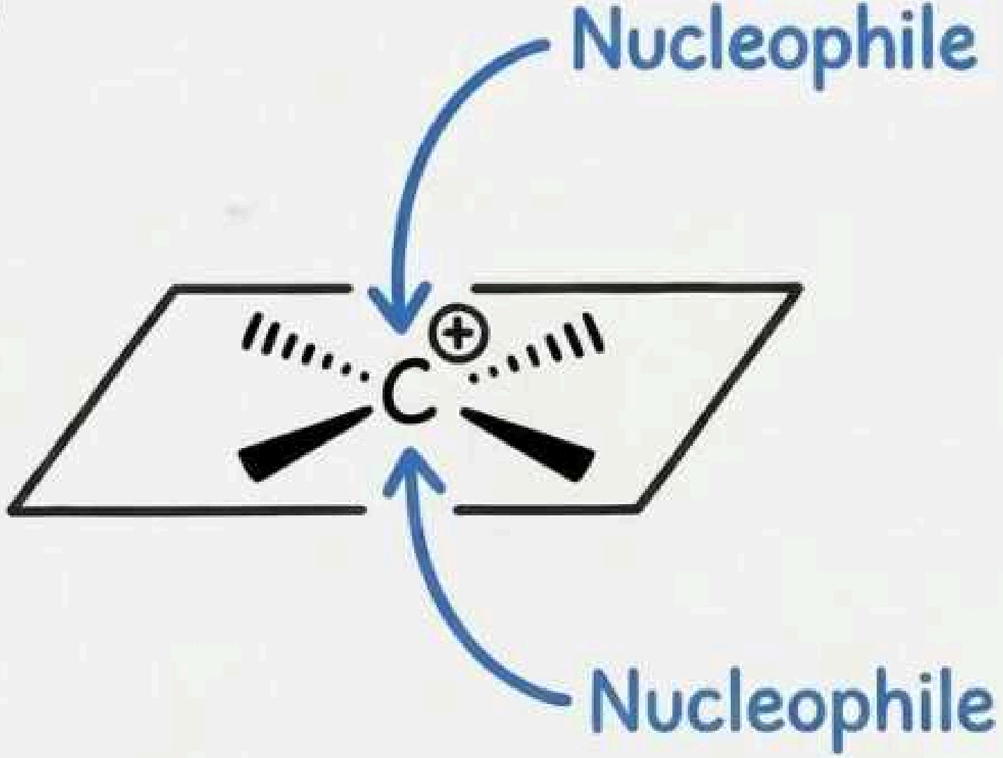
Allyl and benzyl cations gain extra stability from resonance.

Methyl ← 1° → 2° → 3°

Tertiary halides favor S_N1. Primary do not.

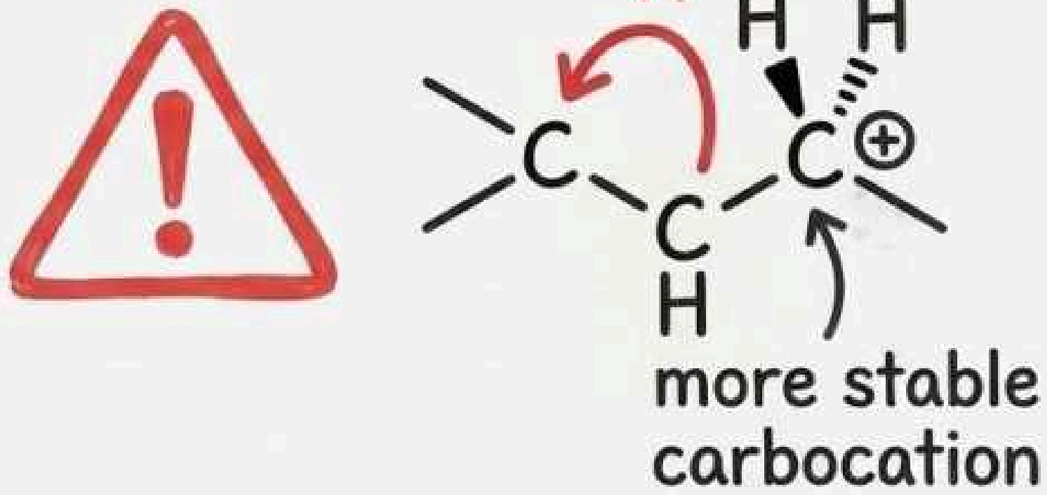
¶ 5.9

A)



