Analyze the spectrum of tribromoethane

- Integration: $2\, \text{H}_A$ and $1\, \text{H}_B$
  - $2/1\, \text{H}_A/\text{H}_B$
  - $h_2 = 2$
  - $h_1$

Splitting of Signals $\rightarrow$ Connectivity of Carbons

- $\text{H}_A$ has 1 neighbor $= 2$ peaks
- $\text{H}_B$ has 2 neighbors $= 3$ peaks

4 main signal types: Singlet, doublets, triplets, quartets

- Singlet: 0 neighbors
- Doublet: 1 neighbor
- Triplet: 2 neighbors
- Quartet: 3 neighbors
NMR - Finer Points

Review: NMR Gives:
1) Type of Proton
2) Number of Protons
3) Connectivity

Splitting → What happens if splitting patterns overlap?

Benzene (Aromatic) Protons

Di

3 Types of Substituted Benzenes

Alcohol Protons and splitting

and N-H

1.0 → 4.5 ppm

2 neighbors but they don't split
More on NMR...
Equivalent Protons don't split
\[ \text{Cl-CH}_2\text{CH}_2\text{-Cl} \] 
\[ \approx 4.2 \]

[J Values] Coupling Constants → This is the magnitude of the split

Normal values (Table 13.3)

\[ \text{CH}_3\text{CH}_2\text{-Cl} \]

Larger than normal

Long Range Coupling

\[ \text{[C = C]} \]

Small splitting

J value ≈ 1-2 Hz

Interesting stuff:

\[ \text{Fast} \]

\[ \text{[H}_A\text{]} \]

- 200 °C

MRI (14.22) → Magnetic Resonance Imaging

\[ \text{O} \]

\[ \text{P}^31 \rightarrow \text{ATP} \]
Chapter 8 Substitution Reactions

Chemical Reactions Review: - Breaking Bonds → Remaking Bonds
- Arrow pushing mechanisms $e^- \rightarrow E^+$
- Valence electrons
- Nucleophilic (electrophilic) $Nu^-$ → $E^+$
- Intermediates → Higher energy species
- Reaction coordinate diagram
- Energy movement

1st mechanism (chem 241)
"Electrophilic addition to a double bond"

\[
\text{C} = \text{C} \overset{\text{S} + \text{S}^-}{\rightarrow} \text{C} - \text{C}^{-} \rightarrow \text{C} - \text{C}^+ \rightarrow \text{C} - \text{Cl}^+ \rightarrow \text{Cl}^{-}
\]

New Mechanism

Substitution Reactions: One group or atom replaced by another group or atom

\[
R - \text{CH}_2 - X + Y^+ \rightarrow R - \text{CH}_2 - Y \quad X^-
\]

Example

\[
\text{CH}_3 - \text{Br} + \overset{\overset{\text{S}}{\text{S}}}{\text{O}} \rightarrow \text{CH}_3 - \overset{\text{O}}{\text{H}} + \overset{\text{B}}{\text{r}}^-
\]

3 elements:
1) Substrate
2) Nucleophile
3) Leaving Group

How this happens

mechanism (arrow pushing)

\[
\text{H} - \overset{\text{O}}{\theta} \rightarrow \text{CH}_3 - \overset{\text{Br}}{\theta} \rightarrow \text{H} - \overset{\text{O}}{\theta} \rightarrow \text{CH}_3 - \overset{\text{Br}}{\theta}
\]

One step

\[
Nu^+ \rightarrow E^+
\]
Reaction Coordinate diagram

- Starting material

Rate of reaction

Rate = \( k \left[ R-\text{Br} \right] \left[ \text{OH} \right] \)

What does \( k \) relate to?

Concentration of reactants

Large if barrier is small

\( \Delta G^+ \) Energy of activation

How do concentrations determine rate? → need to bump into

What does \( S_n2 \) mean?

\( S = \) Substitution

\( N = \) Nucleophile

\( 2 = \) Bimolecular → 2 atoms in the transition state

Rate depends on both

Factors that determine the rate (rate constant \( k \))

\( \sqrt{1} \) Substrate (Table 8.1)

\( \sqrt{2} \) Nucleophile (Table 8.2, Section 8.2)

\( \sqrt{3} \) Leaving Group (pg 339)

\( CH_3- \) > \( \Theta \) > \( Br^- \) > \( I^- \)

- Strong base \( \Theta \): \( OH^- \)
- Large atom \( S \): \( Br^- \)
- Base is stable

Best leaving groups are stable conjugate bases

A stable conjugate base is able to leave.
Chem 242 1/2/12

Sn2 continued

Substrate        Nucleophile        Leaving group

All must be G.K.

