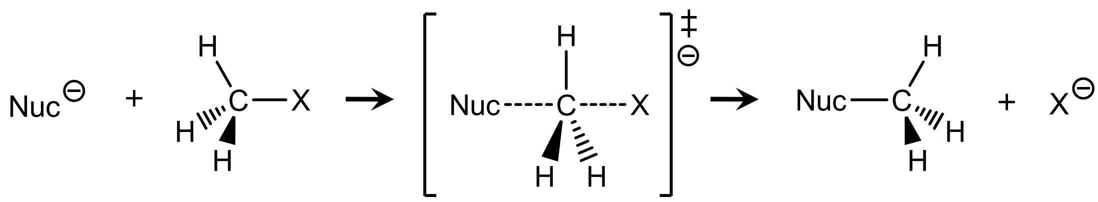
What Makes a Good Nucleophile?



1. Wants to give away electrons (good Lewis base).

HO^- better than H_2O *(bases always better than their conjugate acids)*

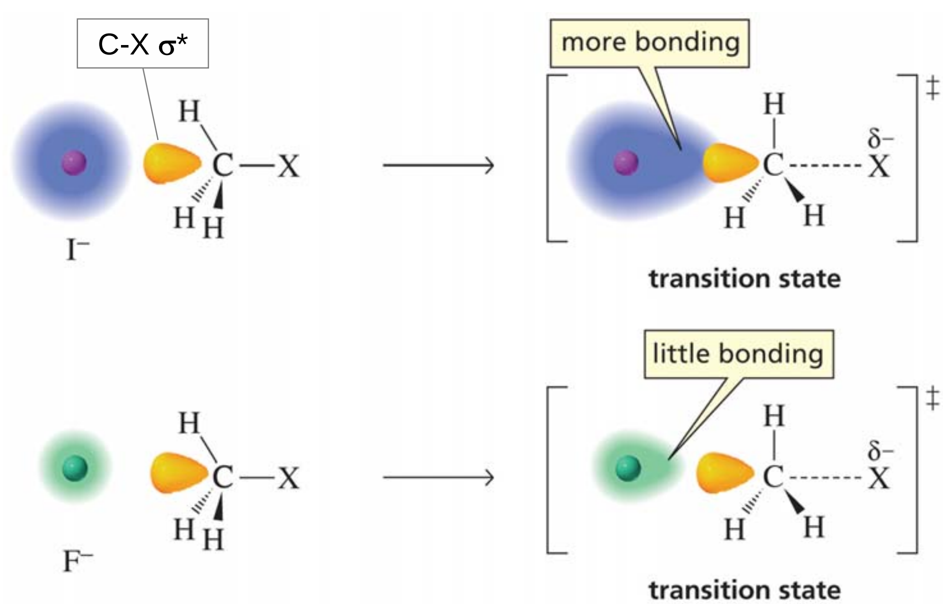
NH_3 better than H_2O

HS^- better than Cl^-

(less electronegative atom means more willing to give up e^-)

What Makes a Good Nucleophile?

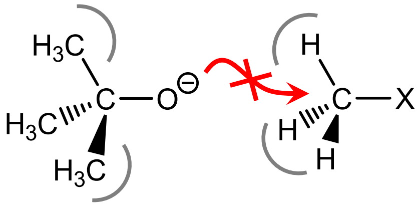
2. More polarizable. (Bigger.)



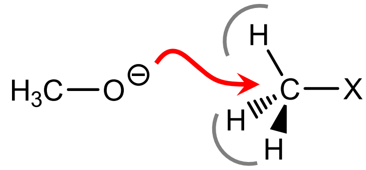
So, I^- is a better nucleophile than F^-.

What Makes a Good Nucleophile?

