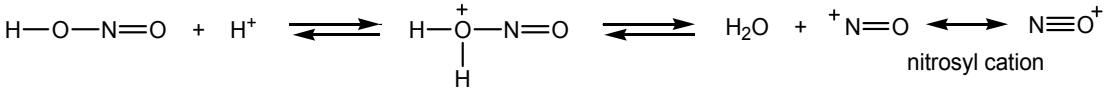
23.8 Reaction with Nitrous Acid

Nitrous acid (아질산, HNO_2) :

Unstable, pK_a = 3.37

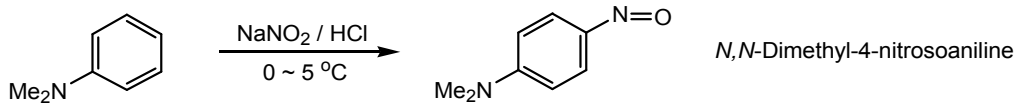
Sodium nitrite ($NaNO_2$) 수용액에 H_2SO_4나 HCl로 처리하여 제조함.

Source of nitrosyl cation



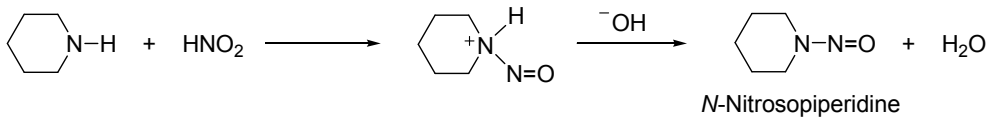
A. Reaction of Nitrous Acid with Tertiary Aromatic Amines

3차 방향족 amine은 nitrous acid와 친전자성 방향족 치환을 일으켜 방향족 nitroso 화합물을 생성함. Nitrosyl cation의 electrophilicity가 매우 약하므로 benzene 고리에 OH, OCH_3, NR_2와 같은 activating group이 있을 경우에만 반응이 일어남.



B. Reaction with Secondary Aliphatic and Aromatic Amines

지방족이거나 방향족인 2차 amine들은 nitrous acid와 반응하여 *N*-nitrosoamine을 생성함.



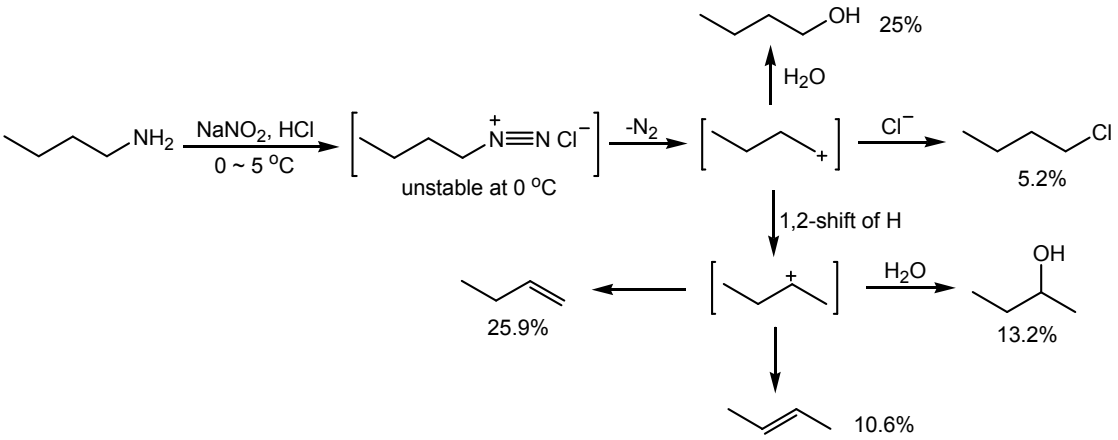
* Property of *N*-Nitrosoamine

Carcinogen, 고기를 굽거나 베이컨을 튀길 때 생성됨

고기의 가공 - 쉽게 변질되는 것을 방지하기 위하여 sodium nitrite를 첨가
$NaNO_2$는 보툴리누스 중독을 일으키는 세균의 성장을 방해함.
FDA 허용 기준 : 50~125 ppm (50~125 μg/1g)

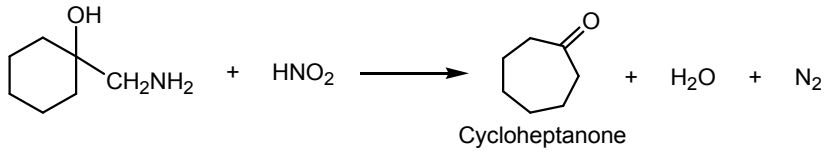
C. Reaction with Primary Aliphatic Amines

지방족 1차 amine은 nitrous acid와 반응하여 여러 가지 혼합물을 생성함.

