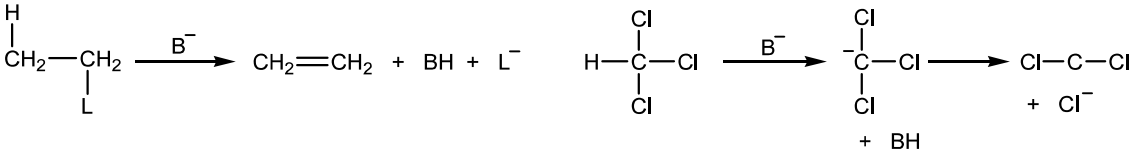
Chap 14 Elimination Reactions – Alkenes and Alkynes

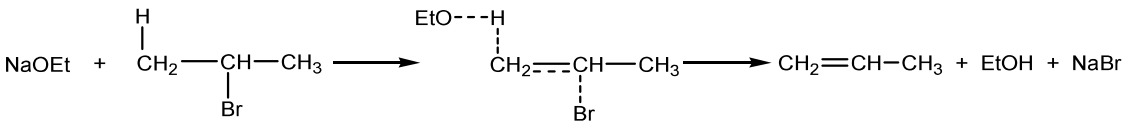
14-1 The Reaction Mechanism

1,2-Elimination and 1,1-elimination :



A. The E2 Mechanism

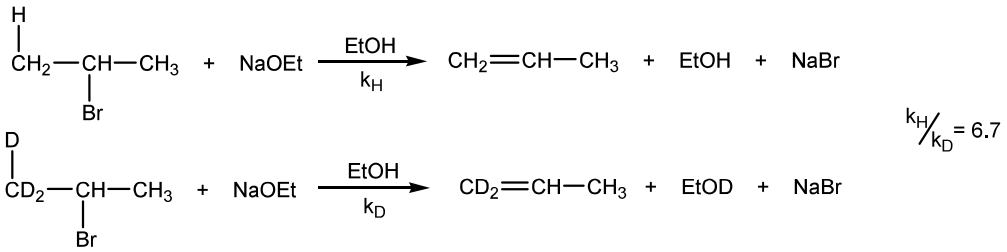
Base가 proton을 뽑는 것과 leaving group의 이탈이 거의 동시에 일어나 C=C의 이중결합을 생성함.



Bimolecular 1,2-elimination, One-step reaction

Rate = k[*iso*-PrBr][$^-$OEt], 2nd order

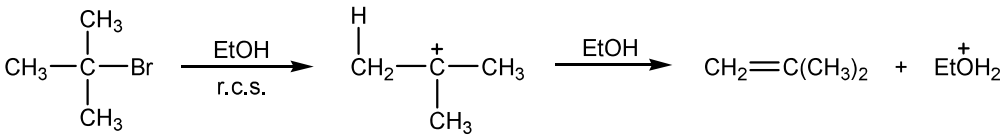
Kinetic isotope effect :



C-H의 bond breaking이 느리게 일어나며, 속도결정단계 (r.c.s.) 에 관여함.

B. The E1 Mechanism

Substrate가 leaving group을 이탈시켜 생성된 carbocation이 deprotonation ($-H^+$) 을 일으켜 C=C의 이중결합이 생성됨.



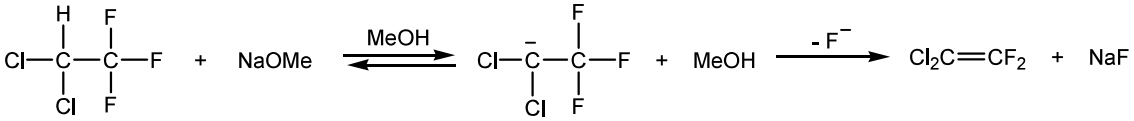
Unimolecular 1,2-elimination, Two-step reaction, Carbocation intermediate

Rate = k[$(CH_3)_3CBr$], independent to [EtOH]

Substitution (S_N1) 과 항상 경쟁적으로 일어남.

C. The E1cB Mechanism

Base가 substrate의 수소를 뽑아 생성된 carbanion에서 leaving group가 이탈되어 C=C의 이중결합을 생성함.



