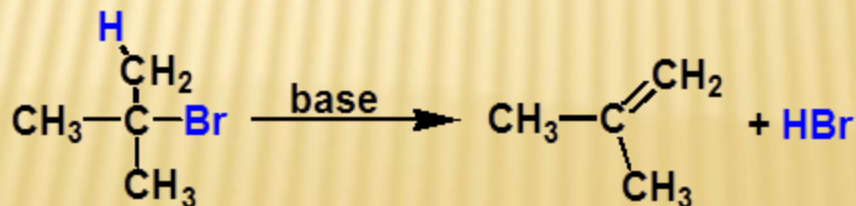
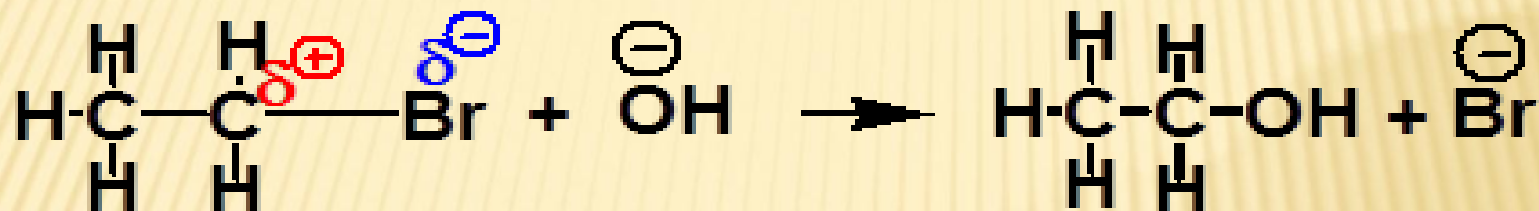


REACTIONS OF ALKYL HALIDES

- ✗ Alkyl halides (R-X) undergo two types of reactions :
- ✗ substitution reactions and elimination reactions.
- ✗ In a substitution reaction, the X group in R-X is
- ✗ replaced by a different group, e.g. $\text{R-X} \rightarrow \text{R-OH} + \text{X}^-$
- ✗ In an elimination reaction, the elements of H-X are
- ✗ eliminated from R-X; the product is very often an
- ✗ alkene.



ALKYL HALIDES – SUBSTITUTION REACTIONS



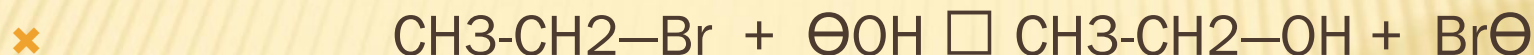
This is a nucleophilic substitution or nucleophilic displacement reaction on which OH displaces Br.

The C-Br bond is polar, and the carbon (δ^+) is susceptible to attack by an anion or any other nucleophile.

OH^- is the nucleophile (species which “loves nuclei” or has an affinity for positive charges).

Br^- is the leaving group

ALKYL HALIDES – SUBSTITUTION REACTIONS



× The general reaction is:



× These are ionic reactions.

× There are two possible ionic mechanisms for nucleophilic substitution, $\text{S}_\text{N}1$ and $\text{S}_\text{N}2$.

× S – substitution; N – nucleophilic;

× 1 – unimolecular (the rate determining, r.d.s., step entails one molecule);

× 2 – bimolecular (the rate determining step entails two species).

ALKYL HALIDES

THE UNIMOLECULAR (SN1) REACTION



- ✗ (a)
- ✗ In the first step, R-X dissociates, forming a carbocation, R⁺, and the leaving group X⁻.
- ✗ This is a slow, rate determining step (r.d.s.) and entails only one species, R-X.
- ✗ (b) $R^+ + Nu^- \rightarrow R-Nu$
- ✗ In the second step the carbocation and the nucleophile combine. This occurs rapidly.
- ✗ The overall reaction is $R-X + Nu^- \rightarrow R-Nu + X^-$
- ✗ The rate of the reaction = $k[R-X]$

ALKYL HALIDES: THE BIMOLECULAR (S_N2) REACTION

- ✗ $A-Nu\ominus + R-X \rightleftharpoons [\ominus Nu \cdots R \cdots X] \ominus$
- ✗ The nucleophile and the alkyl halide combine to form a
- ✗ pentacoordinate transition state. This is the slow rate
- ✗ determining step (r.d.s); it entails two species, R-X and
- ✗ $Nu\ominus$. The dotted lines indicate partially formed or
- ✗ partially broken covalent bonds.

- ✗ $B- [\ominus Nu \cdots R \cdots X] \ominus \rightarrow Nu-R + X\ominus$
- ✗ The pentacoordinate transition state dissociates to form
- ✗ the product, Nu-R, and the halide ion (the leaving
- ✗ group).
- ✗ The rate of the reaction = $k[R-X][Nu\ominus]$
- ✗ The rate is dependent of the concentration of two species;
- ✗ higher concentrations increase the frequency of molecular
- ✗ collisions.

ALKYL HALIDES

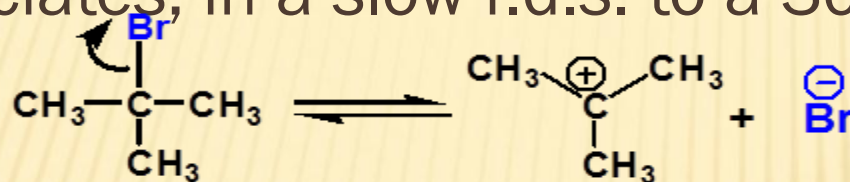
THE UNIMOLECULAR (SN1) REACTION



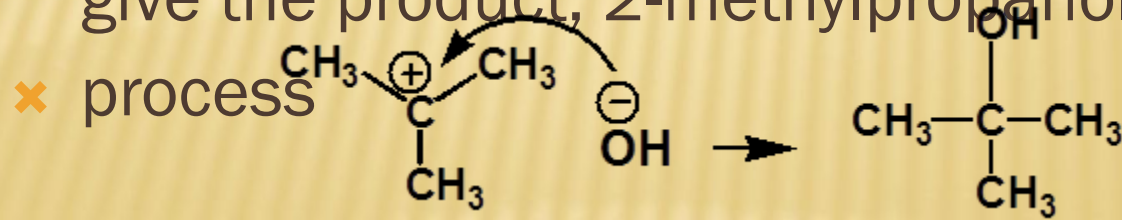
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- ✗ The overall reaction is $R-X + Nu^{\ominus} \rightarrow R-Nu + X^{\ominus}$
- ✗ The rate of the reaction = $k[R-X]$

ALKYL HALIDES: SN1 REACTIONS IN MORE DETAIL

- ✗ A- bromo-2-methylpropane, a 3o alkyl halide dissociates, in a slow r.d.s. to a 3o carbocation and Br^- .