Yields a nearly racemic mixture

B)

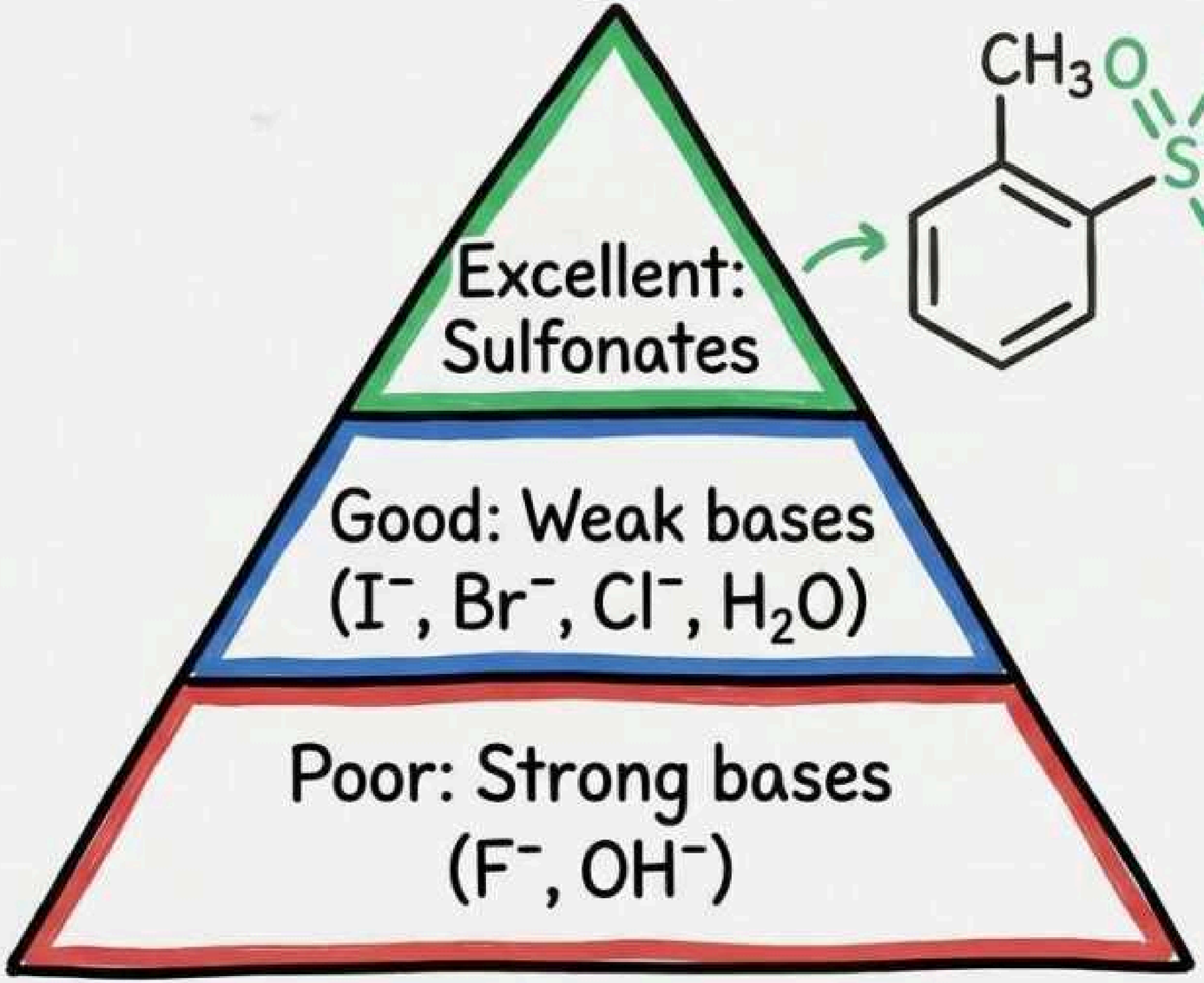


1,2-hydride shift (Rearrangement)

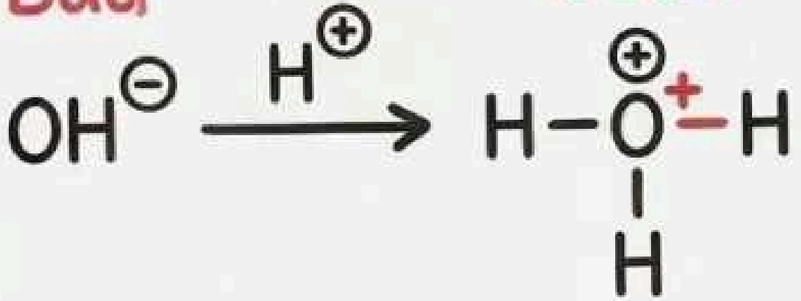
Favored by polar protic solvents (water, methanol, ethanol) which stabilize the cation and leaving group via hydrogen bonds.

