(1) **Today**

Attendance

Review Syllabus

Chap 11: Reactions of Alkyl Halides:
Nucleophilic Substitutions and Eliminations

Sections 11.1 - 11.6: Substitution Reactions

Next Class (2)

Sections 11.1 - 11.6: Substitution Reactions

(3) **Second Class from Today**

Sections 11.1 - 11.6: Substitution Reactions

Sections 10.5, 17.6: Alcohols in Nucleophilic Substitution Reactions

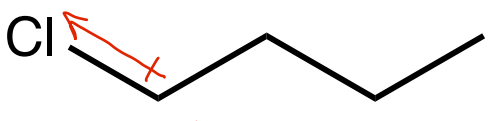
Third Class from Today (4)

Sections 10.5, 17.6: Alcohols in Nucleophilic Substitution Reactions

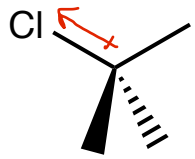
Sections 11:7 - 11:11: Elimination Reactions

LAB STARTS THIS WEEK……PLEASE GO TO YOUR REGULARLY SCHEDULED LAB

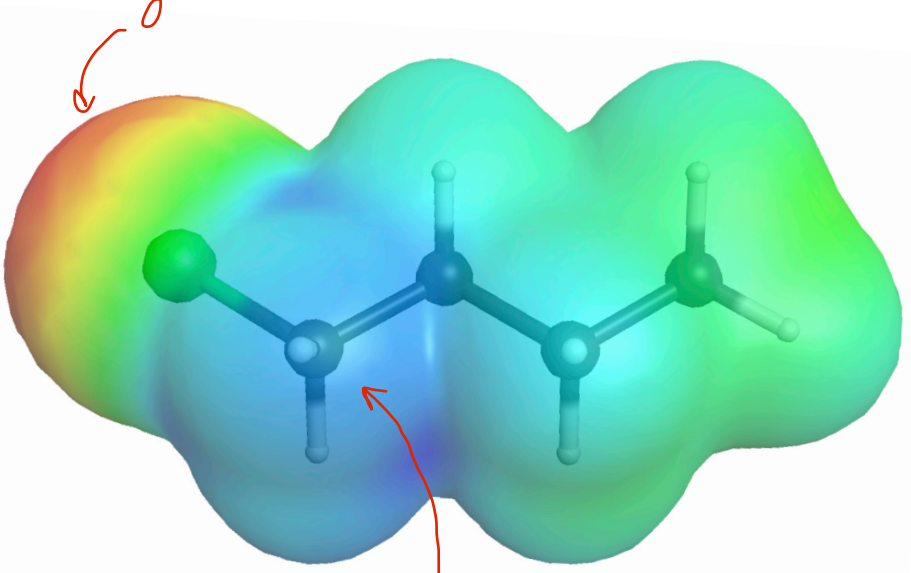
3.16



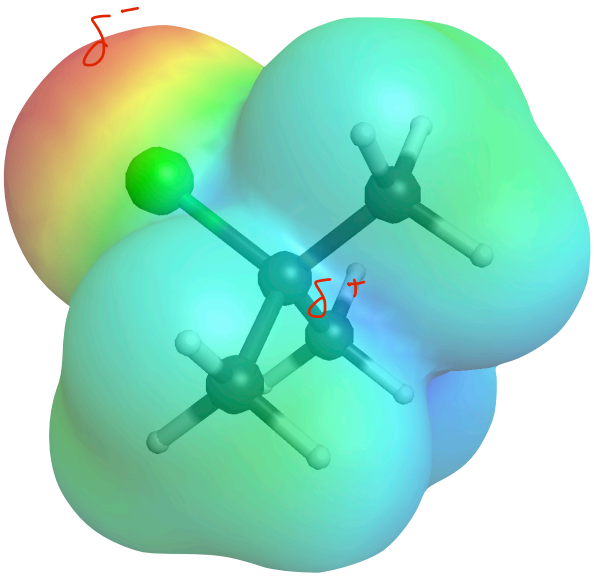
2.5



δ^-



δ^+



Is the C atom nucleophilic or electrophilic?