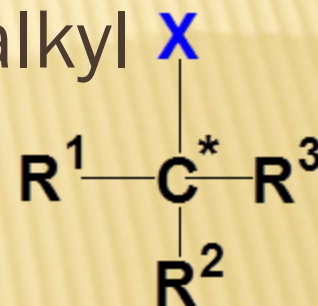


- ✗ The positively charged carbon in a carbocation is sp^2
- ✗ hybridized and carbocations have trigonal geometry.
- ✗ This is a very important point.
- ✗ b) A nucleophile, OH^- , adds to the carbocation to give the product, 2-methylpropanol. This is a fast

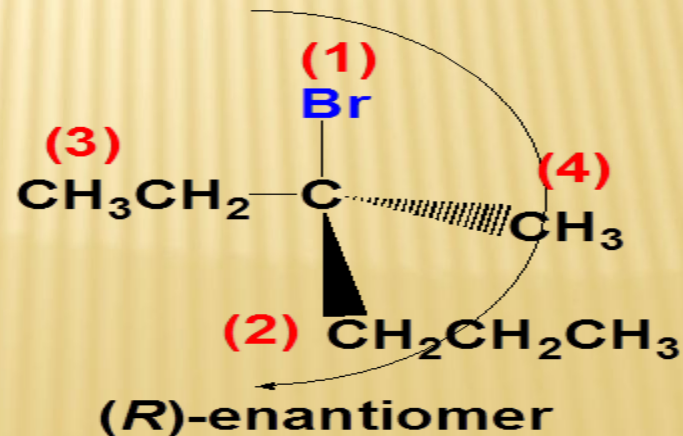
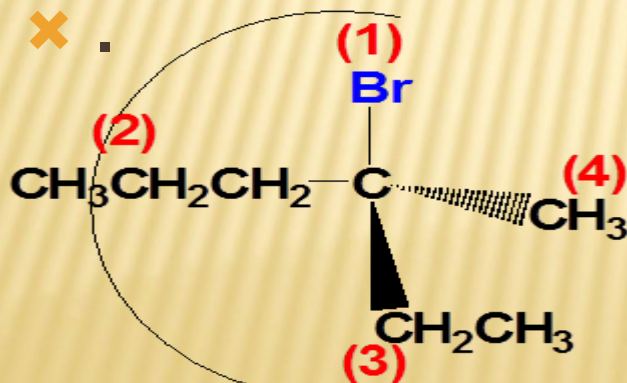


THE STEREOCHEMISTRY OF SN1 REACTIONS

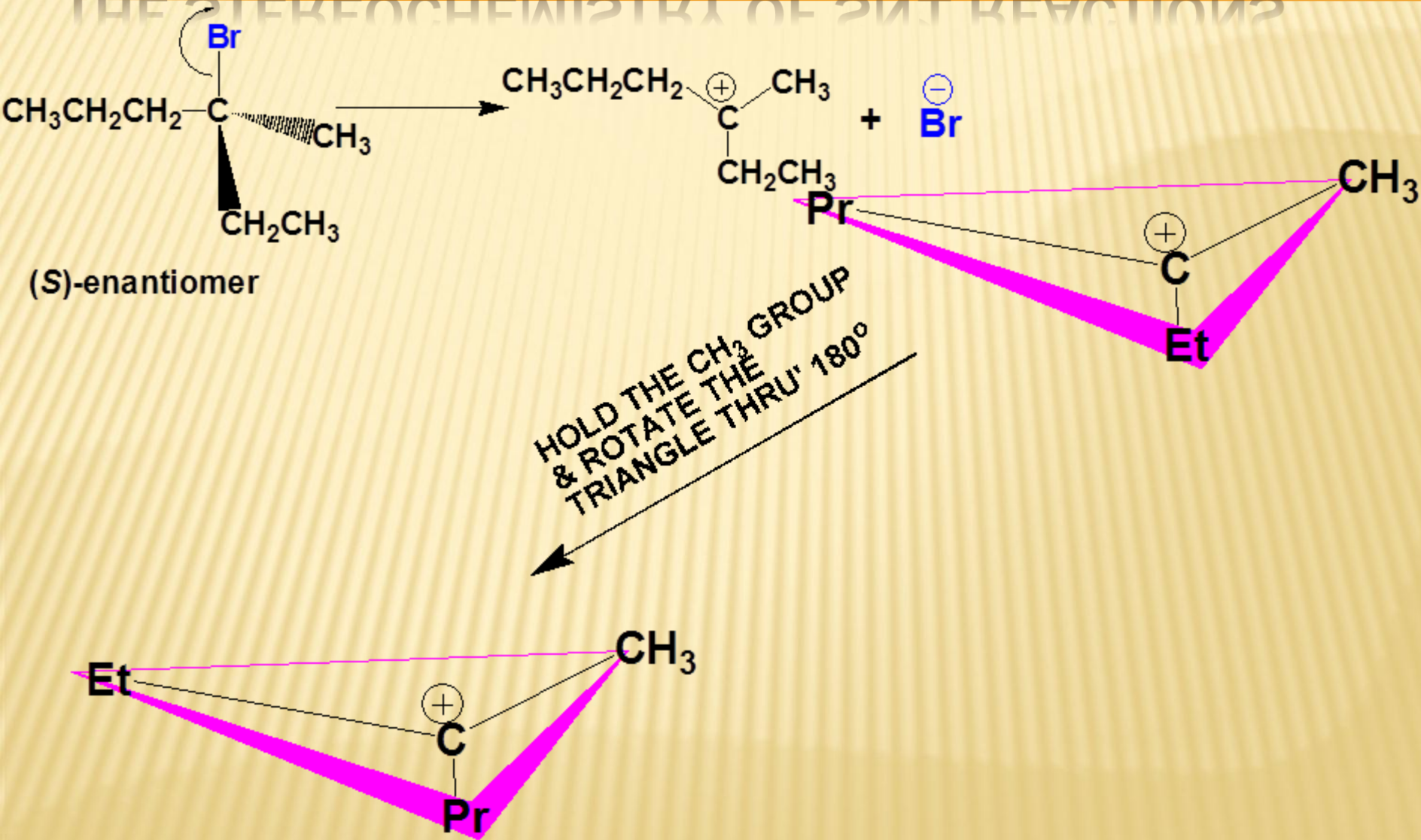
- ✗ A 3° alkyl halide with three different alkyl groups



