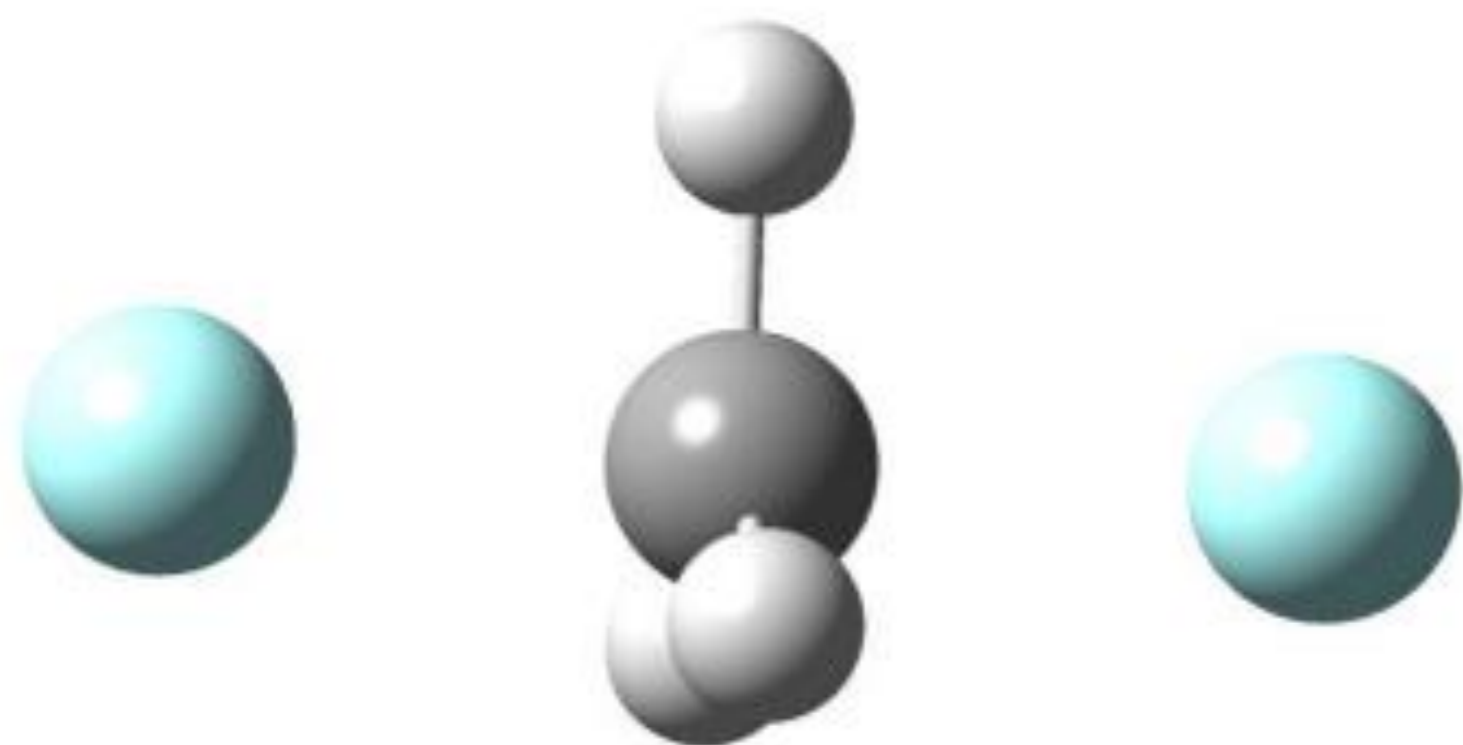




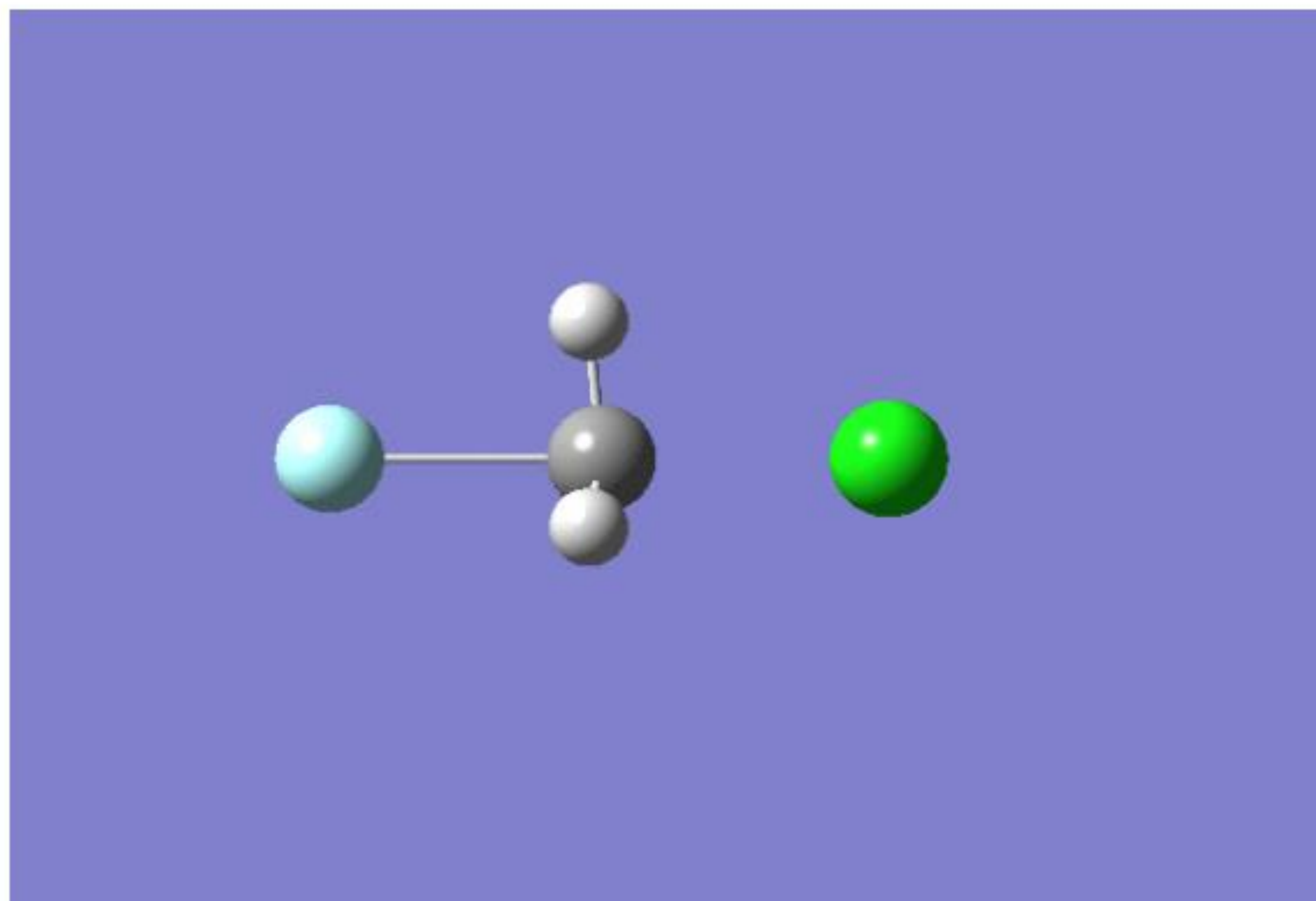
# Organic chemistry

Chapter: 6

Done by: Shahed Zaytoon

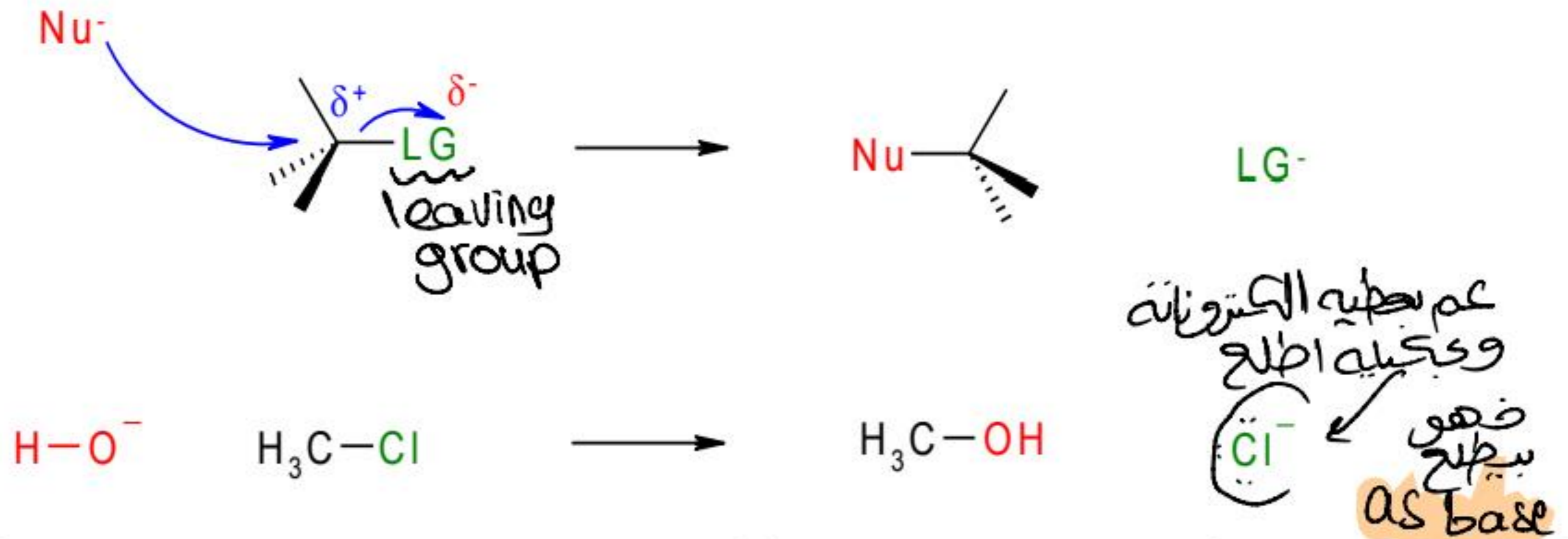


## *Chapter 6: Nucleophilic Substitution and Elimination Reactions*



# Nucleophilic Substitution

A **nucleophilic substitution** reaction involves the replacement of a **leaving group** with a **nucleophile**, i.e.



Note: this reaction is an equilibrium since the leaving group can, in principle, act as a nucleophile.

هذا على ان يكون good leaving group  
لازم يكون stable وكونه stable  
ان كان weak base

افينا سابقا عن ال  
Polar reagents.

# Nucleophiles

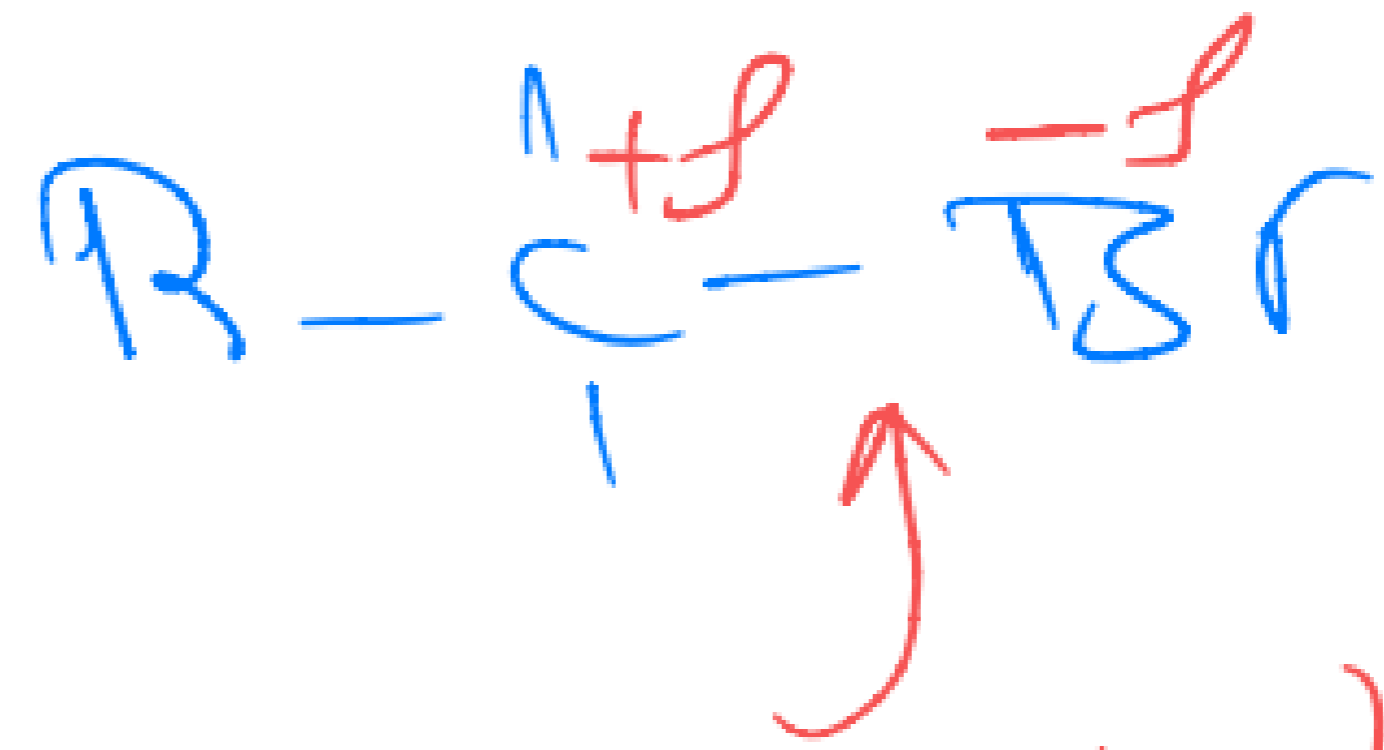
الدها تقسم الى :-

- ① **Nucleophiles** (Nu) are electron rich (i.e. have lone pair(s) of electrons) and are attracted to the positive nuclear charge of an  $e^-$  poor species, the
- ② **electrophile** (E).

يعني قدرته بالله يعطي

**Nucleophilicity** refers to the ability of the nucleophile to react this way, i.e. how available are the  $e^-$  in the nucleophile. The more available the  $e^-$  the more reactive the Nu. These may be lone pair  $e^-$  but  $\pi$  bonding  $e^-$  are also "available".

مبداً لو عندي هاد ال molecule



بلازم انه هاي ال  
bond هي له Polarized

بيجبلنا انه ال C اللي فوق

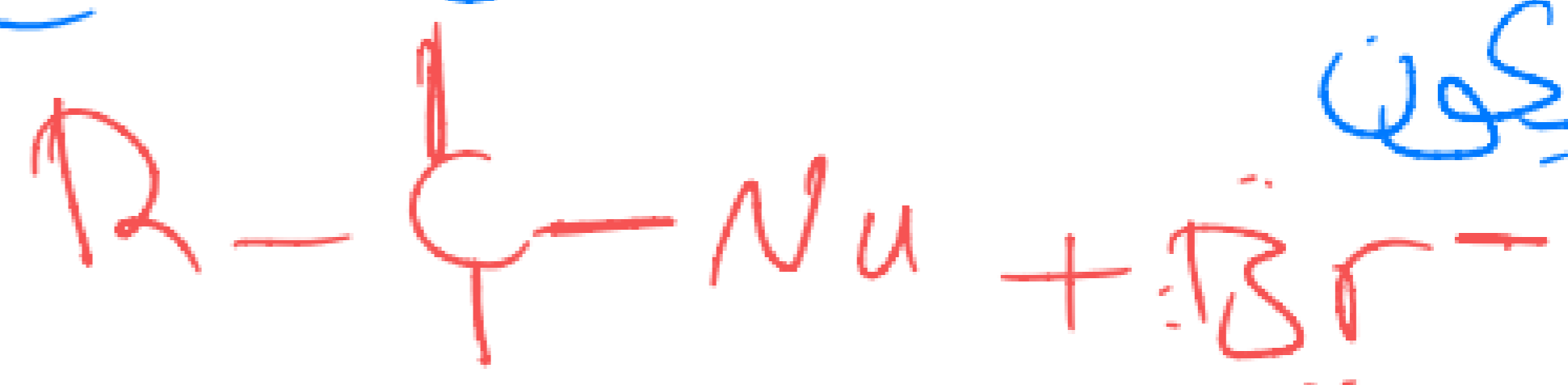
ممكن انها تتصرف electrophile

حيث انه لو جبالها nucleophile

لناسبت ممكن انهم يتفاعلوا سو

ويتم استبدال ال Br فالنتاج

ح يكون



اللي هار عندي انه عملية

## Nucleophilic Substitution

حيث انه انا استبدلنا Br

بال Nu حيث انه Nu

تفاعلت مع ال molecule

وكونت رابطة مع ال C و

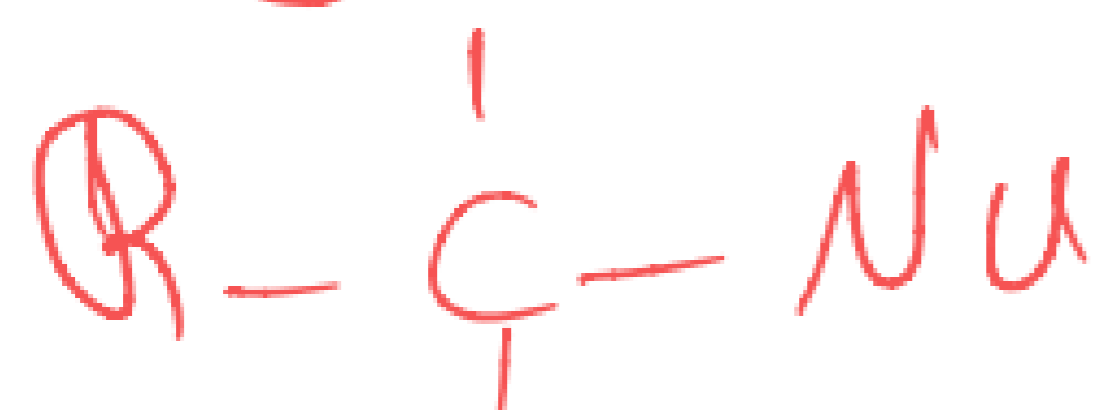
طردت ال Br مع الالكتروناتها

لذلك جزء ال  $Br^-$ :

اللي يتم طرده منسويه ال

leaving group

وار product الناتج هو



ممكن يكونوا neutral  
وهي انions  
**Nucleophiles**

Common nucleophiles include:

| Nucleophile | Neutral  | Anionic   |
|-------------|--|---|
| Halide      |  | I <sup>-</sup> , Br <sup>-</sup> , Cl <sup>-</sup>                |
| Oxygen      | H <sub>2</sub> O, ROH  | OH <sup>-</sup> , RO <sup>-</sup> , RCO <sub>2</sub> <sup>-</sup> |
| Nitrogen    | NH <sub>3</sub> , RNH <sub>2</sub> , R <sub>2</sub> NH, R <sub>3</sub> N | N <sub>3</sub> <sup>-</sup>                                       |
| Sulfur      | RSH, R <sub>2</sub> S  | SH <sup>-</sup> , RS <sup>-</sup>                                 |
| carbon      |  | N≡C <sup>-</sup> , R-C≡C <sup>-</sup>                             |

good nucleophile

بجينا انه في علاقة  
 بين ال nucleophilicity  
 وبين ال basicity حيث انه  
 ال Nu base بيقرر يتصرف كـ

# Nucleophiles

ولو مسيت من اليسار الي اليمين ← ح تتراد ال nucleophilicity

## Nucleophilicity trends (compared with basicity):

1) هاد الجان  
 على نفس  
 ال row  
 2) تغير

1) Across a row in the periodic table nucleophilicity (lone pair donation)  $C^-$   $> N^- > O^- > F^-$  since increasing electronegativity decreases the lone pair availability. This is the **same order** as for basicity. *عندهم ولكن كقدره على اعطاء ح*

2) For the same central atom, higher electron density will increase the nucleophilicity, i.e. an anion will be a better Nu (lone pair donor) than a neutral atom (i.e.  $HO^- > H_2O$ ). This is the **same order** as for basicity.