Leaving Groups

¶5.10

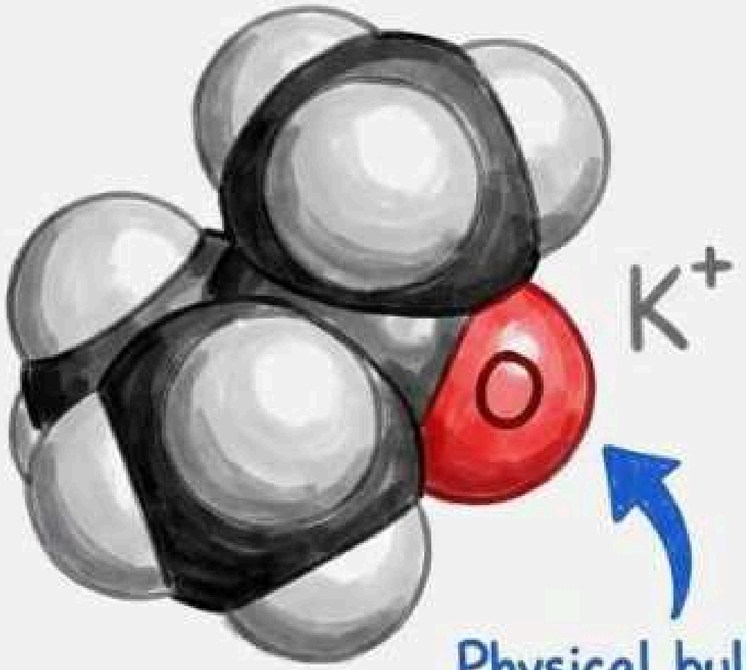


Bad → Good

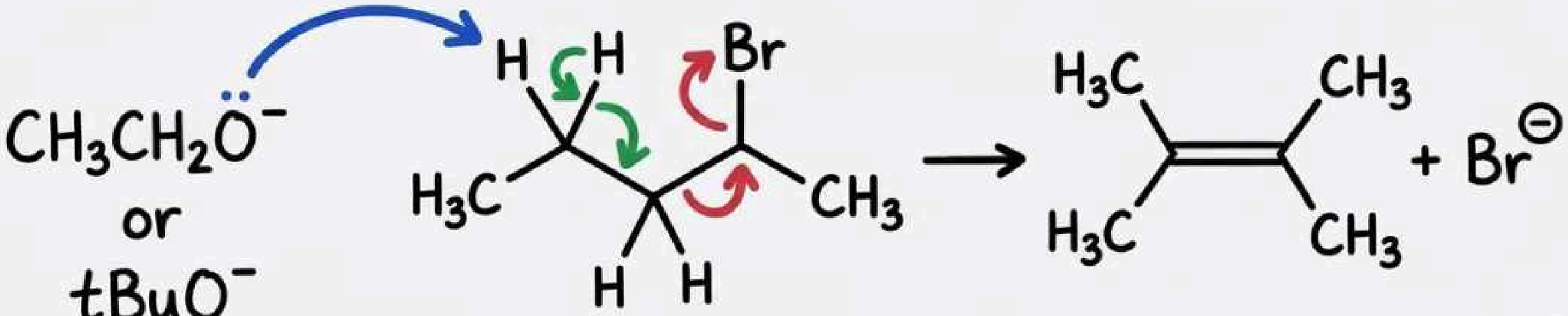


¶ 5.11

Comparison 1 (Size)	Comparison 2 (Charge)
Iodide > Fluoride I^- F^- (larger atoms are better nucleophiles in protic solvents)	OH^- > H_2O (negative charge increases strength)