Bimolecular 1,2-elimination, Two-step reaction, Carbanion intermediate

Rate = $k[Cl_2CHCF_3][^-OMe]$, 2nd order

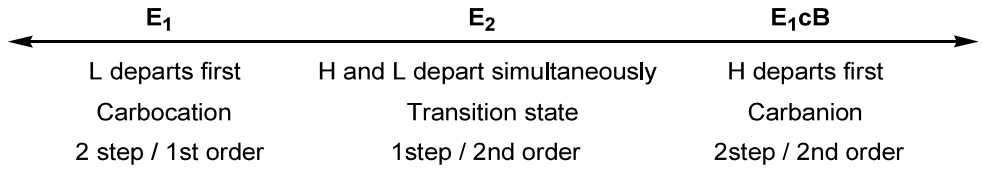
1st step : reversible

Cl_2CHCF_3를 NaOMe/MeOD 하에서 반응할 때 H-D exchange가 일어남. → Problem 14-3 :

2nd step : rate controlling step

F^- - poor leaving group

* E_1, E_2, E_1cB Mechanism :



14-2 Elimination Versus Substitution

A. Basicity Versus Nucleophilicity

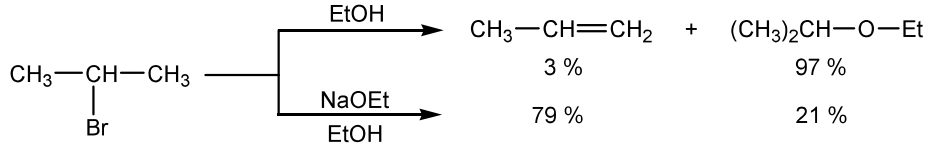
Electron-rich 한 화학종이 base 역할 (abstraction of H) 을 하면 elimination이 일어나며, nucleophile (attack of carbon) 역할을 하면 substitution이 일어남

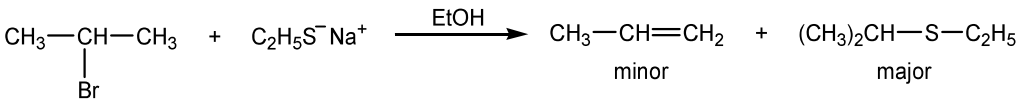
▪ **Basicity와 nucleophilicity에 영향을 미치는 요소들**

1) Property of reagent

Nonbonding electron을 갖는 시약은 anion을 갖는 시약보다 상대적으로 친핵성의 기능이 증가함.

전기음성도가 작은 원소의 anion은 상대적으로 친핵성의 기능이 증가함.

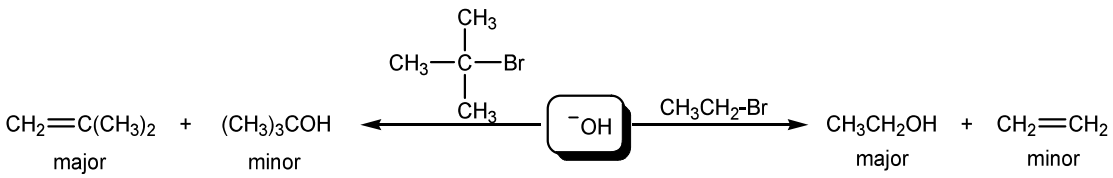




2) Substrate structure

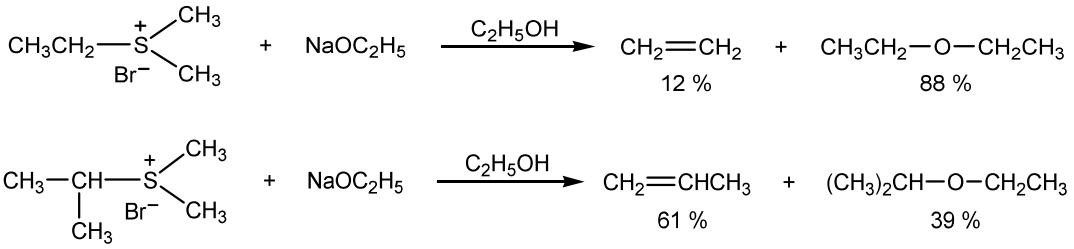
Substrate가 hindered할수록 elimination의 비율이 증가하며, less hindered 할수록 substitution의 비율이 증가함.