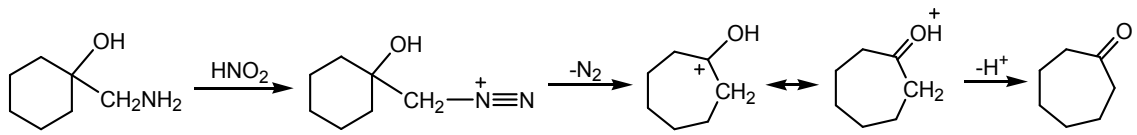


지방족 diazonium ion은 불안정하여 곧바로 N_2를 이탈시켜 carbocation을 생성하므로 alcohol, alkyl chloride, alkene의 혼합물을 생성함.

예외 : Tiffeneau-Demjanov reaction



Mechanism :

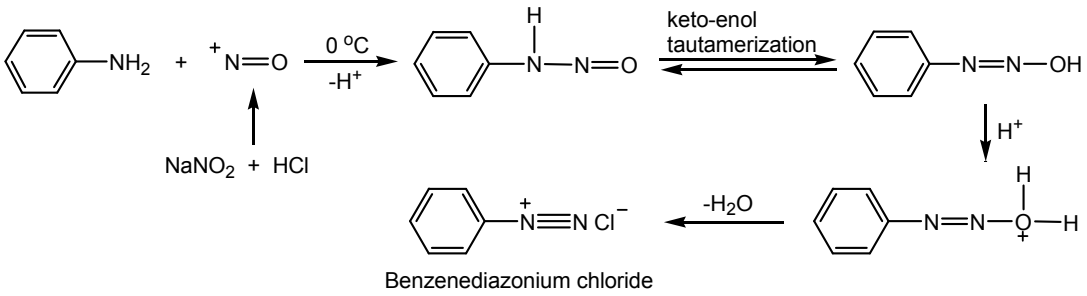


예제 23.11 :

D. Reaction with Primary aromatic Amines

방향족 1차 amine은 nitrous acid와 반응하여 benzendiazonium salt의 중간체를 생성함.

