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MÓDULO V: SUBSTITUIÇÃO NUCLEOFÍLICA DESCRIÇÃO DETALHADA DOS MECANISMOS (INCLUINDO MECANISMOS DE FRONTEIRA), EFEITOS DA ESTRUTURA E DA SOLVATAÇÃO NA REATIVIDADE, PARTICIPAÇÃO DE GRUPOS VIZINHOS, ESTEREOQUÍMICA.

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Outline

Nucleophilic Substitution

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Ambident Substrates

REACTIONS

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Introduction to S_N

$$R\overset{\curvearrowright}{-X} + \overset{-}{Y} \longrightarrow R-Y + \overset{-}{X}$$

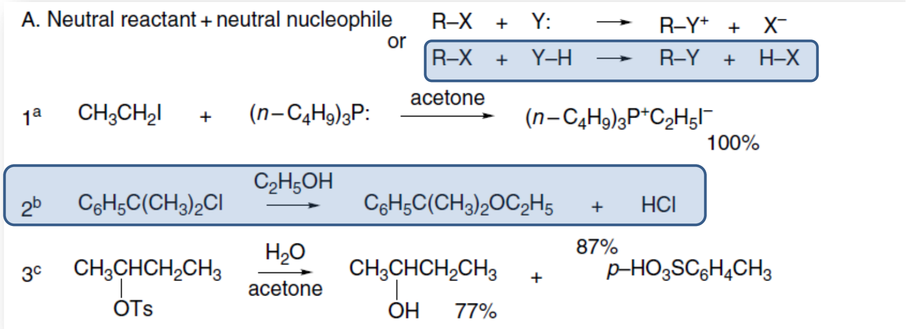
Type I $R-I + OH^- \longrightarrow R-OH + I^-$

Type II $R-I + NMe_3 \longrightarrow R-\overset{+}{N}Me_3 + I^-$

Type III $R-\overset{+}{N}Me_3 + OH^- \longrightarrow R-OH + NMe_3$

Type IV $R-\overset{+}{N}Me_3 + H_2S \longrightarrow R-\overset{+}{S}H_2 + NMe_3$

Representative Nucleophilic Substitution Reactions



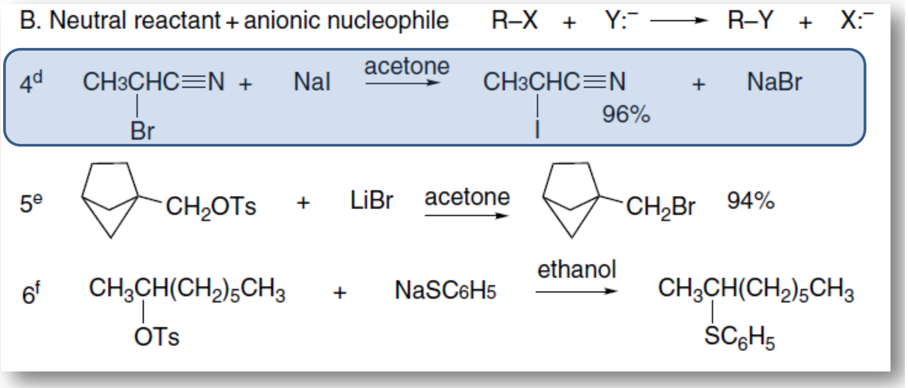
A. Neutral reactant + neutral nucleophile $R{-}X + Y{:} \longrightarrow R{-}Y^+ + X^-$

or $\boxed{R{-}X + Y{-}H \longrightarrow R{-}Y + H{-}X}$

1[a] $CH_3CH_2I + (n{-}C_4H_9)_3P{:} \xrightarrow{\text{acetone}} (n{-}C_4H_9)_3P^+C_2H_5I^-$ 100%

2[b] $C_6H_5C(CH_3)_2Cl \xrightarrow{C_2H_5OH} C_6H_5C(CH_3)_2OC_2H_5 + HCl$ 87%

3[c] $CH_3\underset{\underset{OTs}{|}}{C}HCH_2CH_3 \xrightarrow[\text{acetone}]{H_2O} CH_3\underset{\underset{OH}{|}}{C}HCH_2CH_3$ 77% $+ p{-}HO_3SC_6H_4CH_3$

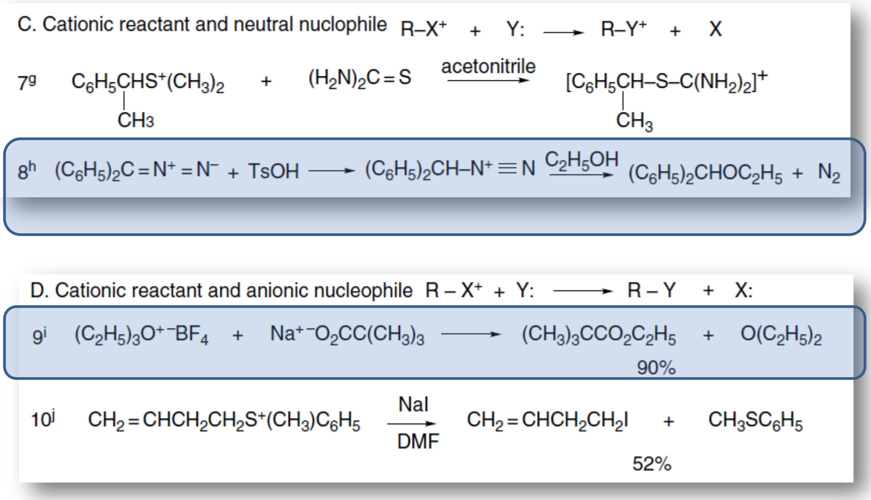


B. Neutral reactant + anionic nucleophile $R{-}X + Y{:}^- \longrightarrow R{-}Y + X{:}^-$

4[d] $CH3\underset{\underset{Br}{|}}{C}HC{\equiv}N + NaI \xrightarrow{\text{acetone}} CH3\underset{\underset{I}{|}}{C}HC{\equiv}N + NaBr$ 96%

5[e] $CH_2OTs + LiBr \xrightarrow{\text{acetone}} CH_2Br$ 94%

6[f] $CH_3\underset{\underset{OTs}{|}}{C}H(CH_2)_5CH_3 + NaSC6H5 \xrightarrow{\text{ethanol}} CH_3\underset{\underset{SC_6H_5}{|}}{C}H(CH_2)_5CH_3$



C. Cationic reactant and neutral nuclophile $R\text{–}X^+ + Y: \longrightarrow R\text{–}Y^+ + X$

7[g] $C_6H_5\underset{\overset{|}{CH_3}}{C}HS^+(CH_3)_2 + (H_2N)_2C{=}S \xrightarrow{\text{acetonitrile}} [C_6H_5\underset{\overset{|}{CH_3}}{C}H\text{–S–}C(NH_2)_2]^+$

8[h] $(C_6H_5)_2C{=}N^+{=}N^- + TsOH \longrightarrow (C_6H_5)_2CH\text{–}N^+{\equiv}N \xrightarrow{C_2H_5OH} (C_6H_5)_2CHOC_2H_5 + N_2$

D. Cationic reactant and anionic nucleophile $R\text{–}X^+ + Y: \longrightarrow R\text{–}Y + X:$

9[i] $(C_2H_5)_3O^{+\,-}BF_4 + Na^{+\,-}O_2CC(CH_3)_3 \longrightarrow (CH_3)_3CCO_2C_2H_5 + O(C_2H_5)_2$ 90%

10[j] $CH_2{=}CHCH_2CH_2S^+(CH_3)C_6H_5 \xrightarrow[\text{DMF}]{\text{NaI}} CH_2{=}CHCH_2CH_2I + CH_3SC_6H_5$ 52%