Elimination : 3° RX > 2° RX > 1° RX Substitution : 1° RX > 2° RX > 3° RX



3) Stability of product

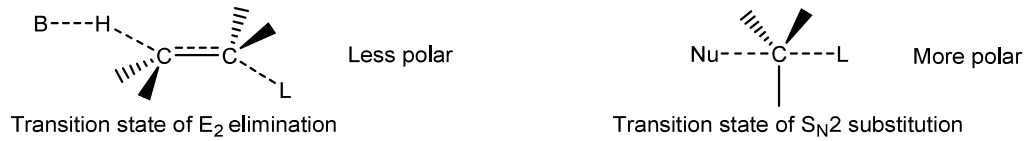
치환이 많이 된 alkene이 생성될수록 elimination의 비율이 증가함.

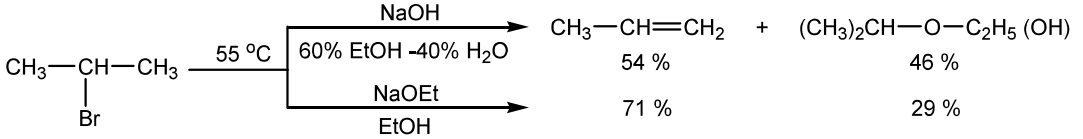


Problem 14-9 :

4) Solvent effect

Solvent의 polarity가 높을수록 substitution의 비율이 증가하며, solvent의 polarity가 낮을수록 elimination의 비율이 증가함.





5) Temperature effect

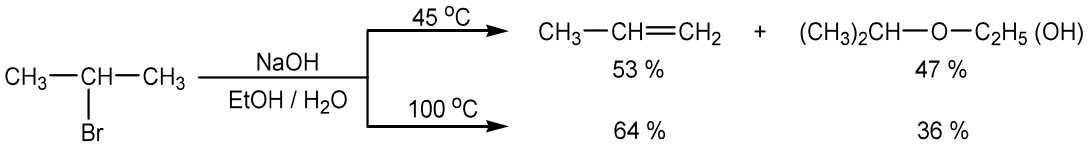
온도가 높을수록 elimination의 비율이 증가하며, 온도가 낮을수록 substitution의 비율이 증가함.

Elimination : σ + σ → π + σ, △H > 0 (endothermic raction)

온도를 증가하면 온도가 감소하는 방향으로의 평형이동 → 정반응

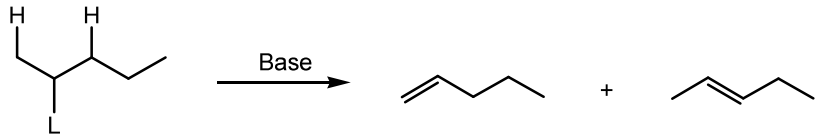
Substitution : σ → σ, Elimination보다 상대적으로 △H가 덜 흡열적임.

온도를 감소하면 상대적으로 substitution의 비율이 증가함.



14-3 The Direction of Elimination

Orientation of elimination :



Saytzeff orientation - 치환이 더 많이 된 alkene이 주 생성물로 생성됨

L = less hindered leaving group (Cl, Br, OTs)

Base = less hindered base (NaOH, NaOEt)

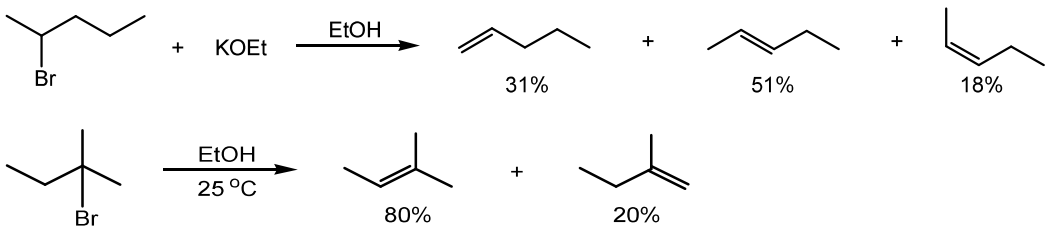
Hofmann orientation - 치환이 더 적게 치환된 alkene이 주 생성물로 생성됨

