Chapter 5. Polar Addition & Elimination Reactions

- Reverse of one another: 473 bottom
  - hydration of alkenes & dehydration of alcohols: 474 top
  - microscopic reversibility: identical reaction pathways;
    intermediates & TS for either reaction; Fig. 5.1

- Polar addition: generalized mechanisms
  - kinetics, regioselectivity & stereochemistry
  - bimolecular electrophilic additions: Ad_E2; 475 bottom
    - carbocation formation free of Y^- or as an intimate ion pair
    - a bridged cationic intermediate: anti
  - termolecular electrophilic addition: Ad_E3; 476 top
    - concerted transfer of E^+ & Y^-: anti
Addition of Hydrogen Halides (I)

- Regioselectivity: Markovnikov’s rule; \[477\text{ mid.}\]
  - more stable carbocation: HX; TS resembles RDS
    - order of reactivity: HI > HBr > HCl
    - anti-Markovnikov addition: HBr; radical mechanism

- kinetics of HBr/HCl addition to isolated alkenes
  - rate = \(k[\text{alkene}][HX]^2\), \(A_dE_3\), anti addition: \[478\text{ & 479}\]
    - temp. & solvent-dependent: mostly syn at -78 °C in \(CH_2Cl_2\)
  - kinetics of HBr/HCl addition to aryl conjugated alkenes
    - rate = \(k[\text{alkene}][HX]\), \(A_dE_2\), syn addition: \[479\text{ middle}\]
  - conjugated dienes: 1,2-addition via ion-pair; \[481\text{ top}\]
    - thermodynamic stability: aryl conjugation; \[481\text{ middle}\]
Addition of Hydrogen Halides (II)

- **Rearranged products: [480 top]**
  - discrete & faster formation of more stable carbocations
    - by hydride or alkyl shift: Ad₃ mechanism: [480 middle]
  - HX with norbornene: exo isomer; [481 bottom]
    - HBr: ~50% rearranged product; symmetrical bridged ion
    - HCl: unequal distribution of isomers; faster ion-pair collapse before the bridged ion achieves symmetry; [482 top]

- **Salt effect: increased C-X bond; LiBr, Bu₄N⁺Cl⁻**
  - competing reactions in nucleophilic solvents: [480 bottom]
Acid-Catalyzed Hydration

The more highly substituted alcohol: 483 middle

- General acid catalysis: RDS is the protonation step
  - Normal solvent isotope effect: $k_{H_2O/D_2O} = 2\sim4$
  - $\sigma^+$: $R=\text{Ar}$ & increased rate with an ERG; 484 Table 5.1
  - No $^2\text{H}$ loss or exchange at the early stage: 483 top

- The nature of carbocation depends on the solvent: 484
  - Weaker acid (acetic acid-HBr): $\text{Ad}_E^3$ & stereospecific anti; via an alkene-acid complex
  - Stronger acid (triflic acid): $\text{Ad}_E^2$ & not stereospecific; formation of discrete carbocation intermediates (rearrangement)

- Related reactions: hydrolysis of enol ethers; 485 middle
**Addition of Halogens (I)**

- rate\(= k_1[\text{olefin}][\text{Br}_2]+k_2[\text{olefin}][\text{Br}_2]^2+k_3[\text{olefin}][\text{Br}_2][\text{Br}^-]\)
  - in MeOH & excess Br\(^-\): \(k_3\), [Br\(_2\)] complex; \(486\) top
  - in nonpolar solvents: \(k_1\) & \(k_2\), \(486\) bottom
    - plausible 2nd order & 3rd order mechanisms
  - styrenes: \(\rho = -4.8\) with \(\sigma^+\) constants; highly ionic TS
  - reversibility of the bromonium ion: \(491\) top
  - summary of the bromination mechanism: \(492\) top

- **Chlorination:** rate\(= k[\text{olefin}][\text{Cl}_2]\);
  - \(487\) Table 5.2
    - larger increase in reactivity with more substituted alkenes
    - competitive elimination of H\(^+\) after migration: greater positive charge due to weaker bridging by chlorine; \(494\) top
Addition of Halogens (II)

- Stereochemistry: *anti* vs *syn*; 488 Table 5.3
  - Br₂: bridged ion vs ion pair; isolated vs conjugated alkenes
    - R = alkyl or aryl with EWGs vs R = aryl with EDGs
  - Cl₂: low selectivity due to poor bridging ability of Cl
    - less polarizable & likely to become positively charged
  - Other reactions: Br₃⁻ & halohydrins; 491-2