The S_N2 Mechanism

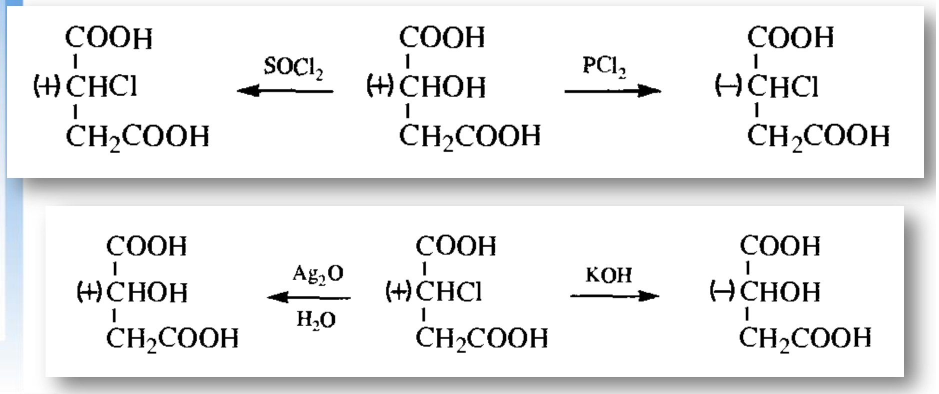
$$\text{Rate} = k[\text{RX}]\,[\text{Y}]$$

Second-order kinetics

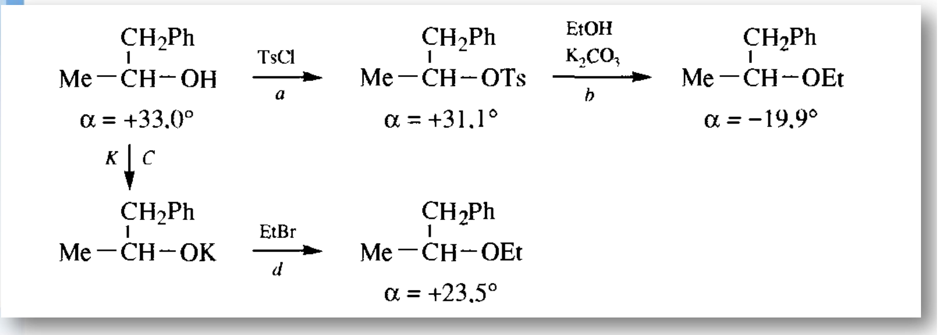
$$R\text{–}X + Y{:}^- \xrightarrow{k} R\text{–}Y + X{:}^-$$

$$\text{rate} = \frac{-d\,[R\text{–}X]}{dt} = \frac{-d\,[Y{:}^-]}{dt} = k\,[R\text{–}X]\,[Y{:}^-]$$

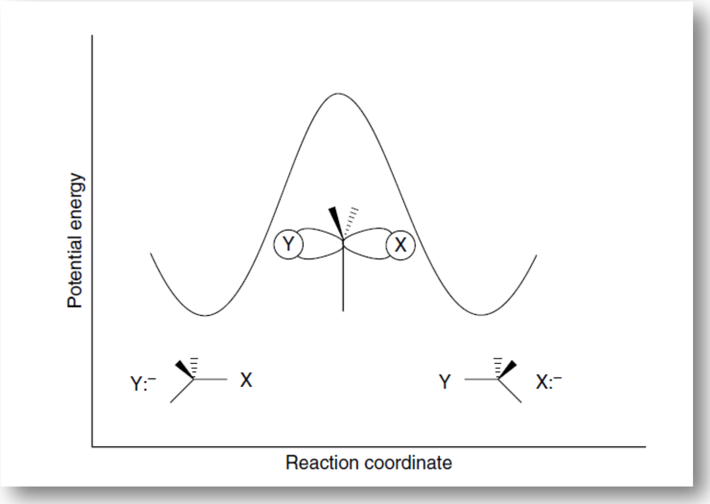
Walden examples



Phillips, Kenyon, and co-workers.

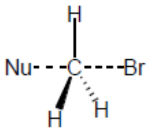


S$_N$2



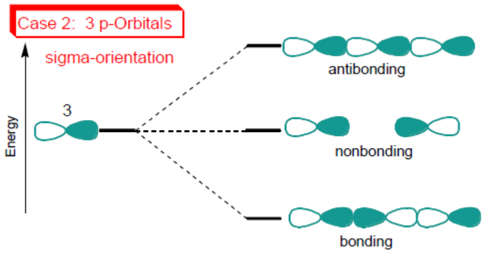
MO description of S$_N$2 TS

The S$_N$2 Transition state: (3-center, 4 electron)

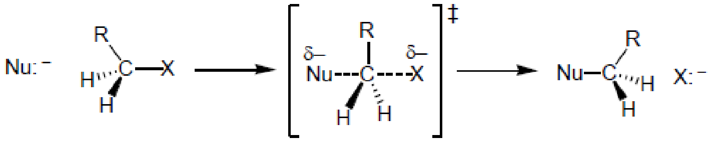


The SN 2 transition state approximates a case 2 situation with a central carbon p-orbital

The three orbitals in reactant molecules used are:
1 nonbonding MO from Nucleophile (2 electrons)
1 bonding MO σ C–Br (2 electrons)
1 antibonding MO σ* C–Br

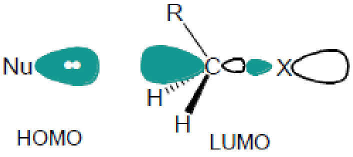


Why do S$_N$2 Reactions proceed with backside displacement?



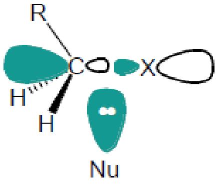
Given the fact that the LUMO on the electrophile is the C–X antibonding orblital, Nucleophilic attack could occur with either inversion or retention.

Inversion



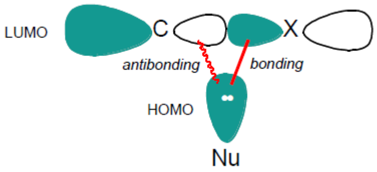
Constructive overlap between
Nu & σ^*C–X

Retention



Overlap from this geometry results
in no net bonding interaction

Expanded view of σ^*C–X



- **Stereoelectronic Effects**

Geometrical constraints placed upon ground and transition states by orbital overlap considerations.

Fukui Postulate for reactions:

"During the course of chemical reactions, the interaction of the highest filled (HOMO) and lowest unfilled (antibonding) molecular orbital (LUMO) in reacting species is very important to the stabilization of the transition structure."

The S_N1 Mechanism

$$R{-}X \xrightarrow[\text{slow}]{k_1} R^+ + X^-$$

$$R^+ + Y^- \xrightarrow[\text{fast}]{k_2} R{-}Y$$

$$\text{rate} = k_1[R{-}X]$$

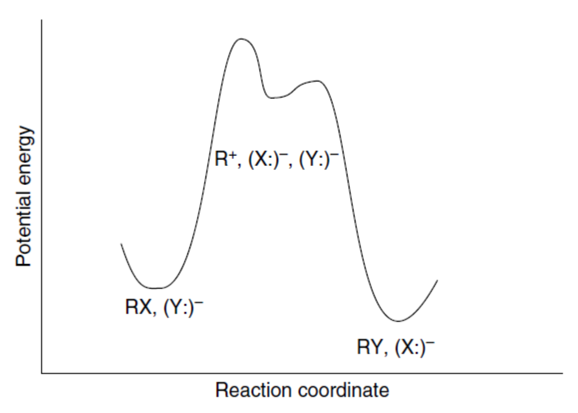
$$RX \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R^+ + X$$

First-order kinetics

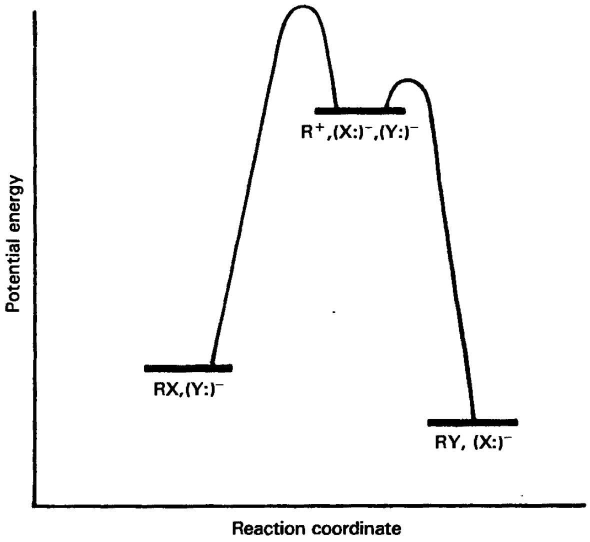
$$R^+ + Y \xrightarrow{k_2} RY$$

$$\text{Rate} = \frac{k_1 k_2 [RX][Y]}{k_{-1}[X] + k_2[Y]}$$

Reaction energy profile for nucleophilic substitution by the ionization S_N1 mechanism.