L= highly hindered leaving group ($^{+}NR_3$, $^{+}SR_2$)

Base = highly hindered base [$NaOC(CH_3)_3$]

A. Formation of the More-Substituted Alkenes

Saytzeff product - more stable alkene

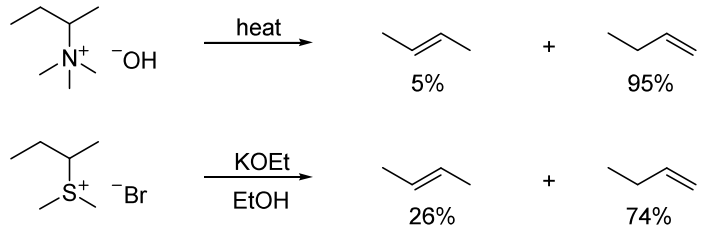


Problem 14-17 : Elimination of 2-bromo-1-phenylpropane

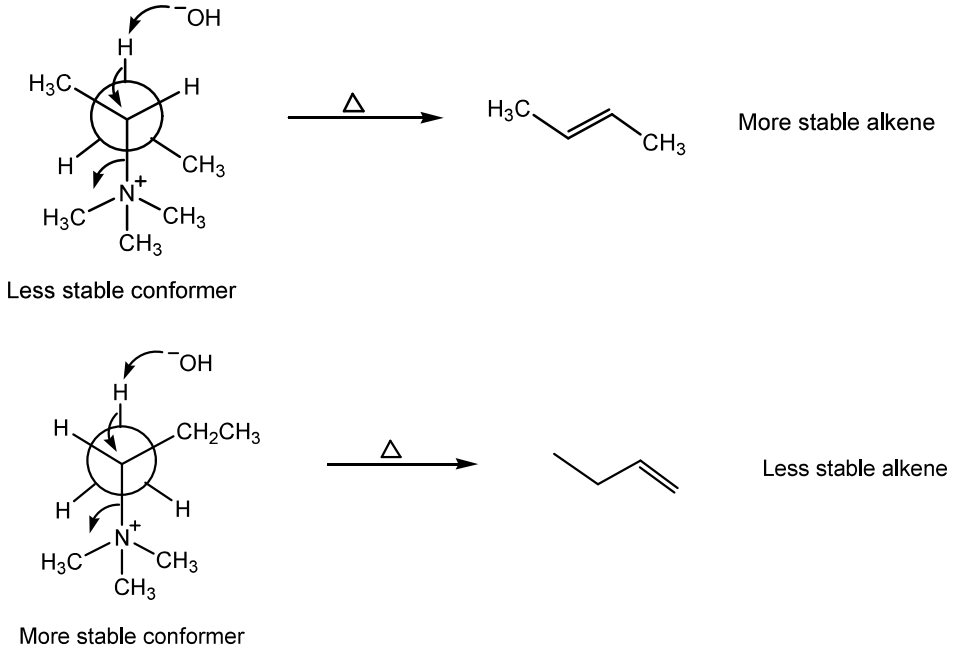
B. Formation of the Less-Substituted Alkene

Hofmann product - Less stable alkene

Product의 안정성보다는 반응물에서 leaving group이 hindered하므로 base가 less hindered한 H에 공격하여 치환이 덜 된 alkene이 주생성물로 얻어짐.