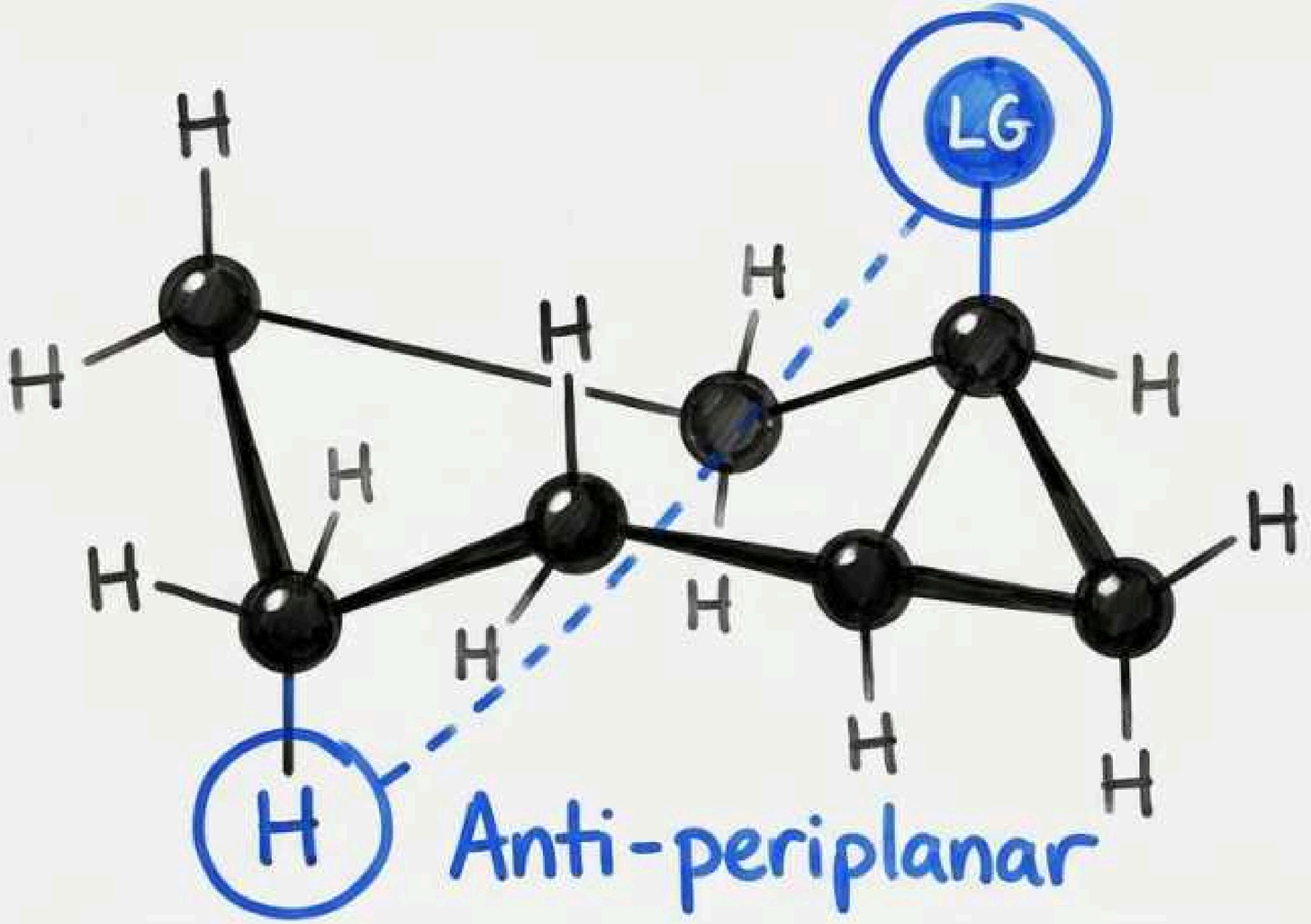
Physical bulk prevents it from acting as a nucleophile. Restricted to removing easily reached exterior protons.