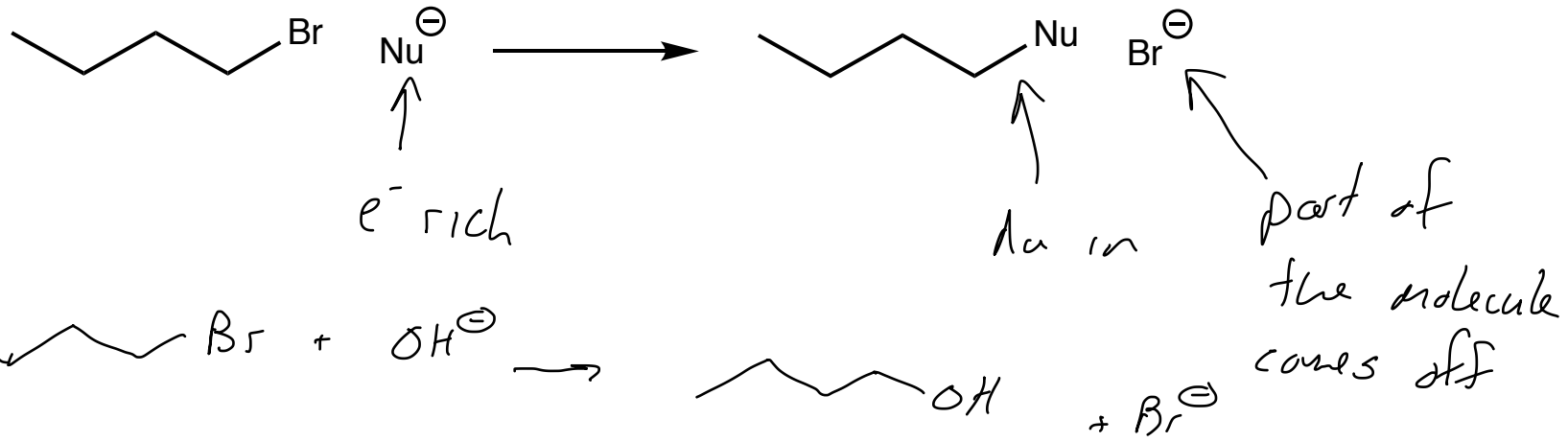
weakly electrophilic C atoms can react with nucleophiles

Both

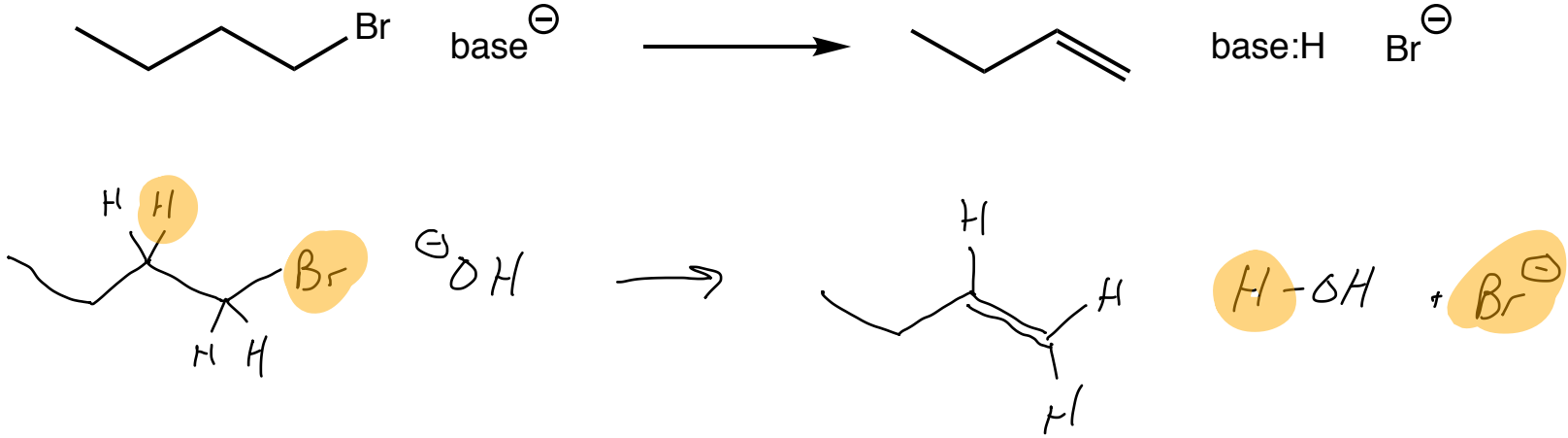
Substitution and Elimination are Possible