Conformational effect에 의한 Hofmann orientation :



Problem 14-18 :

Problem 14-19 :

14-4 Stereochemistry

Stereospecific pathway of elimination :

Anti elimination - H와 leaving group (L) 이 서로 180°의 반대 방향에서 끊어짐.
H와 L이 anti-periplanar에 위치

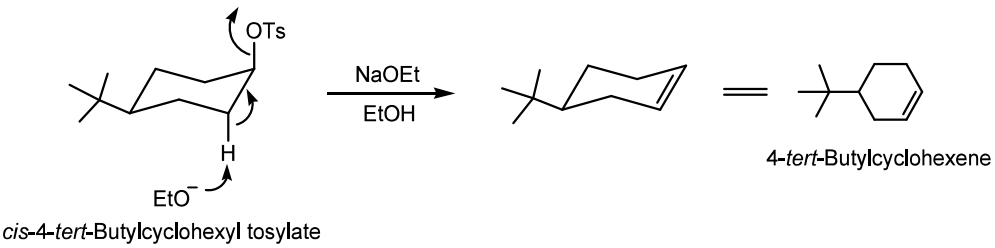
Syn elimination - H와 leaving group (L) 이 서로 같은 방향에서 끊어짐.
H와 L이 syn-periplanar에 위치, cyclic transition state

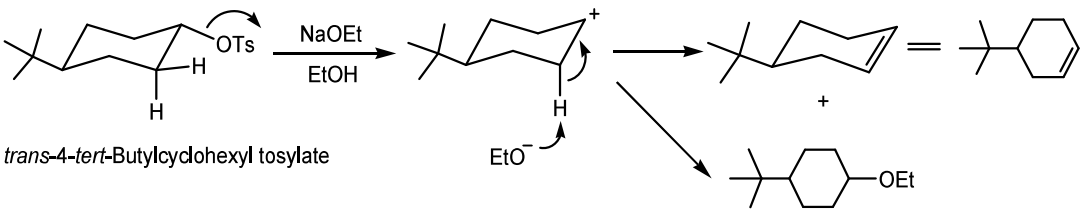
A. Anti Elimination

Elimination of 4-*tert*-butylcyclohexyl tosylate with NaOEt :

cis-4-*tert*-Butylcyclohexyl tosylate - E2 elimination, fast

trans-4-tert-Butylcyclohexyl tosylate - E1 elimination and S_N1 substitution, slow