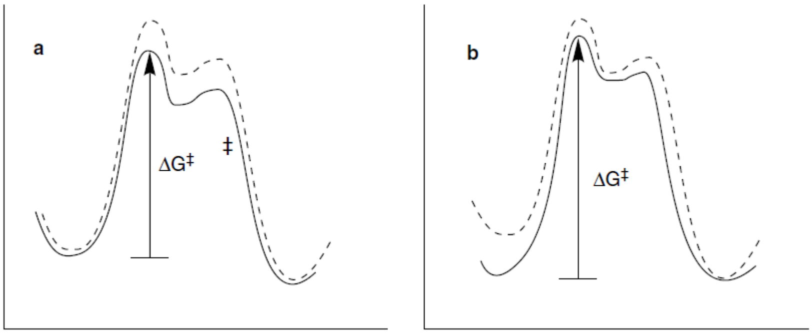


Potential Energy Diagram
Hammond Postulate



Solvent effects

Solid line: polar solvent.
Dashed line: nonpolar solvent

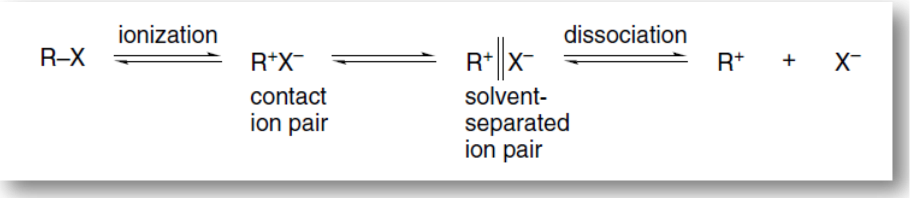


(a) $R–X \rightarrow R^+ + X^-$
Polar solvents increase the rate by stabilization of the $R^{\delta+}$- - -$X^{\delta-}$ TS.

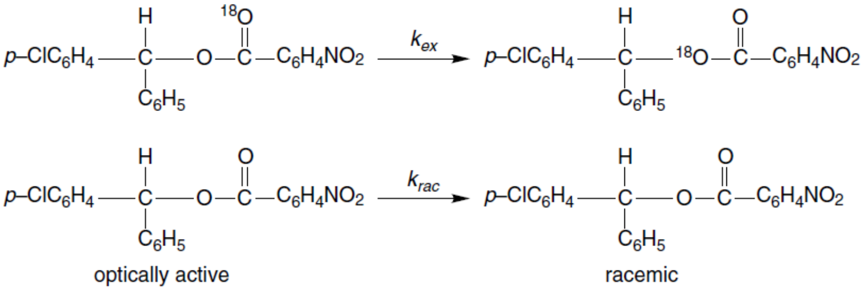
(b) **$R–X^+ \rightarrow R^+ + X$**
Polar solvents decrease the rate because stabilization of R- - $^{\delta+}$- -X TS is less than for the more polar

Ion pair

Detailed mechanism

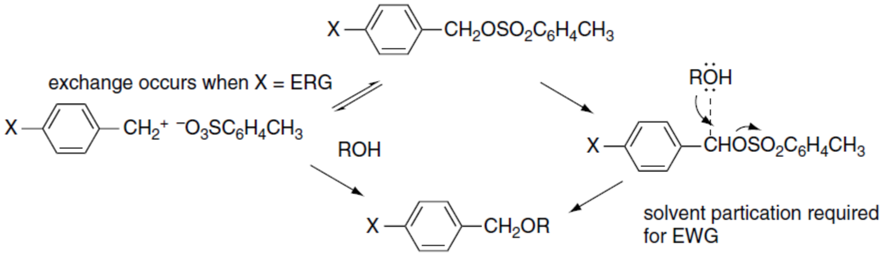


Support to scheme



At 100 °C, $k_{ex}/k_{rac} = 2.3$

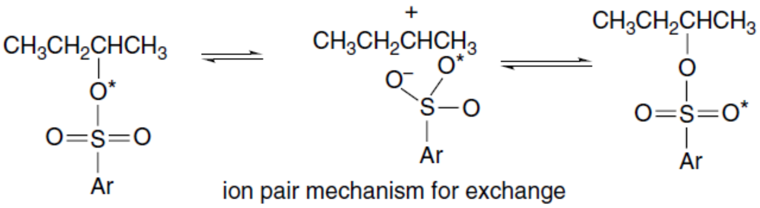
ERG favors exchange



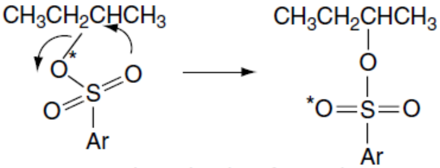
exchange occurs when X = ERG

solvent partication required for EWG

Isotopic scrambling with no racemization



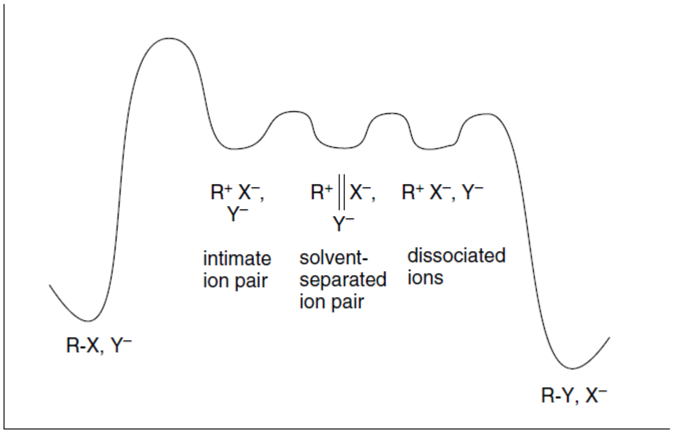
ion pair mechanism for exchange



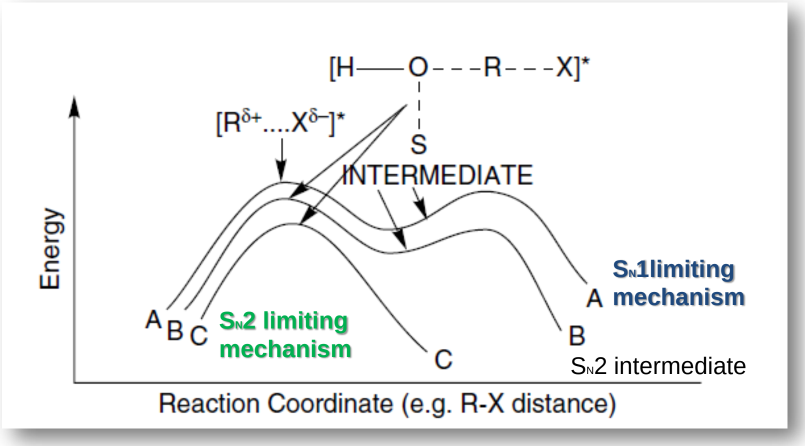
concerted mechanism for exchange

Avoids a carbocation intermediate but requires a front-side displacement!