3) هاد الجان  
 على نفس  
 ال group

3) Within a group in the periodic table, increasing **polarization** of the nucleophile as you go down a group enhances the ability to form the new C-X bond and increases the nucleophilicity, so  $I^- > Br^- > Cl^- > F^-$ . The electron density of larger atoms is more readily distorted i.e. polarized, since the electrons are further from the nucleus. *بجينا انه كل صانتر لنا لتخت بتزيد*

Note: this is the **opposite order** to basicity (acidity increases down a group) where polarizability is much less important for bond formation to the very small proton.

رغم انه بيقرر عن نفس ال center  
 وهاد هو تفسير نقطة 2

بالحالين عندي ال O هي الي  
 ح تعطي @ ولكن قدرتهم  
 بتختلف لانه وهاد anion  
 وهاد neutral فال  
 nucleophilicity ح تكون اعلى  
 OH<sup>-</sup> لانه عندها density @ اعلى

هنا انا عم بيكام على ال Nu ولكن في  
 center هو الي عم بوجيني @  
 مثلا



# Nucleophiles

The following tables ranks the strength of common nucleophiles (as compared in methanol  $\text{CH}_3\text{OH}$ ):

| Strength        | Nucleophile   |
|-----------------|---|
| Very Good       | $\text{I}^-$ , $\text{HS}^-$ , $\text{RS}^-$  |
| Good            | $\text{Br}^-$ , $\text{OH}^-$ , $\text{RO}^-$ , $\text{N}\equiv\text{C}^-$ , $\text{N}_3^-$ |
| Fair (moderate) | $\text{NH}_3$ , $\text{Cl}^-$ , $\text{RCO}_2^-$  |
| Weak            | $\text{H}_2\text{O}$ , $\text{ROH}$   |
| Very weak       | $\text{RCO}_2\text{H}$  |

good nucleophiles

الفرق بين  $\text{RO}^-$  و  $\text{RCO}_2^-$  هو بسبب وجود ال Resonance حيث ال  $\text{RCO}_2^-$  هي delocalized بينما ال  $\text{RO}^-$  هي localized



# Leaving Groups

- A *leaving group*, **LG**, is an atom (or a group of atoms) that is displaced as a stable species taking with it the bonding electrons. Typically the LG is an anion (*i.e.*  $\text{Cl}^-$ ) or a neutral molecule (*i.e.*  $\text{H}_2\text{O}$ ). The better the LG, the more likely it is to depart.
- A "good" LG can be recognized as being the conjugate base of a strong acid.
- What do we mean by this? First we should write the chemical equations for the two processes:



# Leaving Groups

Note the similarity of the two equations: both show heterolytic cleavage of a  $\sigma$  bond to create an anion and a cation.

- For acidity, the more stable  $A^-$  is, then the more the equilibrium will favor dissociation, and release of protons meaning that HA is more acidic.
- For the leaving group, the more stable  $LG^-$  is, the more it favors "leaving".
- Hence factors that stabilize  $A^-$  also apply to the stabilization of a  $LG^-$ .

هنا جدول فقط

# Leaving Groups

The following tables lists some of the common leaving groups.

من ناحية ال leaving group

| Strength  | Leaving Group                                   |
|-----------|---|
| Excellent | $\text{NH}_3$                                   |
| Very Good | $\text{I}^-$ , $\text{H}_2\text{O}$             |
| Good      | $\text{Br}^-$                                   |
| Fair      | $\text{Cl}^-$                                   |
| Poor      | $\text{F}^-$                                    |
| Very poor | $\text{OH}^-$ , $\text{RO}^-$ , $\text{NH}_2^-$ |

من ناحية الامونيا لها تطلع بتطلع بكل صحتان

انه نعمل تفاعل مع R-f شوي صعب

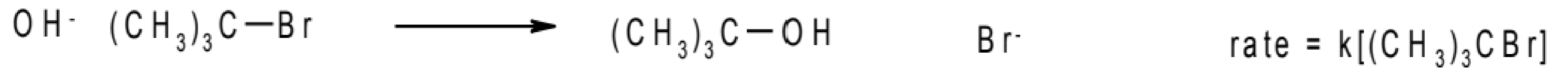
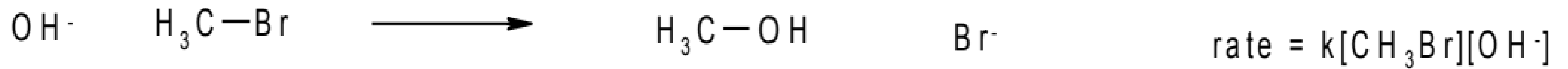
\* مستحيل ال leaving group يكون

Strong bases ← هتكون بطلعوا بسهولة

هكذا انه التفاعل كله عبارة عن استبدال X بال Nu ولكن هار  
 التفاعل الى مسارين / طريقين وهاد مايسمى بال reaction mechanism  
**Mechanism of Substitution Reactions**

هناك حالتين يتم استبدال الـ X بالـ Nu ولكن هدير المسارين مختلفات رغم اني  
 بدير لـ target او لـ product النهائي بالحالتين ولكن اختلاف الطريقه تفسر كثير اشياء

Experimentally if you measure the rate of substitution for the following reactions you will find the following rate laws:



Why the difference?

# Nucleophilic Substitution $S_N$

النوع الأول /  
المسار الأول

## Substitution Reactions: $S_N2$

one step reaction ليس عندي في  
وال Nu يحاج من ال back side

The first reaction is dependent on the concentrations of both the substrate and nucleophile, i.e.

ظبي عليه فكننا 2؟ لأنه اناني عندي reagent 2  
reactants



هكذا فلينا بتخيل سرعة التفاعل على اي تركيز  
يعتمد فيهم فعليا يحققه على الاثنين

This implies it is a bimolecular reaction that occurs in one step.

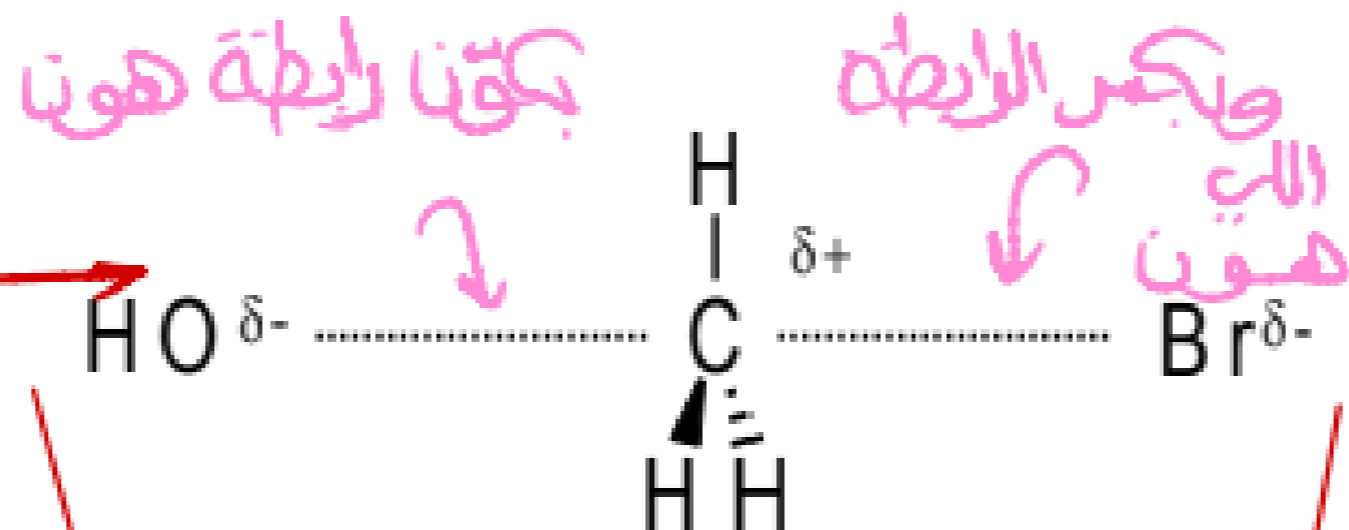
transition state  
There is a single TS in which the new bond to the Nu is forming while the old bond to the LG is breaking, i.e.

المسار يتم من ال  
back side

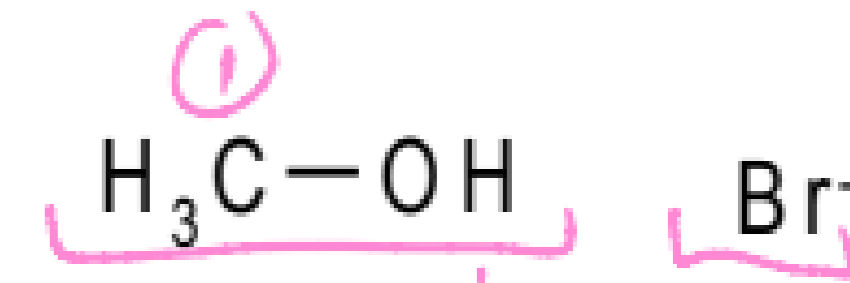
كدهما قرب ال Nu  
يبعد ال leaving group  
ما اوله ل  
تكون رابطة و  
كسر رابطة  
أفري



اللي يهيس انه ال  
Nu يحاج نهاجم  
ال C اللي معهما  
ال leaving group



transition state  
له هده الاعاء طاقة



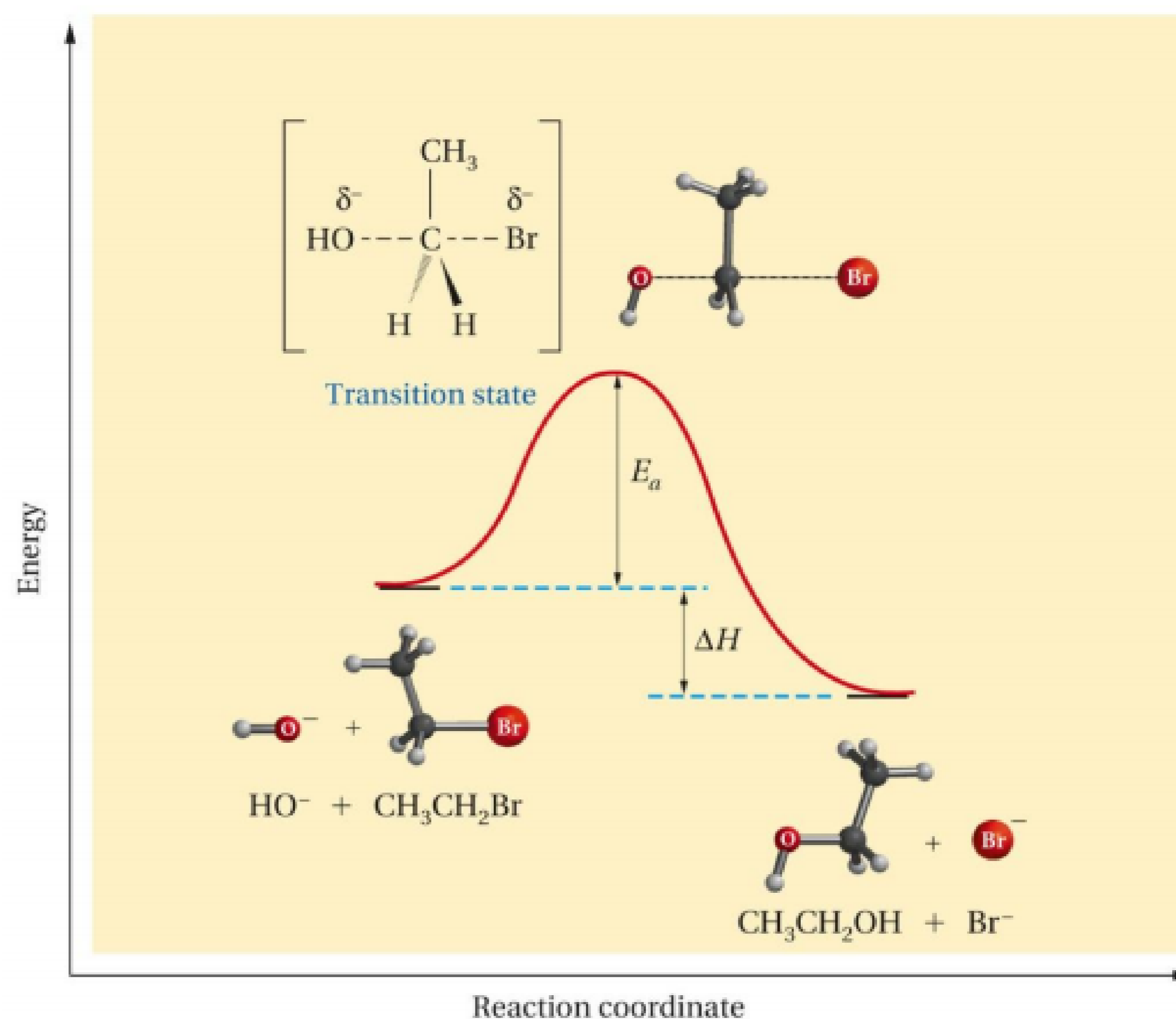
التين هون عبارة  
عن products  
ولكن اللي بهمن هو

# Substitution Reactions: $S_N2$

rate of reaction  
على الترتيب (2 reactants)  
نucleophile  
one step  
back side

The reaction coordinate diagram right indicate this one step mechanism.

- Rate = [substrate] & [nu]
- $S_N2$  results in an inversion of configuration if it occurs at a chiral center. (Back-side attack of the Nu)
- Fastest for  $1^\circ$ , slowest for  $3^\circ$



هون التفاعل له شي بخطوتين الحيات

# Substitution Reactions: $S_N1$

المادة المتفاعلة في  
هون فقط بعينه على تركيز الخطوة الاولى  
rate of reaction

The second reaction is dependent only on the concentration of the substrate, i.e.

يعتمد فقط على تركيز الاكسيل هاليه



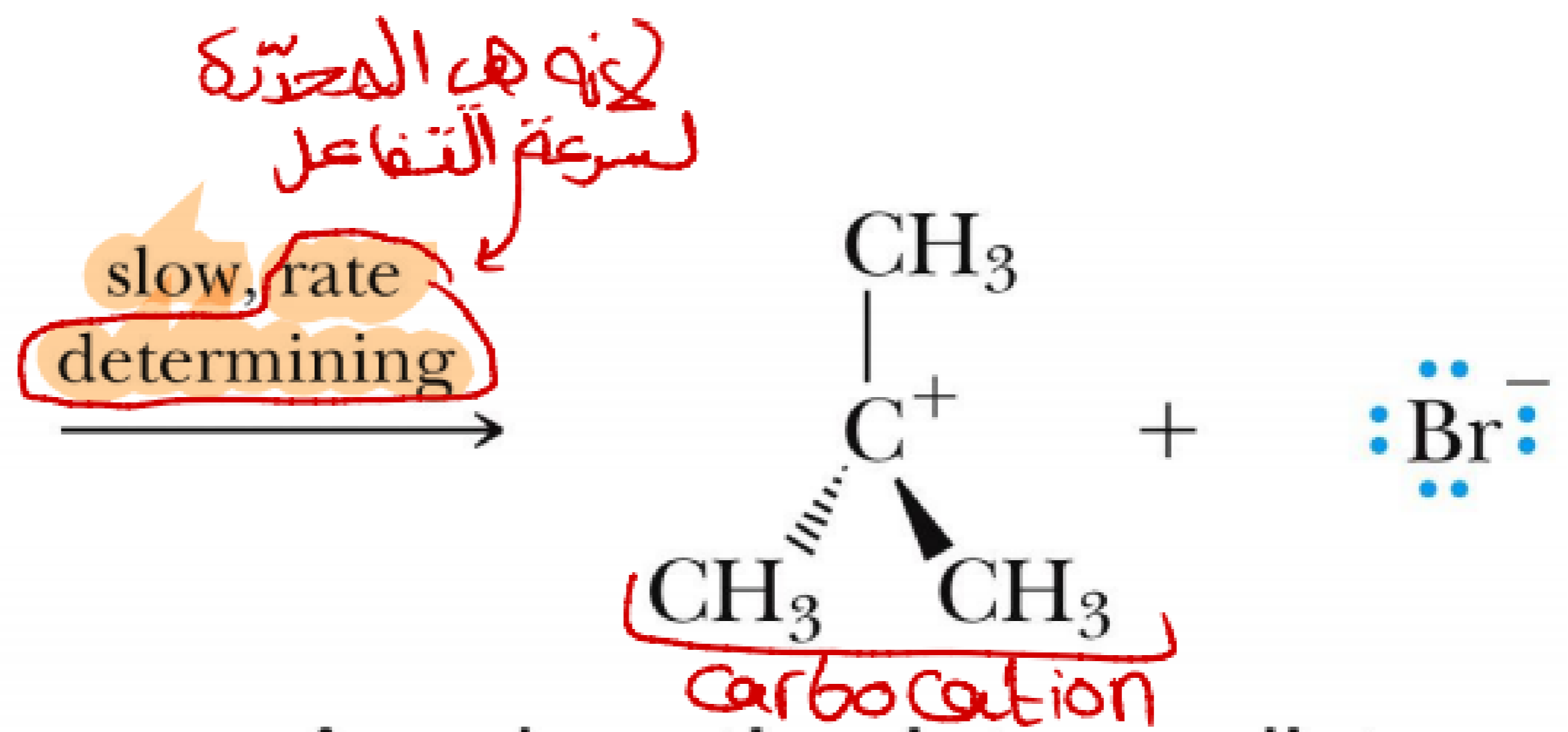
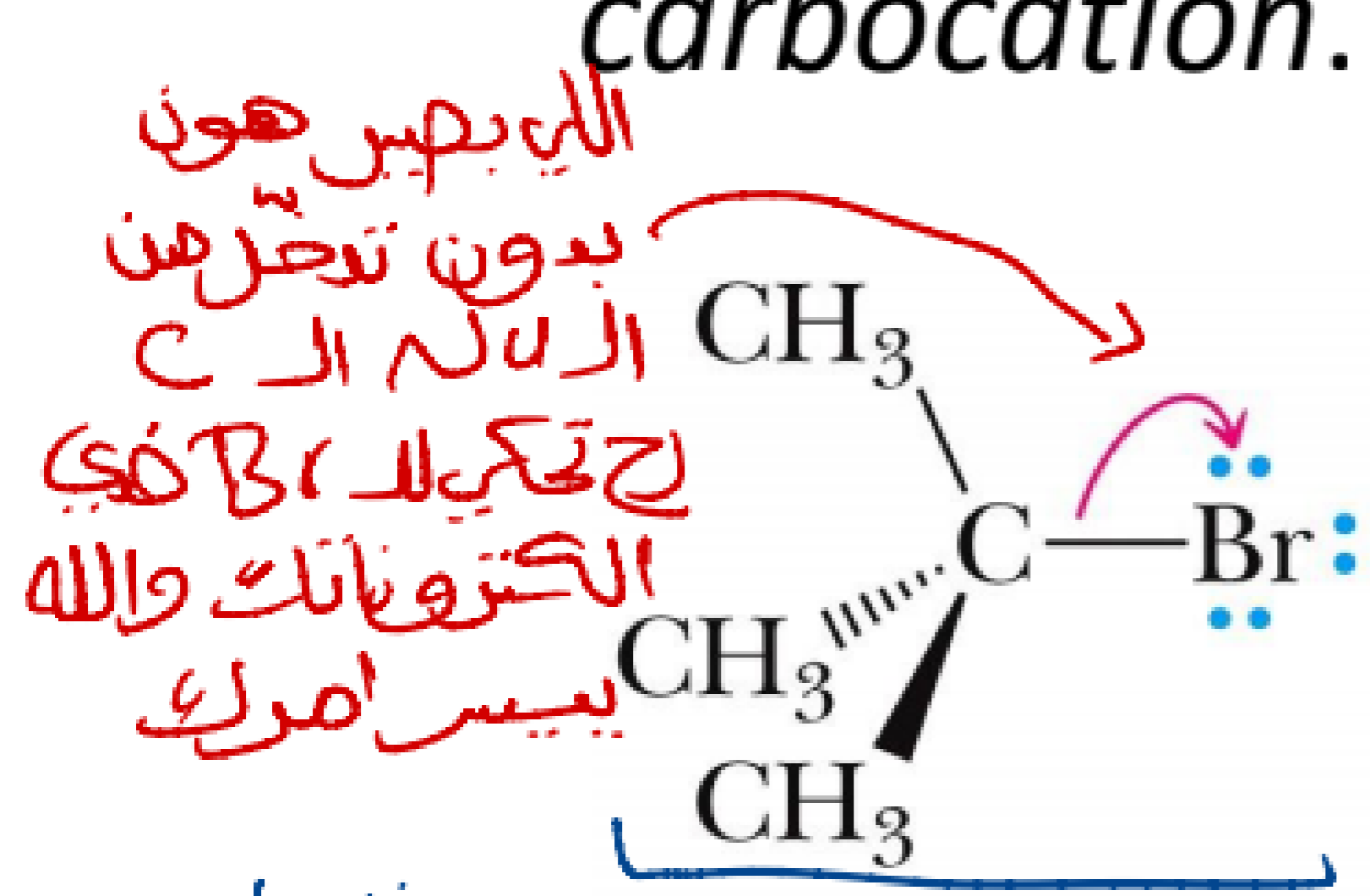
This implies it is a unimolecular reaction that occurs in several steps. The reaction involves the loss of the LG to generate an intermediate carbocation, i.e.