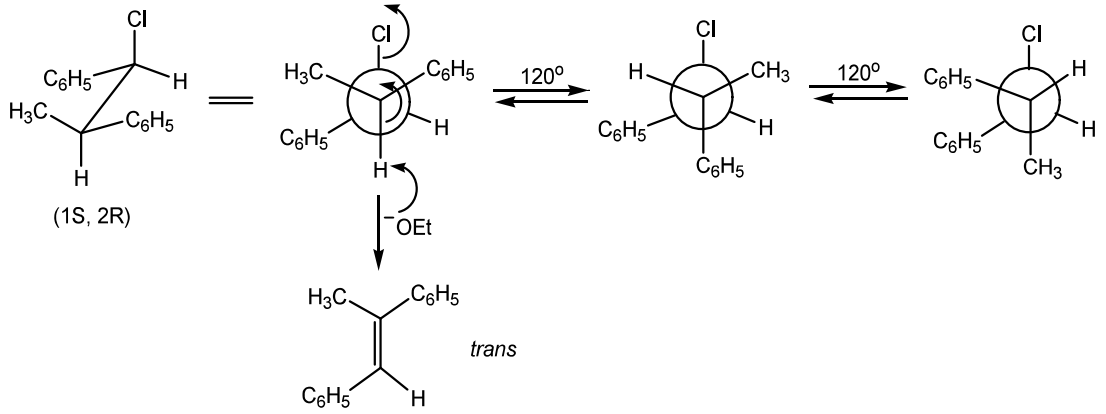


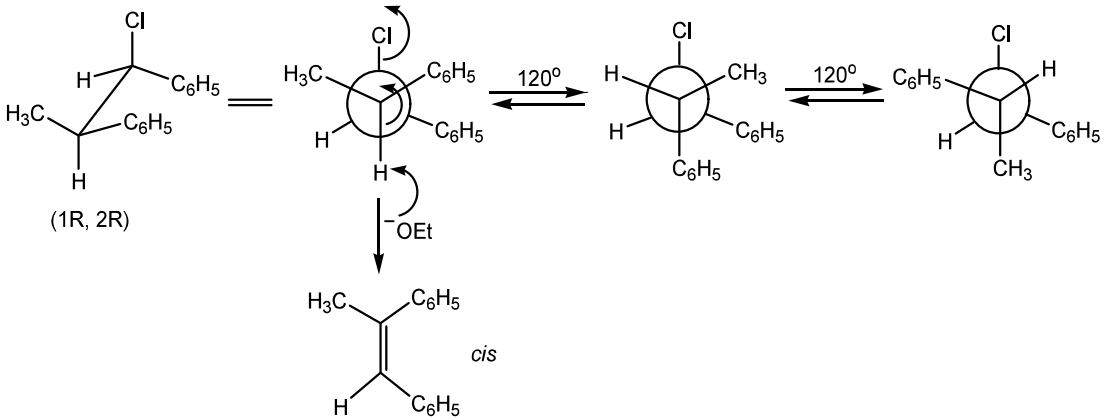
Problem 14-22 : Elimination of *cis*-2-phenylcyclohexyl tosylate and *trans*-2-phenylcyclohexyl tosylate

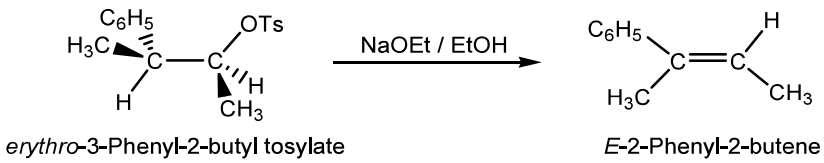
Stereospecific elimination of 1-chloro-1,2-diphenylpropane with NaOEt :

(1S, 2R) or (1R, 2S)-1-Chloro-1,2-diphenylpropane → E-α-Methylstilbene
trans, 100%

(1S, 2S) or (1R, 2R)-1-Chloro-1,2-diphenylpropane → Z-α-Methylstilbene
cis, 98%







erythro-3-Phenyl-2-butyl tosylate

E-2-Phenyl-2-butene

B. Stereoelectronic factors

The most favorable arrangement of elimination :

i) Deprotonation에 의하여 carbon에 발달된 anion (Nu^-) 과 leaving group (L^-) 이 서로 180°의 반대 방향에 위치할 때 반응이 가장 효과적으로 일어남.

ii) 떨어지는 두 group (H, L) 이 서로 180°의 반대 방향에 위치할 때 steric repulsion이 최소화 됨.

→ Anti-periplanar, Anti elimination

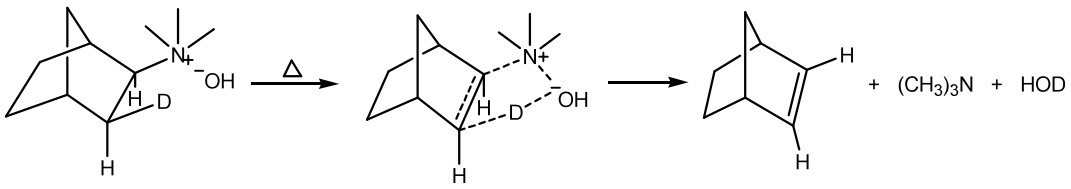
* Evidence of anti elimination

Figure 14-4 : The stereochemical course of menthyl chloride and neomenthyl chloride elimination

C. Syn Elimination

Rigid molecule에서 H(D) 와 leaving group (L) 이 cyclic transition state를 거쳐서 서로 같은 쪽에서 제거되는 반응