- Evidences for the bridged bromonium ions
  - NMR spectrum in superacid conditions: 489-90
  - X-ray structure of sterically hindered ions: 490 Fig. 5.2
Addition of Halogens (III)

- Fluorination: violent reactions with F₂; mixtures
  - mild fluorinating agents: XeF₂, AcOF, dilute F₂ at low temp.
    - syn product from collapse of the ion pair: 496 middle
- Iodination: easily reversible to alkenes; anti
- Conjugated dienes: 1,2- vs 1,4-adduct & anti vs syn
  - Br₂: 1,4-syn addition via ionic intermediate; 496 bottom
  - mild pyr•Br₂/Br₃⁻: 1,2-anti addition via AdE₃; 497 top
Stereochemistry of Fluorination

NaOAc + F₂ → CH₃CO₂F

CH₂Cl₂ -75 °C

acetyl hypofluorite

no bridged fluoronium ion involved
Sulfenylation

Sulfenylation: bridged intermediates; 498 bottom

- sulfenylating reagents: 498 Scheme 5.1
- less electrophilic & better bridging: less rate increase (10^2 times) with 2,3-dimethyl-2-butene than Cl_2 (10^6)/Br_2 (10^7)
- regioselectivity: substrate & reagent; 500 Table 5.4
  - often anti-Markovnikov addition due to steric factors
  - electrophilic CF_3CH_2SX: Markovnikov & anti; 500 middle
Selenenylation

- Selenenylation: bridged seleniraniums; 501 mid.
  - rate-acceleration by ERG-Ar: concerted addition/ionization
  - selenenylation reagents: 498 Scheme 5.1
  - rate-enhancing: alkyl groups; 502 Table 5.5
    - phenyl: rate-retarding; steric & stabilized alkene
  - regioselectivity: anti-Markovnikov; 501 bottom
    - rearrangement to the thermodynamic Markovnikov product
    - styrene: the Markovnikov product
  - stereoselectivity: anti & diaxial; 502-3
  - utility of selenide intermediates: 501 top
Epoxidation with Peroxides

- Concerted mechanism: syn addition; 504 middle
  - common epoxidizing reagents: mCPBA etc.
  - faster rate: strained/ERG-alkenes & EWG-peroxy acids
    - \( k_{\text{norbornene}} = 2 \ k_{\text{cyclopentene}}, \ k_{\text{trans-cyclooctene}} = 90 \ k_{\text{cyclohexene}} \)
    - Aryl-conjugated alkene: stabilized & less reactive
  - stereoselectivity: less hindered face; 505 top
    - hydroxy-directing effect: H-bonding; 505 middle
    - inductive effects: syn-EWG vs anti-ERG; 506 bottom
  - DMDO: (in-situ) preparation & reactions; 509 top
    - more reactive to Z-alkenes: 510 top
    - more nucleophilic than peroxyacids: 510-511
MCPBA

peroxyacetic acid

dimethyldioxirane (DMDO)

dimethyldioxirane (DMDO)

peroxytrifluoroacetic acid

Oxone (potassium peroxymonosulfate)

2 HOOSO$_3$K
KHSO$_4$
K$_2$SO$_4$
Transformations of Epoxides (Oxiranes)

- Ring-opening: steric/electronic; § 511 bottom
  - basic conditions: less substituted carbons (steric)
  - acidic conditions: degree of the C-O rupture; § 512 top
    - pH-rate profile: stable with weak base; § 512 middle
  - cyclohexene epoxides: regio/stereospecific; § 514 bottom
    - via cations: not stereospecific but regiospecific; § 513 bottom
    - reaction conditions: catalyzed/uncatalyzed; § 514 top
  - propylene oxide with HBr: anti-Markovnikov; § 515 top
    - possible reversal of regioselectivity with a stabilized cation intermediate
Electrophilic Addition with Metal Ions

Formation of alkene-metal ion complex: 515 mid.