اسمه  $S_N1$  لأنه يعتمد على  
تركيبه  $S_N1$  Mechanism

- $S_N1$  is illustrated by the solvolysis of *tert*-butyl bromide.

الخطوة الأولى هي الأهم  
لذلك هي الأبطأ وبالتالي  
الأبطأ هي التي يتحدد سرعة التفاعل

ionization **Step 1: Break a bond to form a stable ion or molecule.** Ionization of the C-X bond gives a carbocation.



A carbocation intermediate; carbon is trigonal planar

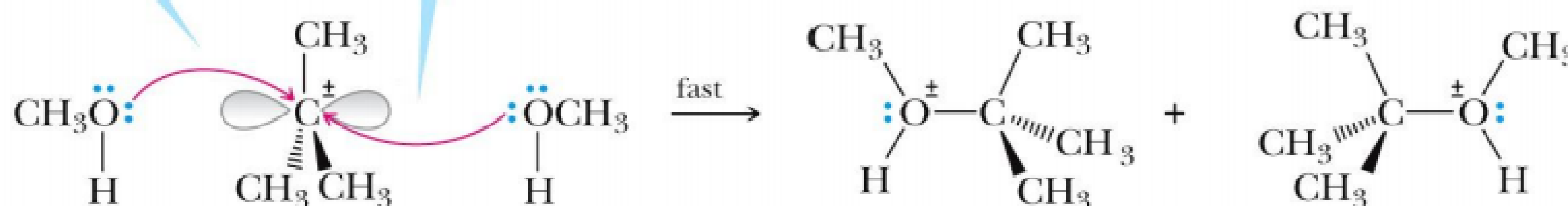
↑ الأجل عاليه هو فقط  
الذي موجود بالخطوة الأولى  
ضالتي الى ان ما الله يفل  
بالخطوة المحددة لسرعة  
التفاعل



بجبال Nu  
ويشجع عني ان  
Product

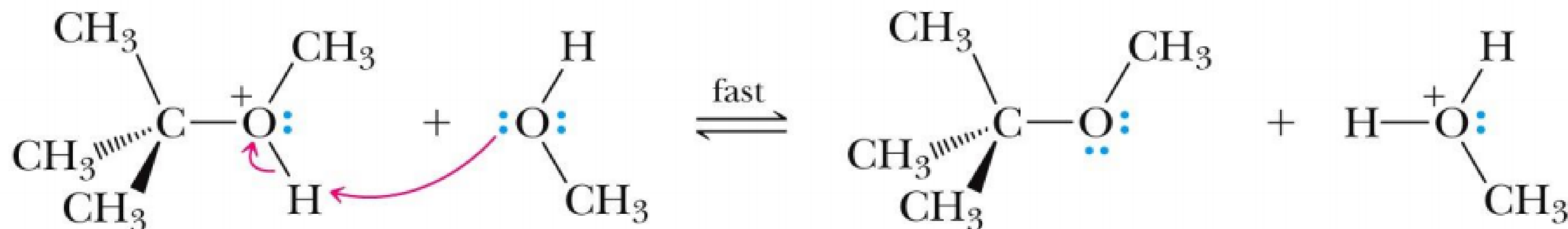
## – Step 2: Reaction of a nucleophile and an electrophile to form a new covalent bond.

the locations of the two lobes of the empty  $p$  orbital of the carbocation allow the nucleophile to attack from either face



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## – Step 3: Take a proton away. Proton transfer to methanol completes the reaction.



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## SN1

خطوتين

التفاعل يحدث على خطوتين  
الخطوة الأولى هي الأهم والأبطأ<sup>4</sup>  
والحددة للـ rate

الذي يحدد سرعة التفاعل  
(substrate)

يح ينتج عنى Racemic  
mixture

$3^\circ > 2^\circ > 1^\circ > \text{methyl}$

Protic

## SN2

خطوة واحدة

التفاعل يحدث مع  
بعضها (Nu + substrate)

الذي يحدد سرعة التفاعل  
(Nu + substrate)

يح ينتج عنى inversion  
of configuration

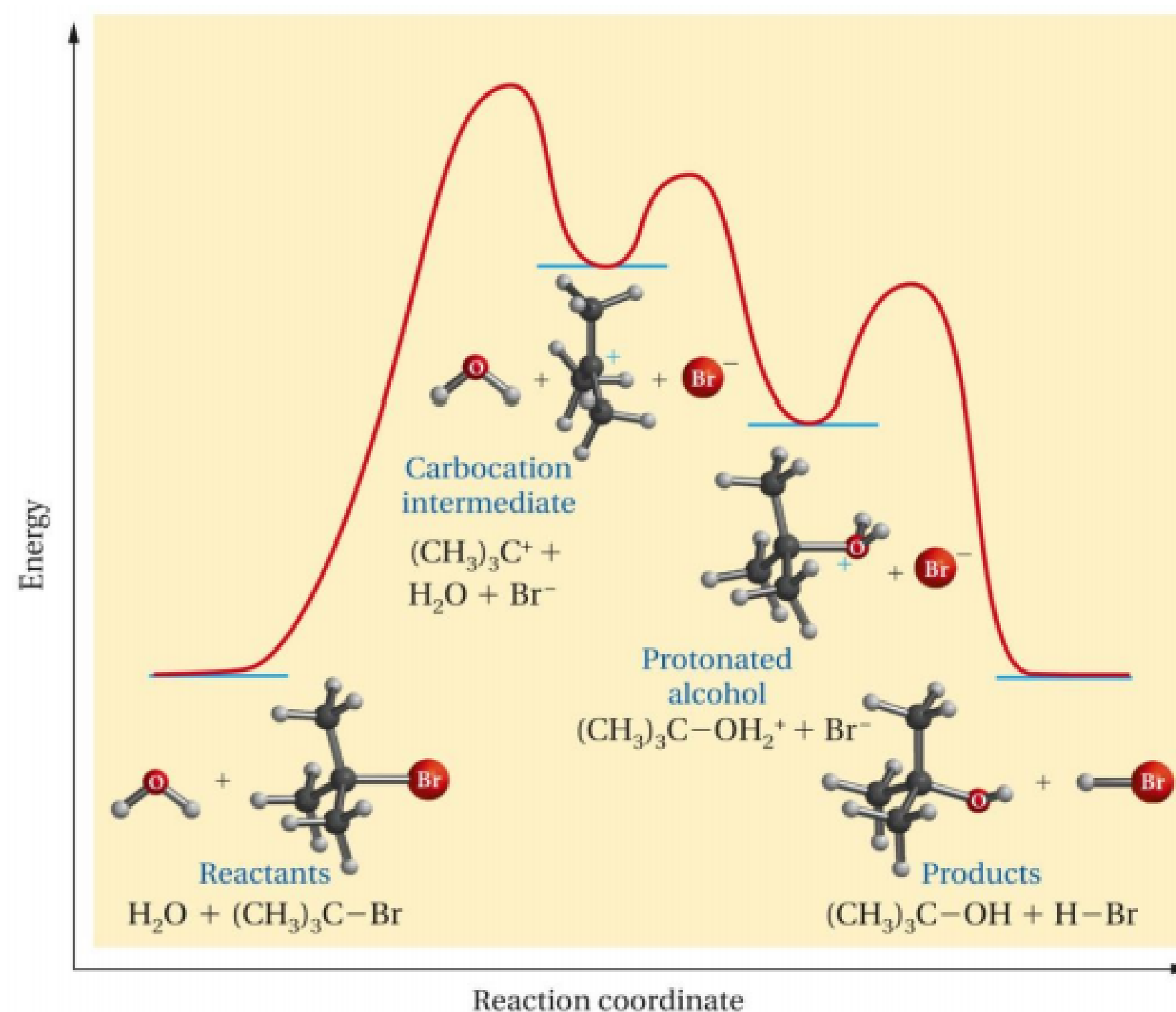
$\text{methyl} > 1^\circ > 2^\circ > 3^\circ$

Aprotic

# Substitution Reactions: S<sub>N</sub>1

The reaction coordinate diagram right indicate this multi-step mechanism.

- Rate = [substrate]
- Generate intermediate carbocation
- S<sub>N</sub>1 results in racemization of configuration if it occurs at a chiral center.
- Fastest for 3°, slowest for 1° (parallels C<sup>+</sup> stability)

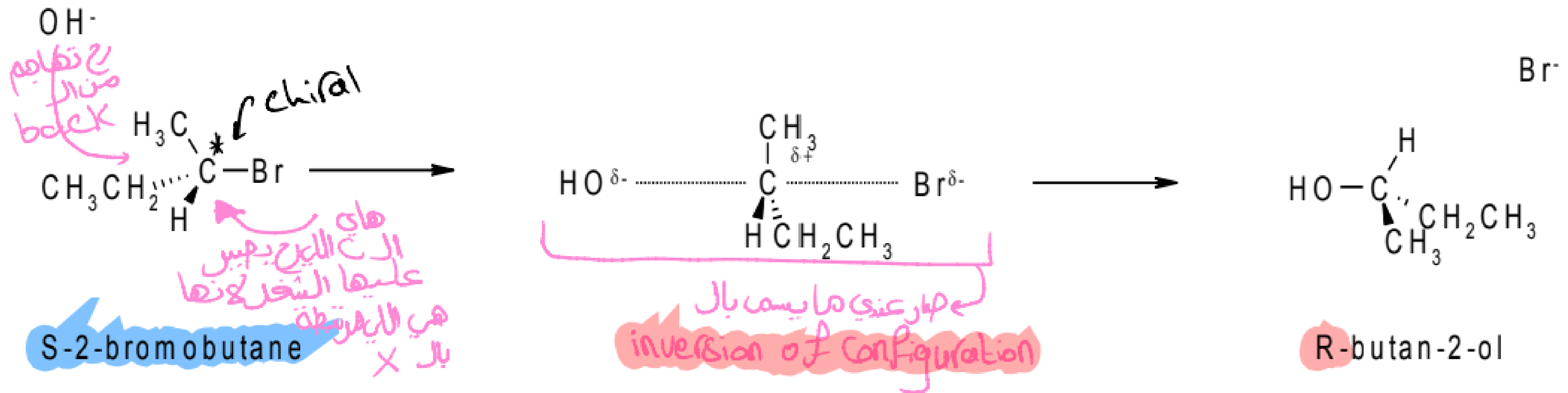


# S<sub>N</sub>2: Stereochemistry

هذا الكلام منقلم فيه اذا كان غنا  
Chirality

Inversion of configuration for chiral atoms, i.e.

هذا التفاعل عبارة عن  
S<sub>N</sub>2



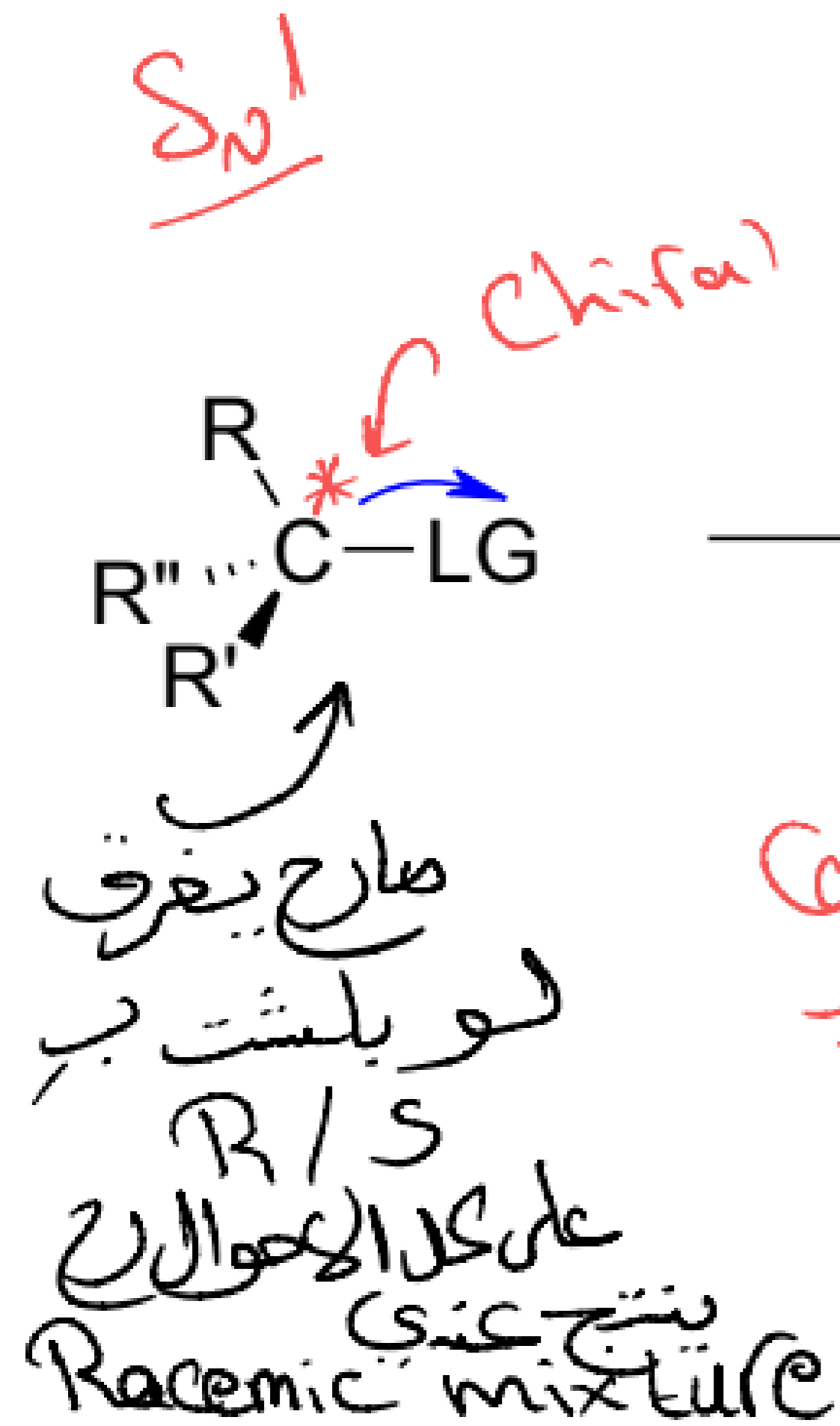
\* المختصر :-  
اذا ال C اللي ملكة مع X (leaving G.) كانت ال وقتها ال (R)  
كانت ال وقتها ال (S) ← اذا كان ال Starting (S) ← ال product (R)  
والعكس صحيح

# $S_N1$ : Stereochemistry

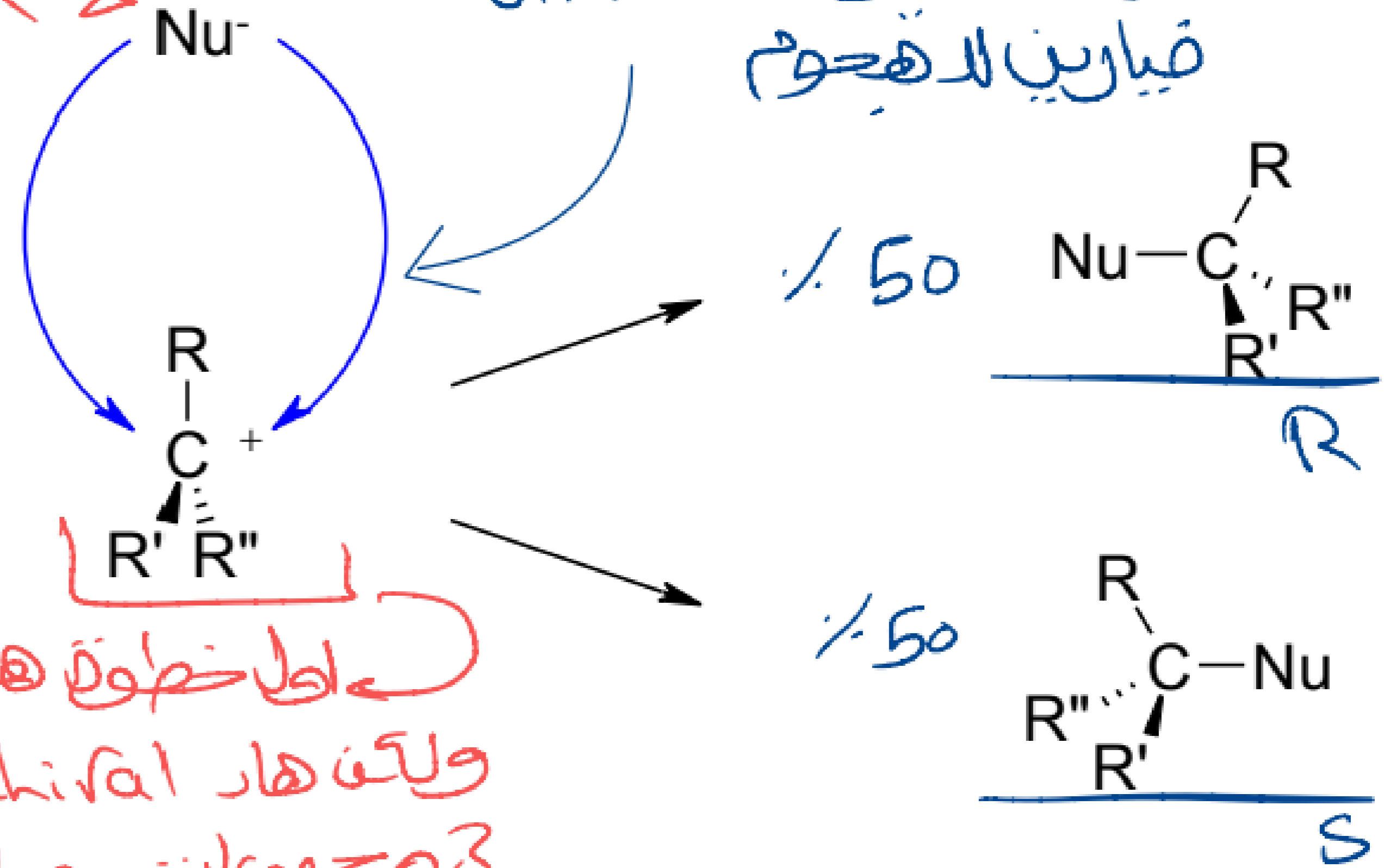
اوچھل جان  
Racemic mixture  
Racemization of chiral atoms, i.e.

\* لہذا اگر انت ہیئت ب  $S/R$  - القتیف  
(ال carbocation) ح یققتہ ال Chirality ارا هو  
لا R ولا S

Carbocation ہوا مولینا  
کل ال R ہمن ہیستوی  
واہ لہیک ال Nu ال  
قیارین لا ہجو



اول خطوتہ ہی تاوین Carbocation  
ولکن ہاں Achiral لاندہ مربوط ب  
3 مجموعت مو



لہذا ال R و S ہیستہم  
Racemic mixture ← 50%

هذه "أنا عم، خذني عن الكيل هاليه ولتف هاه الحكي كمان رح ينطبق لإقفاً  
 على الأحوال هك جيبك انه الحلييل هاليه همن انواع

# $S_N1$ vs. $S_N2$ : Nature of Substrate

primary/secondary/tertiary وفي عنا حالة خاصة ( $H_3CX$ )

The substrate itself has an effect on the mechanism.  $S_N1$  requires an intermediate carbocation, while  $S_N2$  requires a backside attack of the nucleophile (steric effects), i.e.