1) Preparation of Benzenediazonium Salt



1st step : Nucleophilic addition of aniline to nitrosyl cation

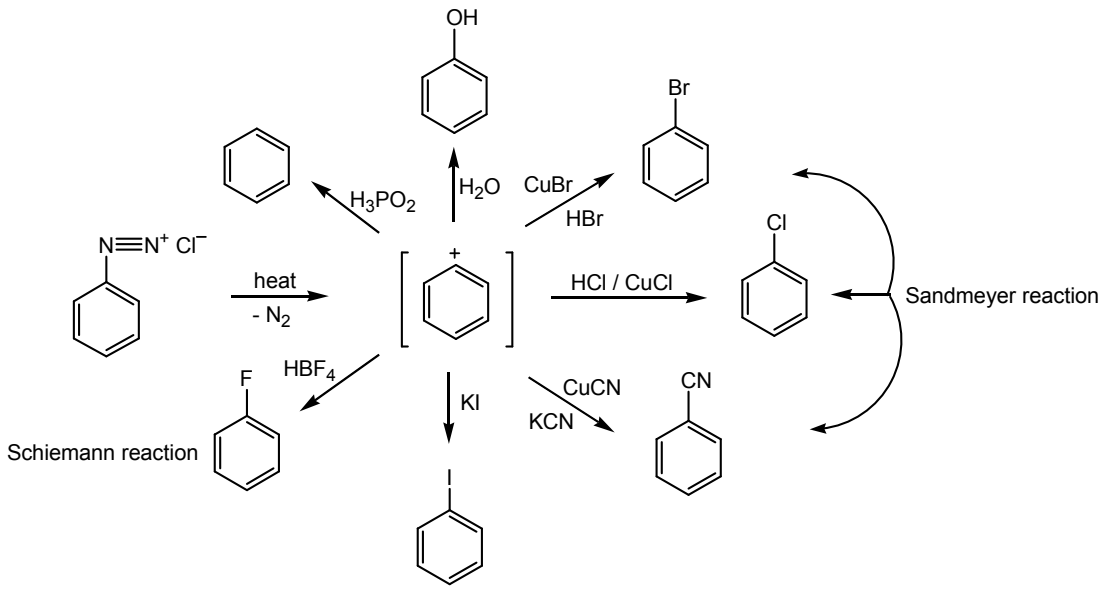
2nd step : Keto-enol tautomerization

3rd step : OH의 protonation

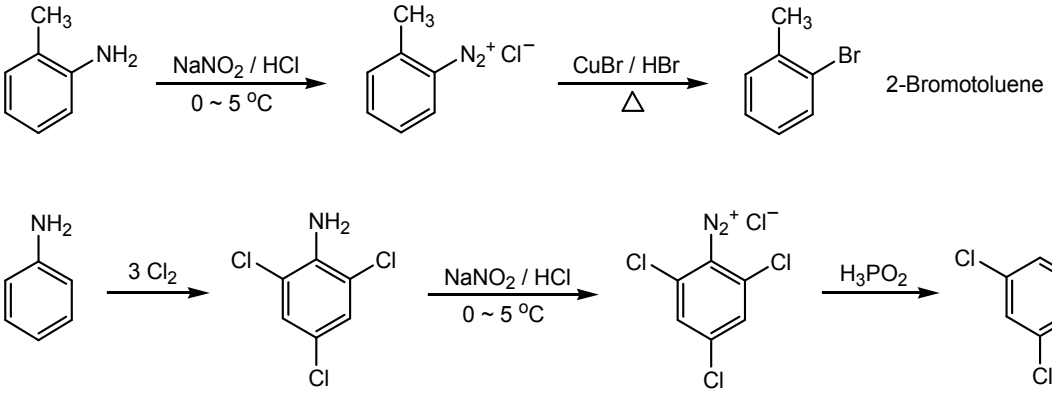
4th step : H_2O의 이탈에 의하여 benzenediazonium chloride의 생성

Benzenediazonium chloride - stable at 0 °C, 짧은 기간 동안 용액으로 보관함.
$C_6H_5^+$의 동등체 (N_2 -excellent leaving group)

2) Reaction of Benzenediazonium chloride



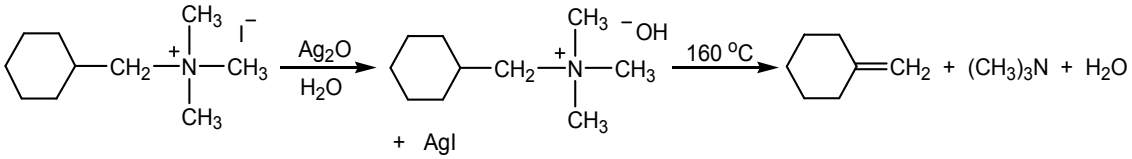
* Some reaction using benzenediazonium chloride



예제 23.12 :

23.9 Hofmann Elimination

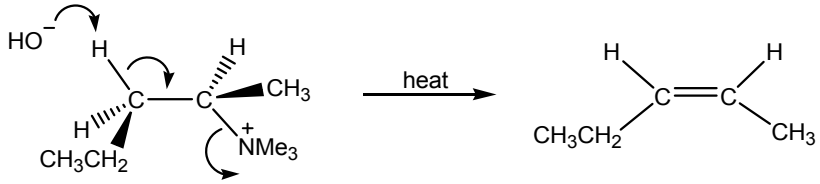
Quaternary ammonium hydroxide를 가열할 때 E2 elimination에 의하여 alkene이 생성되는 반응



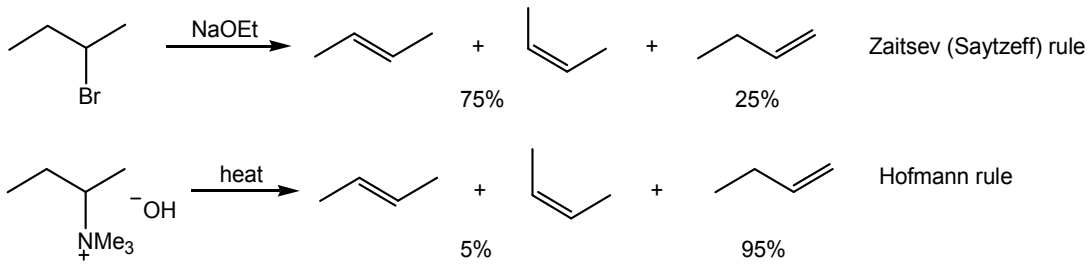
Hofmann elimination :

1) E2 elimination by concerted reaction

2) Anti elimination - H와 이탈기는 서로 180° 방향에서 떨어짐.



3) Less substituted alkene이 주생성물로 얻어짐.

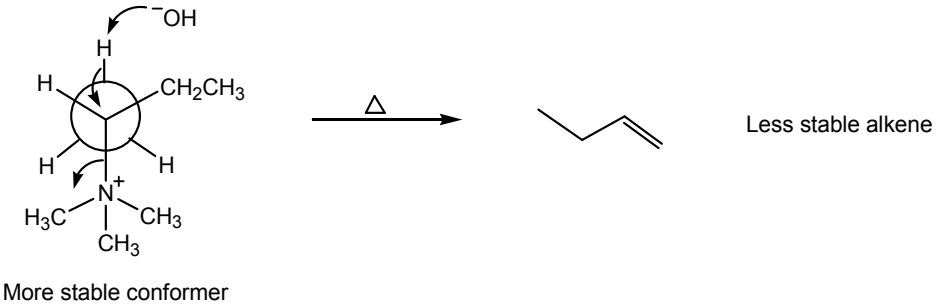


Zaitsev rule - 떨어지는 이탈기가 bulky하지 않을 경우는 생성되는 **alkene의 안정성이 반응을 지배**하여 치환이 많이 된 alkene이 주생성물로 얻어진다. (이탈기 = Cl^-, Br^-, I^-, ^-OTs)