- Hg$^{2+}$: stable mercurinium ions; 517 top
  - alkene reactivity: steric hindrance to Hg$^{2+}$; Table 5.6
  - reagent activity: Hg(O$_2$CCF$_3$)$_2$, Hg(ClO$_4$)$_2$ > Hg(OAc)$_2$ >> HgCl$_2$
  - styrene: $\rho = -3.16$; a cationic character
  - regioselectivity: Markovnikov addition
    - but at the sterically less hindered position: 516 middle
  - anti addition: acyclic/monocyclic alkenes; 517 bottom
  - syn addition: bicycles, group transfer from Hg$^{2+}$; 518 top
    - remote attack from polar groups: 518 mid & 518 mid
- argentation: reversible complex formation; 520 bottom
  - analysis & separation of alkenes, no intermolecular Nu attack
Hydroboration and Functionalization

- Concerted syn electrophilic addition: \( 522 \) top
  - reagent reactivity vs stability: \( 521 \) bottom
  - less hindered & more e-\(-\)rich site: \( 523 \) Table 5.7
  - less hindered face & higher selectivity with bulky reagents
  - rearrangement to terminal sites: > 160 °C; \( 525 \) middle
    - intramolecular migration via e-\(-\)poor \( \pi \)-complex: \( 526 \) bottom
    - thermodynamic control: \( 525-6 \)

- Concerted migration of the R: functionalization
  - hydroxylation (\( 527-8 \)), amination (\( 528-9 \))
  - enantioselective hydroboration: chiral boranes; \( 530 \)
Comparison of Electrophilic Additions

- Correlation between reactivity & IP: 
  - protonation: substitution degree at the more substituted C
    - the major factor: carbocation stability
  - bromination: total No of substituents; symmetrical bridge
  - sulfenylation/selenenylation: less sensitive to substitution
  - epoxidation: similar to bromination but a reduced slope
  - mercuration: carbocation-like but a large steric effect
  - hydroboration: dominant steric effect and less e⁻ demand

- Polar addition intermediates:
  - electronic/steric control: regio-/stereoselectivity
Polar Addition to Alkynes (I)

- Basic mechanisms: via a complex; 
  - Addition of HCl: vinyl cation (sp); 
  - aryloalkynes: mainly syn, $A_{dE}2$; stabilized by aryl groups
  - alkyl alkynes: $A_{dE}2$ (540) or $A_{dE}3$ (539, added X⁻)
- Hydration: ketones via vinyl cations; 
  - solvent isotope effect: rate-determining protonation step
- Chlorination of aryloalkynes: vinyl cations; 
  - phenylacetylene: $\rho = -4.2$ with $\sigma^+$ constants; vinyl cation
  - rate = $k[\text{alkyne}][\text{Cl}_2]$; nonstereospecific; solvent capture
❖ Polar Addition to Alkynes (II)

❖ Chlorination of alkyl alkynes: 541 top
   ◆ disubstituted: anti via bridged ions; very fast \( k_{\text{di}}/k_{\text{mono}} \approx 100 \)
   ◆ monosubstituted: syn; short lifetime for the vinyl cation pair

❖ Bromination: alkyne-Br\(_2\) complex; 541 bottom
   ◆ aryl alkynes: not stereospecific via a vinyl cation (Ad\(_E\)3)
     ○ anti: EWG on aryl rings (bridged) & added Br\(^-\) salts
   ◆ alkyl alkynes: anti with Ad\(_E\)3; 542 middle

❖ Mercuration: E or Z-addition; to ketones, 544 mid

❖ Reactivity of alkynes and alkenes: 537 Table 5.10
   ◆ vinyl cations: 10-15 kcal higher than alkyl cations
   ◆ bridged ions with a double bond: very strained
Addition to Allenes

- Vinyl cation: kinetically favored; 545 middle
  - twisted allyl cations: 36-38 kcal higher than vinyl cations
  - RDS: protonation step to the vinyl cation
- Addition of HX: vinyl halides; 545-6
  - geminal dihalides with 2 HX: stabilized by the 1st halogen
- Addition of H₂O: ketones via enols; 546 middle
- Addition of X₂/Hg²⁺: bridged ions; 546 middle
  - nucleophilic attack at the terminal carbon
Mechanism in Allenes: Vinyl vs Allylic Cation

\[ RH^+C\text{CH} = \text{CHR} \quad \xrightarrow{H^+} \quad RHC = \text{C} = \text{CHR} \quad \xrightarrow{H^+} \quad RH_2C = \text{C} = \text{CHR} \]

allylic cation

vinyl cation

‘kinetically favored’
Polar Elimination Reactions: Mechanisms

- Classification of elimination modes: 547 top
  - relative to X: \( \alpha \)-, \( \beta \)-, \( \gamma \)-elimination; 548 Scheme 5.2
- Limiting mechanisms of \( \beta \)-eliminations: 548-9
- Variable (E2) TS theory: CH\(_3\)CH\(_2\)X; 549 Fig. 5.11
  - 2-/3-D potential energy diagrams: 550 Fig. 5.12
  - change of TS: substituent effects (Z or R); 551 Fig. 5.13
- SAR (structure-[re]activity relationship): E1 / E1cb
  - EDG / EWG, more / less substitution, good / poor leaving group, solvents with high / low Y, stronger & harder bases (E1 over S\(_N\)1) / stronger bases: 548-9 Schemes 5.3-5.4
Change of TS in Eliminations: Substituents