- ✗ attached to the head carbon is chiral.
- ✗ There are two enantiomers of such a compound, e.g. 3-bromo-3-methylhexane

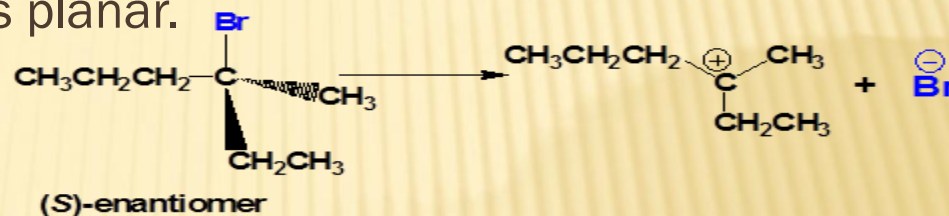


THE STEREOCHEMISTRY OF SN1 REACTIONS

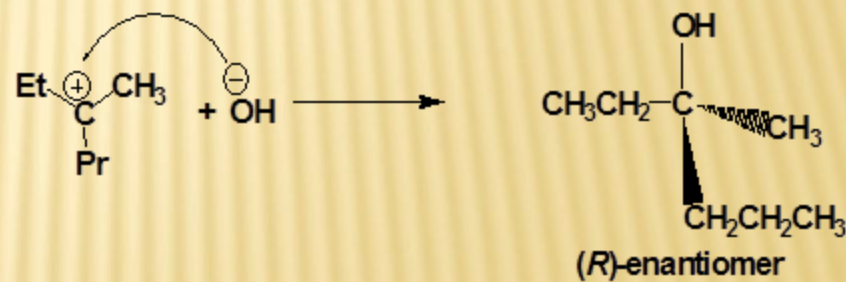
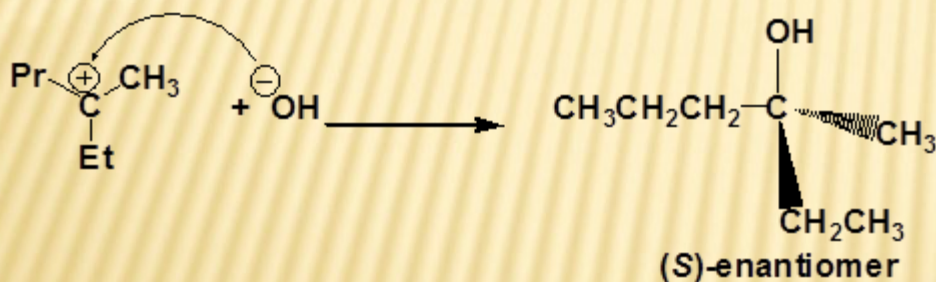


THE STEREOCHEMISTRY OF SN1 REACTIONS

- ✗ The initially formed carbocation is planar.

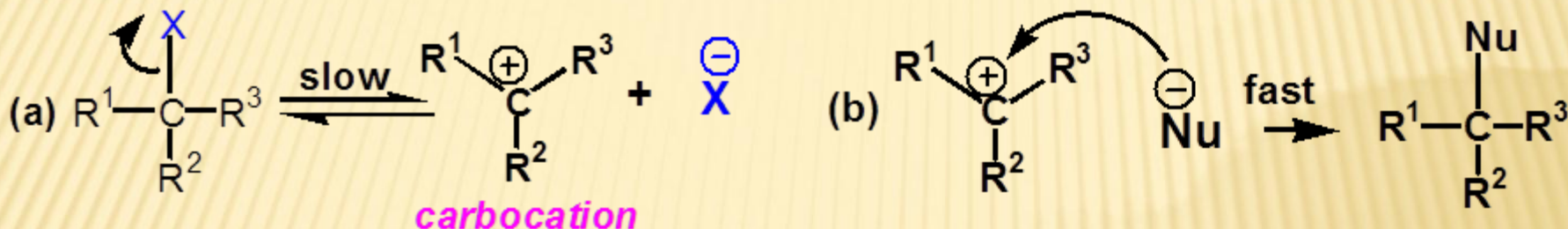


- ✗ In the second step, the nucleophile will add from either face
- ✗ of the carbocation.



- ✗ Both enantiomers of the product are formed in equal amounts.
- ✗ The same result is obtained starting with the R enantiomer of the alkyl halide, because exactly the same carbocation is formed.

OTHER ASPECTS OF SN1 REACTIONS

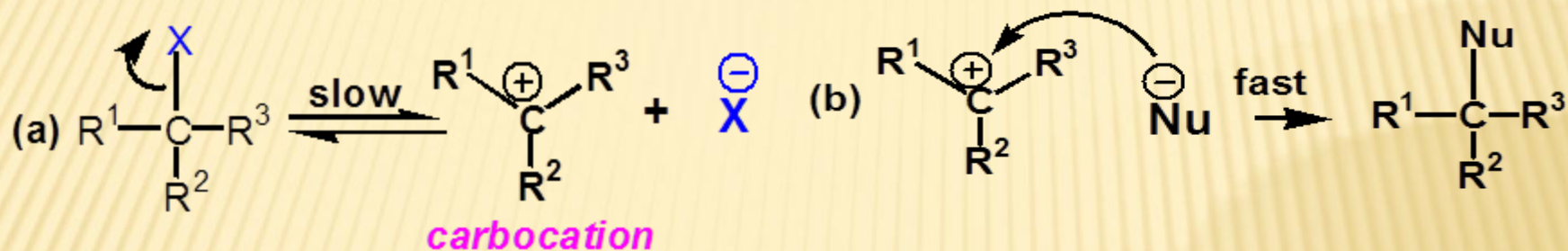


The most important feature of SN1 reactions is the carbocation intermediate.

