Basic Organic Chemistry L9-3

These are study notes for Basic Organic Chemistry L9-3: Do You Really Understand Substitution and Elimination Reactions of Alcohols?.

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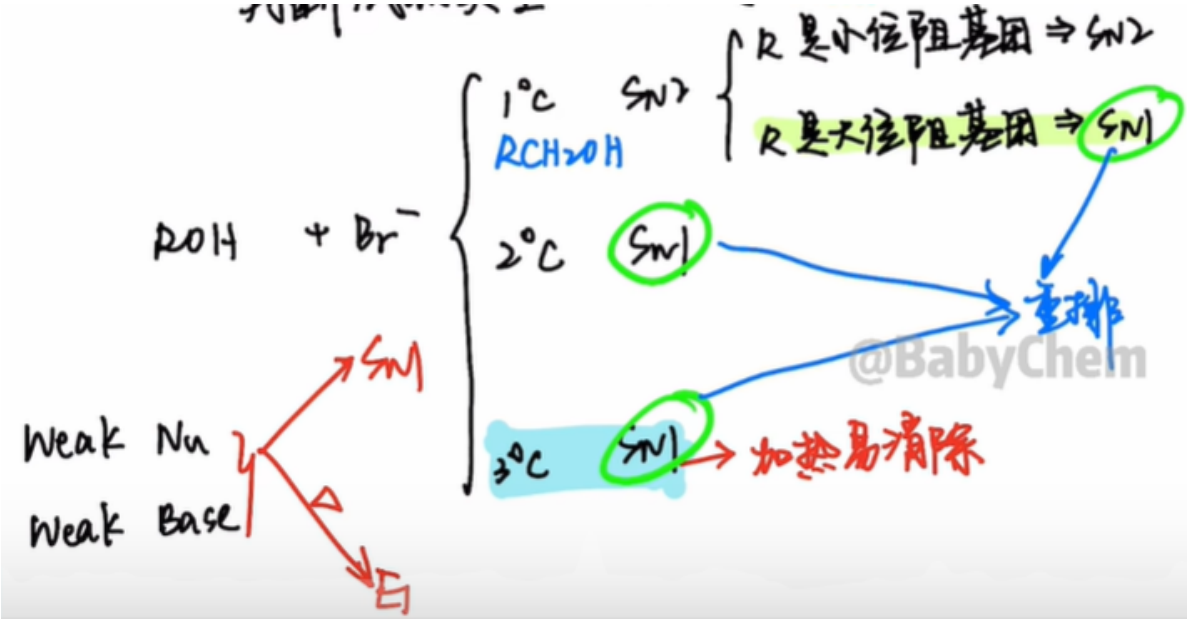
#PartI:Alcohol substitution

ROH + HX



Conclusion:

1. Mechanism: hydroxyl oxonium ion (water is a good leaving group)
2. Small sterically hindered primary alcohol, otherwise S_{N1} will rearrange
3. Alcohol reactivity: allyl type, benzyl type, 3°>2°>1°
4. Hydrohalic acid reactivity: $\mathrm{HI} > \mathrm{HBr} > \mathrm{HCl}$

在氢卤酸中，氢碘酸酸性最强，氢溴酸其次，浓盐酸相对最弱，而卤离子的亲核能力又是$I^- > Br^- > Cl^-$，故氢卤酸的反应性为 HI＞HBr＞HCl。例如，若用一级醇分别与这三种氢卤酸反应，氢碘酸可直接反应，氢溴酸需用硫酸来增强酸性，而浓盐酸需与无水氯化锌混合使用，才能发生反应。

$$CH_3(CH_2)_3OH + HI\ (57\%) \longrightarrow CH_3(CH_2)_3I + H_2O$$

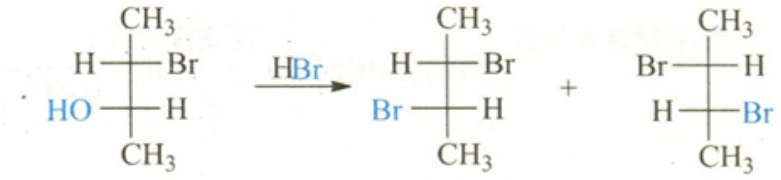
$$CH_3(CH_2)_3OH + HBr\ (48\%) \xrightarrow[\triangle]{H_2SO_4} CH_3(CH_2)_3Br + H_2O$$

$$CH_3(CH_2)_3OH + HCl\ (36\%) \xrightarrow[\triangle]{ZnCl_2} CH_3(CH_2)_3Cl + H_2O$$