Syn-periplanar

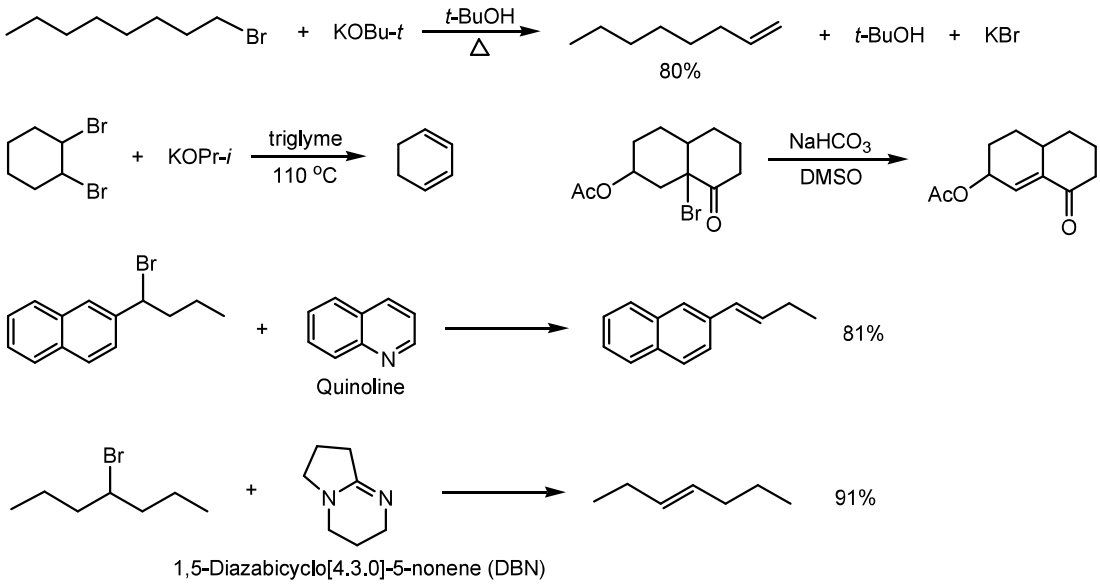


D과 $(CH_3)_3N$ group이 eclipsing되어 반발력이 유발되므로 anti elimination보다는 unstable 하다. 그러나 ring의 C-C σ bond가 회전하지 못하므로 D과 $(CH_3)_3N$ group은 anti-periplanar하게 위치할 수 없으며, 5-membered cyclic transition state를 거쳐서 syn elimination이 일어나게 된다.

14-5 Formation of Alkenes

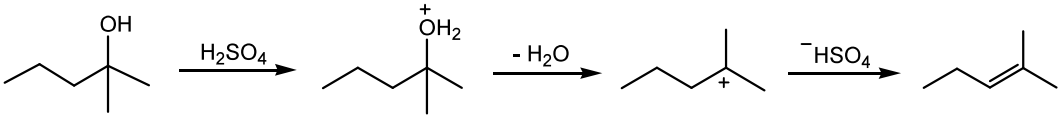
A. Dehydrohalogenation

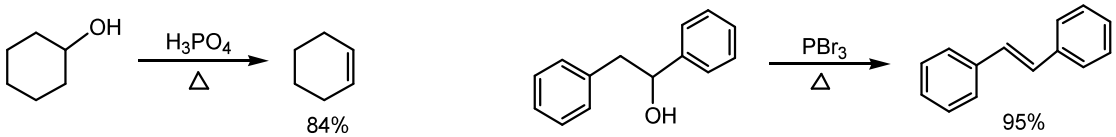
Elimination of hydrogen halide (HX) - formation of alkene



B. Dehydration

Acidic 조건에서 H_2O의 이탈



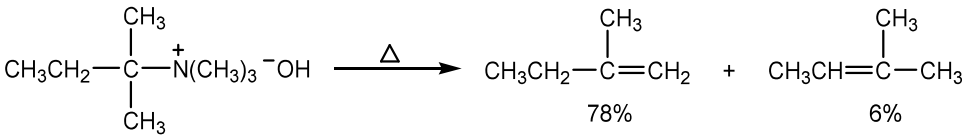


Problem 14-34 :

C. The Hofmann Elimination

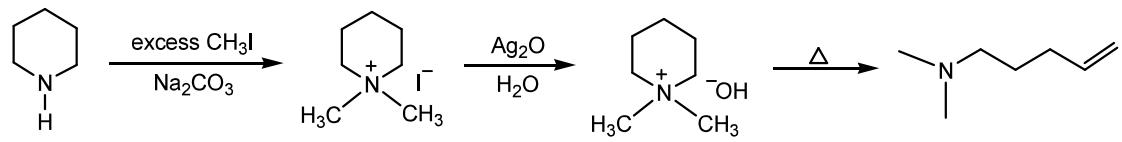
Quaternary ammonium salt로부터 trialkylamine과 β-H의 elimination