Sections 11.1 and 11.7

Nucleophilic substitution



Elimination reaction



Overview

Nucleophilic Substitution and Mechanisms of Nucleophilic substitution

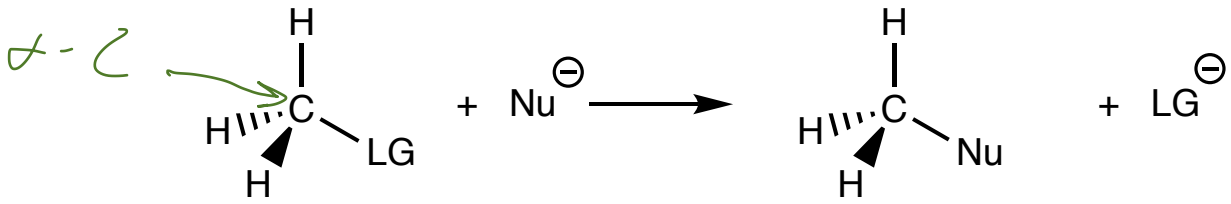
- Factors affecting nucleophilic substitution
- Competition between S_N1 and S_N2 Mechanisms

Elimination Reactions and Mechanisms of Elimination Reactions

- Factors affecting elimination reactions
- Competition between E1 and E2 Mechanisms

Competition between Substitution and Elimination Reactions

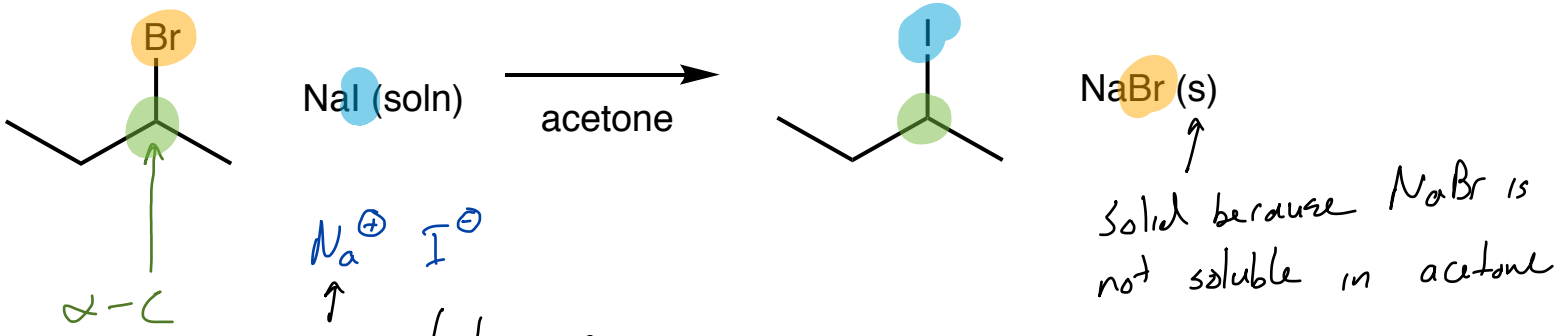
Alcohols as Substrates in Substitution and Elimination Reactions