ل الان النوع هون بهم بدنيا اختيار المريقة اللي بعه بيشيها التفاعل بال

\* مكينا اهم اش بيس بال  $S_N2$  هو مهاجمه ال Nu من ال back له بكيلا انه اضافة Nu على ال primary اسهل من ال tertiary لونه ال (H) حجمها اصغر وليكن ال (R) هي اكبر بكيث

فعلياً همن ما بيشيوا  
 $3^\circ > 2^\circ > 1^\circ > \text{methyl}$   
 primary secondary tertiary

$S_N1$  reactivity

Nucleophilic Substitution

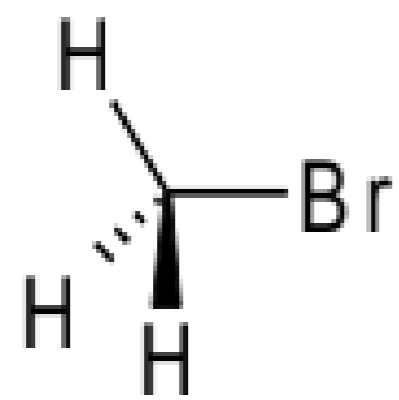
$S_N2$  reactivity

$3^\circ > 2^\circ > 1^\circ > \text{methyl}$   
 فعلياً ال ح ما بيشي بال ( $S_N2$ )

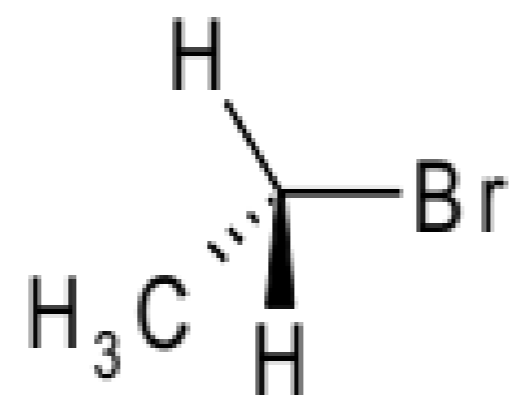
مكينا الخلوقة الاساسيه بال ال  $S_N2$  هي تكوين ال carbocation واقنا سابقاً انه تكوين ال carbocation يكون اكثر استقراراً بال ح

# $S_N1$ vs. $S_N2$ : Nature of Substrate

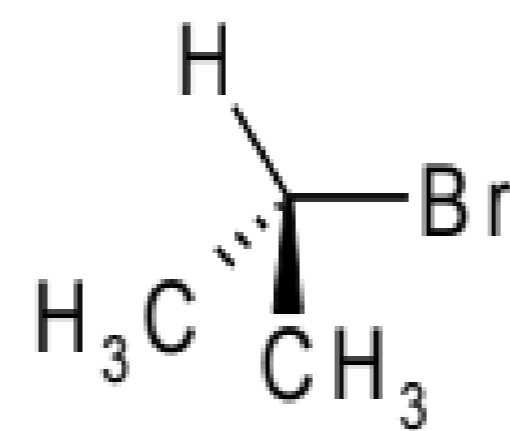
Reactivity of Alkyl bromide to  $S_N1$  mechanism:



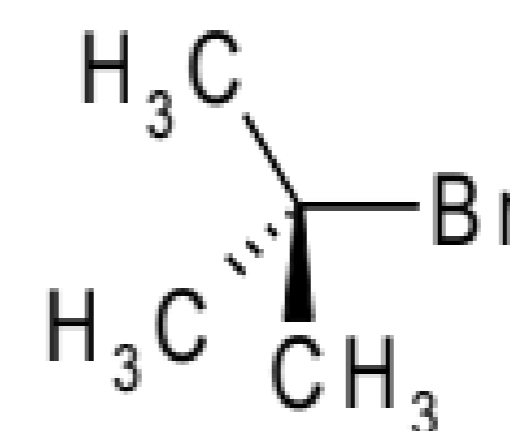
1



2



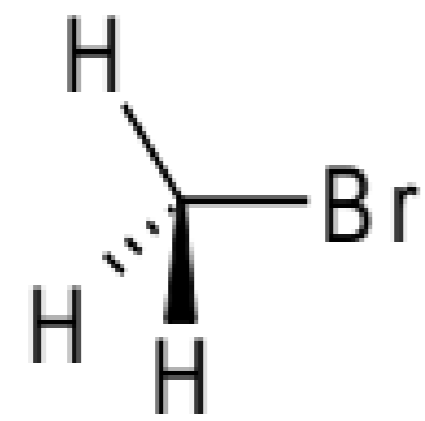
43



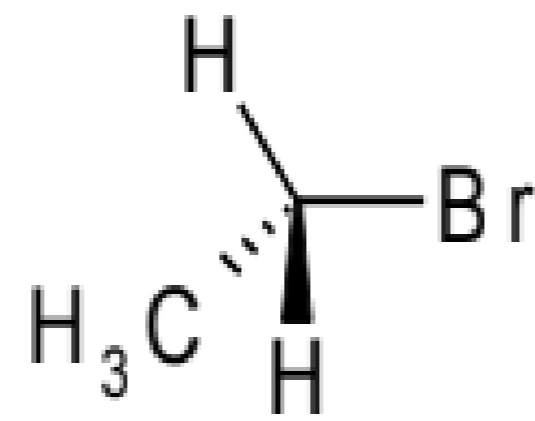
100,000,000

الارقاد بيتثبت  
انه ال  $S_N1$   
افضل شيء الة هو  
ال  $S_N1$

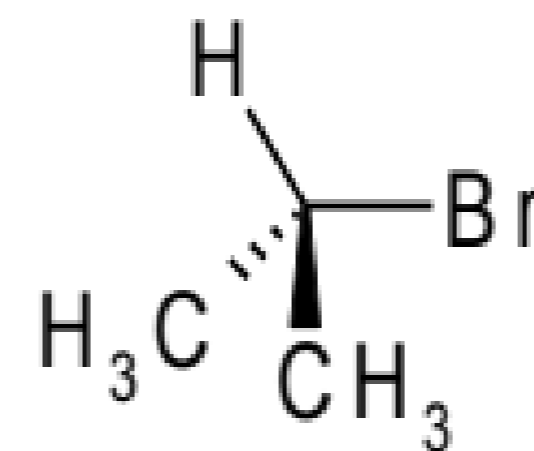
Reactivity of Alkyl bromide to  $S_N2$  mechanism:



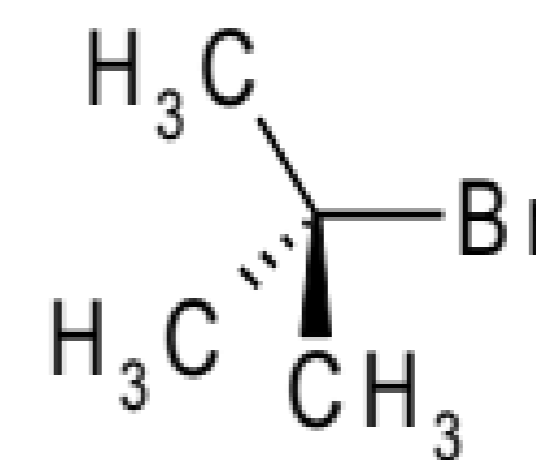
220,000



1350



1



too small to measure

وال  $S_N2$   
افضل شيء  
لانه هو ال  $S_N2$   
1° methyl

التفاعلات التي يمكننا بتقوّلها بر solvent معين

# S<sub>N</sub>1 vs. S<sub>N</sub>2: Solvent Effects

وال solvent له دور مهم جداً باختيار طريقة سير التفاعل

The solvent can effect the rate of formation and stability of charged species. In general two types of solvents are used:

هنا بالحالتين

S<sub>N</sub>1 or S<sub>N</sub>2

اننا مختار ال

Polar Solvent

لكن ال Polar solvent يقسم إلى قسمين:

1. **Polar protic solvents:** a solvent that contains an

like: -OH group, they are good for dissolving anions and cations. This increases the rate of S<sub>N</sub>1 but decreases S<sub>N</sub>2 by solvating the Nu. (water, alcohols, acids)

ال S<sub>N</sub>1

يعني

توجد هنا ال

Protic

H<sub>2</sub>O  
CH<sub>3</sub>OH  
R-C-OH

2. **Polar aprotic solvents:** only solvate cations well

like: therefore good for S<sub>N</sub>2 as the Nu is very reactive in these conditions. (acetone, DMSO, DMF, acetonitrile)

ال S<sub>N</sub>2

يكون

افضل

مع ال aprotic

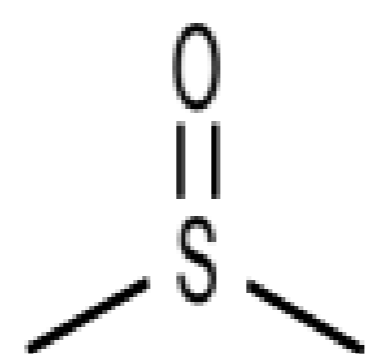
DMSO  
DMF  
acetone



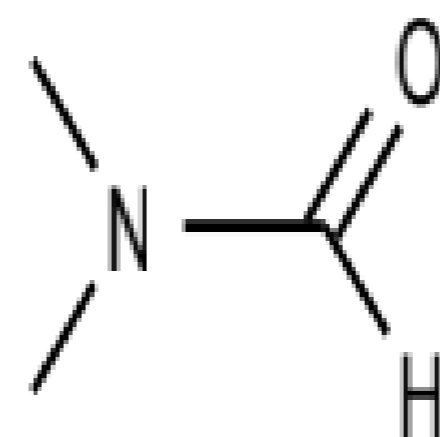
# $S_N1$ vs. $S_N2$ : Solvent Effects

Effects of polar protic/aprotic solvent polarity on  $S_N2$  mechanism

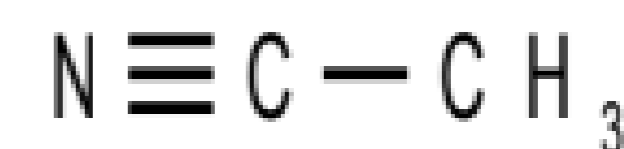
| Protic /aprotic Solvent                    | Relative Rate |
|--|---------------|
| CH <sub>3</sub> OH                         | 1             |
| H <sub>2</sub> O                           | 7             |
| (CH <sub>3</sub> ) <sub>2</sub> SO (DMSO)  | 1,300         |
| (CH <sub>3</sub> ) <sub>2</sub> NCHO (DMF) | 2,800         |
| CH <sub>3</sub> C≡N                        | 5,000         |



dimethyl sulfoxide



dimethylformamide



acetonitrile

لكننا انهم قوي او ضعيف  
و في انيون او قوت neutral

## $S_N1$ vs. $S_N2$ : Nucleophile

بميت ان nucleophile ح تاثير يتفاعل  $S_N1$  or  $S_N2$ ?  
الجواب هو  $S_N2$  لانها ال  $S_N1$  ال Nu ما يتفاعل بال rate

- 1) Anions are stronger nucleophiles than neutral molecules, i.e.  $\text{HO}^-$  vs.  $\text{H}_2\text{O}$  (but more basic).  
↑ هو الاقوى فوقتها  
ح يختار  $S_N2$   $S_N1$
- 2) Nucleophilic strength increases down a column in the Periodic Table (polarizability).
- 3) Across a row in the periodic table nucleophilicity (lone pair donation)  $\text{C}^- > \text{N}^- > \text{O}^- > \text{F}^-$  since increasing electronegativity decreases the lone pair availability.

# $S_N1$ vs. $S_N2$ : Summary

Summary of  $S_N1$  &  $S_N2$  reactions:

| Variable             | $S_N1$                                       | $S_N2$                                   |
|----------------------|--|--|
| Halide: 1° or methyl | NO   | YES                                      |
| 2°                   | Yes  | Yes                                      |
| 3°                   | YES (Stable Carbocation)                     | NO                                       |
| Stereochemistry      | Racemization                                 | Inversion                                |
| nucleophile          | Neutral ok as rate<br>doesn't depend on [Nu] | Best when anionic                        |
| Solvent              | Polar protic                                 | Polar aprotic best,<br>Polar protic slow |

ازالة  
Chiral →

التينى Polar

# $S_N1$ vs. $S_N2$ : Summary

Summary of  $S_N1$  &  $S_N2$  reactions:

- $1^\circ$  - react  $S_N2$ ! Can't make stable carbocation
- $3^\circ$  - react  $S_N1$ ! Too sterically crowded for  $S_N2$
- $2^\circ$  - reacts either  $S_N1$  or  $S_N2$ , this is the one you have to use nucleophilic strength and solvent conditions to control the mechanism if needed.

Example: -

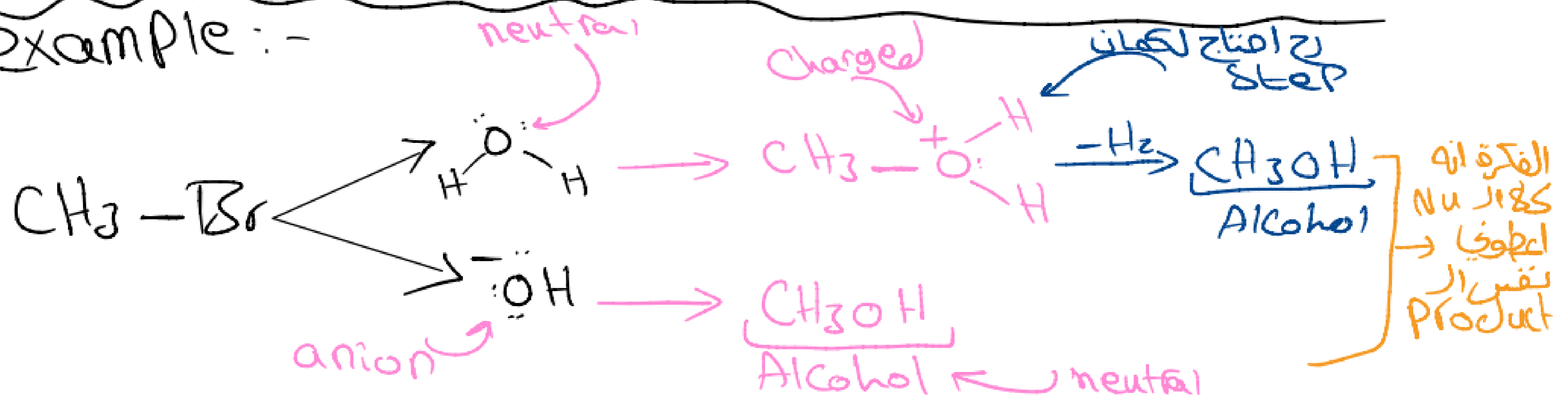


Table 6.1 Reactions of Common Nucleophiles with Alkyl Halides (Eqs. 6.2 and 6.3)

| Nu  |                 | R-Nu                                    |                         | Comments   |
|---|-----------------|---|-------------------------|--|
| Formula                                     | Name            | Formula                                 | Name                    |  |
| <b>Oxygen nucleophiles</b>                  |                 |   |                         |  |
| 1. $\text{HO}^-$                            | hydroxide       | $\text{R}-\text{OH}$                    | alcohol                 | These ions lose a proton and the products are alcohols and ethers.   |
| 2. $\text{RO}^-$                            | alkoxide        | $\text{R}-\text{OR}$                    | ether                   |  |
| 3. $\text{HOH}$                             | water           | $\text{R}-\text{O}^+\text{H}_2$         | alkyloxonium ion        |  |
| 4. $\text{ROH}$                             | alcohol         | $\text{R}-\text{O}^+\text{R}$           | dialkyloxonium ion      |  |
| 5. $\text{R}-\text{C}(=\text{O})\text{O}^-$ | carboxylate     | $\text{R}-\text{C}(=\text{O})\text{OR}$ | ester                   |  |
| <b>Nitrogen nucleophiles</b>                |                 |   |                         |  |
| 6. $\text{NH}_3$                            | ammonia         | $\text{R}-\text{NH}_3^+$                | alkylammonium ion       | With a base, these ions readily lose a proton to give amines.  |
| 7. $\text{RNH}_2$                           | primary amine   | $\text{R}-\text{NH}_2\text{R}^+$        | dialkylammonium ion     |  |
| 8. $\text{R}_2\text{NH}$                    | secondary amine | $\text{R}-\text{NHR}_2^+$               | trialkylammonium ion    |  |
| 9. $\text{R}_3\text{N}$                     | tertiary amine  | $\text{R}-\text{NR}_3^+$                | tetraalkylammonium ion  |  |
| <b>Sulfur nucleophiles</b>                  |                 |   |                         |  |
| 10. $\text{HS}^-$                           | hydrosulfide    | $\text{R}-\text{SH}$                    | thiol                   |  |
| 11. $\text{RS}^-$                           | mercaptide      | $\text{R}-\text{SR}$                    | thioether (sulfide)     |  |
| 12. $\text{R}_2\text{S}$                    | thioether       | $\text{R}-\text{SR}_2^+$                | trialkylsulfonium ion   |  |
| <b>Halogen nucleophiles</b>                 |                 |   |                         |  |
| 13. $\text{I}^-$                            | iodide          | $\text{R}-\text{I}$                     | alkyl iodide            | The usual solvent is acetone. Sodium iodide is soluble in acetone, but sodium bromide and sodium chloride are not. |
| <b>Carbon nucleophiles</b>                  |                 |   |                         |  |
| 14. $^-:\text{C}\equiv\text{N}:$            | cyanide         | $\text{R}-\text{C}\equiv\text{N}$       | alkyl cyanide (nitrile) | Sometimes the isonitrile, $\text{R}-\text{N}\equiv\text{C}:$ , is formed.  |
| 15. $^-:\text{C}\equiv\text{CR}$            | acetylide       | $\text{R}-\text{C}\equiv\text{CR}$      | alkyne                  |  |

بكل الحالات هون عنده قيرق انا  
 نيقه H عنان يبرقع neutral

$\text{R}-\text{NH}_3^+$   
 $\text{R}-\text{NH}_2\text{R}^+$   
 $\text{R}-\text{NHR}_2^+$   
 $\text{R}-\text{NR}_3^+$

\* إذا انت بدأت بـ  
 anion (Nu) بك

تعرف انك رح توهل  
 neutral one

وإذا انت بدأت  
 بـ neutral (Nu)

رح ينتج عندي

لهو charged ولكن  
 انت جابته لكان  
 فطوق بحيث

انها رح لهو charged  
 molecule يبرقع  
 neutral one

\* هو يجب يبرقع  
 neutral  
 state

\* إذا كان ال Nu  
 Neutral

الناتج رح يكون عندي  
 charged

وبها الناتج افتح  
 لكان step 5 يبرقع  
 فيها ال H و يبرقع  
 لـ neutral state

\* إذا كان ال Nu  
 (Anion)

الناتج رح يكون عندي  
 neutral

هكذا انه الـ OH هي Nu لـ good ولكن المشكلة انها

ممكن تتصرف كـ base

## Elimination Reactions

لذلك النوع محققا أكثر من 2<sub>N</sub> و 1<sub>N</sub> لأنه ممكن يكونا عني  
التفاعلات أحي

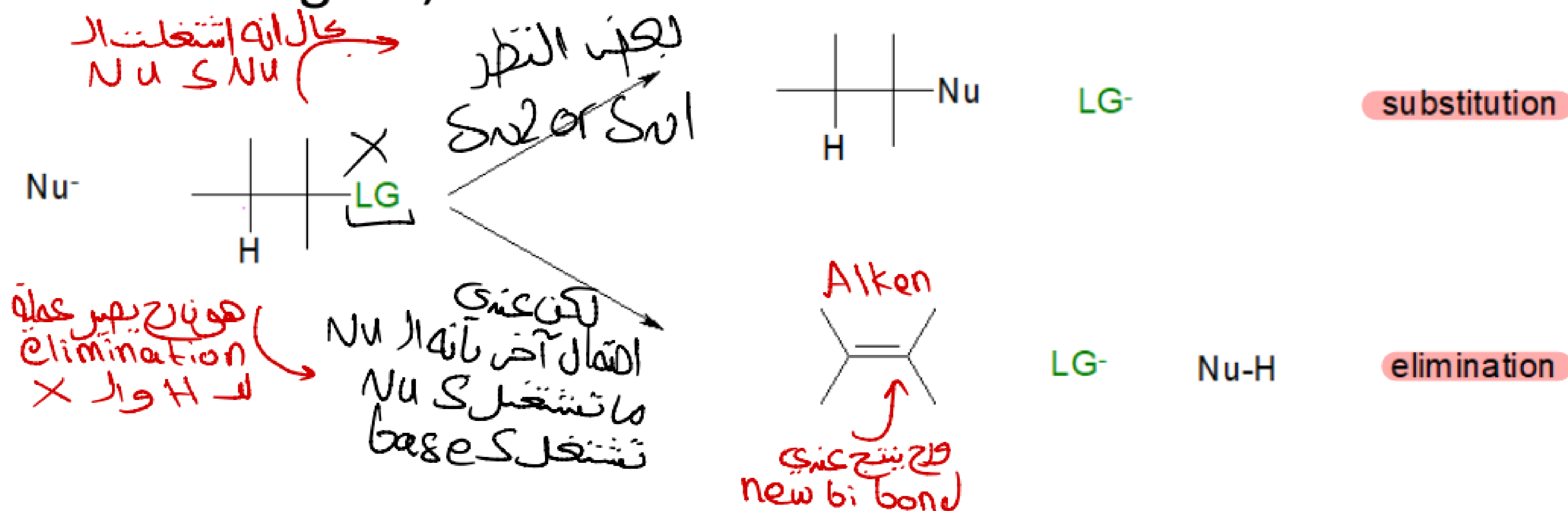
A problem arises in nucleophilic substitution reactions in that nucleophiles are also **bases**. This is especially true for anionic nucleophiles, i.e.