Neighbor participation effect

2. 邻基参与效应

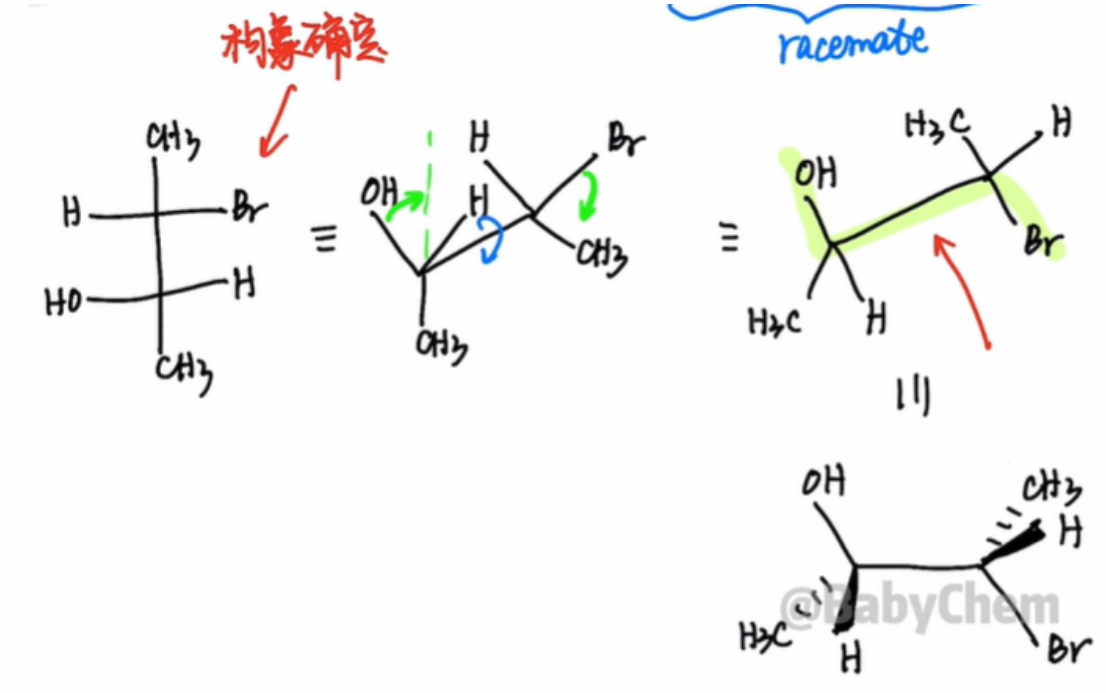
(2S,3S)-3-溴-2-丁醇用浓氢溴酸处理，得外消旋体二溴化物(i)和(ii)：



苏型 (i) (ii)