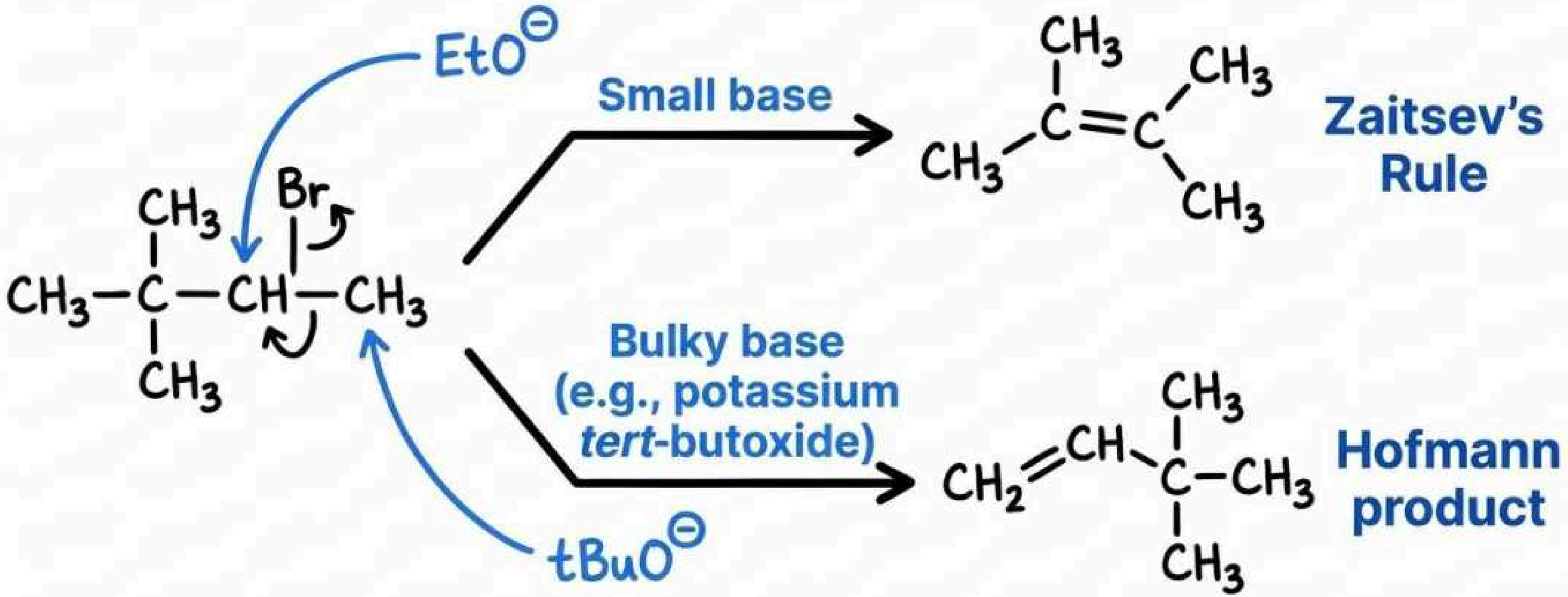
Rate depends on both substrate and base.

Reagents:
Ethoxide, tert-butoxide (strong bases).