3. Not too sterically hindered.



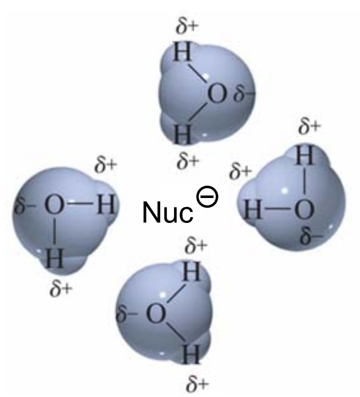
t-butoxide anion
strong base,
hindered nucleophile

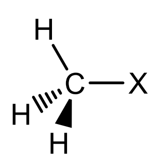


methoxide anion
smaller, attacks
more easily

What Makes a Good Nucleophile?

4. Not obscured by too polar a solvent.





solvent hinders
nucleophile from
approaching
electrophile.

So, S_N2 reactions are usually run in medium polarity solvents;
polar enough to dissolve ionic species, not so polar to cage the nucleophile.

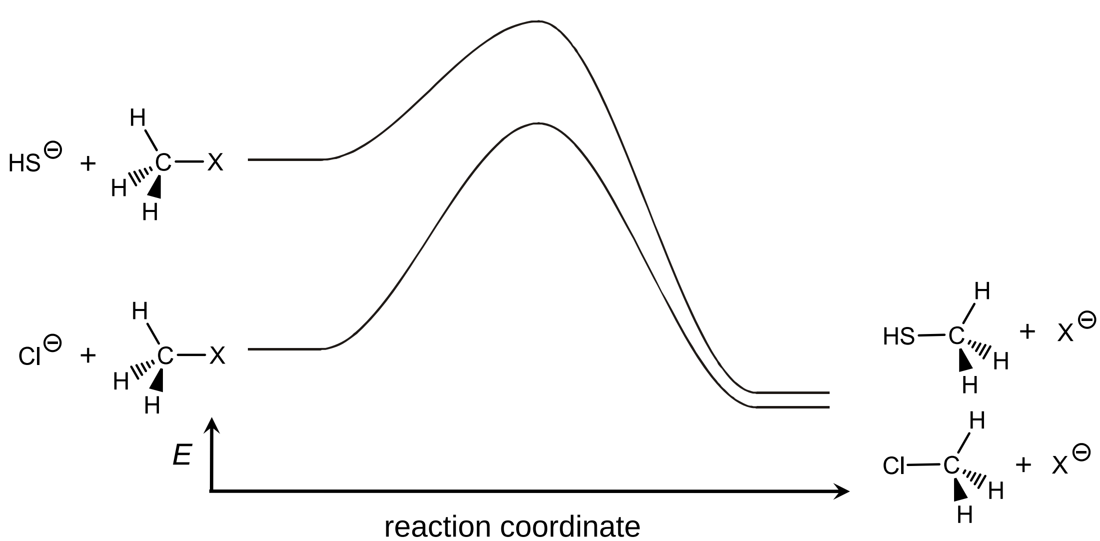
Some Common Nucleophiles

TABLE 6-3 Some Common Nucleophiles. Listed in Decreasing Order of Nucleophilicity in Hydroxylic Solvents Such as Water and Alcohols