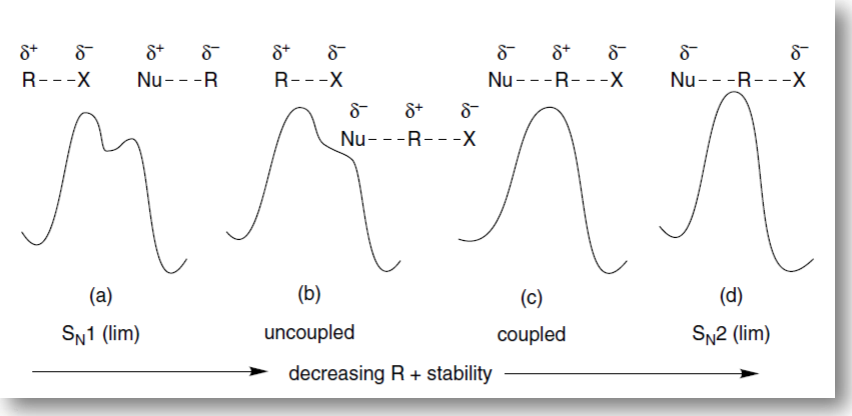
Schematic relationship between reactants, ion pairs, and products in substitution proceeding through ion pairs.



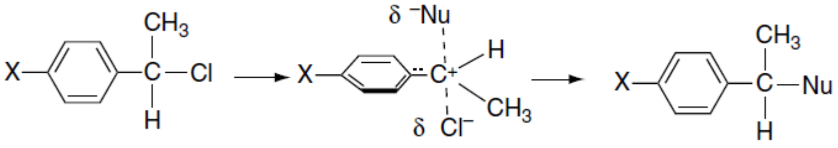
The gradation from S_N1 to S_N 2 mechanisms can be summarized in terms of the shape of the potential energy diagrams for the reactions



Jencks: reaction energy profiles showing decreasing carbocation stability in change from S_N1(lim) to S_N2(lim) mechanisms.



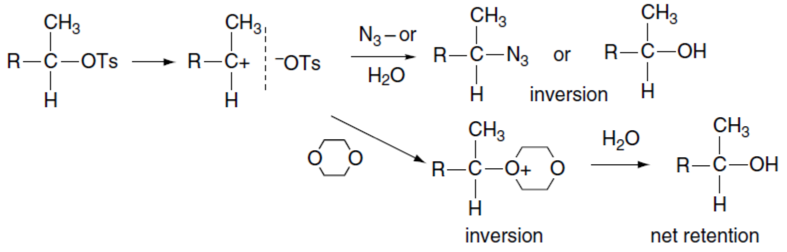
An example of a coupled displacement: the “exploded” SN2 TS.



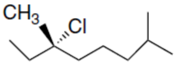
Second-order kinetics with a substantially ρ+

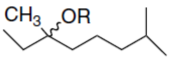
Stereochemistry of Nucleophilic Substitution Reactions

	Reactant[a]	Conditions	Product	Sterechemistry
1[b]	$CH_3CH_2CH_2CHDOBs$	HCO_2H 99° C	$CH_3CH_2CH_2CHDO_2CH$	99 ± 6% inv.
2[c]	$C_6H_5CHDOTs$	CH_3CO_2H 25° C	$C_6H_5CHDO_2CCH_3$	82 ± 1% inv.
3[c]	$CH_3\underset{OTs}{CH}(CH_2)_5CH_3$	$Et_4N^{+-}O_2CCH_3$ acetone, 56° C	$CH_3\underset{O_2CCH_3}{CH}(CH_2)_5CH_3$	100% inv.
4[d]	$CH_3\underset{OTs}{CH}(CH_2)_5CH_3$	75 % aq. dioxane 65° C	$CH_3\underset{OH}{CH}(CH_2)_5CH_3$	77% inv.
		75 % aq. dioxane 0.06 *M* NaN_3, 65° C	$CH_3\underset{OH}{CH}(CH_2)_5CH_3$ 22%	100% inv.
			$CH_3\underset{N_3}{CH}(CH_2)_5CH_3$ 78%	100% inv.



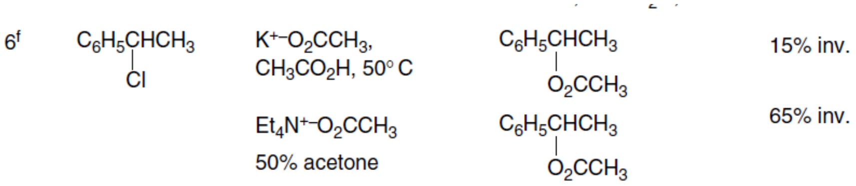
5[e]



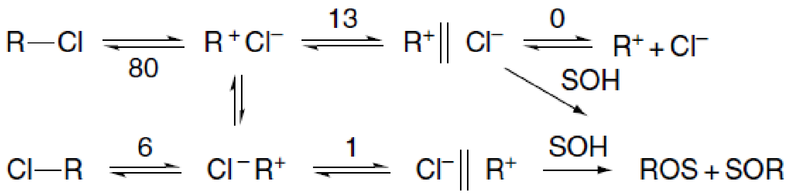


CH_3OH, DTBP, 25° C	78% inv.
C_2H_5OH, DTBP, 40° C	55% inv.
HCO_2H, DTBP, 0° C	42% inv.
CF_3CH_2OH, DTBP, 25° C	13% ret.
t-BuOH, 20% H_2O, 25° C	49% inv.
dioxane, 20% H_2O, 25° C	98% inv.

Stereochemical, kinetic, and isotope effects on solvolysis reactions of 1-phenylethyl chloride in several solvent systems



6[f]	$C_6H_5CH(Cl)CH_3$	$K^{+-}O_2CCH_3$, CH_3CO_2H, 50° C	$C_6H_5CH(O_2CCH_3)CH_3$	15% inv.
		$Et_4N^{+-}O_2CCH_3$ 50% acetone	$C_6H_5CH(O_2CCH_3)CH_3$	65% inv.



Structural and Solvation Effects on Reactivity Characteristics of Nucleophilicity

1. **Strong solvation lowers the energy of an anionic nucleophile relative to the TS**, in which the charge is more diffuse, and results in an increased E_a.

2. Because the **S_N2 process is concerted**, the strength of the partially formed new bond is reflected in the TS.

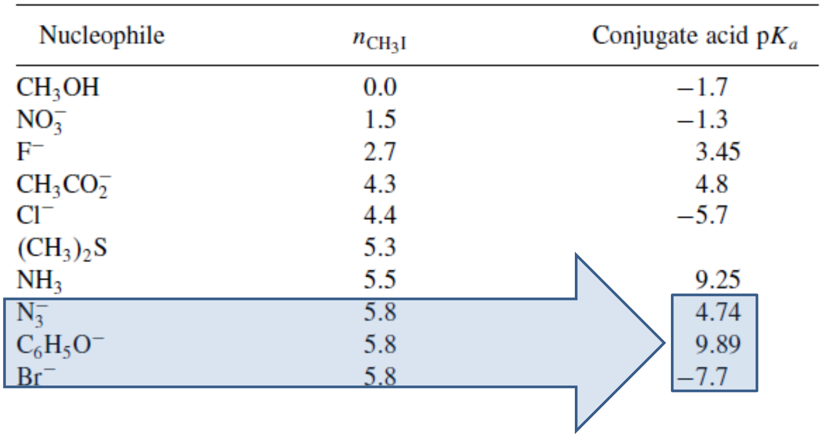
3. A more **electronegative** atom binds its electrons more tightly than a less electronegative one.

4. **Polarizability** describes the ease of distortion of the electron density of the nucleophile.

5. A **sterically congested nucleophile** is less reactive than a less hindered one. The trigonal bipyramidal geometry of the S_N2 transition state is sterically more demanding than the tetrahedral reactant so steric interactions increase as the TS is approached.