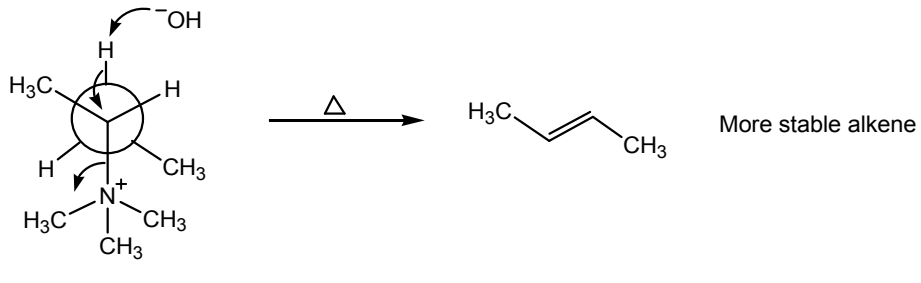
Hofmann rule - 떨어지는 이탈기가 bulky할 경우는 ^-OH가 less hindered proton을 뽑게 되므로 less hindered alkene이 주생성물로 얻어지며, **반응물의 conformation이 반응을 지배**한다.
[이탈기 = $(CH_3)_3N$, $(CH_3)_2S$]

또한 염기의 size가 크면 [$(CH_3)_3COK$] Hofmann이 주생성물이고, 염기의 size가 작으면 (CH_3ONa, NaOEt) Zaitsev가 주생성물로 얻어진다.

◆ Conformational effect



More stable conformer

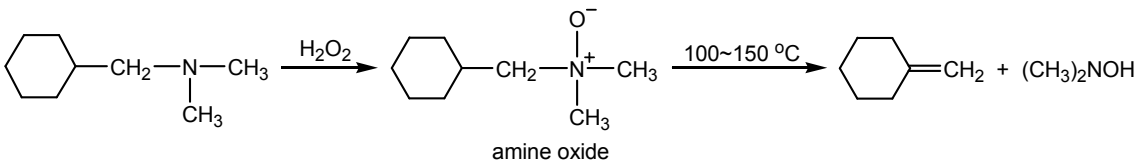


Less stable conformer

예제 23.14 :

23.10 Cope Elimination

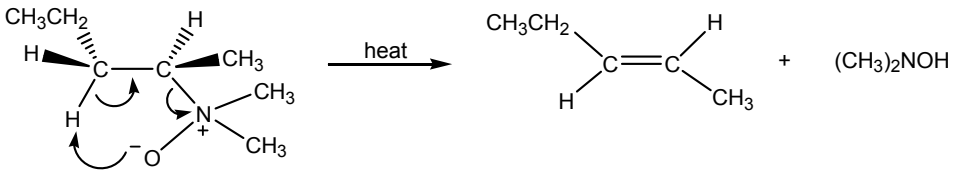
Amine oxide를 가열할 때 elimination에 의하여 alkene이 생성되는 반응



Cope elimination :

1) E2 elimination by concerted reaction

2) Syn stereoselective elimination - H와 이탈기가 서로 같은 방향에서 떨어짐.



예제 23.15 :

Problems

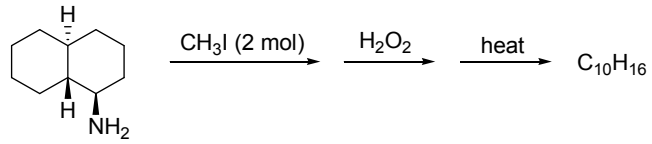
23.25 : Stronger base

23.30 : Acid-base reaction

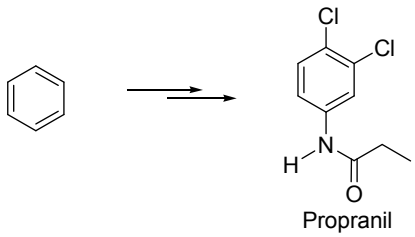
23.33 : Synthesis of 1-hexanamine from bromoalkane of five carbon atoms

23.37 : Nitrous acid deamination of β-aminoalcohol v.s.
Pinacol rearrangement

23.40 : Reaction product



23.44 : Reagent for each step in the synthesis of the herbicide Propranil from benzene



23.46 : Synthesis of 2,4-dihydroxytoluene from toluene