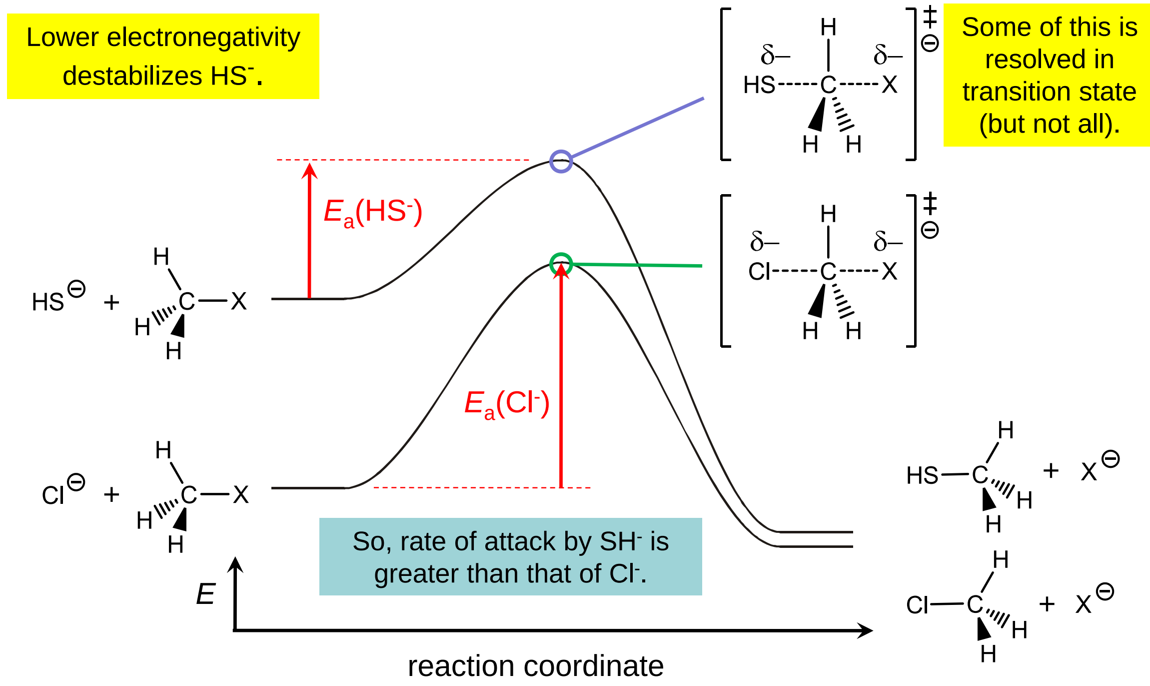
strong nucleophiles	$(CH_3CH_2)_3P:$	moderate nucleophiles	$:Br:^-$
	$^-:S-H$		$:NH_3$
	$:I:^-$		CH_3-S-CH_3
	$(CH_3CH_2)_2NH$		$:Cl:^-$
	$^-:C\equiv N$		$CH_3C(=O)-O:^-$
	$(CH_3CH_2)_3N:$		
	$H-O:^-$	weak nucleophiles	$:F:^-$
	$CH_3-O:^-$		$H-O-H$
			CH_3-O-H