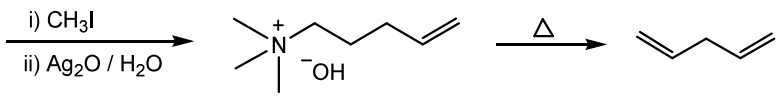
Formation of less substituted alkene



▪ Hofmann degradation (Hofmann exhaustive methylation)

연속적인 Hofmann elimination에 의하여 diene 화합물의 합성

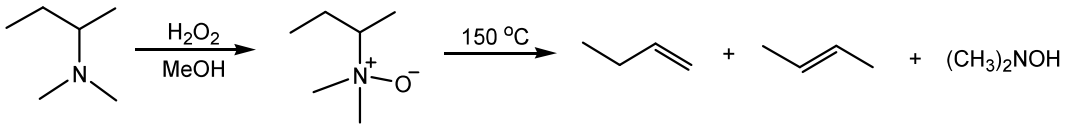




▪ Cope reaction

Pyrolysis of amine oxide

Formation of less substituted alkene

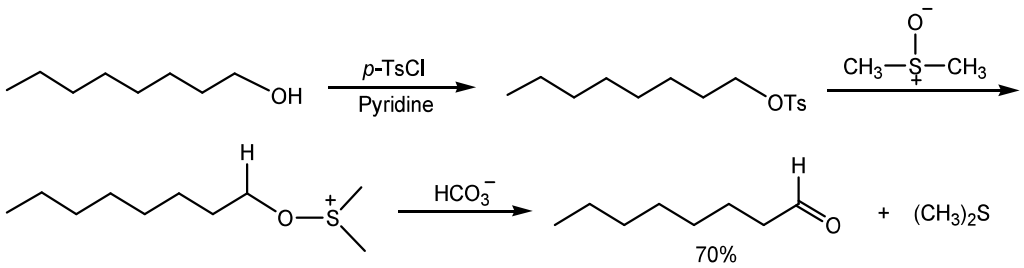


14-6 Other Double and triple Bonds

A. DMSO에 의한 alcohol의 oxidation

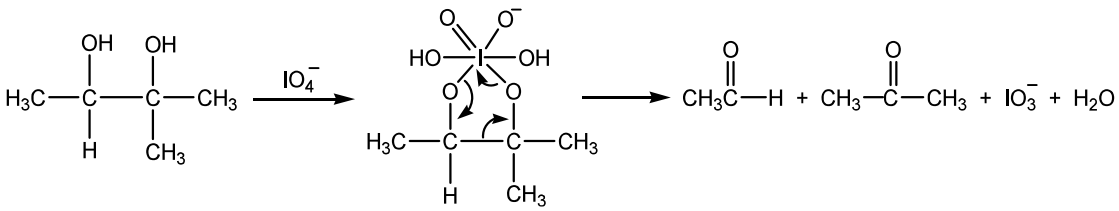
CH_3SOCH_3 - nucleophilic Me_2S (dimethyl sulfide) - good leaving group

Mild한 조건에서 산화가 일어남.



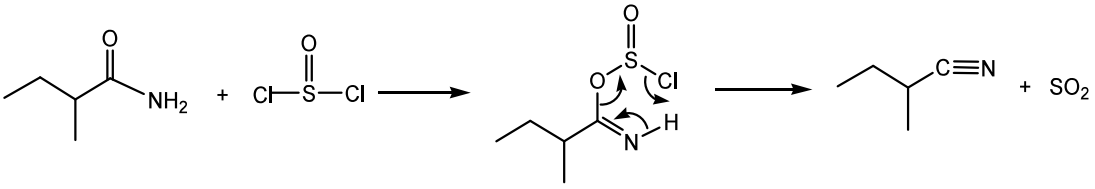
▪ Periodic acid에 의한 1,2-diol의 oxidation

Periodic acid (HIO_4) -oxidizing agent



B. Nitriles

Preparation from the reaction of primary amide with $SOCl_2$ or P_2O_5



Supplementary Problems

14-54 Major product of reaction

14-59 Major product of reaction

14-63 Fragmentation mechanism of β-haloacid

14-64 Explanation for observations