This can occur by the Nu abstracting a proton (i.e. acting as a base) from the substrate giving an elimination reaction.

# Dehydrohalogenation Reactions

A dehydrohalogenation is an elimination reaction of alkyl halides. It will compete with a substitution to some degree, i.e.



It is used to produce alkenes from alkyl halides

# E Mechanisms

Like substitution there are several possible mechanisms for elimination reactions. We will examine two of them: E1 and E2

Substitution  
SN1 SN2  
E1 and E2  
Mechanisms

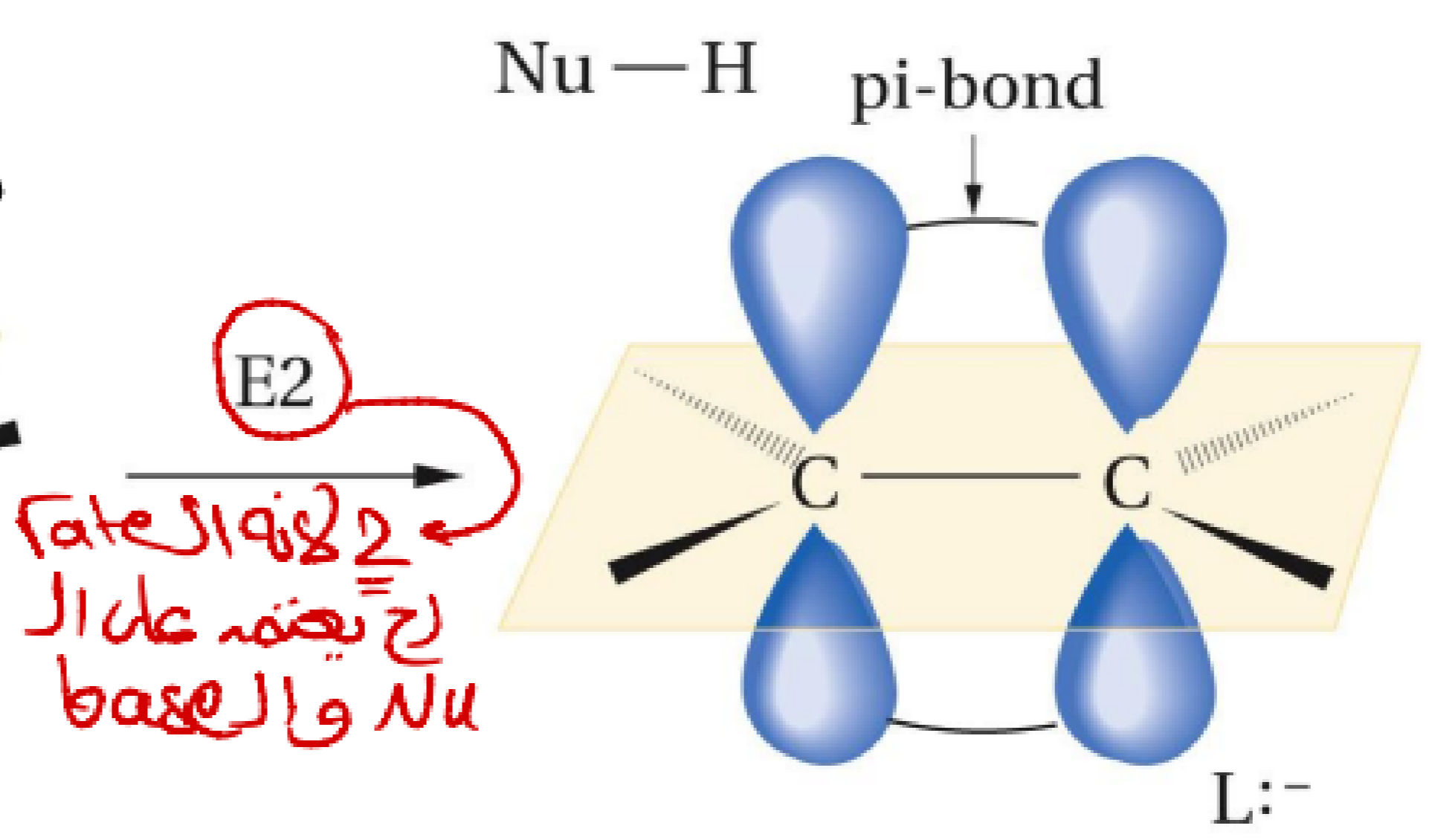
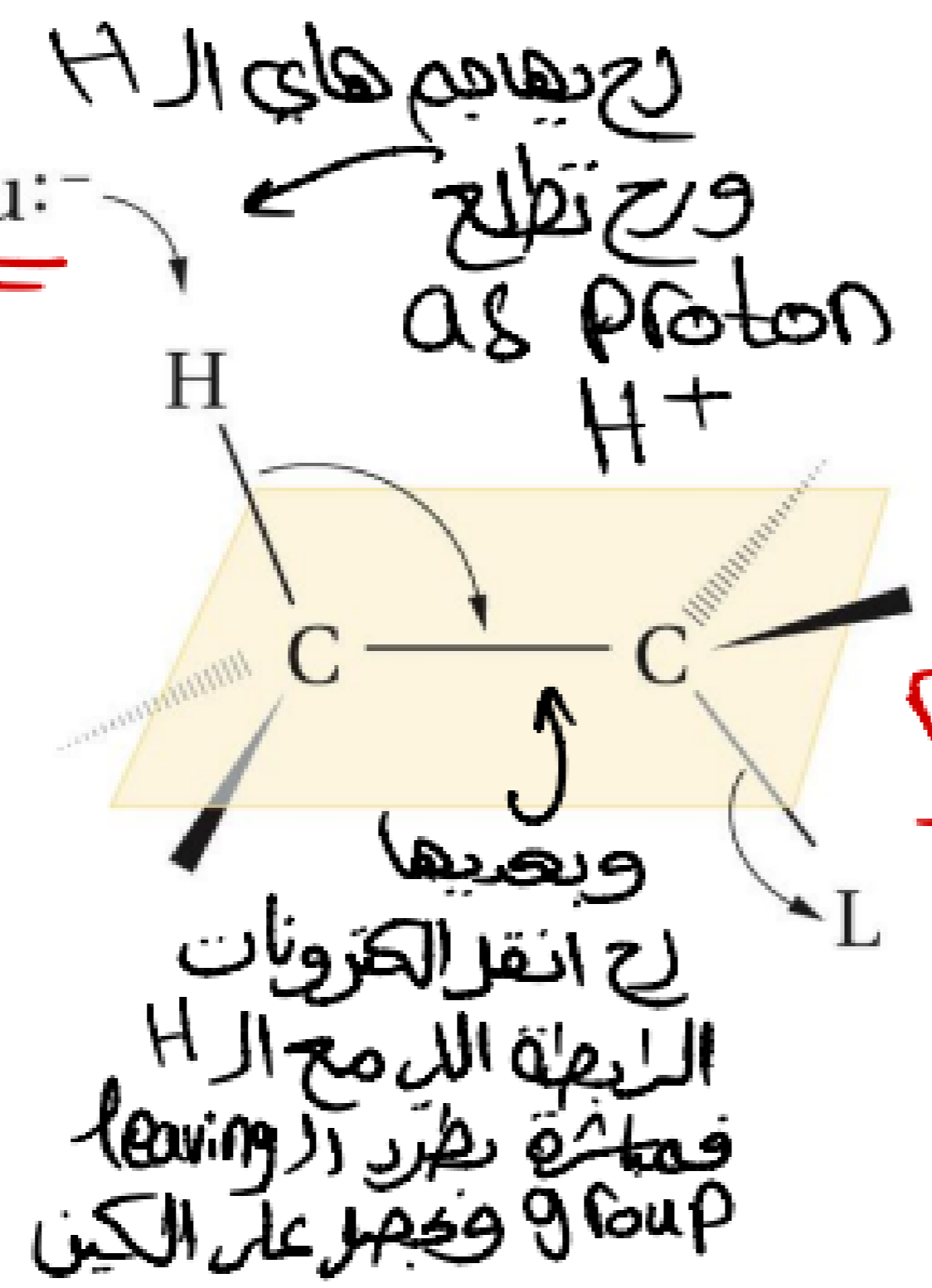


نفس قهبة ال SN  
 من ناحية انه ال Nu  
 Substitutions  
 صرح تهاجم ال back

one step  
**E2 Mechanism**

- Rate = k[alkyl halide][base] (bimolecular)
- Stereochemical requirement: **anti-periplanar** arrangement of the H atom and LG is required
  - This results from an orbital interaction that allows the  $\pi$  bond to form.

اللي ح يهجم ال Nu  
 ح يهاجم ال H  
 ال الموجودة على ال C  
 المجاورة لـ C اللي  
 معها ال leaving  
 group



\* Note:  
 لو كان عني  
 كذا ال H الـ H  
 اللي بنتم مهاجمتها  
 هي ال H اللي  
 تكون anti  
 بالنسبة لـ X

# E2 Mechanism

tetra > tri > di

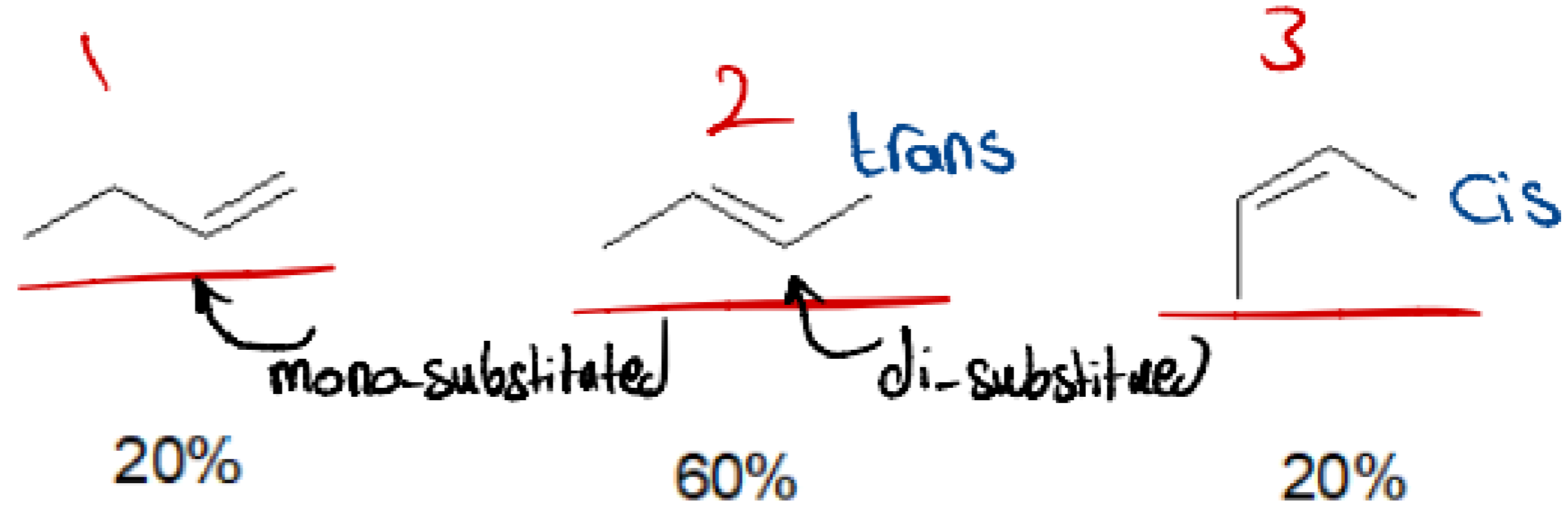
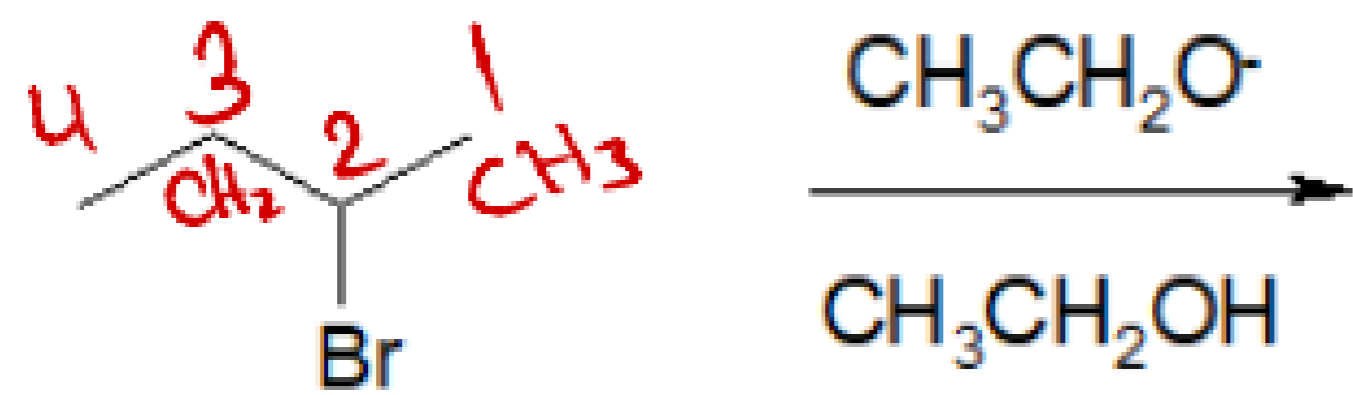
Regioselectivity: where does the double bond form: **Zaitsev's**

**rule:** most highly substituted alkene (watch for sterically hindered bases)

Stereoisomers: **trans > cis**

ال trans أكثر استقراراً

يعني لو انا عندي tetra-substituted مقارنة ب tri-substituted Alken وقتها ح ينتج عندي tetra بكل الاكثر



لانه انه Trans اكثر من ال Cis

هونا عندي احتفاليين:-

1- يا إما بسحب ال X مع H اللوعار ال

2- او بسحب X مع H اللوعار ال C3

لهيكلح ينتج عندي

2 products (structural isomers)

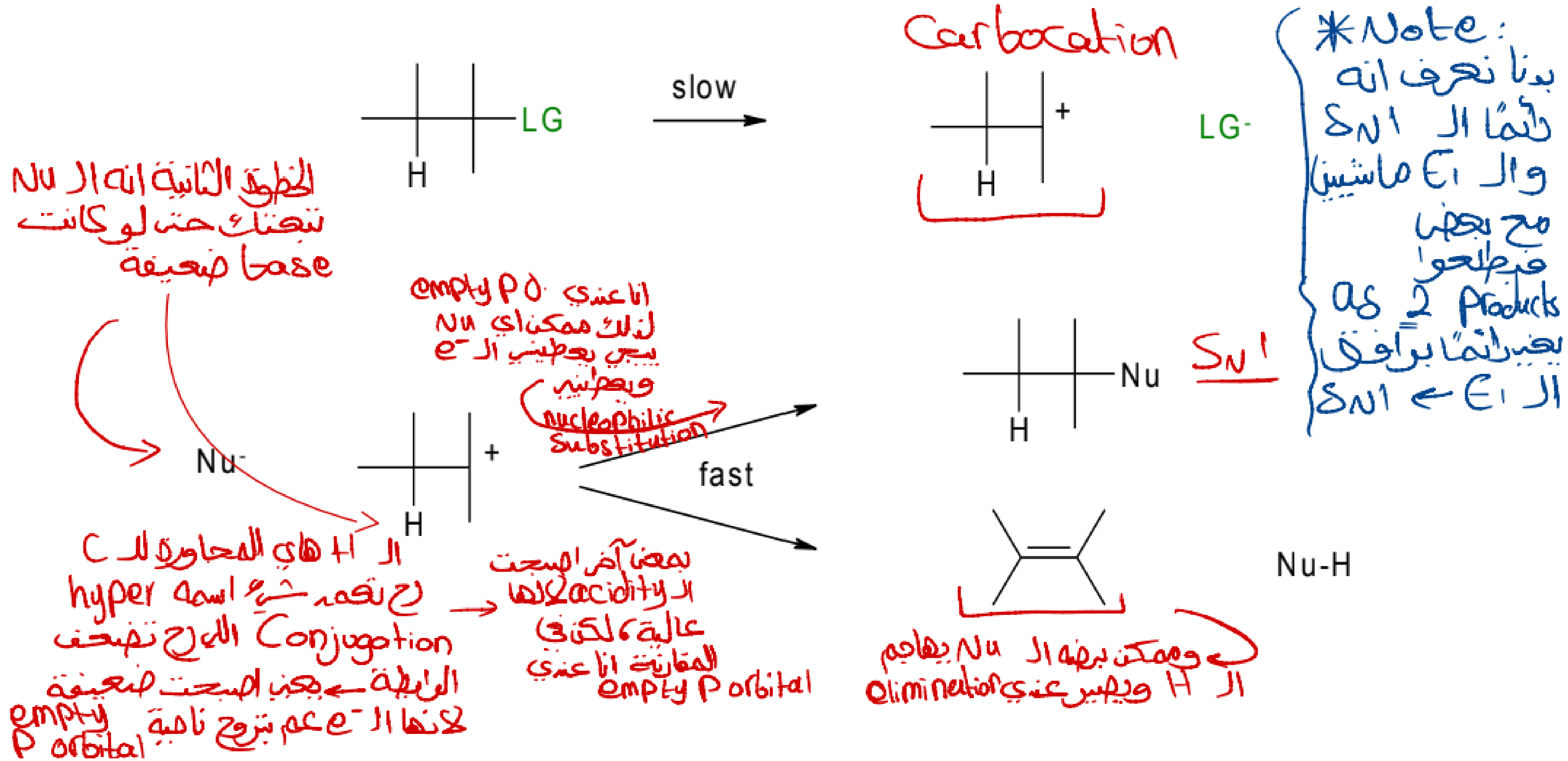
\* ملاحظ انه ال Product رقم 2 نسبتة اعلى والسبب وجود ال factor اوده واحد اسمه (Zaitsev) عمل تجارب عملية واكتشف انه رايثماً الاكثي الناتج الي معاه R اكثر Major product (more substituted) يكون هو ال

تفسر فكرة انه  
انه يتم اولاً تكوين  
Carbocation

لما تكون Carbocation ما يلزمها  
base و Nu ال

# E1 Mechanism

• Rate = k[alkyl halide] (unimolecular)