A. Alkyl halides which form stable carbocations will undergo SN1 reactions.

3o alkyl halides form 3o carbocations (stable) and will ☐ undergo SN1 reactions.

OTHER ASPECTS OF SN1 REACTIONS



Alkyl halides which form stable carbocations will undergo SN1 reactions.

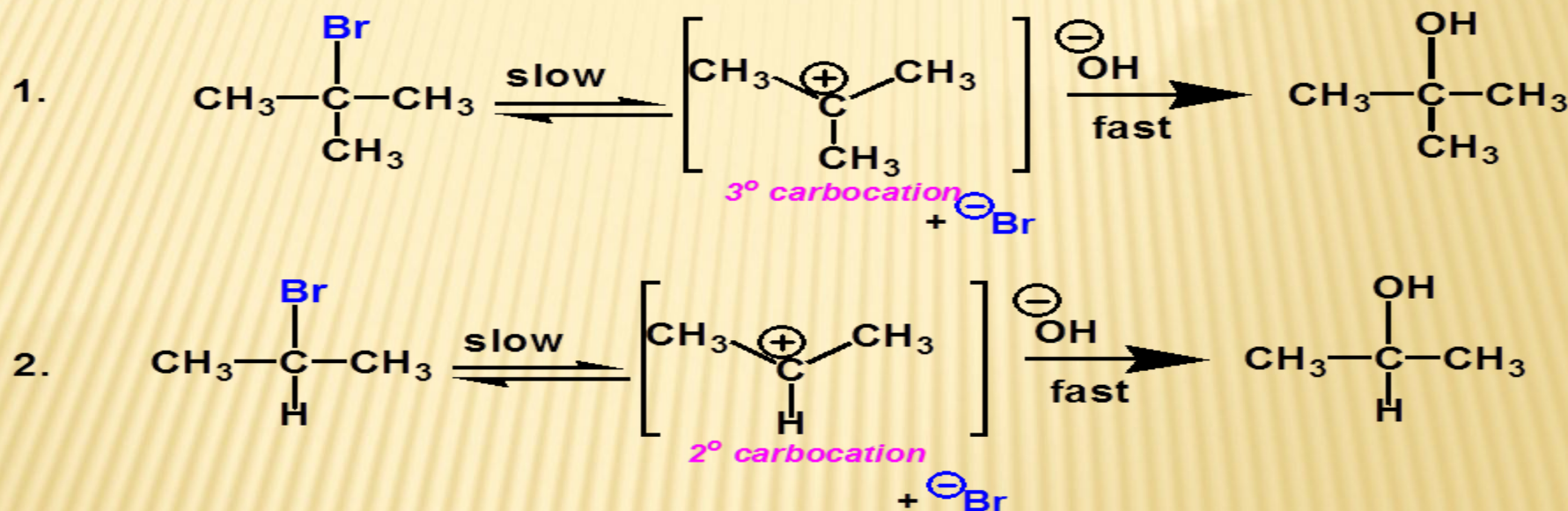
2o alkyl halides form 2o carbocations (fairly stable) and ☐ undergo SN1 reactions.

1o carbocations are unstable, 1o alkyl halides will not undergo SN1 reactions.

Substitution reactions of 1o alkyl halides proceed via the SN2 mechanism.

OTHER ASPECTS OF SN1 REACTIONS

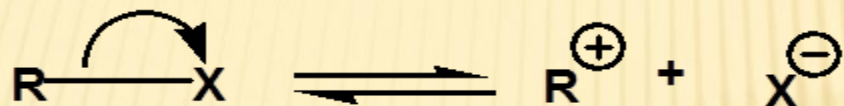
- ✗ The RATE of SN1 reactions increases with increasing stability of the carbocation.



- ✗ The carbocation formed in reaction 1 is more stable than that
- ✗ formed in reaction 2, □ reaction 1 is faster than reaction 2.

OTHER ASPECTS OF SN1 REACTIONS

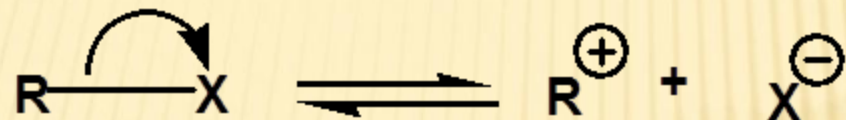
- ✗ Polar solvents STABILIZE carbocations, and accelerate SN1 reactions.
- ✗ The first step of an SN1 reaction is



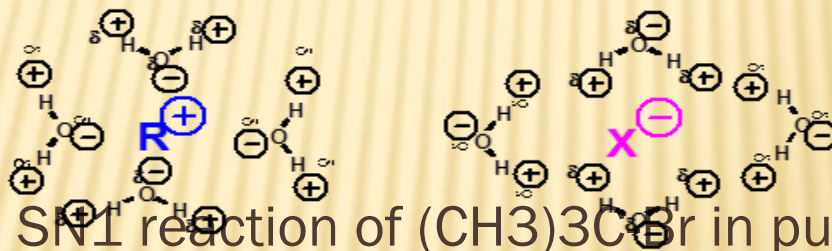
- ✗ If R^{\oplus} is stabilized via interactions with the solvent, the
- ✗ equilibrium is pulled to the RIGHT, and the overall process is accelerated.
- ✗
- ✗ The DIELECTRIC CONSTANT (ϵ , “epsilon”) is an index of
- ✗ solvent polarity.
- ✗
- ✗ H_2O (ϵ 79) is a polar, protic solvent.
- ✗ $\text{CH}_3\text{CH}_2\text{OH}$ (ethanol, ϵ 25) is also protic, but much less polar than H_2O .

OTHER ASPECTS OF SN1 REACTIONS

- ✖ Polar solvents STABILIZE carbocations, and accelerate SN1 reactions.