Comparing Nucleophile Quality with Potential Energy Diagrams

We said HS^- better than Cl^- *(based on electronegativity).*

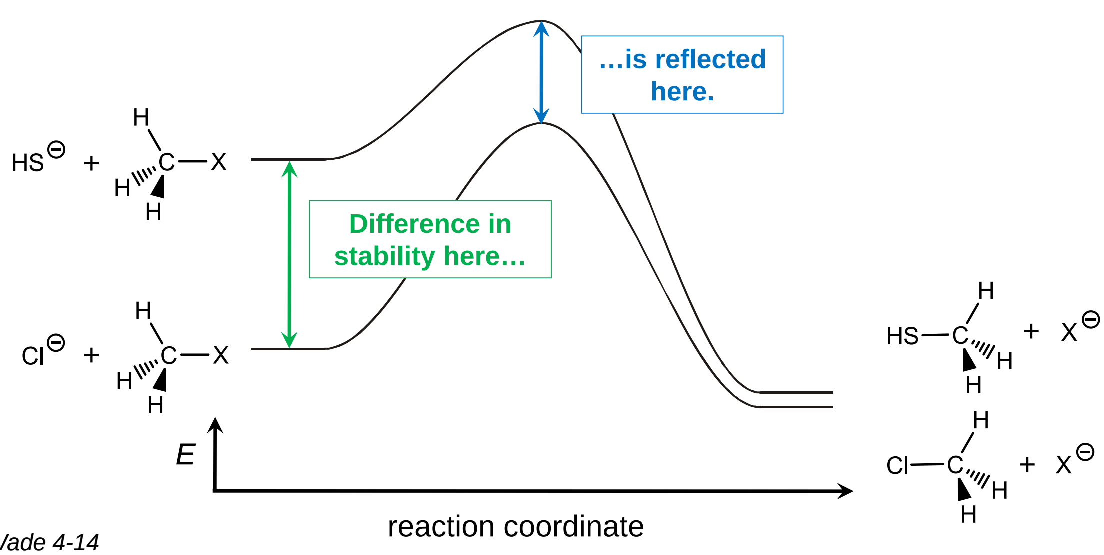


Comparing Nucleophile Quality with Potential Energy Diagrams



The Hammond Postulate

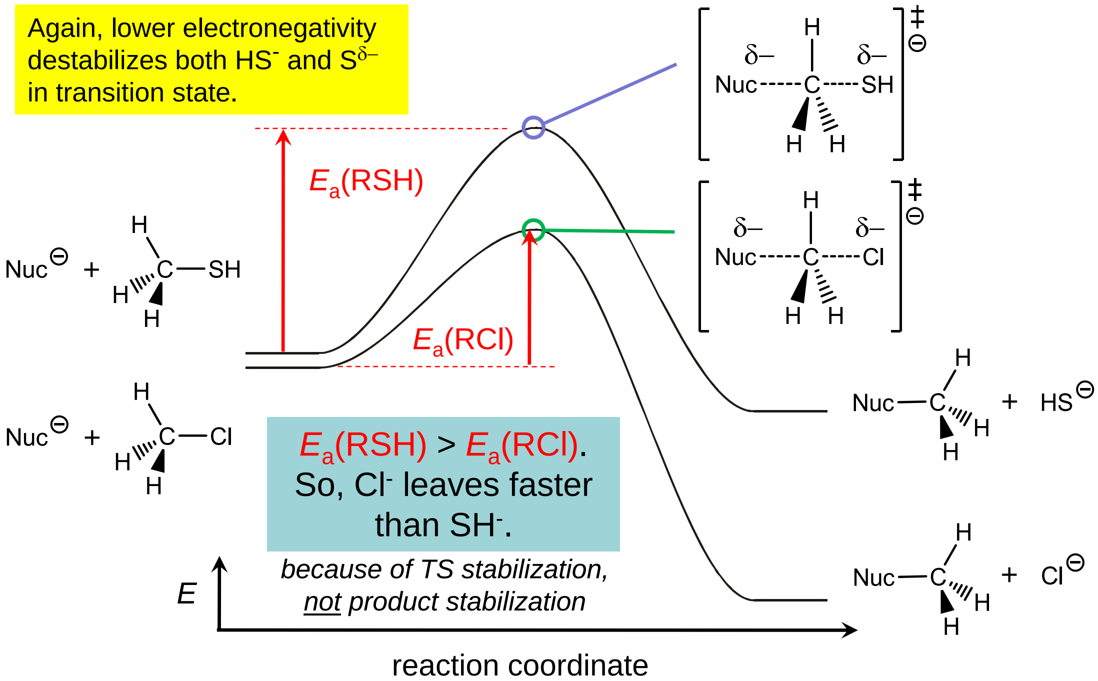
For similar reactions, differences in starting material or product stabilities will be reflected in transition state (to a lesser degree).



Wade 4-14

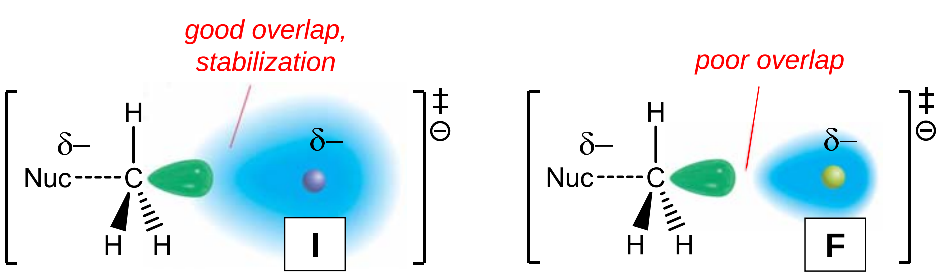
What Makes a Good Leaving Group?

1. Wants to take electrons (electronegative).



What Makes a Good Leaving Group?