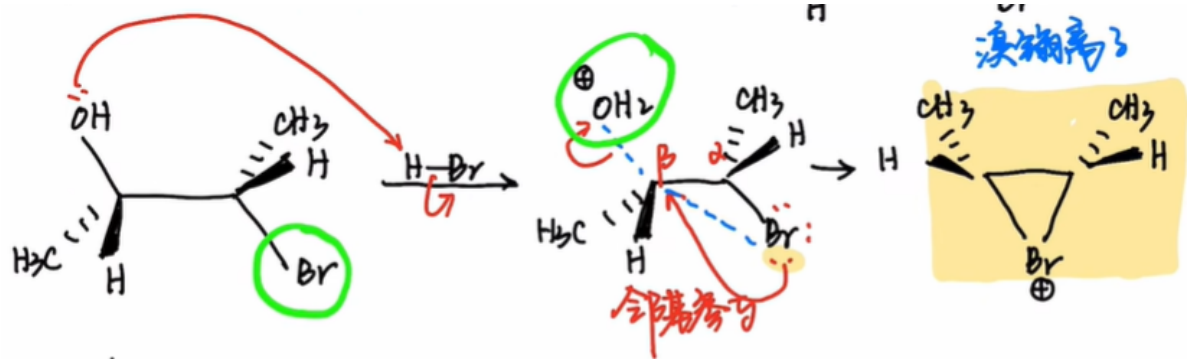
(2S, 3S)-3-溴-2-丁醇 外消旋体

In order to explain the racemic product and the faster reaction rate, in connection with the three pairs of lone pairs of electrons of the Br atom, the neighbor group participation effect was proposed.

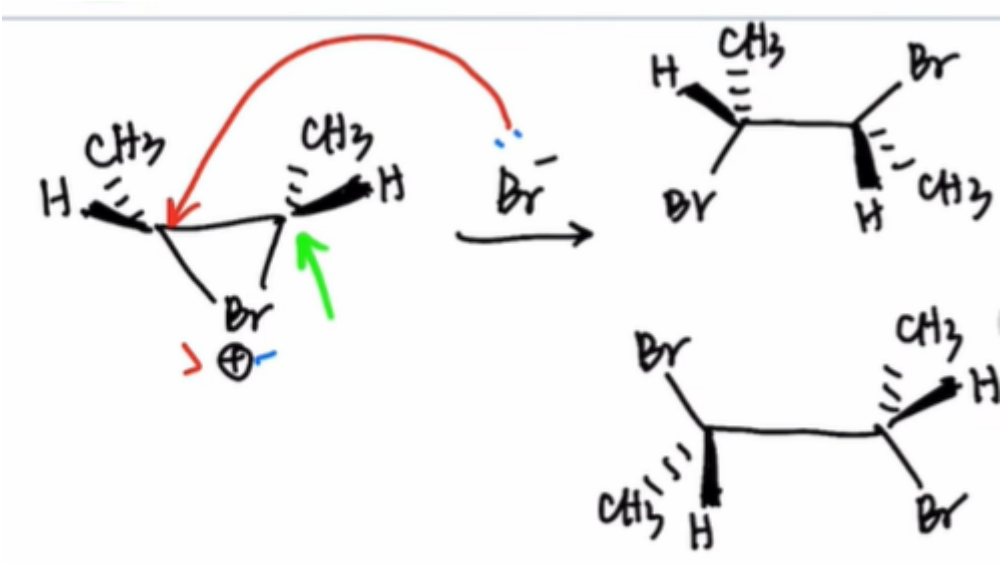


Neighbor group participation requires stereochemistry: trans coplanar

The lone pair of electrons of the bromine atom fills the antibonding orbital of the carbon-oxygen bond, causing the departure of water to form **Bronium ion**.



Next, the bromium ion is attacked by Br^- to open the ring, and attacks from the left and right are possible, so two **racemates** with a chirality ratio of 50:50 are generated.

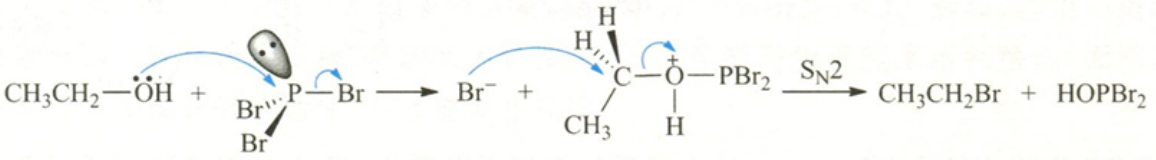


ROH + PBr3

$$3\,\mathrm{ROH} + \mathrm{PX_3} \longrightarrow 3\,\mathrm{RX} + \mathrm{H_3PO_3}$$
$$\mathrm{ROH} + \mathrm{PX_5} \longrightarrow \mathrm{RX} + \mathrm{POX_3} + \mathrm{HX}$$

P is a third period element, so the P atom in $\mathrm{PBr_3}$ has a 3d orbital and can be attacked by the oxygen lone pair of electrons of the hydroxyl group, turning the hydroxyl group into a good leaving group and producing the nucleophile Br^-.