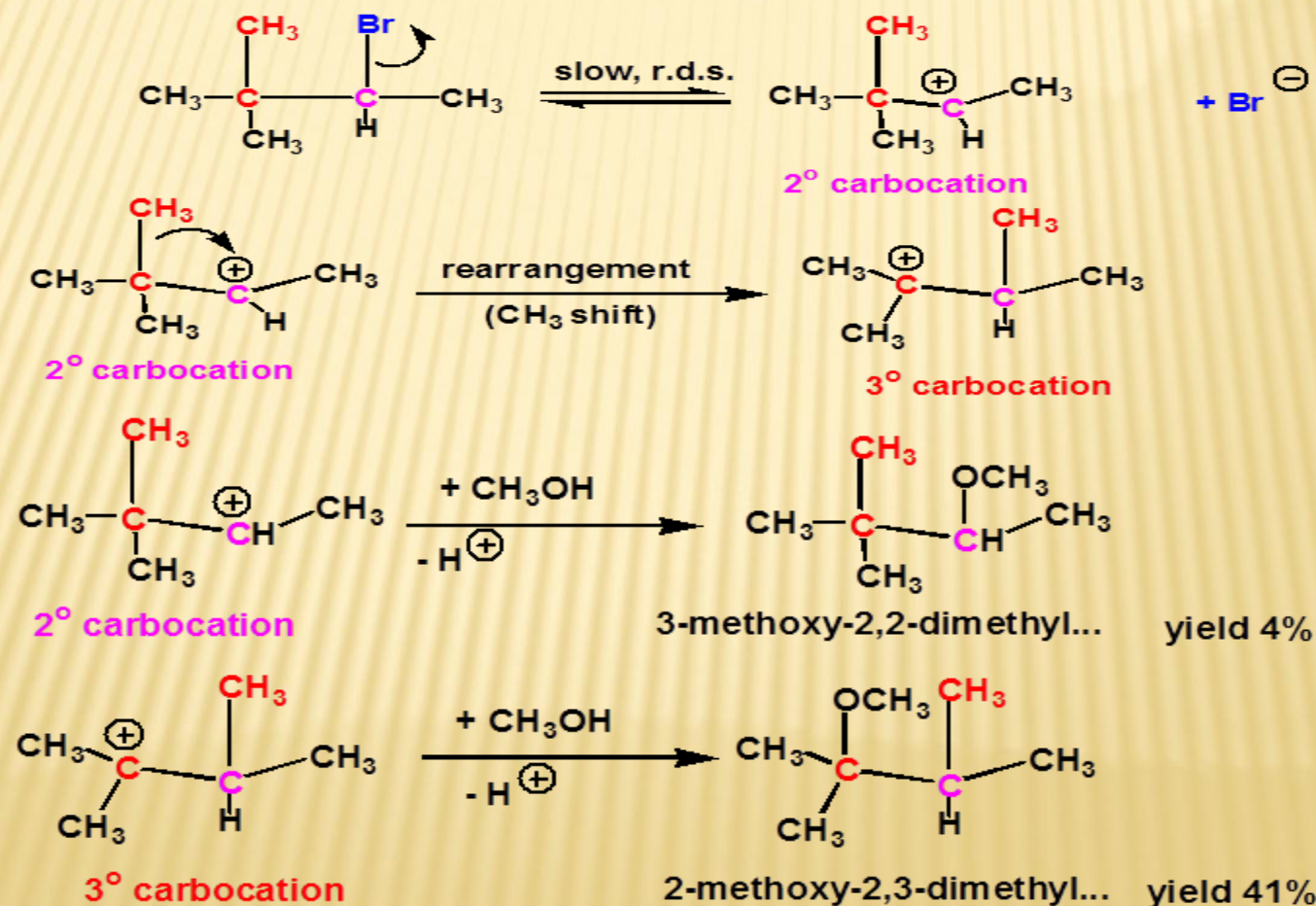
- ✖ H₂O (□ 79) interacts with R[⊕] and X[⊖] as shown here.



- ✖ The rate of an SN1 reaction of (CH₃)₃COBr in pure
- ✖ H₂O (□ 79) is approximately 12,000 times the rate in
- ✖ pure CH₃CH₂OH (ethanol, □ 25).

OTHER ASPECTS OF SN1 REACTIONS

- When some 2° alkyl halides undergo the SN1 reaction, products of rearrangement are observed.



ALKYL HALIDES: THE BIMOLECULAR (S_N2) REACTION

- ✗ $\text{Nu}^- + \text{R-X} \rightleftharpoons [\text{Nu}^{\delta-} \cdots \text{R} \cdots \text{X}^{\delta-}]^{\ddagger}$
- ✗ The nucleophile and the alkyl halide combine to form a
- ✗ pentacoordinate transition state. This is the slow rate
- ✗ determining step (r.d.s); it entails two species, R-X and
- ✗ Nu^- . The dotted lines indicate partially formed or
- ✗ partially broken covalent bonds.

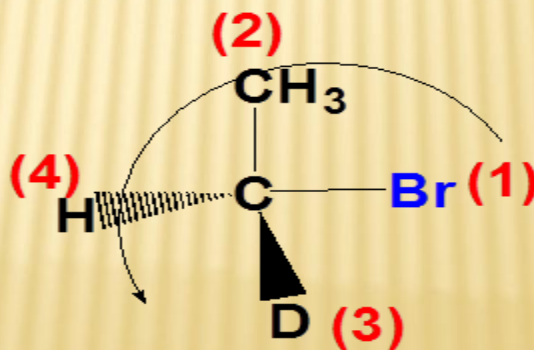
- ✗ $[\text{Nu}^{\delta-} \cdots \text{R} \cdots \text{X}^{\delta-}]^{\ddagger} \rightarrow \text{Nu-R} + \text{X}^-$
- ✗ The pentacoordinate transition state dissociates to form
- ✗ the product, Nu-R, and the halide ion (the leaving
- ✗ group).
- ✗ The rate of the reaction = $k[\text{R-X}][\text{Nu}^-]$
- ✗ The rate is dependent of the concentration of two species;
- ✗ higher concentrations increase the frequency of molecular
- ✗ collisions.