- For E1cb-like reaction
  - Transition State (TS)

- For E1-like reaction
  - Transition State (TS)
Regiochemistry of Eliminations

- **E2 via an ‘E1-like’ TS: regioselectivity of E1**
  - E1 TS (RDS) resembles the carbocation: Fig. 5.14
    - the more stable carbocation: hyperconjugation giving the more substituted alkene: the Saytzeff product / rule; middle

- **E2 via an ‘E1cb-like’ TS: regioselectivity of E1cb**
  - E1cb TS (RDS): significant bond between H & base
    - low $\Delta E_a$: easier removal of H; less hindered & more acidic $\beta$-H (kinetic acidity), stronger/bulky bases (the Hofmann rule)

- **Concerted E2: significant C=C bond at TS**
  - more substituted alkenes & (anti)periplanar conformations
  - effects of leaving groups, base strength & bulkiness: Table 5.11, 5.12 & 5.13, 557 & 558
Stereochemistry of E2 Eliminations

- Periplanar conformation: anti & syn; 558 bottom
  - Cyclicks: mostly anti in cyclohexanes; 560 middle
    - 90% syn for 4-ring; 50% syn for 5-ring
    - syn elimination: no anti conformation possible; 561 top
  - Acyclics: usually anti favored; stereospecific, 559 top
    - Competitive syn elimination possible: 559 mid & Table 5.14
    - syn elimination in acyclic systems: 560 Table 5.15
      - Poor X, longer chain, nonpolar solvent, strong base
      - An ion pair: less syn with crown ethers; 561 bottom
      - Steric effect: 562 bottom Table & 563 top
  - Z-selectivity: arene sulfonates; 563 middle
Anti Elimination in Acyclic Compounds
❖ Dehydration of Alcohols

❖ Acid-catalyzed elimination: E1; 563 bottom

❖ reverse of acid-catalyzed hydration: cation intermediates
  ❖ reactivity: 3o > 2o >> 1o alcohols
  ❖ more substituted alkenes predominant
  ❖ rearranged products: 564 top
  ❖ secondary kinetic isotope effect at β-position: 564 middle
Eliminations Not Involving C-H Bonds (1)

Vicinal dibromides: *anti* with NaI; \( \text{564-5} \)
- lower selectivity with Zn/Cr: nonstereospecific formation of an organometal intermediate

Acid-catalyzed deoxymercuration: \( \text{566 bottom} \)
- \( \text{CH}_3\text{CH(OH)CH}_2\text{HgI} \): 10\(^{11}\) faster than \( \text{CH}_3\text{CH(OH)CH}_3 \)
  - bridged \( \text{Hg}^+ \): faster with the *trans* isomer; \( \text{566 bottom} \)
- other metals: \( \text{IHg~Ph}_3\text{Pb~Ph}_3\text{Sn} \) > \( \text{Ph}_3\text{Si} \) (10\(^6\) slower) > H
  - weaker bond energies: Hg-C 27 < Pb-C 31 < Sn-C 54 < Si-C 60 < H-C 96 kcal/mol
  - stabilized \( \beta \)-cation via a bridged ion or e- donation; \( \text{566 top} \)
Eliminations Not Involving C-H Bonds (II)

- Elimination of $\beta$-hydroxysilanes/tins: 566 middle
  - *anti* elimination under acidic conditions

- Elimination of $\beta$-halo/carboxysilanes: 566-7
  - *anti* elimination under basic conditions: 567 top
  - $\beta$-sulfonyloxsilanes: mild conditions; 567 middle

- Vinyl silanes/stannanes: substitution; 567 bottom
  - activated olefins & *anti* addition to silanes

- Allyl silanes/stannanes: active $E^+$; 568
  - allyl anion equivalents: rearrangement of double bonds