¶ 5.13



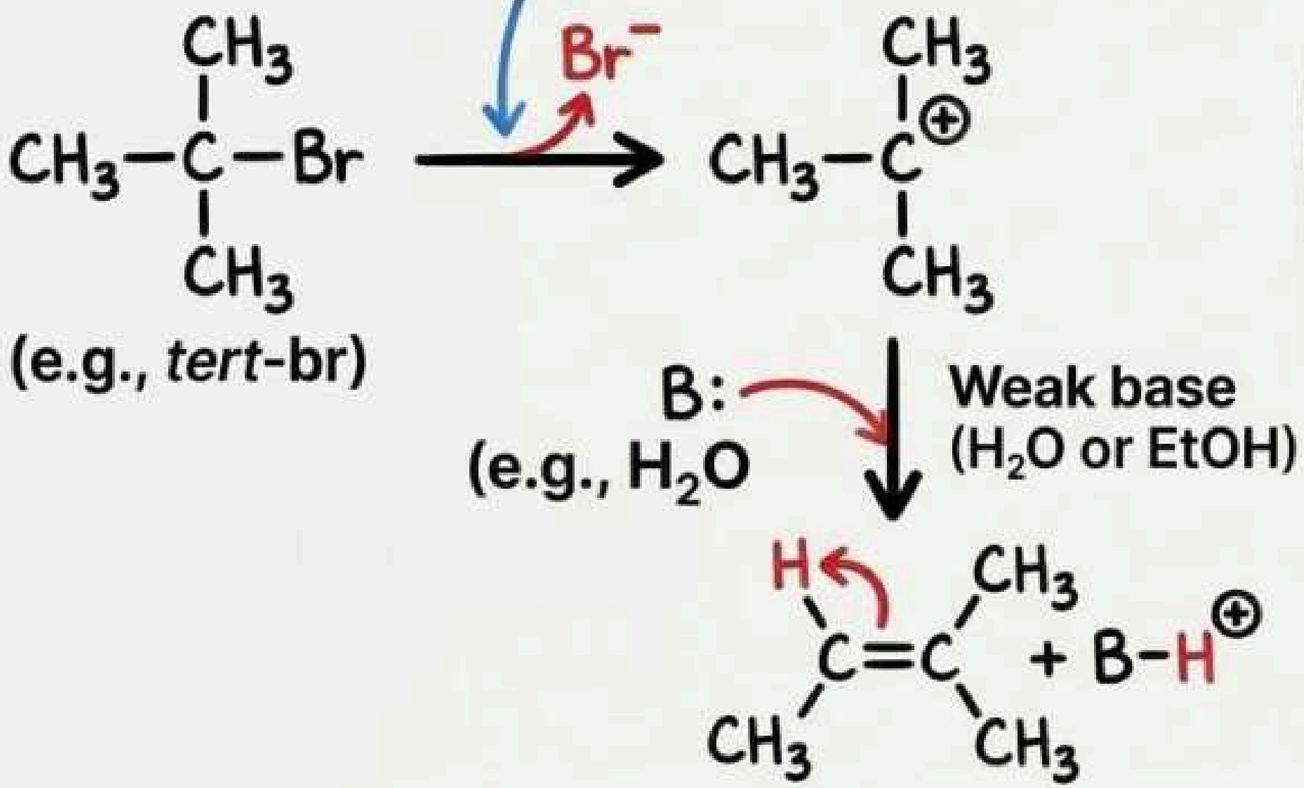
The geometric rule dictates reaction speed and which stereoisomer forms.


EtO⊖
Small base
Zaitsev's Rule
Bulky base
(e.g., potassium
tert-butoxide)
Hofmann
product
tBuO⊖

¶ 5.15

E1 Mechanism

Shares the exact same initial step as S_N1.



(e.g., *tert*-br)