Why does substrate matter? Why $1^\circ > 2^\circ > 3^\circ$? 3-D

methyl substrate (faster?)

\[ \text{(H)} \quad \overset{\text{H}}{\text{C}} \rightarrow \quad \overset{\text{Cl}}{\text{C}} \]

Backside attack

\[ \text{small} \quad \overset{\text{C}}{\text{C}} \rightarrow \quad \overset{\text{Cl}}{\text{C}} \]

1° substrate (not as good)

steric hindrance

Too crowded

Stereochemistry of the Sn2 mechanism: Backside attack

\[ \text{CH}_3 \rightarrow \text{C} \rightarrow \text{I} \rightarrow \overset{-1/2}{\overset{\text{C}}{\text{O}}} \rightarrow \overset{-1/2}{\overset{\text{C}}{\text{C}}} \rightarrow \overset{+}{\overset{\text{I}}{\text{C}}} \rightarrow \]

\[ \text{CH}_3 \quad \text{I} \]

1/2 way point

2° (slower) Transition state - highest energy point

\[ \text{CH}_3 \rightarrow \text{C} \rightarrow \text{Br} \rightarrow \overset{-1/2}{\overset{\text{C}}{\text{O}}} \rightarrow \overset{-1/2}{\overset{\text{C}}{\text{C}}} \rightarrow \overset{+}{\overset{\text{Br}}{\text{C}}} \rightarrow \]

\[ \text{CH}_3 \quad \text{Br} \]

(R) Inversion of configuration

100% (S)
Section 8.4

Substrate: $\text{CH}_3\text{CBr}$, $\text{NaN}_3$ + $\text{ICH}_3$

$L$: $\text{Br}_0$, 0.10
$N$: $\text{Cl}_0$, 0.10

Fast $\xrightarrow{\text{EtOH}}$ $\text{Br}^-$

$\text{CH}_3\text{CBr} + \text{ICH}_3 \rightarrow \text{CH}_3\text{C} - \text{Cl}^-$

Rate law: $\text{rate} = k [\text{substrate}]$

Effect on substrate on rate (Table 8.4): $\text{No Effect}$

Effect of Nucleophile on Rate? $\text{No Effect}$

Effect of leaving group on rate? $\text{Yes} - \text{same as in } \text{SN}_2$

Mechanism that explains the results above:

- $\text{SN}_1$ – unimolecular
- only substrate matters
- $\text{SN}_2$ – bimolecular
- only substrate matters in the rate
- $\text{Nu}$ doesn’t matter

$\text{CH}_3\text{C} - \text{Cl}^-$
Sn₁ Reaction: Effect of the Substrate (Table 8.4)

(See 8.4)

\[ \text{CH}_3 \quad \text{CH}_3 \]
\[ \quad \beta \quad \beta \quad \beta \quad \beta \]
\[ \text{CH}_3 \quad \text{CH}_3 \quad \text{CH}_3 \]

Fastest: 3° cation more stable

Slowest: methyl cation

Order of Reactivity:

3° > 2° > 1° > CN₃

Most stable: 3° cation

Stable - will form

Effect of Leaving Group:

- Same as Sn₂: I⁻ > Br⁻ > Cl⁻

Effect of Nucleophile: Doesn't matter

\[ \text{OH just as fast as O-H} \]

Stereochemistry of the Sn₁ Reaction

CH₃

C - Br + Cl⁻ →

CH₃CH₂ (R)

1st step

Carbocation

Reaction Coordinate Diagram?
Water/Alcohols as Nucleophiles (Sn1)

\[(CH_3)_3C-Cl + H_2O \rightarrow \text{Excess Solvent Salolysis} \]

Summary of Sn1
- $3^\circ > 2^\circ >> 1^\circ$
- Any nucleophile works
- Leaving group the same as Sn2
- Other cations to consider see 8.7

Allylic
\[CH_2=CH-CH_2-Cl + Bu^+ \rightarrow \text{Sn1?} \rightarrow \text{Fast} \rightarrow \text{CH}_2=\text{CH-CH}_2\text{Cl} \rightarrow \text{Bu}^+ \rightarrow \text{Resonance} \rightarrow \text{Product} \]

Benzyllic
\[CH_2=Cl \rightarrow \text{Bu}^+ \rightarrow \text{Resonance} \rightarrow \text{Stable Cation} \rightarrow \text{Product} \]

Vinyllic
\[H \rightarrow \text{Cl} \rightarrow \text{Form} \rightarrow \text{H} \rightarrow \text{Cl} \rightarrow \text{No Resonance} \]

Aryl
- $Sn_2$ continued, can affect the rate/speed

**Solvent effects**

$Sn_2 \rightarrow$ solvating the nucleophile
Solute $= $stabilization

\[ S+ \cdot N-O \cdot H^+ \]
\[ S+ \cdot H-O \cdot H^+ \]
\[ S+ \cdot O-H \]

Stabilized in polar protic

Good $Sn_2$ uses which solvent $\rightarrow$ Acetone $-$ want a destabilized nucleophile

Fast $y$ use polar aprotic solvents

**Polar protic**

has $O-H$ group

H$_2$O, Alcohol, Ethanol/methanol

DMSO

**Polar aprotic**

NO, O-H

\[ \text{DMSO} \]

\[ \text{Acetone} \]

In acetone, not solvated well, not stabilized

\[ \text{Steric hindrance} \]

$\Theta$ and $S+$ can't get close

\[ \text{in acetone} \]

\[ \text{No} \]

\[ \text{Acetone} \]

\[ \text{Want a destabilized nucleophile} \]

**Sn$_1$ Solvent effects**

For $Sn_1$, please:

- polar protic solvents

- Want to stabilize

- Stabilize the intermediate
Biological $S_N_2$ Reactions (sec 8.11)

Methylation agents (add CH$_3$ group to a substrate)

$Nu^\ominus + CH_2-I \rightarrow Nu-CH_3$  $\Theta$

In Biology, $\text{S-adenosylmethionine (SAM)}$ - water soluble

$R-NH_2 \rightarrow CH_3\text{--I}$

used to methylate norepinephrine