Nucleophilic constant, n, defined by Swain and Scott

$$n_{CH_3I} = \log(k_{nucl}/k_{CH_3OH}) \text{ in } CH_3OH, 25\,°C$$



Nucleophile	n_{CH_3I}	Conjugate acid pK_a
CH_3OH	0.0	−1.7
NO_3^-	1.5	−1.3
F^-	2.7	3.45
$CH_3CO_2^-$	4.3	4.8
Cl^-	4.4	−5.7
$(CH_3)_2S$	5.3	
NH_3	5.5	9.25
N_3^-	5.8	4.74
$C_6H_5O^-$	5.8	9.89
Br^-	5.8	−7.7

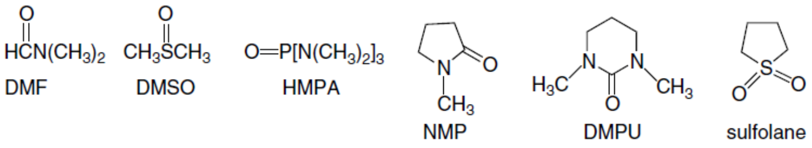
Effect of Solvation on Nucleophilicity

In **protic hydrogen-bonding solvents**, anions are subject to strong interactions with solvent.

Hard nucleophiles are more strongly solvated by protic solvents than soft nucleophiles, and this difference contributes to the greater nucleophilicity of soft anions in such solvents.

Nucleophilic substitution reactions of anionic nucleophiles usually occur more rapidly in **polar aprotic solvents than they do in protic solvents**, owing to the fact that anions are weakly solvated in such solvents

Common polar aprotic solvents



DMF DMSO HMPA NMP DMPU sulfolane

But, in methanol, the relative reactivity order
$N_3^- > I^- > CN^- > Br^- > Cl^-$

Becomes, in DMSO
$CN^- > N_3^- > Cl^- > Br^- > I^-$

The nucleophilicity of the solvent.

The Winstein-Grunwald equation

$$\log(k/k_0) = lN + mY$$

Standard reactant l = 1.00; Standard solvent N = 0.00, for solvolysis of t-butyl chloride.
The scale has also been assigned for 2-adamantyl tosylate.
Ethanol-water in the ratio 80:20 is taken as the standard solvent.

	t-Butyl chloride		2-Adamantyl tosylate	
Solvent	*N*	*Y*	N_{Tos}	Y_{Tos}
Ethanol	+0.09	−2.03	0.00	−1.75
Methanol	+0.01	−1.09	−0.04	−0.92
50% Aqueousethanol	−0.20	1.66	−0.09	1.29
Water	−0.26	3.49		
Acetic acid	−2.05	−1.64	−2.35	−0.61
Formic acid	−2.05	2.05	−2.35	3.04
Trifluoroethanol	−2.78	1.05	−3.0	1.80
97% $(CF_3)_2CHOH$-H_2O	−3.93	2.46	−4.27	3.61
Trifluoroacetic acid	−4.74	1.84	−5.56	4.57

Leaving group effects

Relative Solvolysis Rates of 1-Phenylethyl Esters and Halides

Leaving group	k_{rel}
$CF_3SO_3^-$ (triflate)	1.4×10^8
p-Nitrobenzensulfonate (nosylate)	4.4×10^5
p-Toluenesulfonate (tosylate)	3.7×10^4
$CH_3SO_3^-$ (mesylate)	3.0×10^4
I^-	91
Br^-	14
$CF_3CO_2^-$	2.1
Cl^-	1.0
F^-	9×10^{-6}
p-Nitrobenzoate	5.5×10^{-6}
$CH_3CO_2^-$	1.4×10^{-6}

Relative rates of solvolysis of 1-phenylethyl esters and halides in 80% aqueous ethanol at 75 °C.

Ionization exhibits greater dependence on LG

R	k_{Tos}/k_{Br}
Methyl	11
Ethyl	10
Isopropyl	40
t-Butyl	4000
1-Adamantyl	9750

Tosylate/Bromide Rate Ratios for Solvolysis of RX in 80% Ethanol[a]

Relative Reactivity of Leaving Groups in S_N2 Substitution Reactions

Nucleophile	CH_3I		CH_3Br		CH_3OTs	
	MeOH	DMF	MeOH	DMF	MeOH	DMF
N_3^-	8.0×10^{-5}	3.2	5.0×10^{-5}	4.0×10^{-1}	5.0×10^{-4}	5.0×10^{-2}
NCS^-	5.0×10^{-4}	8.0×10^{-2}	2.5×10^{-4}	1.3×10^{-2}	1.3×10^{-4}	8.0×10^{-4}
NC^-	6.4×10^{-4}	3.2×10^{2}				
ArS^-	6.4×10^{-2}	16			1.6×10^{-2}	6.4×10^{-1}

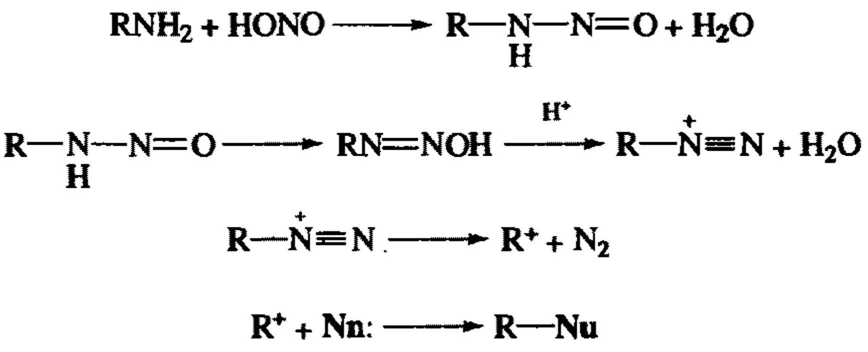
A poor leaving group can be made more reactive by coordination to an electrophile.

$$CH_3OH + Br^- \longrightarrow CH_3Br + {}^-OH$$

It is endothermic by 16 kcal mol^{-1}

$$CH_3(CH_2)_2CH_2OH \xrightarrow[H_2SO_4]{NaBr} CH_3(CH_2)_2CH_2Br$$

N_2 best LG



$$RNH_2 + HONO \longrightarrow R\!-\!\underset{H}{N}\!-\!N\!=\!O + H_2O$$

$$R\!-\!\underset{H}{N}\!-\!N\!=\!O \longrightarrow RN\!=\!NOH \xrightarrow{H^+} R\!-\!\overset{+}{N}\!\equiv\!N + H_2O$$

$$R\!-\!\overset{+}{N}\!\equiv\!N \longrightarrow R^+ + N_2$$

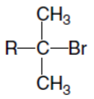
$$R^+ + Nu{:} \longrightarrow R\!-\!Nu$$

Steric & strain effects

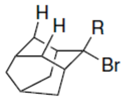
Rate Constants for Nucleophilic Substitution of Primary Alkyl Bromides and Tosylates

$k \times 10^5$ for $RCH_2{-}X^b$	R = H	CH_3	CH_3CH_2	$(CH_3)_2CH$	$(CH_3)_3C$
$RCH_2Br + LiCl$, acetone, 25 °C	600	9.9	6.4	1.5	2.6×10^{-4}
$RCH_2I + n\text{-}Bu_3P$, acetone, 35 °C	26,000	154	64	4.9	
$RCH_2Br + NaOCH_3$, methanol	8140	906	335	67	
RCH_2OTs, acetic acid. 70 °C^c	5.2×10^{-2}	4.4×10^{-2}		1.8×10^{-2}	4.2×10^{-3}

In contrast to S_N2 reactions, rates of reactions involving TSs with cationic character increase with substitution.



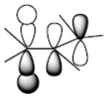
$k_{rel}\ \frac{R=CH_3}{R=H} = 10^{3.7}$



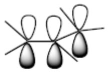
$k_{rel}\ \frac{R=CH_3}{R=H} = 10^{8.1}$

A high CH_3/H rate ratio is expected if nucleophilic participation is weak and stabilization of the cationic nature of the TS is important.

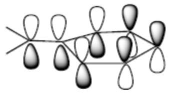
Effects of conjugation



interaction of sp^2 hybridized substitution center with π LUMO



interaction of empty sp^2 orbital with π HOMO



interaction of empty sp^2 orbital of benzyl cation with HOMO aromatic π system

For example, allyl chloride is 33 times more reactive than ethyl chloride toward iodide ion in acetone!