Thermodynamics

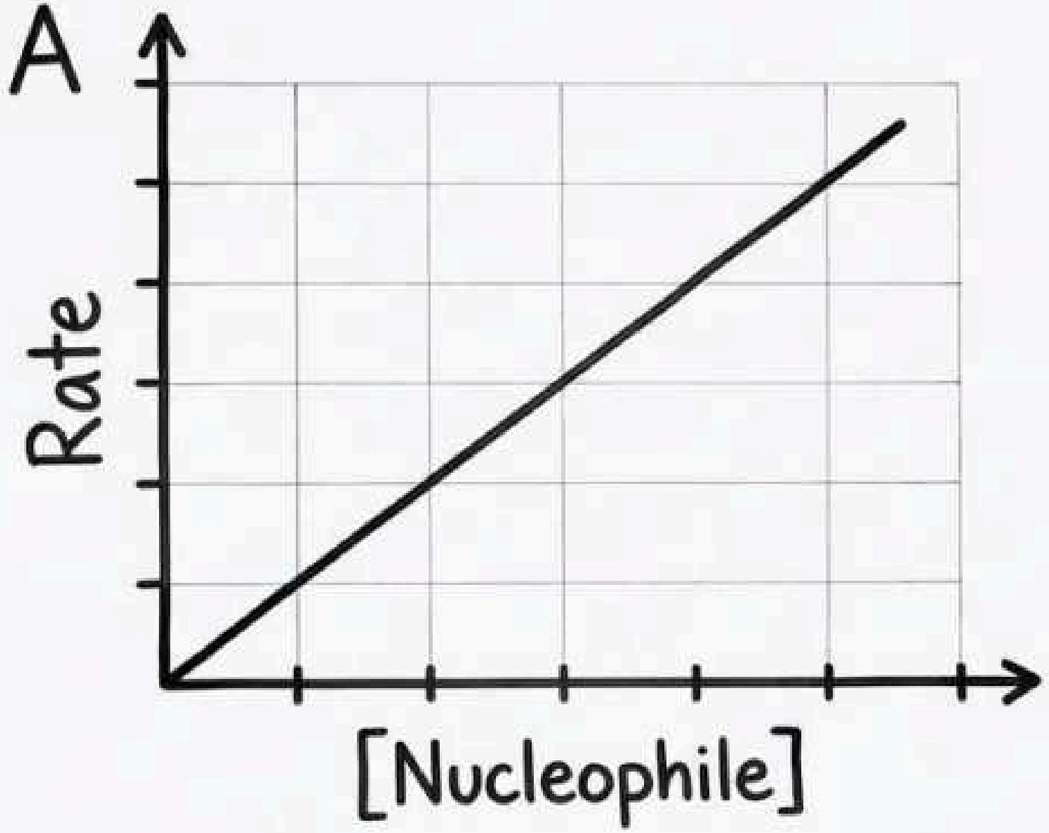
$$\Delta G = \Delta H - T\Delta S$$

Heat (T) multiplies the entropy (ΔS) gained from creating more molecules. Heat favors elimination.

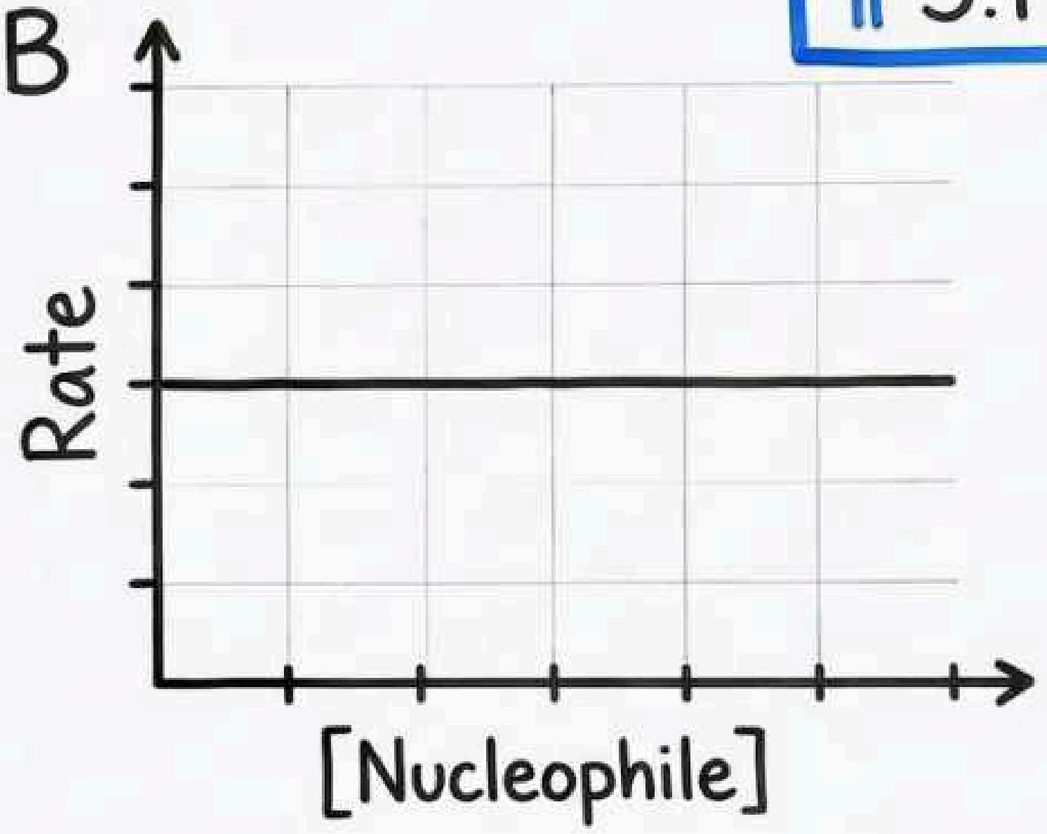
¶ 5.16

	Strong Nucleophile / Weak Base	Strong Base
Methyl	mostly S_N2 (unless bulky base forces E2)	
1°	mostly S_N2 (unless bulky base forces E2)	
2°	The hard case: Reagent decides (Nucleophile = S_N2, Base = E2)	
3°	S_N1/E1 without base	E2 with strong base

¶ 5.17



S_N2 (e.g., methyl iodide + cyanide).



S_N1 (e.g., tert-butyl bromide).

Kinetics reveals the invisible mechanism.

¶ 5.18

S_N2	S_N1
1-step, inversion	2-step, carbocation, racemic
E2	**E1**
alkene formation, concerted base removes proton	alkene formation, stepwise base removes proton