2. Polarizable. (Stabilizes transition state.)



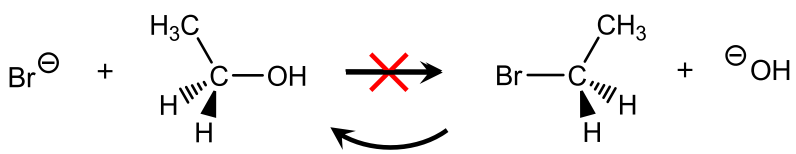
So, $I^{\ominus}$ is a better leaving group than $F^{\ominus}$.

Interesting consequence: $I^{\ominus}$ is both a good nucleophile *and* a good leaving group.

What Makes a Good Leaving Group?

3. Products are stable; S_N2 wouldn't work much better in reverse.

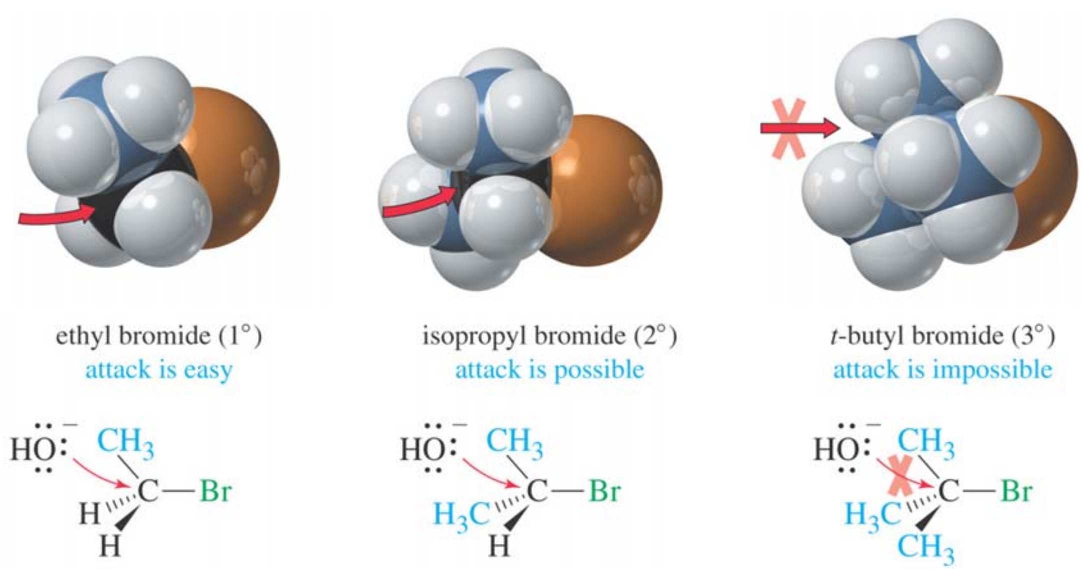
Example:



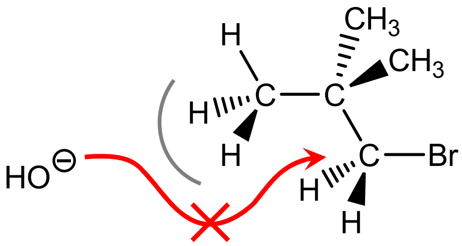
⊖OH is a much better nucleophile than Br⊖;
this reaction would revert if it ever happened.

So it doesn't happen.

Steric Hindrance at the S_N2 Reaction Center Inhibits Reaction



Inhibition of S_N2 by Neopentyl Groups



neopentyl bromide

(primary, but still hindered)

TABLE 6-5 Effect of Substituents on the Rates of S_N2 Reactions

Class of Halide	Example	Relative Rate
methyl	CH_3-Br	>1000
primary (1°)	CH_3CH_2-Br	50
secondary (2°)	$(CH_3)_2CH-Br$	1
tertiary (3°)	$(CH_3)_3C-Br$	<0.001
n-butyl (1°)	$CH_3CH_2CH_2CH_2-Br$	20
isobutyl (1°)	$(CH_3)_2CHCH_2-Br$	2
neopentyl (1°)	$(CH_3)_3CCH_2-Br$	0.0005