α-Substituent Effect

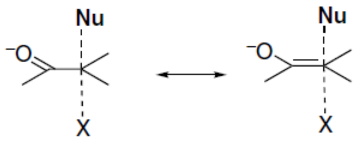
Substituent Effects of α-EWG Substituents

$Z{-}CH_2{-}Cl \; + \; I^- \longrightarrow Z{-}CH_2{-}I$

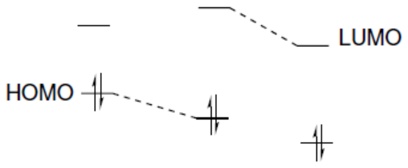
Z	Relative rate	Z	Relative rate
$CH_3CH_2CH_2$	1	$PhC{=}O$	3.2×10^4
$PhSO_2$	0.25	$N{\equiv}C$	3×10^3
$CH_3C{=}O$	3.5×10^4	$C_2H_5OC{=}O$	1.7×10^3

Steric effects may be responsible for part of the observed acceleration.

Stabilizing π orbital TS

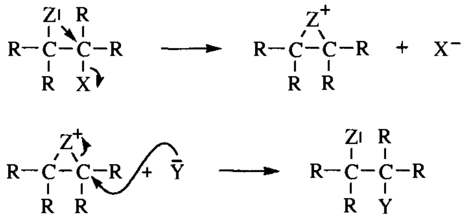


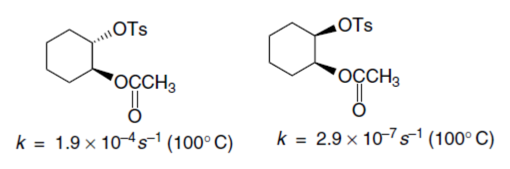
resonance representation of electronic interaction with carbonyl group and substitution center to delocalize negative charge



MO representation of stabilization of substitution transition state through interaction with C═O π* orbital

Neighboring-Group Participation

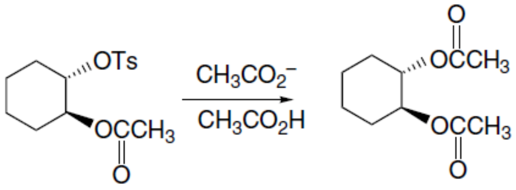


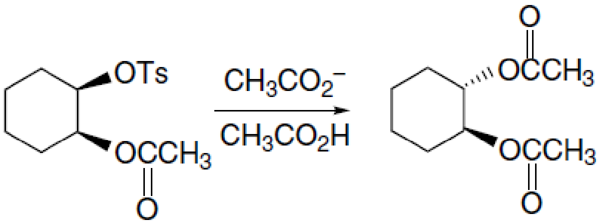


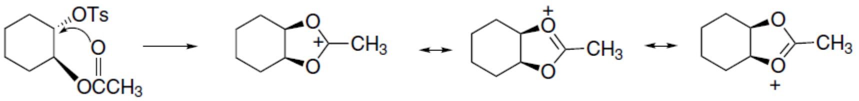
$k = 1.9 \times 10^{-4}\,s^{-1}$ (100° C)

$k = 2.9 \times 10^{-7}\,s^{-1}$ (100° C)

The rates of solvolysis of the *cis* and *trans* isomers of 2-acetoxycyclohexyl p-toluenesulfonate differ by a factor of about 655!

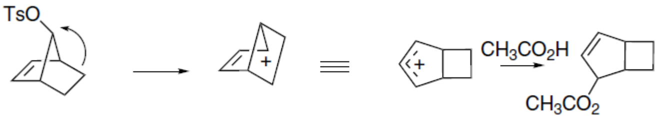






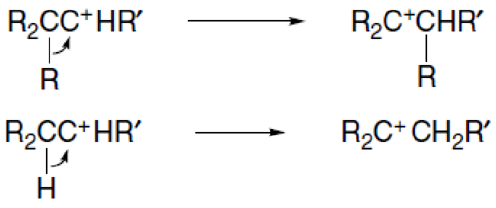
The π electrons of C=C can also become involved in S_N

It is more reactive by a factor of about 10^{11} than the saturated analog toward acetolysis



It reacts 10^7 times slower than the *anti* isomer.

Mechanism of Rearrangements of Carbocations

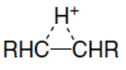


$$\underset{\text{R}}{\overset{}{\text{R}_2\text{C}}}\text{C}^+\text{HR}' \longrightarrow \text{R}_2\underset{\text{R}}{\text{C}^+}\text{CHR}'$$

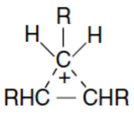
alkyl shift

$$\underset{\text{H}}{\text{R}_2\text{C}}\text{C}^+\text{HR}' \longrightarrow \text{R}_2\text{C}^+\,\text{CH}_2\text{R}'$$

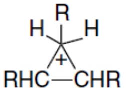
hydride shift



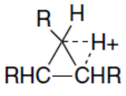
hydride – bridged carbocation



alkyl – bridged carbocation

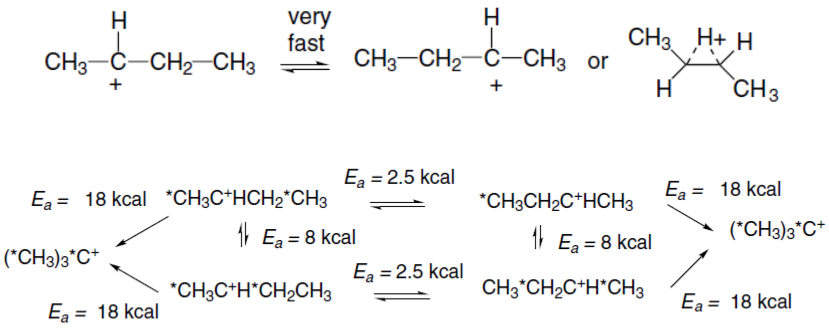


corner – protonated cyclopropane

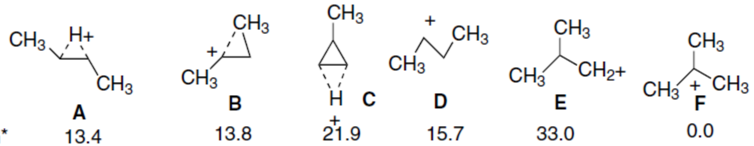


edge – protonated cyclopropane

The 2-butyl cation

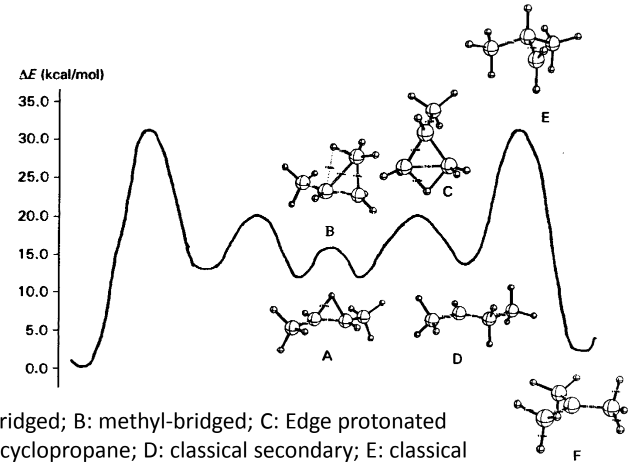


The methyl-bridged ion is only slightly less stable.

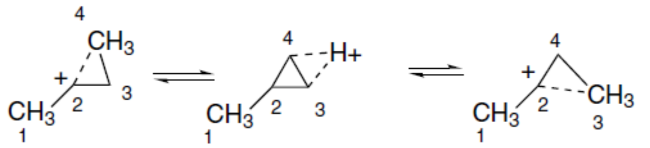


	A	B	C	D	E	F
MP/6-311G*	13.4	13.8	21.9	15.7	33.0	0.0
MP/6-31G**	12.8	12.0	20.5		32.6	0.0

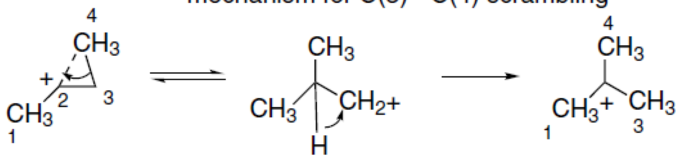
The 2-butyl to t-butyl rearrangement gives the following energy surface



A: H-bridged; B: methyl-bridged; C: Edge protonated methycyclopropane; D: classical secondary; E: classical primary; F: tertiary.