大多数 1°ROH 按 S_N2 机理进行反应。例如



Conclusion:

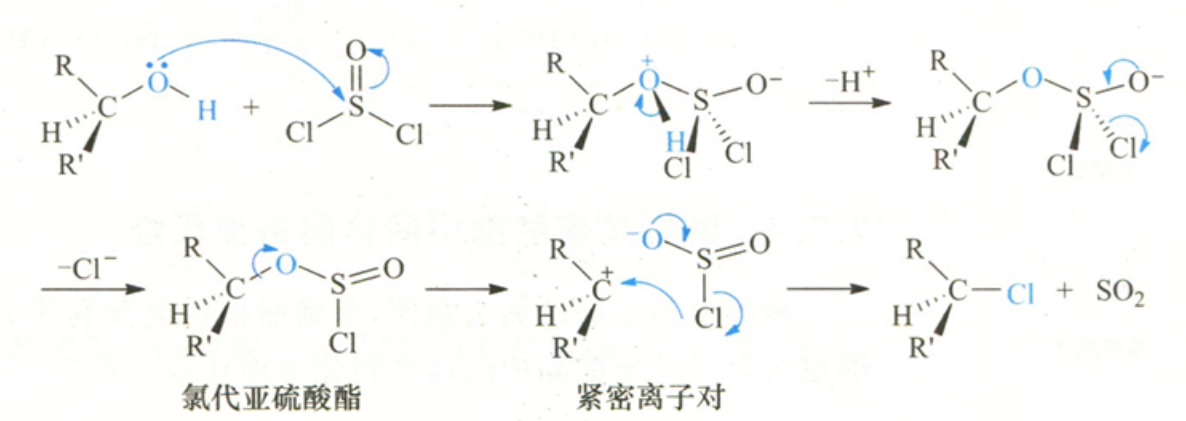
1. Chlorination: PCl_3/PCl_5 Bromination: PBr_3 (phosphorus pentabromide is unstable) Iodination: $P + I_2$
2. Mainly used for 1°, 2°
3. Low temperature to avoid rearrangement

ROH + SOCl2

$$ROH + SOCl_2 \xrightarrow{\triangle} SO_2\uparrow + HCl\uparrow + RCl$$

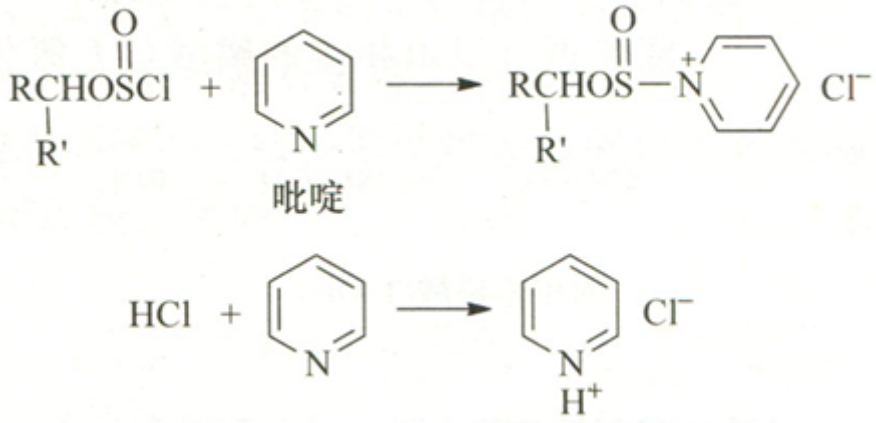
Reaction advantages: directly obtain alkyl chloride, mild conditions, fast rate, high yield, and the product is easy to purify.