THE STEREOCHEMISTRY OF SN2 REACTIONS

- ✗ (a) $\text{Nu}^- + \text{R-X} \rightleftharpoons [\text{Nu}^-\cdots\text{R}\cdots\text{X}]^\ddagger$ (slow, r.d.s)
- ✗ (b) $[\text{Nu}^-\cdots\text{R}\cdots\text{X}]^\ddagger \rightarrow \text{Nu-R} + \text{X}^-$ (fast)

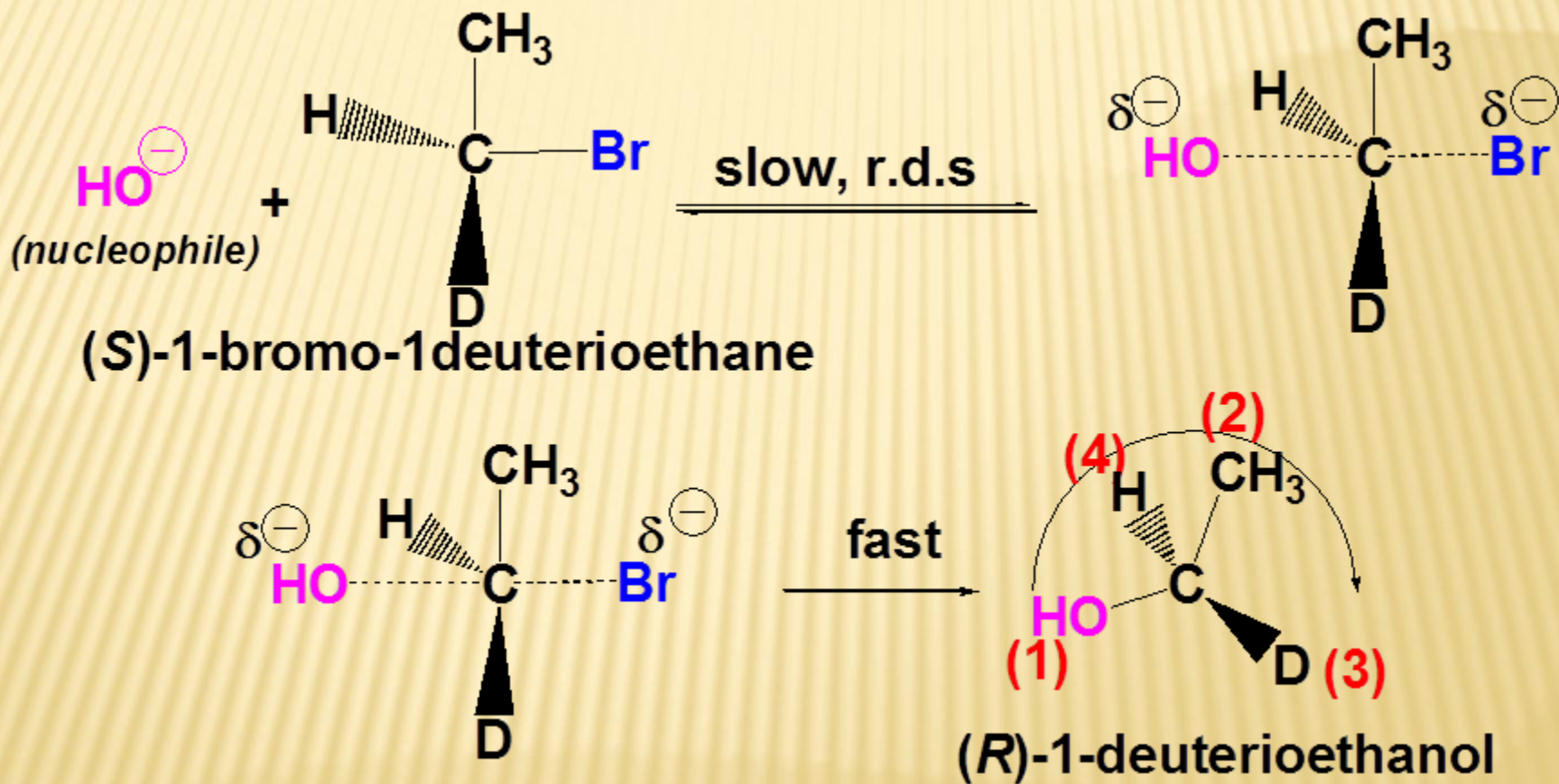
✗ Let us consider a chiral substrate undergoing an

✗ SN2 reaction.