\* انزل على الجدول بعدين  
ارجع للاضائة

# E1 Mechanism

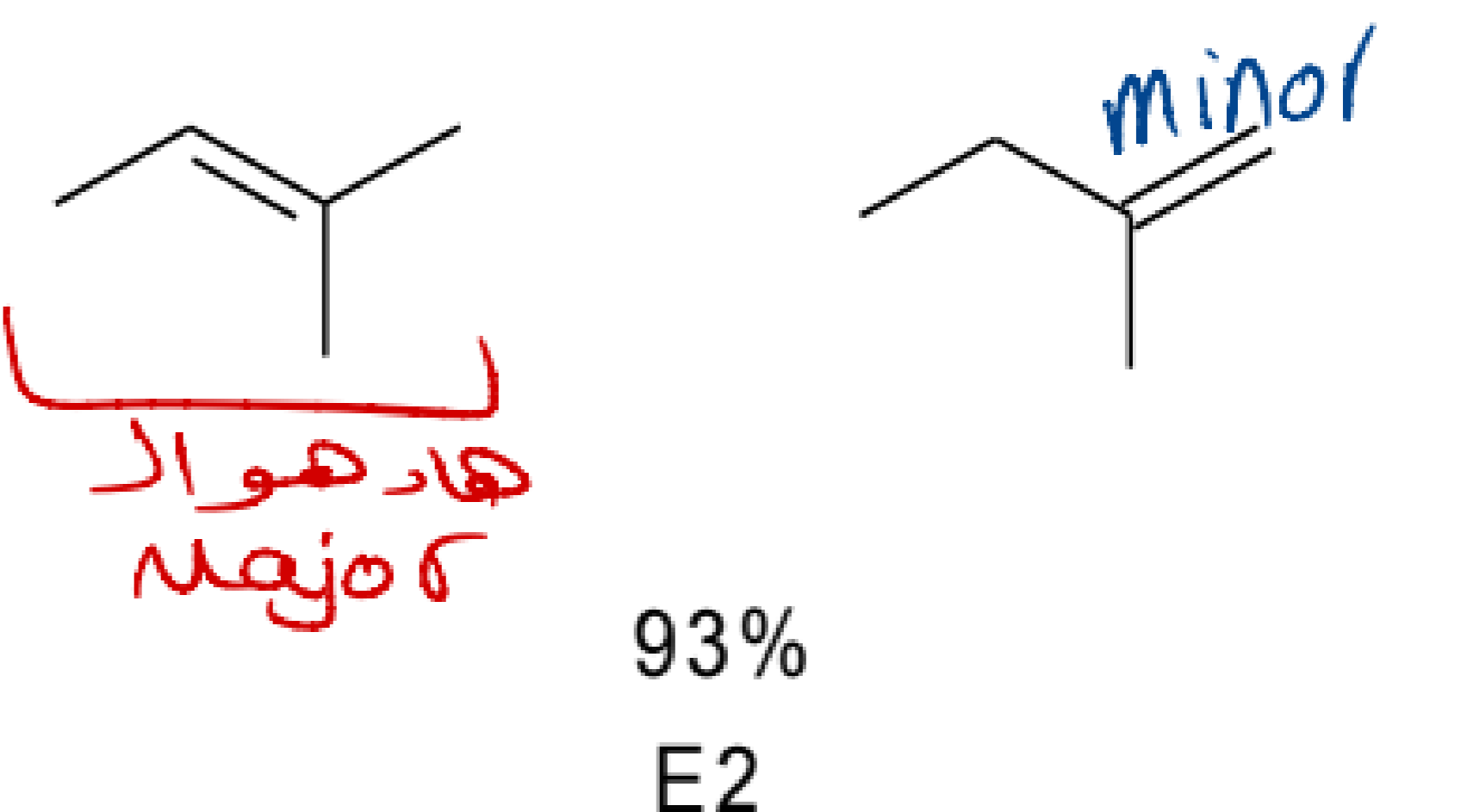
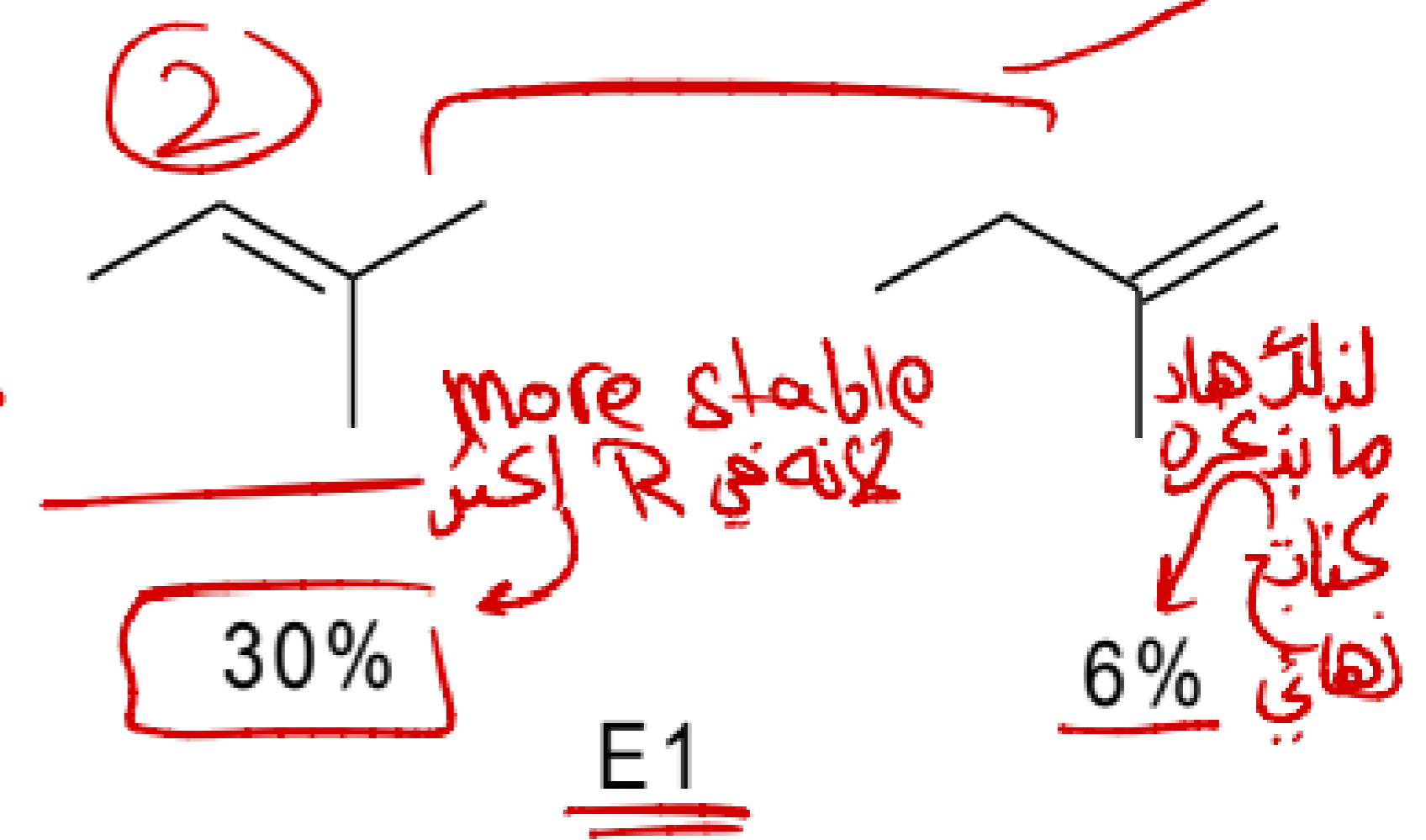
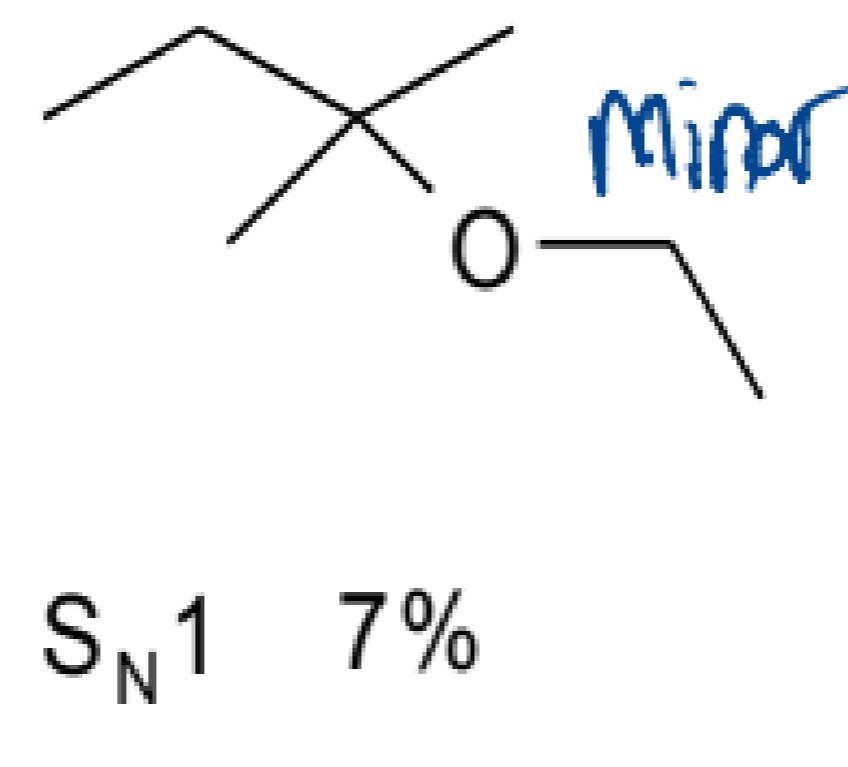
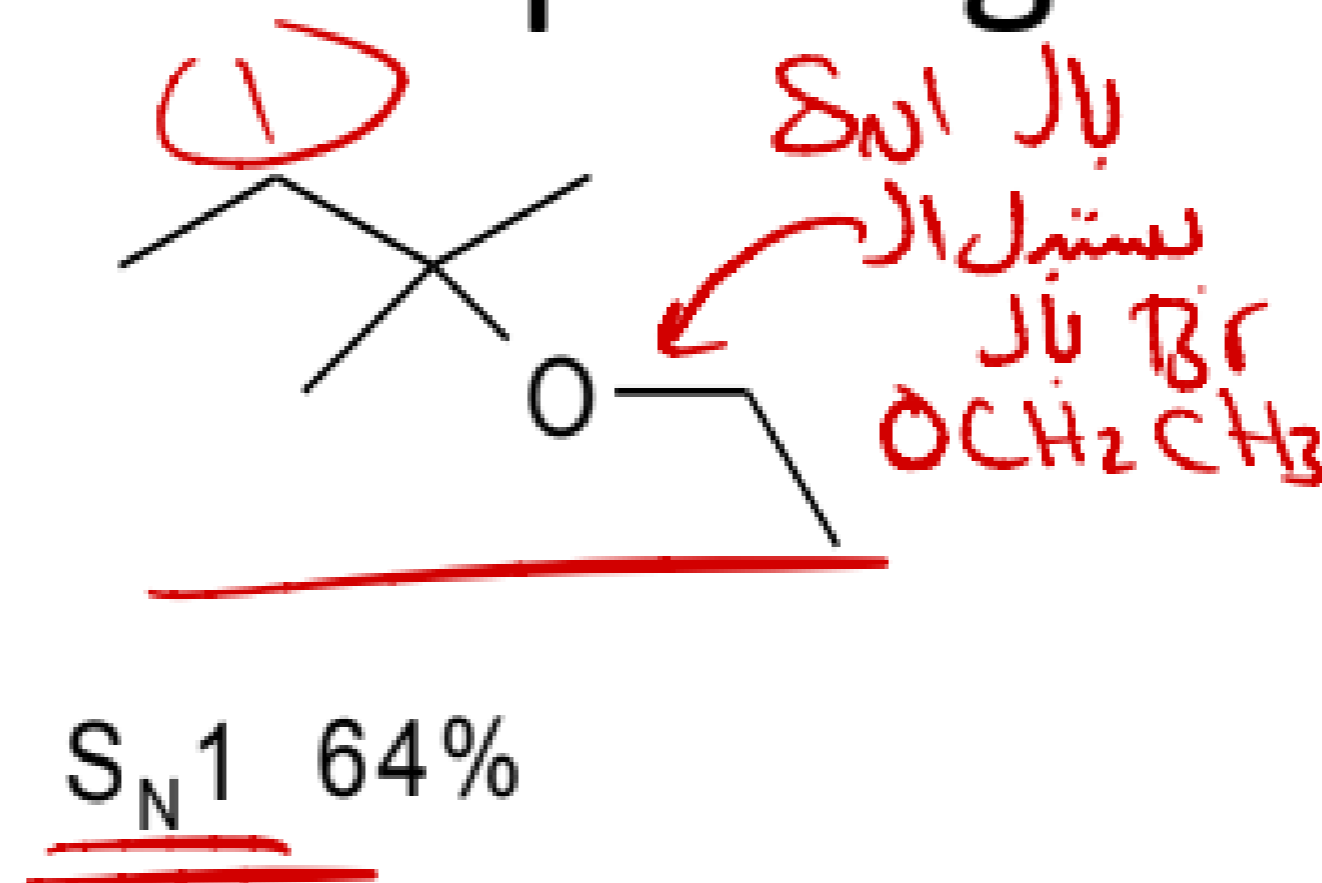
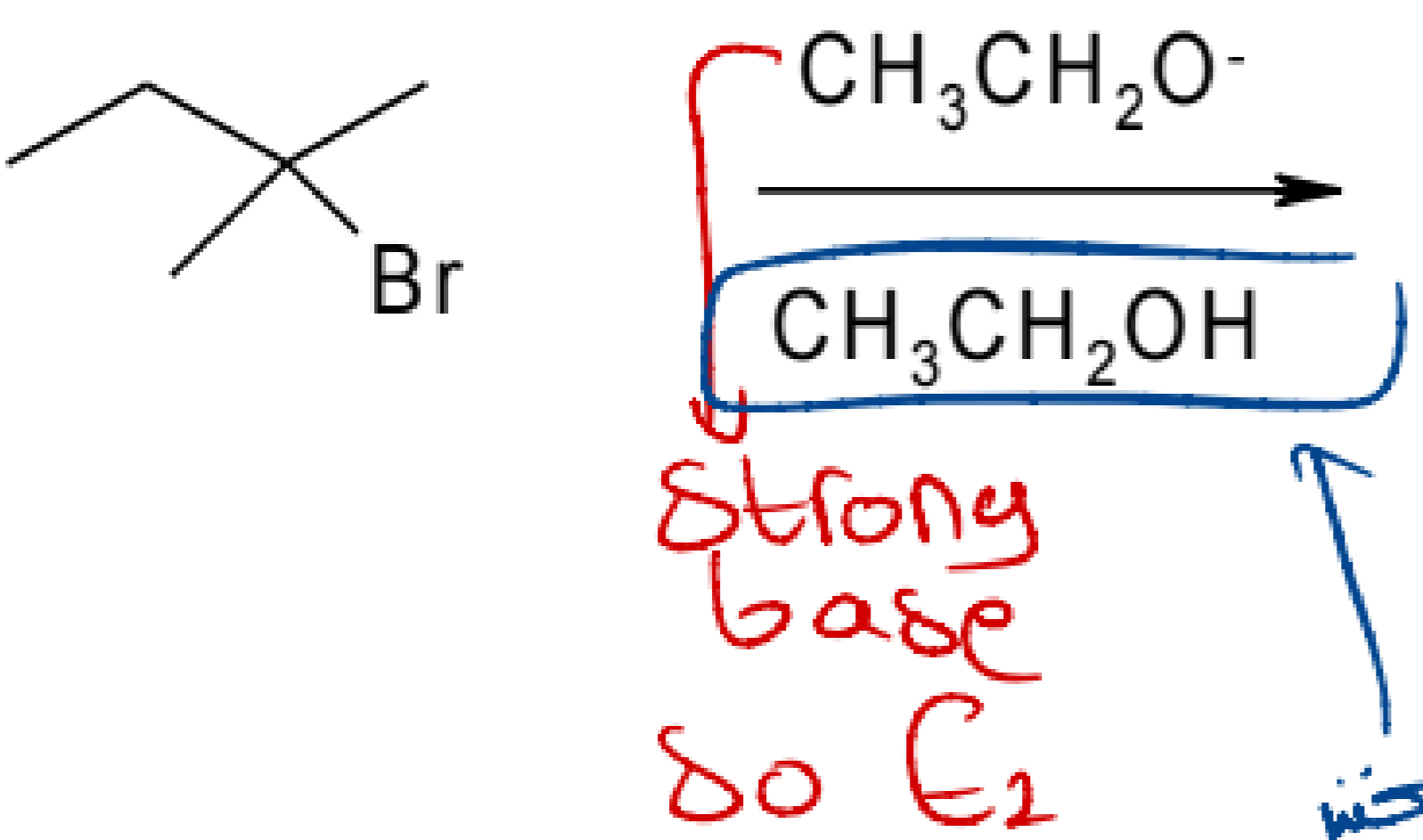
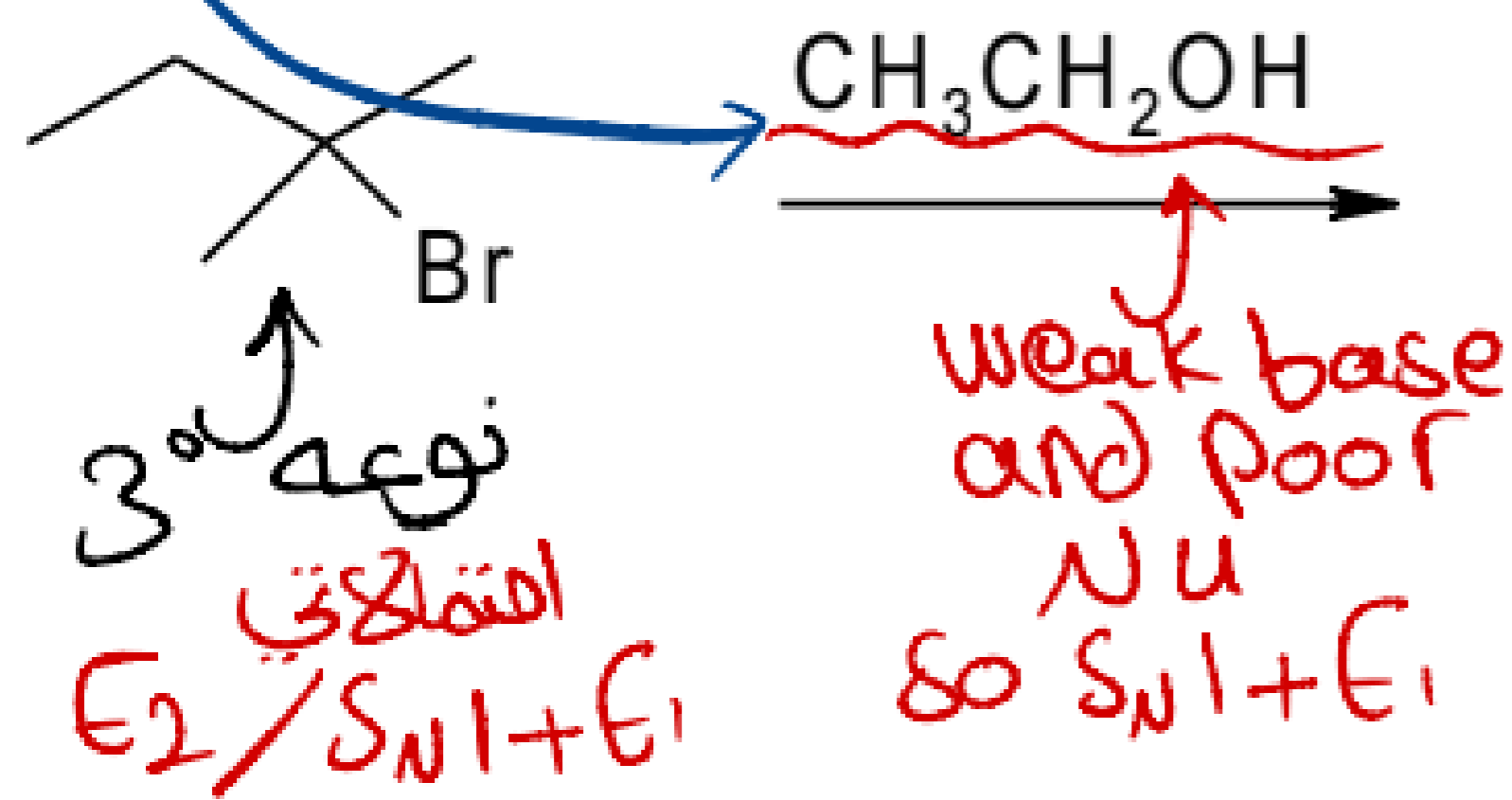
\* او 2 همن ال Major Products  
الثالثا ما يذكر