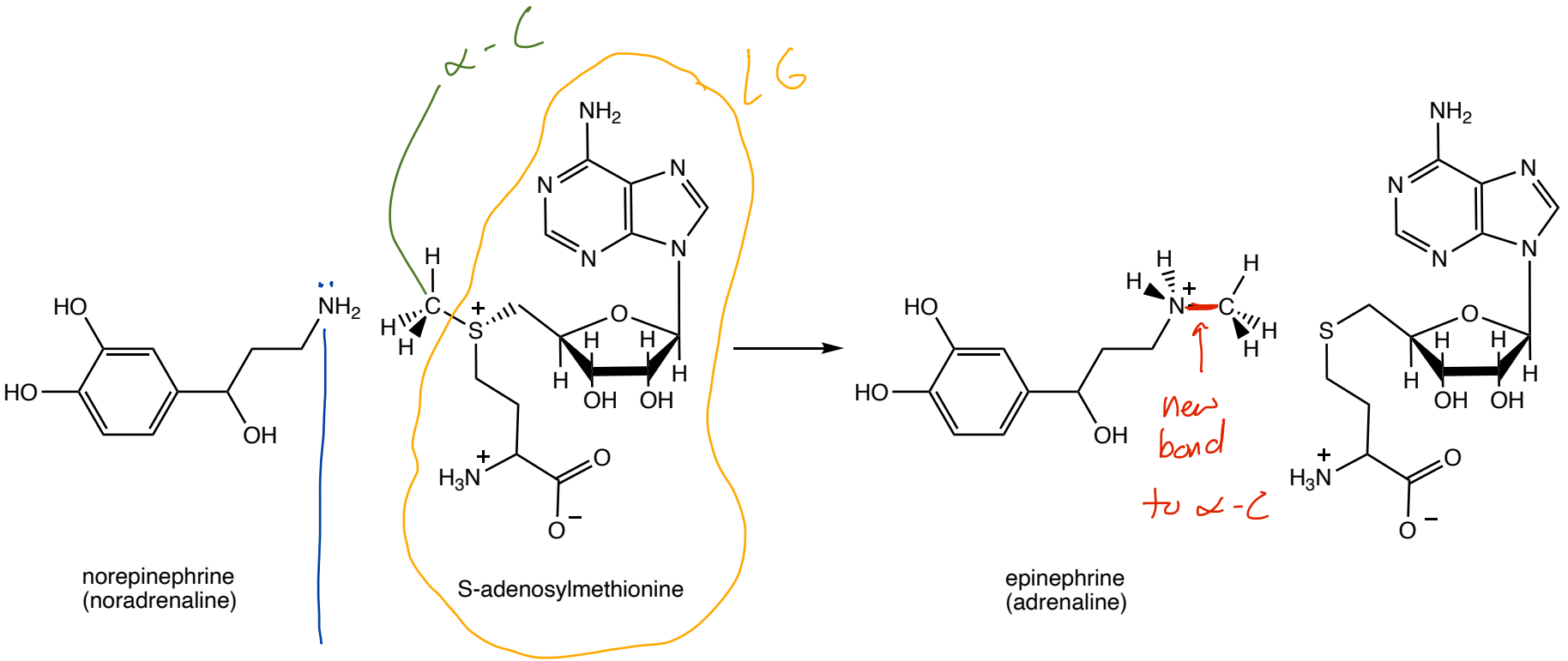
α-Carbon – the carbon where the substitution occurs

Nucleophile – the e⁻ rich atom, ion, or molecule that forms a new bond to the α-C

Leaving Group – leaves and carries away e⁻'s making room for the nucleophile to form a new bond



Nucleophilic Substitution Reactions in Biology



Nucleophile

this $-NH_2$ like ammonia $H-\ddot{N}-H$ (H) has a lone pair of electrons, which make this N an electron rich nucleophilic atom

Nucleophilic Substitution Reactions in Biology

The lysozyme mechanism sorted — after 50 years

Anthony J Kirby

Unambiguous evidence for a glycosyl-enzyme intermediate on the lysozyme reaction pathway has recently been reported, finally settling what kind of mechanism this textbook enzyme uses.