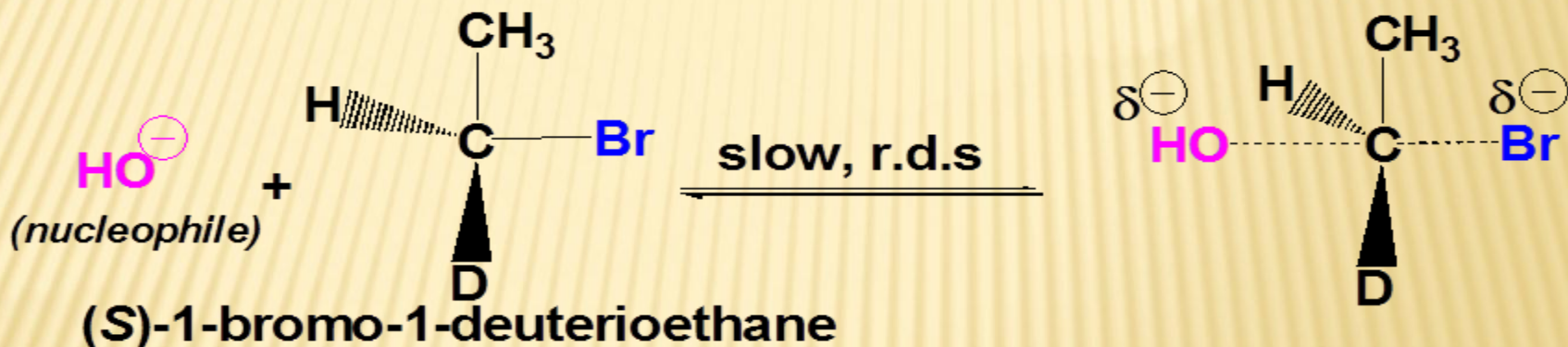
(S)-1-bromo-1-deuterioethane

THE STEREOCHEMISTRY OF SN2 REACTIONS



THE STEREOCHEMISTRY OF SN2 REACTIONS

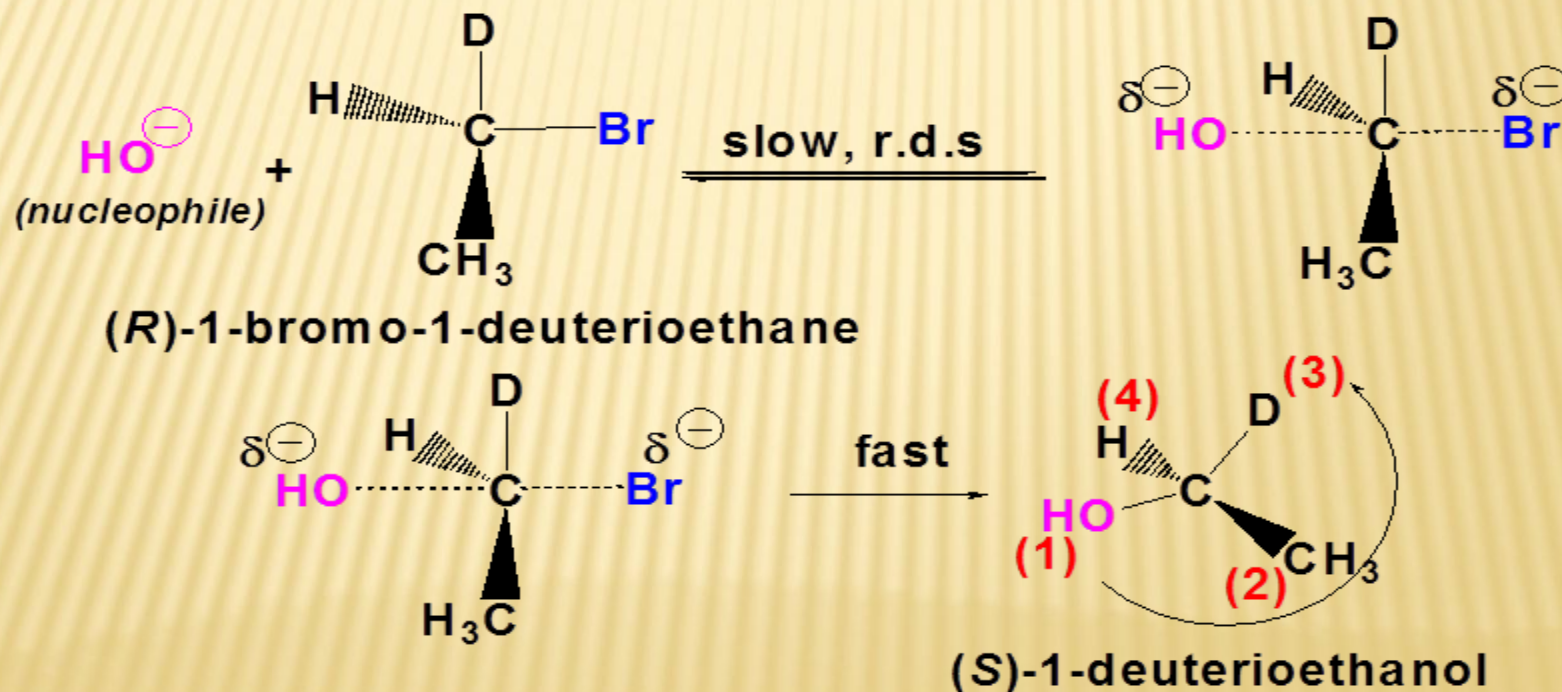
- ✗ (a) $\text{Nu}^- + \text{R-X} \rightleftharpoons [\text{Nu}^{\delta-} \cdots \text{R} \cdots \text{X}^{\delta-}]^{\ddagger} \text{ (slow, r.d.s)}$
- ✗ (b) $[\text{Nu}^{\delta-} \cdots \text{R} \cdots \text{X}^{\delta-}]^{\ddagger} \rightarrow \text{Nu-R} + \text{X}^- \text{ (fast)}$



- ✗ The pentacoordinate transition state formed at the end of the
- ✗ first, slow, rate-determining step is a trigonal bipyramid:
- ✗ a three-sided plane perpendicular to the screen;
- ✗ the OH and Br groups form apices on either side of the
- ✗ pentacoordinate carbon, in the plane of the screen.