بال E1 عندي خيارين

## Base strength and competing mechanisms:

هون هاد Solvent  
وينفس الوقت  
Nu

الخطوة الثانية تكون ال Nu

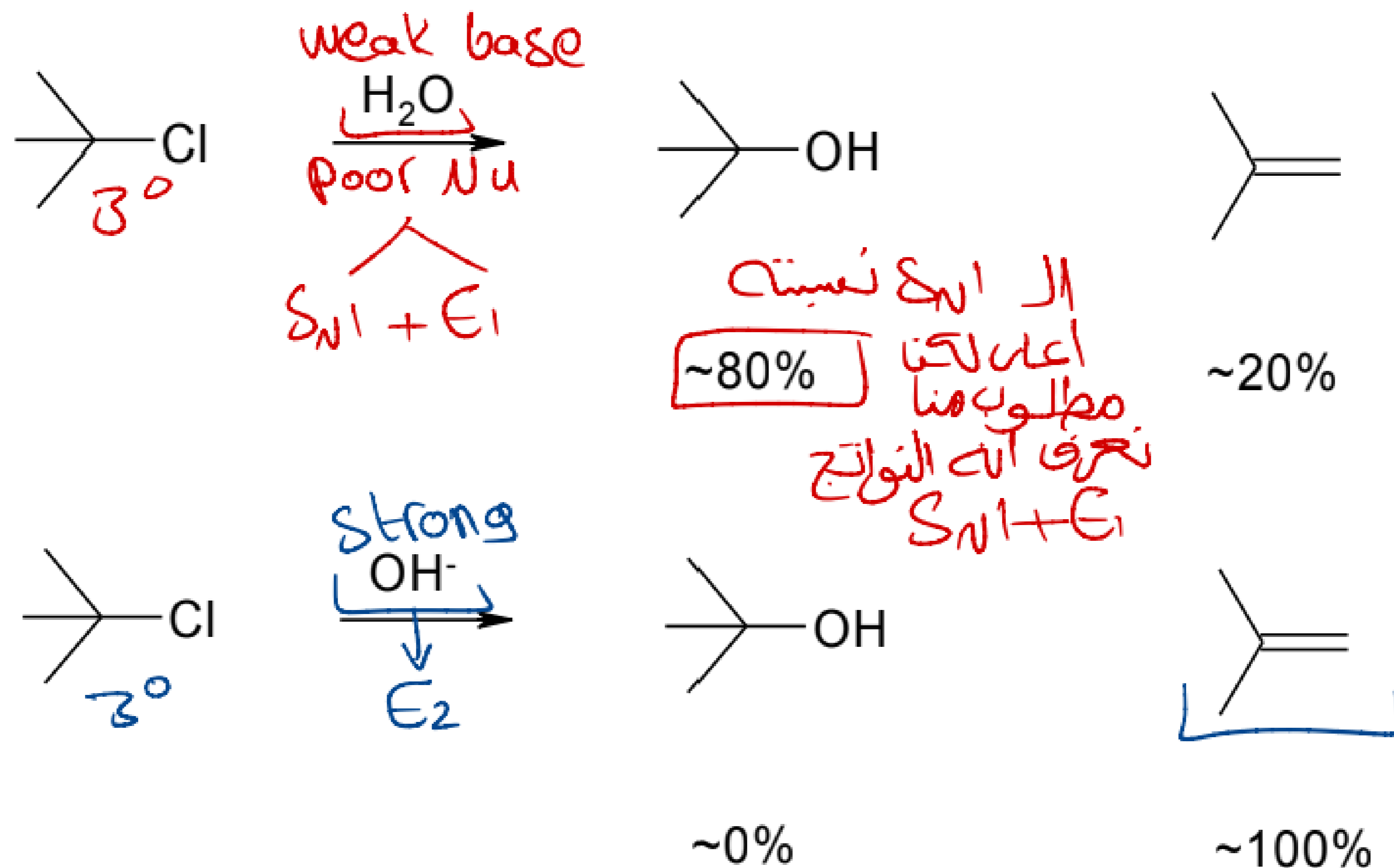


هون بعدين  
Solvent S  
فقط

# Substitution vs. Elimination

3° alkyl halides: only S<sub>N</sub>1 but either (E1 or E2)

– Weak Nu and polar solvent: S<sub>N</sub>1 and E1 compete



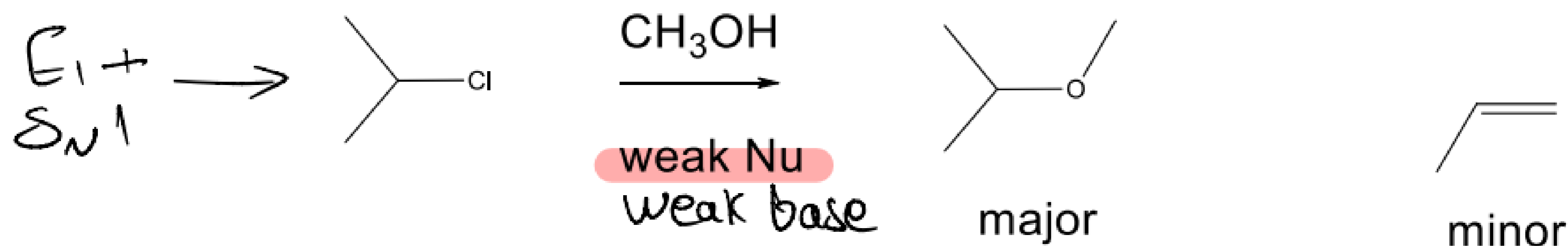
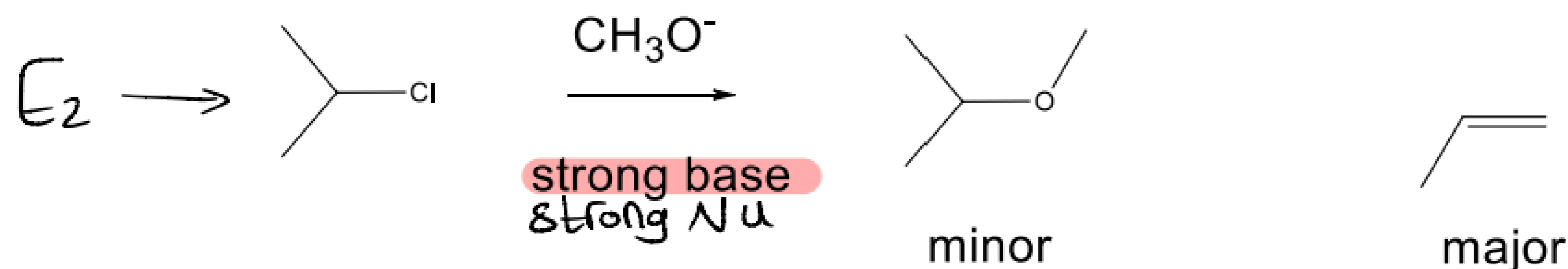
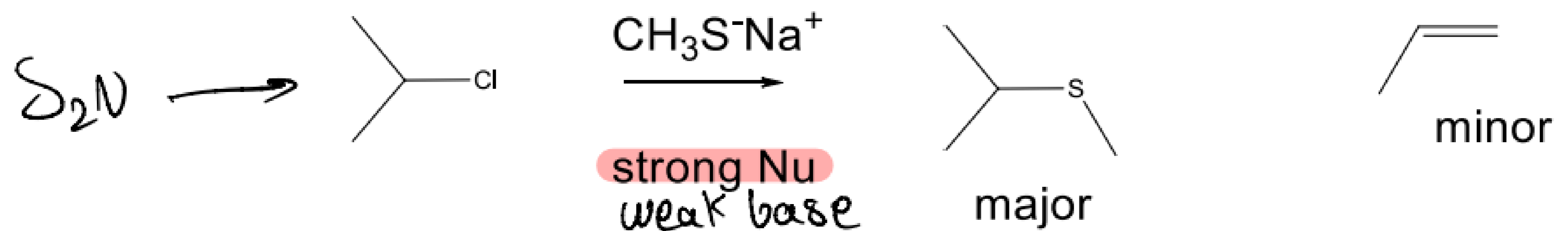
# Substitution vs. Elimination

2° alkyl halides:  $S_N1$ ,  $S_N2$ , E1 or E2 are all possible.

- Weak Nu  $\rightarrow$  substitution
- Strong base  $\rightarrow$  elimination
- Can use solvent to control  $S_N1$  vs.  $S_N2$

# Substitution vs. Elimination

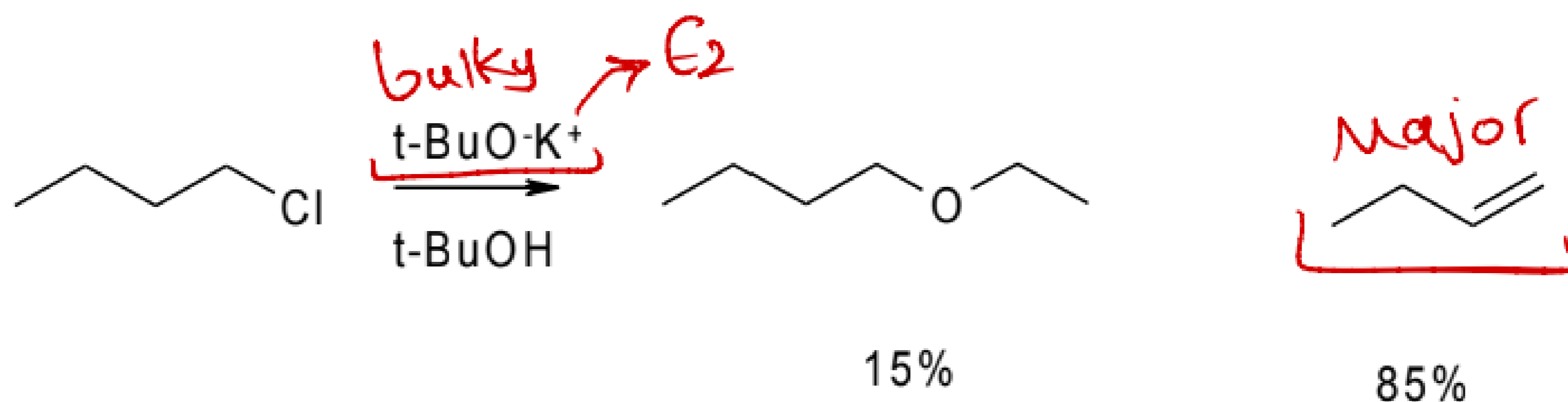
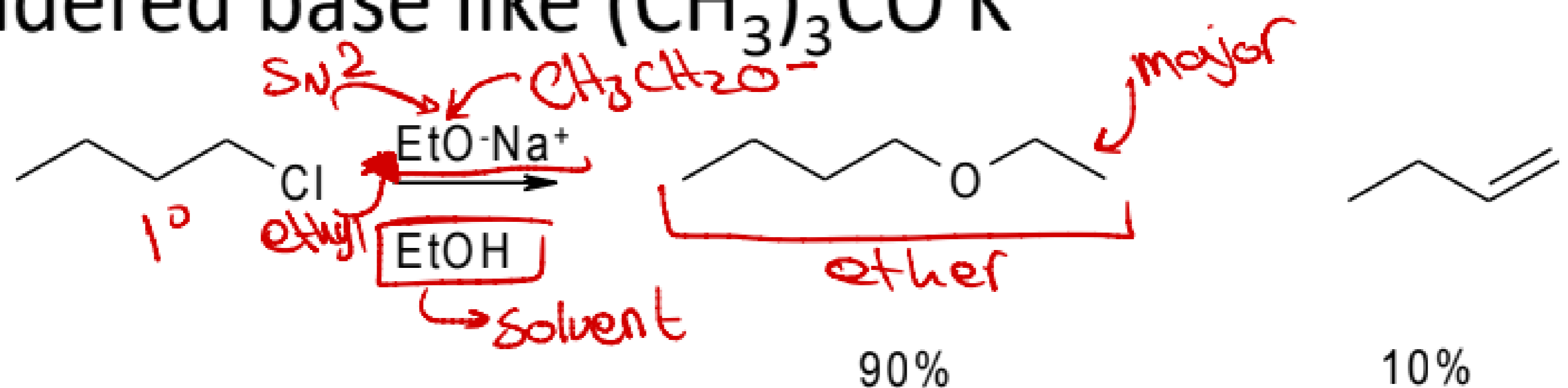
2° alkyl halides: i.e.



# Substitution vs. Elimination

1° alkyl halides:

- Only  $S_N2$  and E2 are possible (no carbocations)
- Substitution dominates unless you use a sterically hindered base like  $(CH_3)_3CO^-K^+$





# Summary of $S_N$ versus E for Haloalkanes

هناك بدنا تعرف  
 كيف نفرق  
 بين ال  
 reaction  
 mechanisms

For Methyl and Primary Haloalkanes

ما ج لمشي بفرقة  $E_1/E_2$   
 لانه ما ج كربون تالبا  
 بفرقة  $E_1/E_2$

TABLE 7.7 Summary of Substitution versus Elimination Reactions of Haloalkanes

| Halide              | Reaction  | Comments   |
|---------------------|-----------|--|
| Methyl<br>$CH_3X$   | $S_N2$    | The only substitution reactions observed.  |
| Primary<br>$RCH_2X$ | $S_N2$    | The main reaction with strong bases such as $OH^-$ and $EtO^-$ . Also, the main reaction with <u>good nucleophiles/weak bases</u> , such as $I^-$ and $CH_3COO^-$ .<br>like $RS^-/RSH$ |
|                     | E2        | The main reaction with strong, bulky bases, such as potassium <i>tert</i> -butoxide.   |
|                     | $S_N1/E1$ | Primary cations are never formed in solution; therefore, $S_N1$ and E1 reactions of primary halides are never observed.  |

$S_N1$   
 لانه لا يكوون  
 Carbocation

هو ما يكون  
 Carbocation  
 ب بقدر يجعل  
 Elimination

$S_N1/E1$   
 لانه ما ج  
 Carbocation

\* Note:  
 ال Primary ال  $S_N2$  مع ال  
 bulky base

فعلية ال Primary هو ج بفرقة  $S_N2$  ال  $S_N1$  لوانا بي ايجو  
 بفرقة  $E2$  ال بقدر لعمل الاطيا: لو اجبت استعملت  $base$  ما يكون  
 bulky زي  $CH_3-C(CH_3)_2-O^-$  هاد هوب يوهل لل  $back$  side  
 فوفتها ج يجعل Elimination

ليه مهم اني افرق بين ال Reaction  
Mechanisms

لانه بالنهاية انا اللي مطلوب مني هو  
معرفة ال final product

---

كيف نفرق بينهم؟

عنا 3 خطوات لازم نمشي فيهم  
بالترتيب :-

1- Type of Alkyl Halide

2- The strength of  
Nu vs. basicity

3- Solvent effect on the  
reaction mechanism

# Summary of $S_N$ versus E for Haloalkanes

– For Secondary and Tertiary Haloalkanes

**TABLE 7.7 Summary of Substitution versus Elimination Reactions of Haloalkanes**

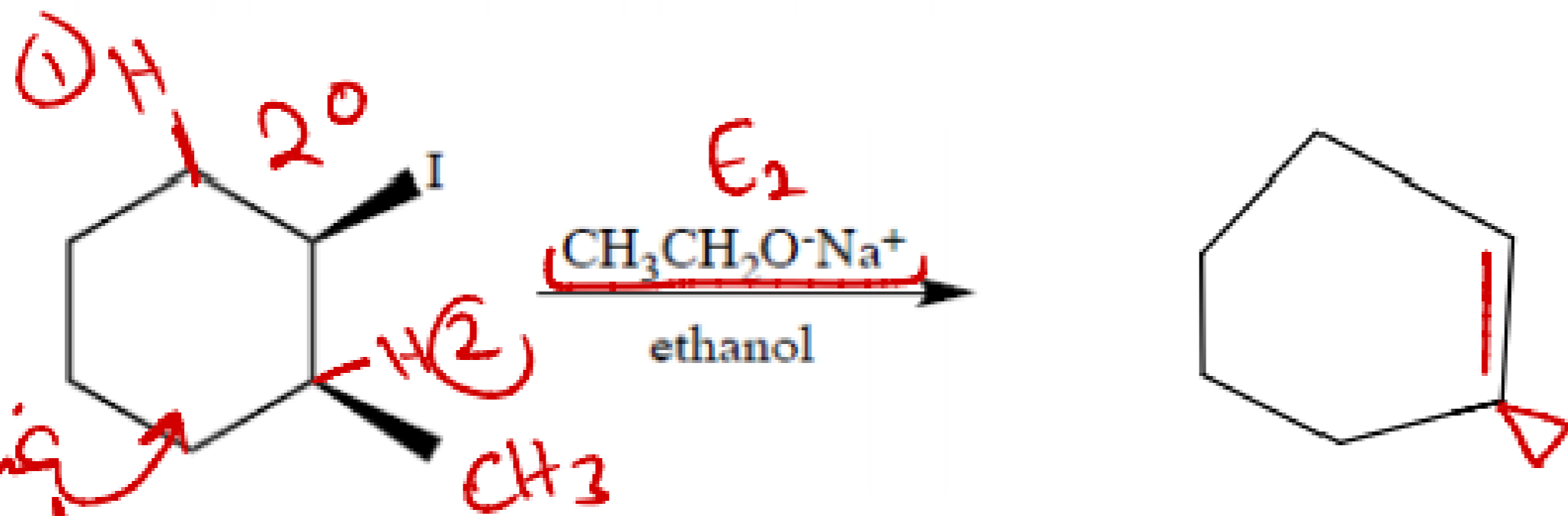
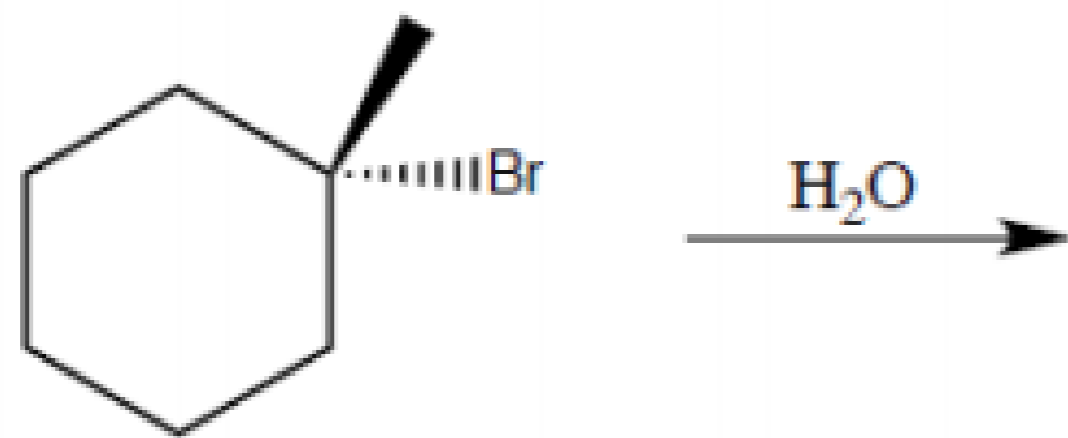
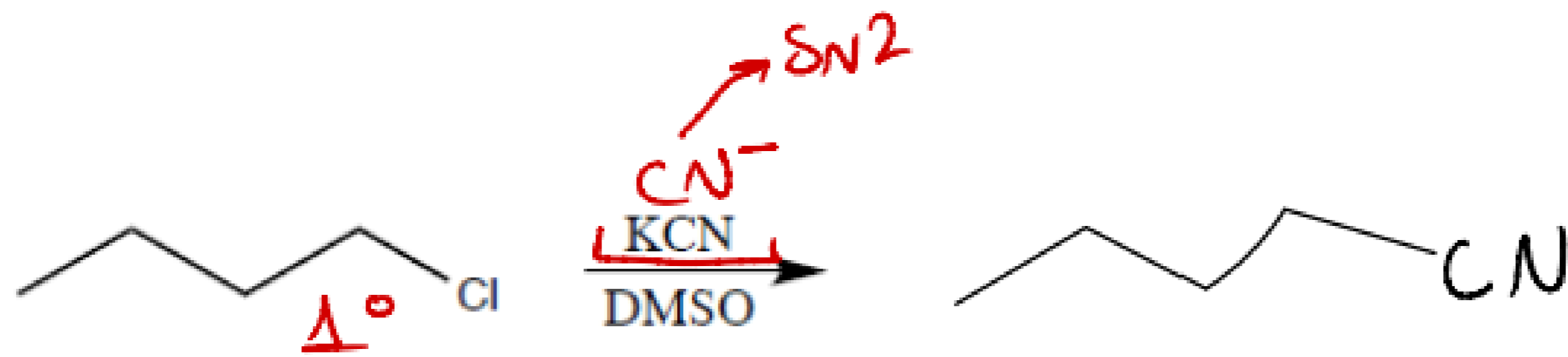
| Halide                | Reaction  | Comments  |
|-----------------------|-----------|---|
| Secondary<br>$R_2CHX$ | $S_N2$    | The main reaction with weak bases/good nucleophiles, such as $I^-$ and $CH_3COO^-$ . / $RS^-$                                       |
|                       | E2        | The main reaction with strong bases/good nucleophiles, such as $OH^-$ and $CH_3CH_2O^-$ . / $RO^-$                                  |
|                       | $S_N1/E1$ | Common in reactions with weak nucleophiles in polar protic solvents, such as water, methanol, and ethanol. like $H_2O / CH_3O$      |
| Tertiary<br>$R_3CX$   | $S_N2$    | $S_N2$ reactions of tertiary halides are never observed because of the extreme crowding around the $3^\circ$ carbon. like $CH_3O^-$ |
|                       | E2        | Main reaction with strong bases, such as $HO^-$ and $RO^-$ . like $CH_3OH / H_2e$   |
|                       | $S_N1/E1$ | Main reactions with poor nucleophiles/weak bases.   |