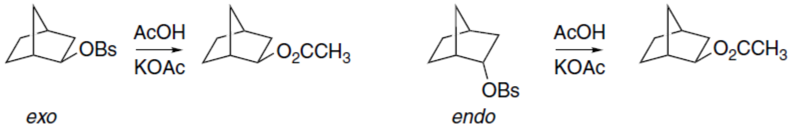


mechanism for C(3) - C(4) scrambling



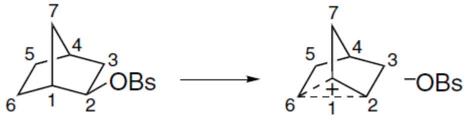
mechanism for isomerization to *t*-butyl cation

The Norbornyl Cation Nonclassical Carbocations

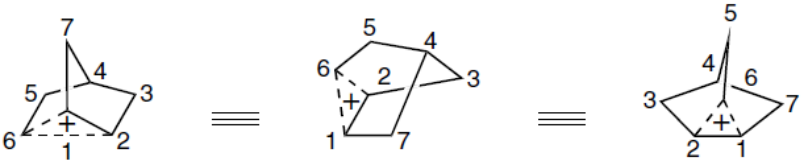


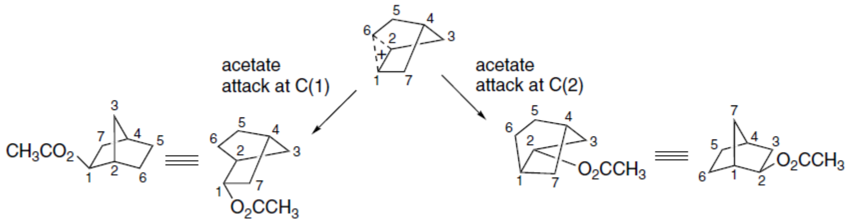
Racemic!

The exo-brosylate is more reactive than the endo isomer by a factor of 350.

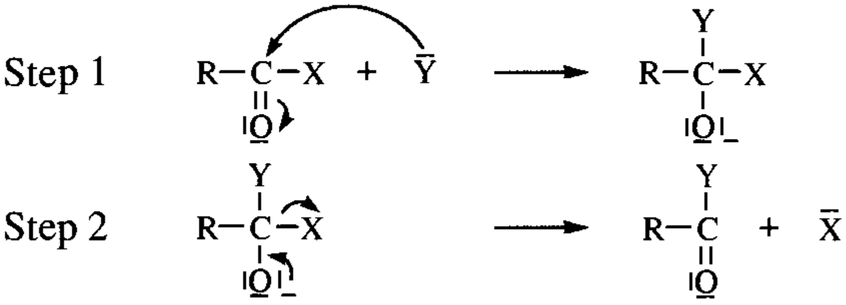


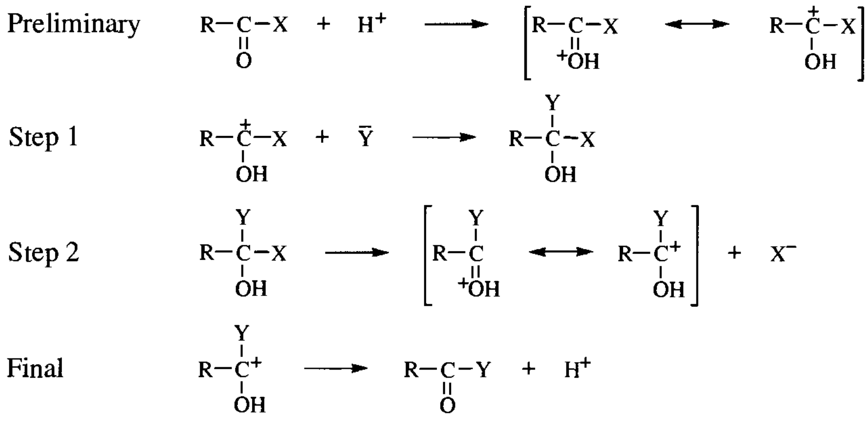
The plane of symmetry: intermediate explains racemic product



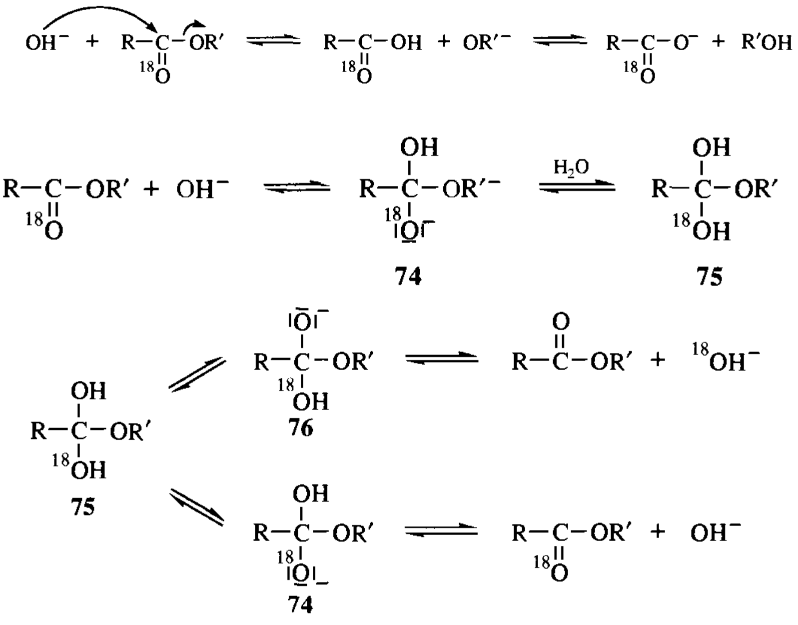


Nucleophilic Substitution at an Aliphatic Trigonal Carbon: The Tetrahedral Mechanism



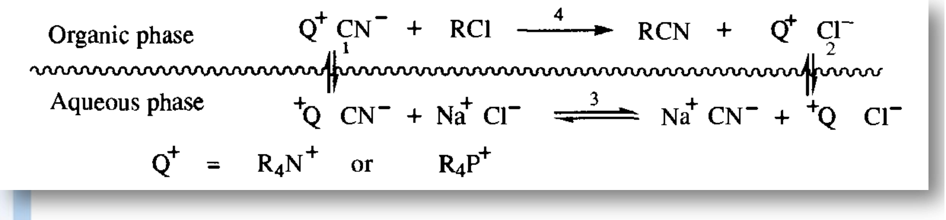


Evidence

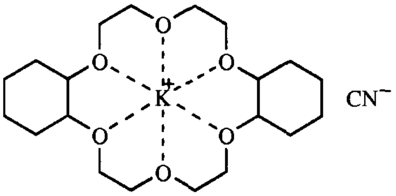


Phase-Transfer Catalysis

1. Quaternary Ammonium or Phosphonium Salts.

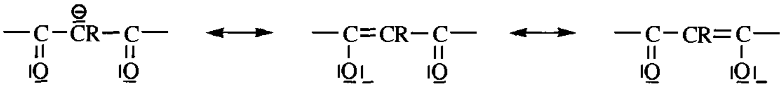


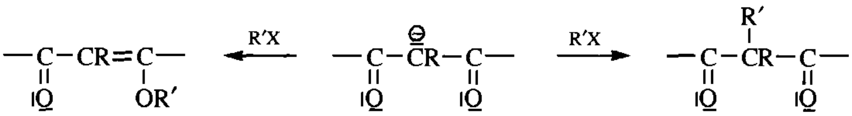
2. Crown Ethers and Other Cryptands (no water needed)