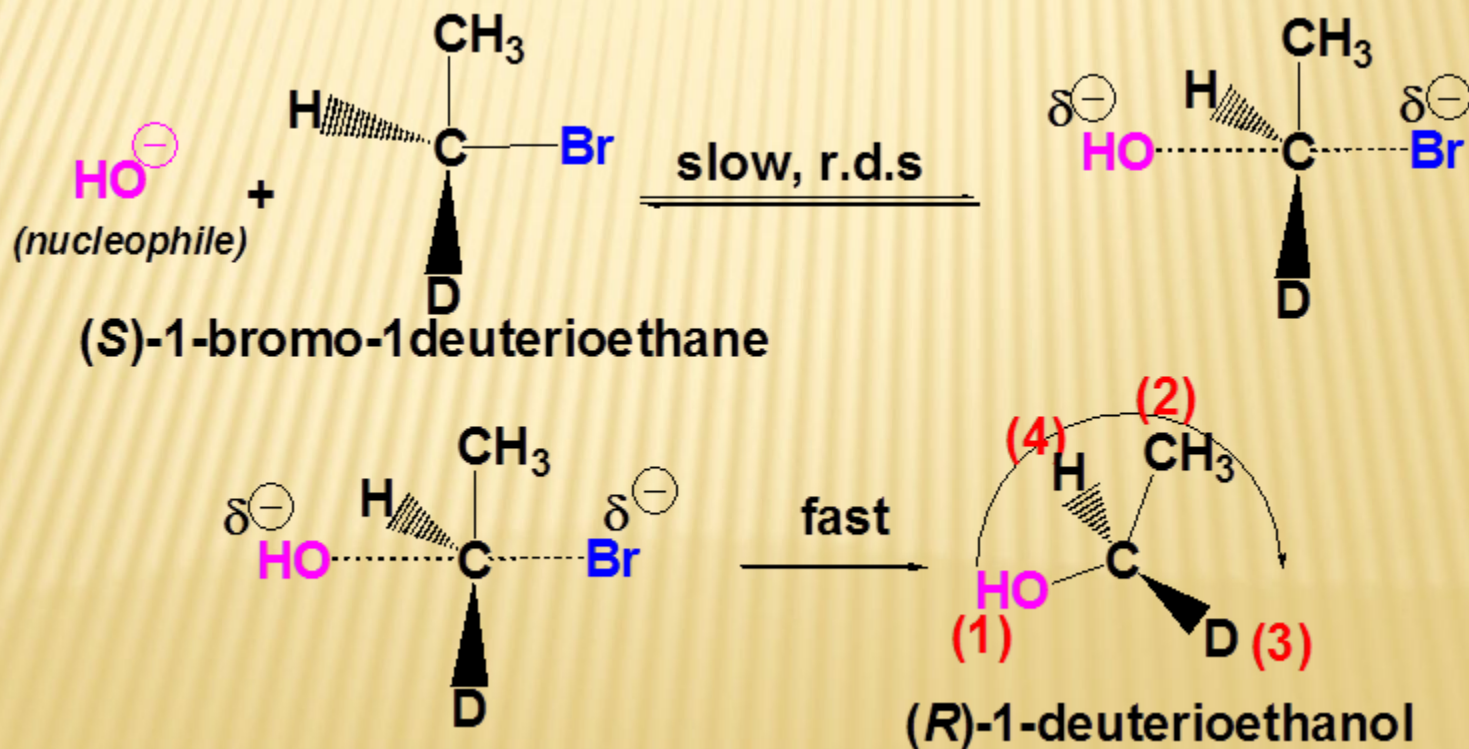
THE STEREOCHEMISTRY OF SN2 REACTIONS

- ✗ The nucleophile attacks the substrate from the side
- ✗ opposite to the leaving group.
- ✗ The stereochemistry of the product is INVERTED,
- ✗ relative to that of the starting material.



THE STEREOCHEMISTRY OF SN2 REACTIONS

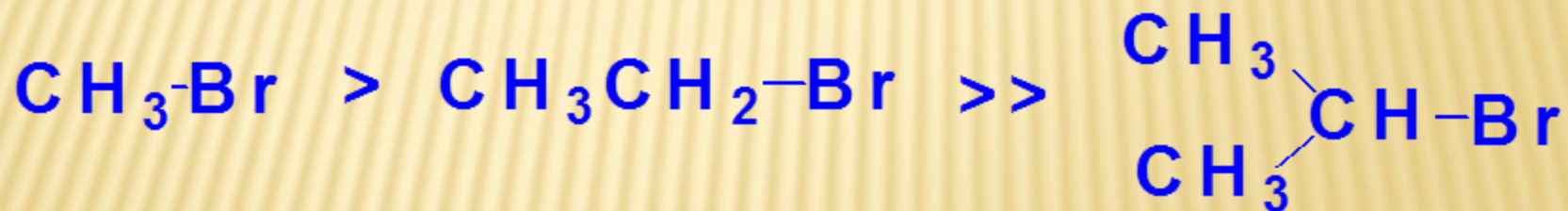
- ✗ For chiral substrates, reactions proceeding via the
- ✗ SN2 mechanism result in inversion of configuration.
- ✗ This is a consequence of the “back side” attack by
- ✗ the nucleophile.



OTHER ASPECTS OF SN2 REACTIONS

- ✗ SUBSTRATE

- ✗ The SN2 reaction involves a transition state with
- ✗ pentacoordinate carbon, so sterically hindered alkyl
- ✗ halides do not react via this mechanism.
- ✗ The RATE of the SN2 reaction for the following
- ✗ substrates therefore follow the trend:



- ✗ Tertiary alkyl halides do not undergo the SN2 reaction.

OTHER ASPECTS OF SN2 REACTIONS

- ✗ NUCLEOPHILE
- ✗ The SN2 reaction is bimolecular, and more
- ✗ effective nucleophiles will react faster.
- ✗ Order of nucleophilicity: $\ominus\text{CN} > \ominus\text{OR} > \ominus\text{OH}$.
- ✗ Therefore,
- ✗ $\text{CH}_3\text{Br} + \ominus\text{CN} \rightarrow \text{CH}_3\text{CN} + \text{Br} \ominus$ is a faster
- ✗ reaction than
- ✗ $\text{CH}_3\text{Br} + \ominus\text{OR} \rightarrow \text{CH}_3\text{OR} + \text{Br} \ominus$, and this in
- ✗ turn is faster than
- ✗ $\text{CH}_3\text{Br} + \ominus\text{OH} \rightarrow \text{CH}_3\text{OH} + \text{Br} \ominus$.

OTHER ASPECTS OF SN2 REACTIONS

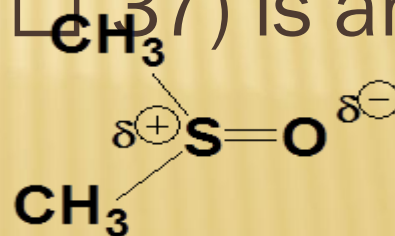
✗ POSSIBILITY OF REARRANGEMENT

- ✗ When an alkyl halide undergoes
- ✗ substitution via the SN2 mechanism, the
- ✗ product has the same carbon skeleton as
- ✗ the starting material. No rearrangement
- ✗ takes place.

OTHER ASPECTS OF SN2 REACTIONS

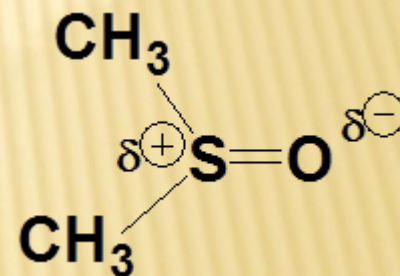
- ✗ SOLVENT
- ✗ The rate of SN2 reactions (involving negatively charged nucleophiles) increases when the reactions are carried out in polar APROTIC solvents.

- ✗ Dimethyl sulfoxide (DMSO, $\chi_{\text{DMSO}} = 37$) is an example of a polar aprotic solvent.



OTHER ASPECTS OF SN2 REACTIONS

- ✗ SOLVENT: Dimethyl sulfoxide (DMSO, \square 37) is an
- ✗ example of a polar aprotic solvent.



- ✗ If, for example, the nucleophile is $\ominus\text{CN}$, and the
- ✗ source is KCN (potassium cyanide) DMSO will
- ✗ solvate the K^+ ion, thus making $\ominus\text{CN}$ readily
- ✗ available for reaction.