لأنه متوفر من الجانب الخلفي  
لكنه صعب  
لأنه متوفر من الجانب الخلفي  
لكنه صعب

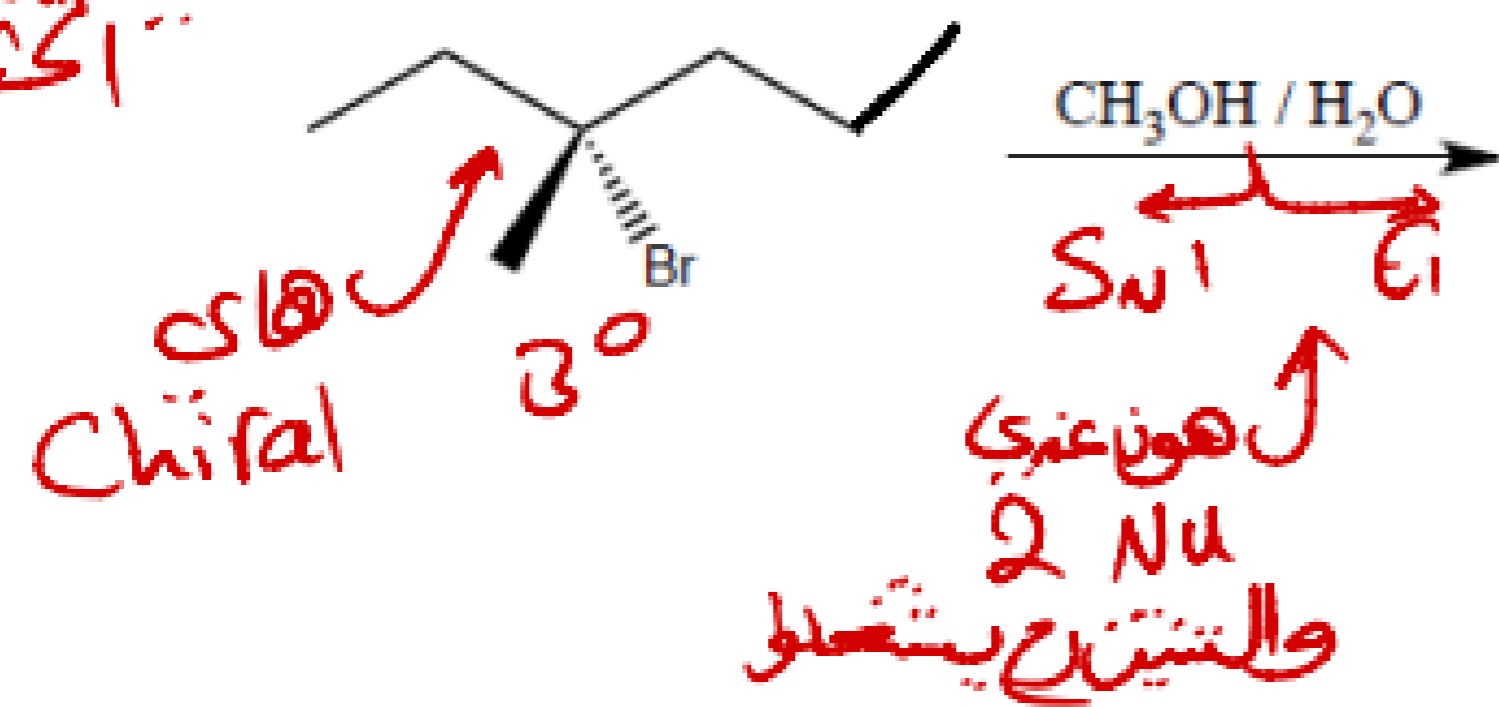
سهل جداً تكوينه  
Carbocation  
لأنه مستقر

لذلك هو راجع إلى  
 $S_N1$  and  $E_1$

الاحتمال الثاني هو أنه ليس  $E_2$  لأنه يدار  
من الجانب الخلفي  
\* Strong bases  
Good Nu  
ولكن العكس غير صحيح



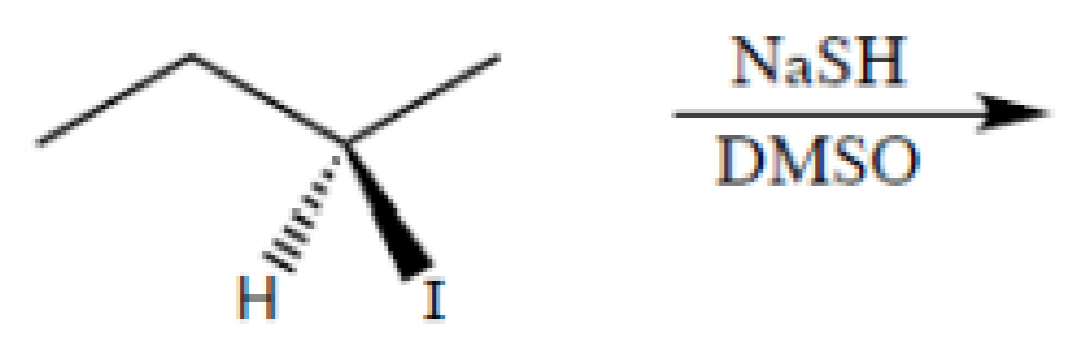
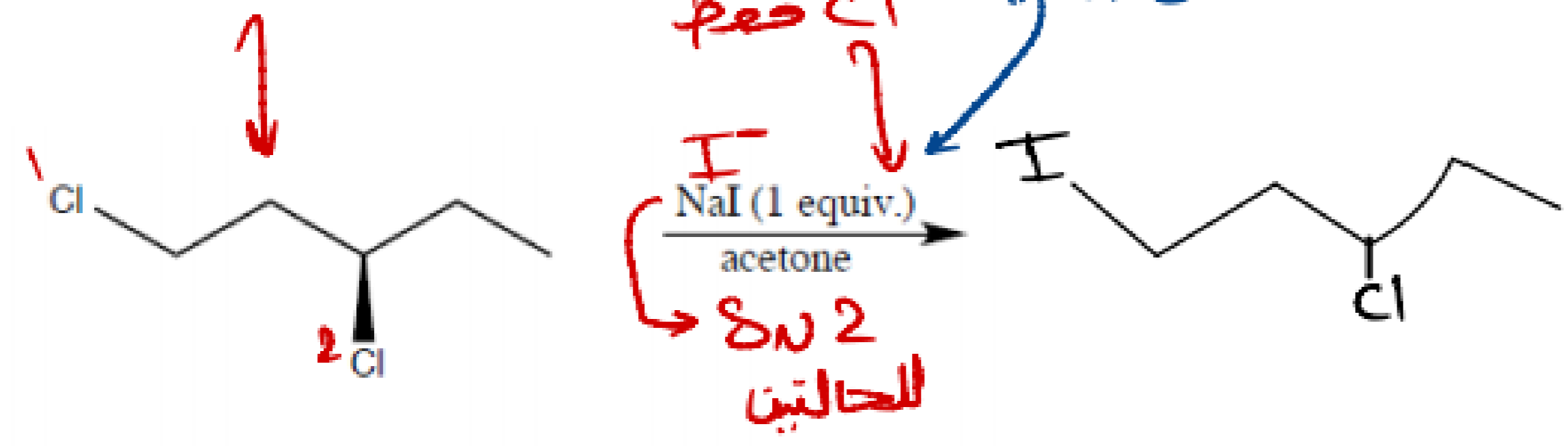
هنا قيارنا  
 لسبب ② افضل  
 لأنه في R group  
 أكثر



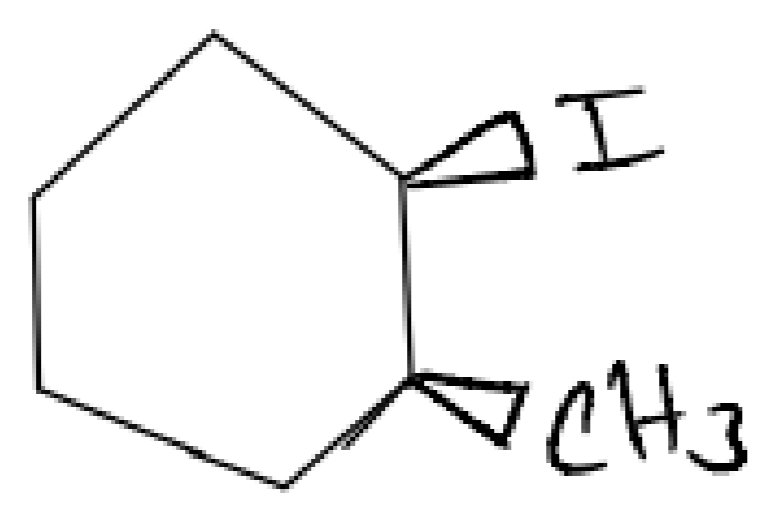
Substitute as  
 5 products  
 4  $\rightarrow$   $\text{S}_{\text{N}}1$   
 لأنه عندي racemic  
 1  $\rightarrow$   $\text{E}_1$

هون اليرج بيتم استبدالها  
هي الالنهال SN2  
اسهل مع ال primary

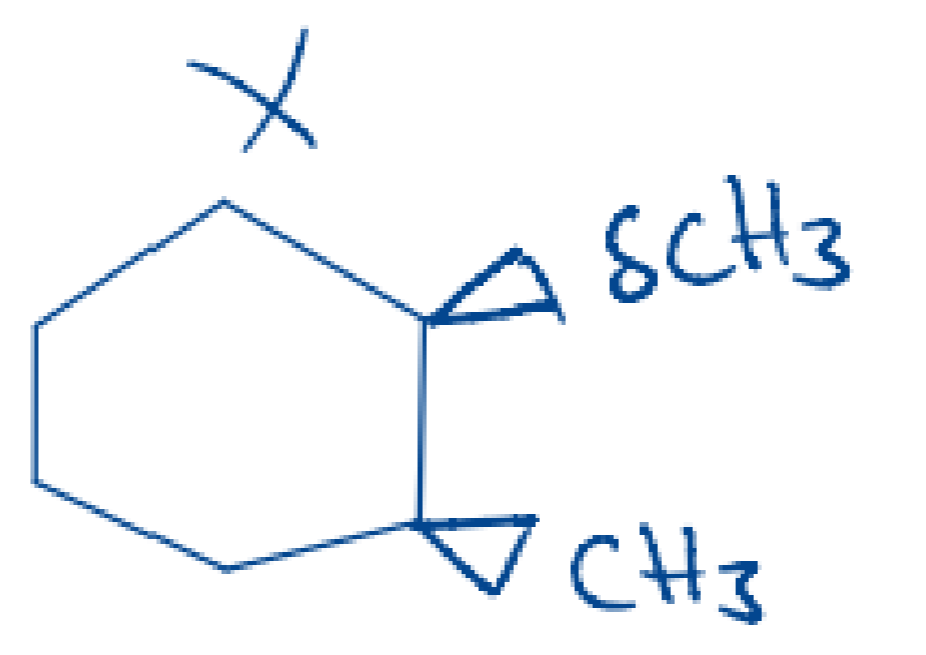
لو اعطاك مكان  
واحد يستبدل  
ال ال الثاني  
هون جكيك استبدال وهدية  
ال فقط



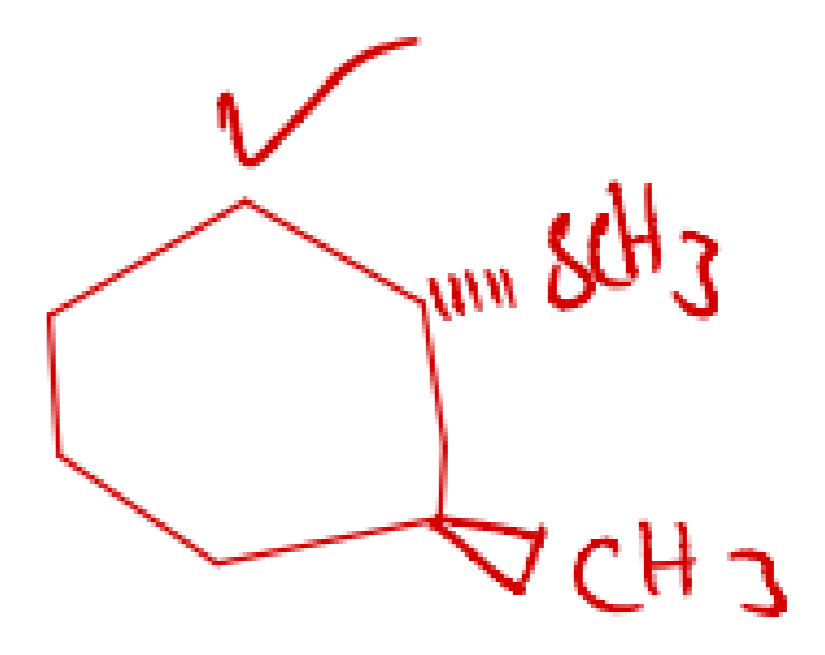
صالح  
ال دكتور



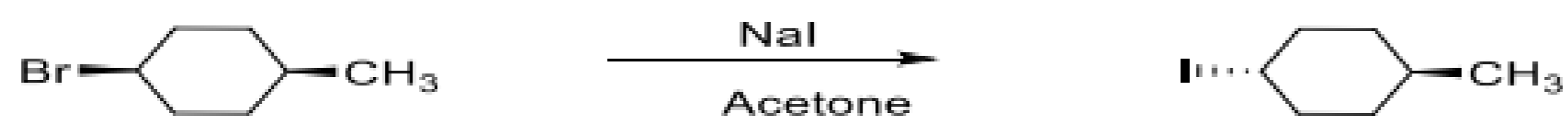
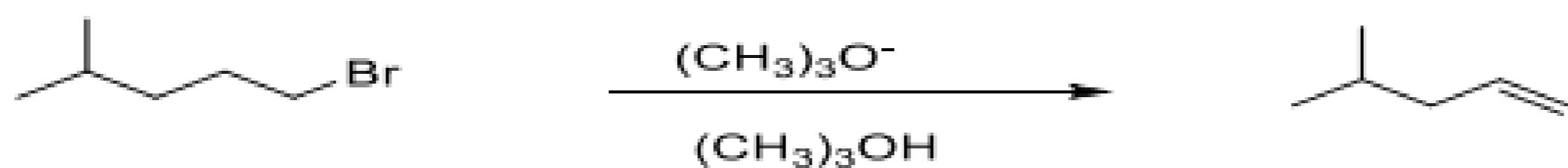
weak base  
good Nu  
SN2



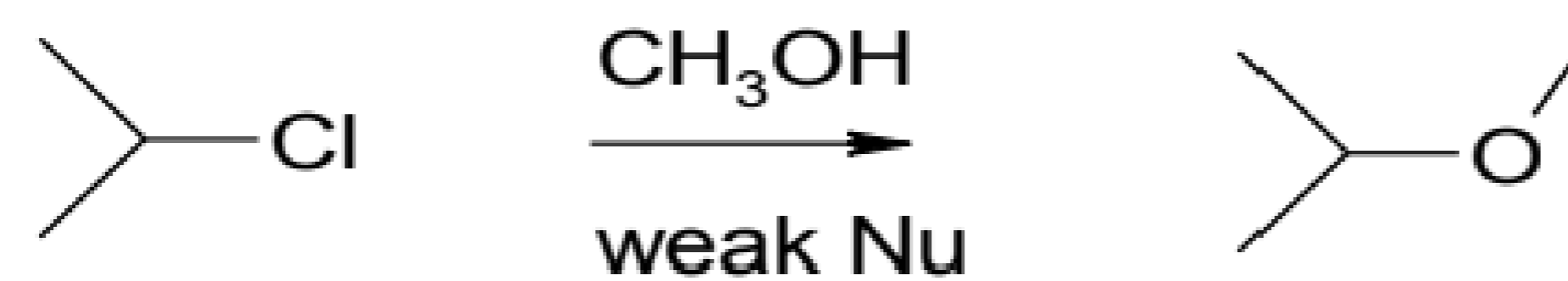
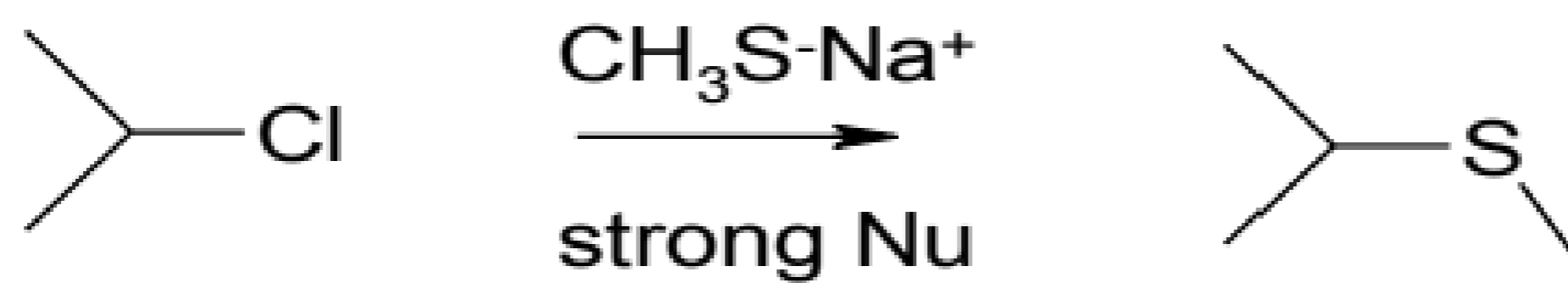
هاد خطا  
لانه ال CH3 ال  
رج تعاليم من ال  
back



هاد الصبح



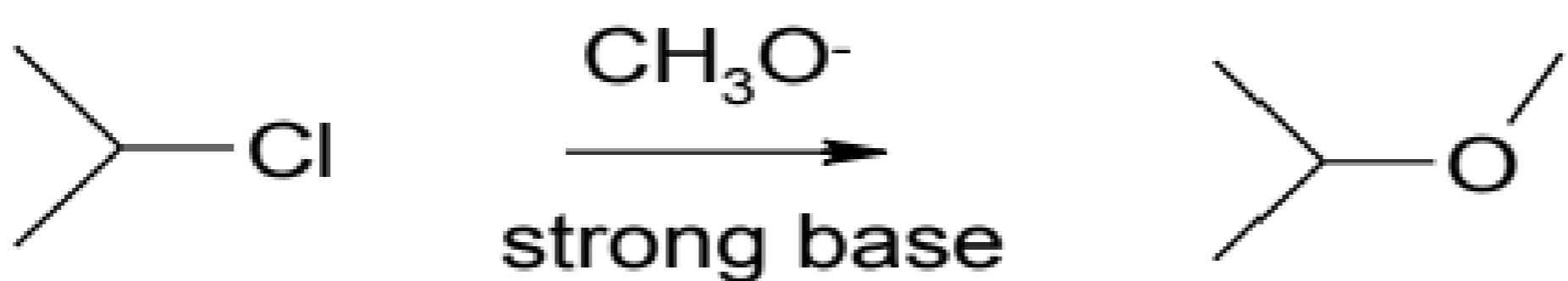
93%  
E2



major



minor



minor



major

# Summary of $S_N$ versus E for Haloalkanes

– **Examples:** Predict the **major** product and the **mechanism** for each reaction.