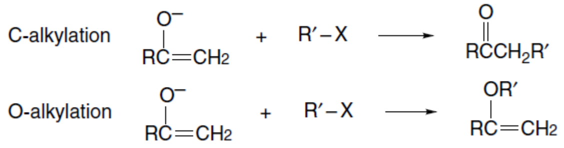


Ambident Nucleophiles: Regioselectivity

1. Ions of the Type. —CO—C:⁻R—CO—

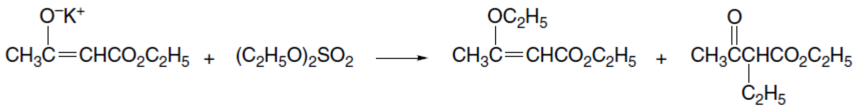






C-alkylation $R\overset{O^-}{\overset{|}{C}}=CH_2 + R'-X \longrightarrow R\overset{O}{\overset{\|}{C}}CH_2R'$

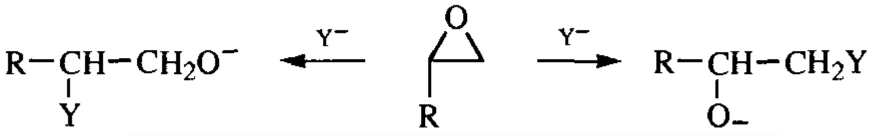
O-alkylation $R\overset{O^-}{\overset{|}{C}}=CH_2 + R'-X \longrightarrow R\overset{OR'}{\overset{|}{C}}=CH_2$



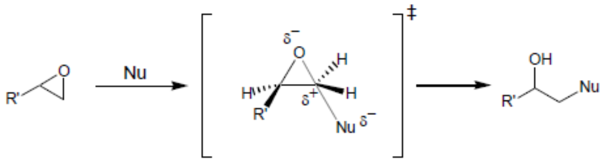
$CH_3\overset{O^-K^+}{\overset{|}{C}}=CHCO_2C_2H_5 + (C_2H_5O)_2SO_2 \longrightarrow CH_3\overset{OC_2H_5}{\overset{|}{C}}=CHCO_2C_2H_5 + CH_3\overset{O}{\overset{\|}{C}}\underset{C_2H_5}{\underset{|}{C}}HCO_2C_2H_5$

HMPA	83%	15%
t-Butyl alcohol	0%	94%
THF	0%	94%

Ambident Substrates



$R-\underset{Y}{\underset{|}{CH}}-CH_2O^- \xleftarrow{Y^-}$ (epoxide with R) $\xrightarrow{Y^-} R-\underset{O^-}{\underset{|}{CH}}-CH_2Y$



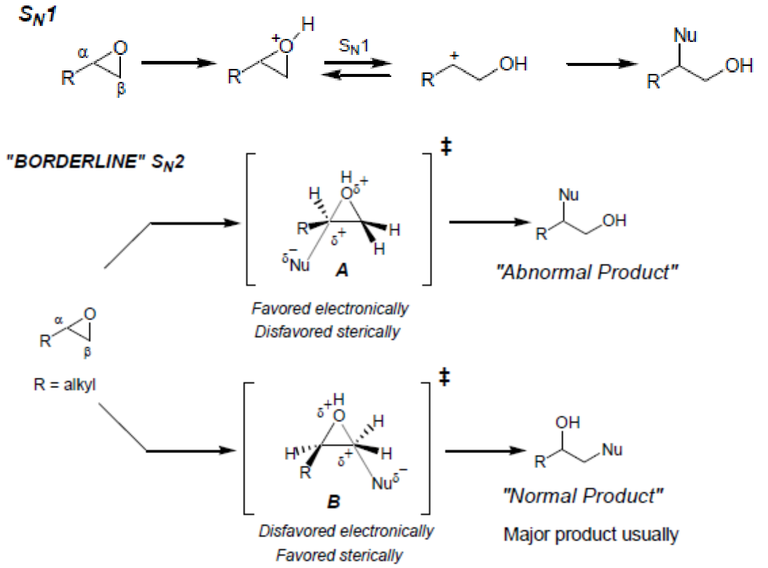
S$_N$2 Transition-State

Nu = H^-
N_3^-
RO^-
RS^-
RNH_2
R_2NH
NH_3
R^-

R = various alkyl, aryl, or vinyl substituents

REGIOSELECTIVITY OF EPOXIDE RING OPENING

ACIDIC CONDITIONS: BORDERLINE S_N2 TO S_N1



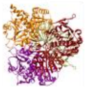
Favored electronically
Disfavored sterically

"Abnormal Product"

Disfavored electronically
Favored sterically

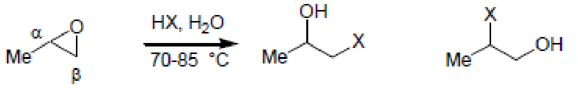
"Normal Product"

Major product usually

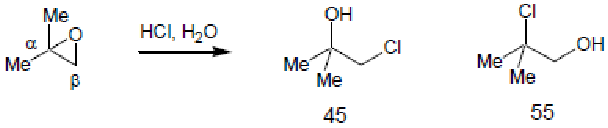


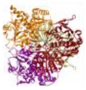
REGIOSELECTIVITY OF EPOXIDE RING OPENING

ACIDIC CONDITIONS: BORDERLINE S_N2 TO S_N1

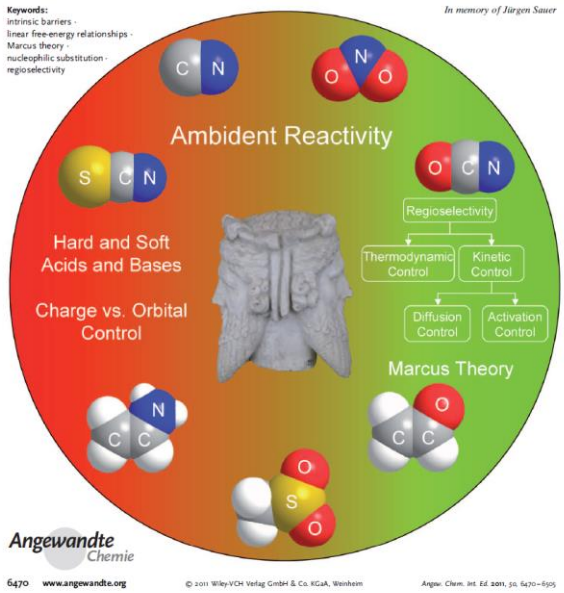


HX	Normal Prod	Abnormal Prod
HCl	56	44
HBr	71	29
HI	82	18
HCl, Et_2O, Δ	74	26





Exercício do dia



Keywords:
intrinsic barriers ·
linear free-energy relationships ·
Marcus theory ·
nucleophilic substitution ·
regioselectivity

In memory of Jürgen Sauer

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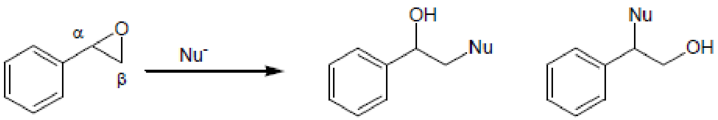
REGIOSELECTIVITY OF EPOXIDE RING OPENINGS

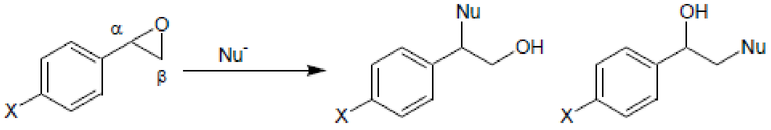
EFFECT OF CONJUGATING SUBSTITUENTS



Nucleophile	Ratio
$LiAlH_4$	100: 00
$LiBH_4$	74:26
PhLi	100: 00
MeONa	70:30
MeOH, H_2SO_4	10:90
NaN_3	00:100
NaOPh	24:76
HOPh	12:88
HOPh, TsOH	06:94

REGIOSELECTIVITY OF EPOXIDE RING OPENINGS

EFFECT OF CONJUGATING SUBSTITUENTS



Nu	substituent (X)	Ratio
NaOPh	$-NO_2$	36:64
	-H	76:24
	-OMe	100:0
NaOMe	-H	30:70

Portinari

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