The publication in 1965[1] of the hen egg white lysozyme crystal structure — the first such structure of any enzyme — was a major landmark, offering the prospect of detailed explanations of enzyme mechanisms at the molecular level. Such mechanisms involve some of the most subtle relationships between structure and function in all of biology, as enzymes have to recognize and thus stabilize transition states, which probably exist for only femtoseconds. Because the structure of lysozyme was a first, and because of the coherent messages the structure seemed to provide, lysozyme has been a textbook example of enzyme mechanism ever since. Now, in a recent issue of *Nature*, Vocadlo *et al.*[2] report new evidence about the mechanism of lysozyme, information that has been sought after for almost 50 years.

Lysozyme is the most prominent member of the very large class of glycosidases or glycohydrolases, enzymes that catalyze the transfer of a glycosyl group to water. *In vivo* lysozyme catalyzes the hydrolysis of a polysaccharide component of the cell wall of Gram-positive bacteria. To do this it accelerates enormously the extraordi-

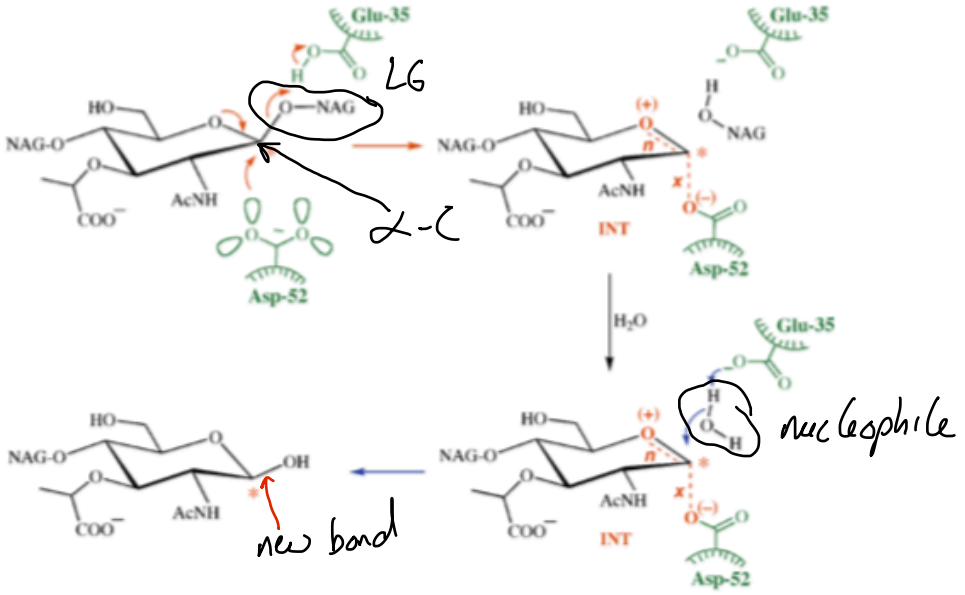
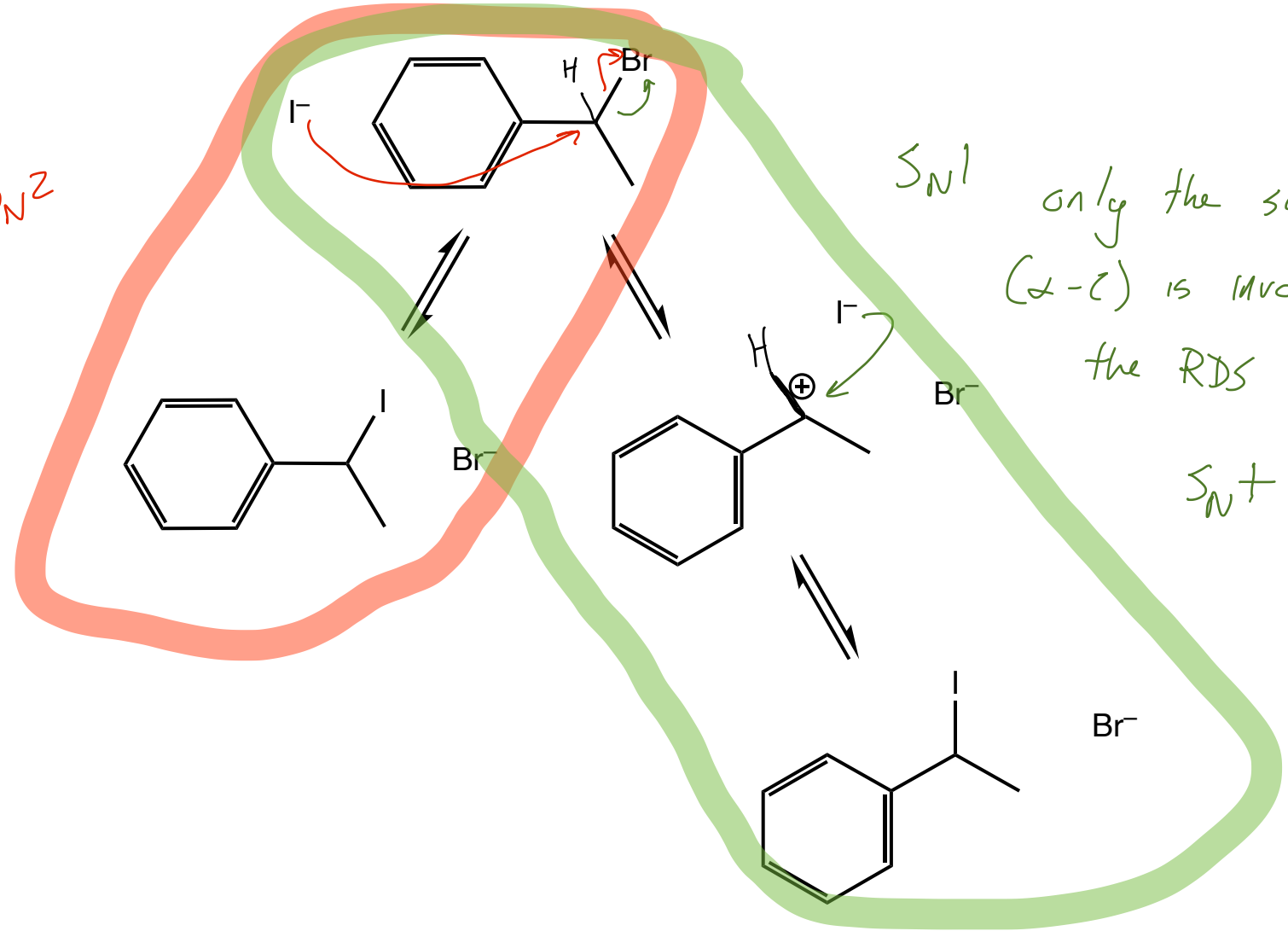


Fig. 1 The reaction catalyzed by lysozyme. The substrate is bound so that the leaving group oxygen, the 4-OH group of an N-acetylglucosamine (NAG) residue, is protonated as it leaves by the COOH group of Glu 35. Groups on the enzyme are colored green, electron movements and the key developing bonds and charges in red. Only one of the dashed *exo* and *endo* (*x* and *n*) bonds of the intermediate (INT) is actually present: which one defines the mechanism. Thus *n* is missing in mechanism (i), *x* in mechanism (ii).

Nature structural biology (2001), v8(9), p73

Mechanisms of Nucleophilic Substitution: S_N1 and S_N2

Sections 11.2 and 11.4



S_N2

two things collide in RDS

S_N1

only the substrate (α-C) is involved in the RDS

S_N1

Substitution Nucleophilic unimolecular rate determining step (1)

Substitution Nucleophilic bimolecular rate determining step (2)