The configuration of the alcohol is maintained before and after the reaction, and chlorosulfite can be separated at low temperature and decomposed into alkyl chloride and SO_2 upon heating, which indicates that the reaction mechanism is:

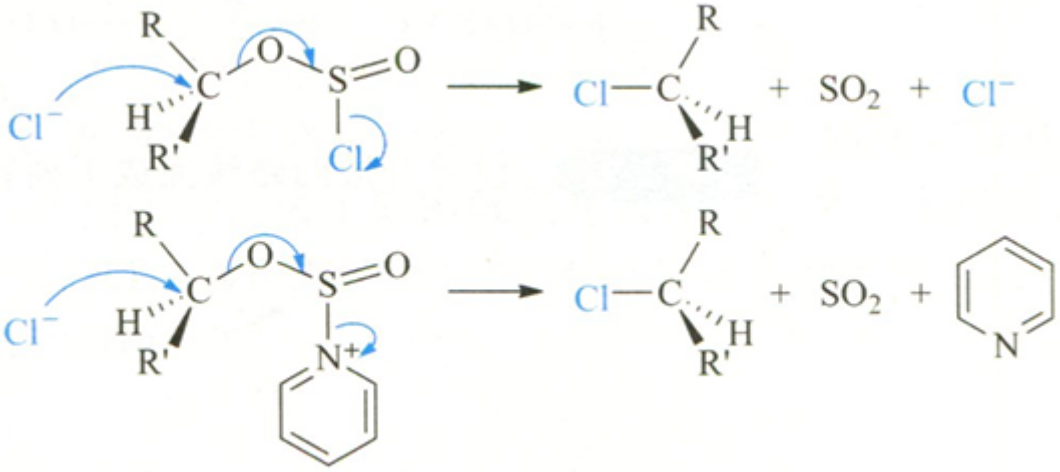


During the reaction, chlorosulfite is first generated, and then decomposes into a tight ion pair. Cl^- attacks the carbocation as part of the leaving group (LG), that is, "returns internally" to obtain the product chloroalkane with maintained configuration. Since the substitution seems to be carried out within the molecule, it is called intramolecular nucleophilic substitution, represented by S_Ni.

If the weak nucleophile pyridine is added to a mixture of alcohol and thionyl chloride, a product with a configuration flip is obtained.



The generated Cl^- is used as a nucleophile to attack chlorosulfite from the back side of the carbon-oxygen bond to obtain a configuration-inverted product (S_N2)

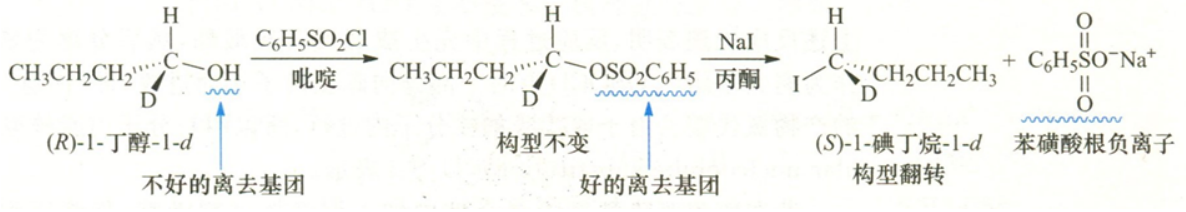


> The reaction of tertiary amines (R_3N) and HCl is also conducive to the formation of chloride ions, so tertiary amines, like pyridine, can catalyze this reaction:
>
> $$R_3N + HCl \rightarrow R_3NH^+ + Cl^-$$

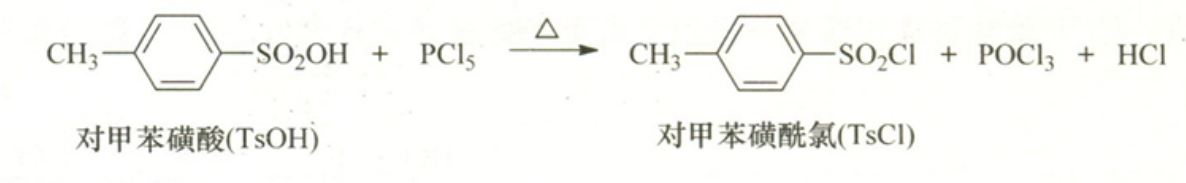
ROH + TsCl

Ts=Tosyl=p-toluenesulfonic acid group

醇羟基不是好的离去基团，苯磺酸根负电荷利于分散，是很好的离去基团，因此醇也可以经苯磺酸酯中间体再转化为卤代烃。例如



磺酰氯可以由相应的磺酸与五氯化磷反应来制备，例如

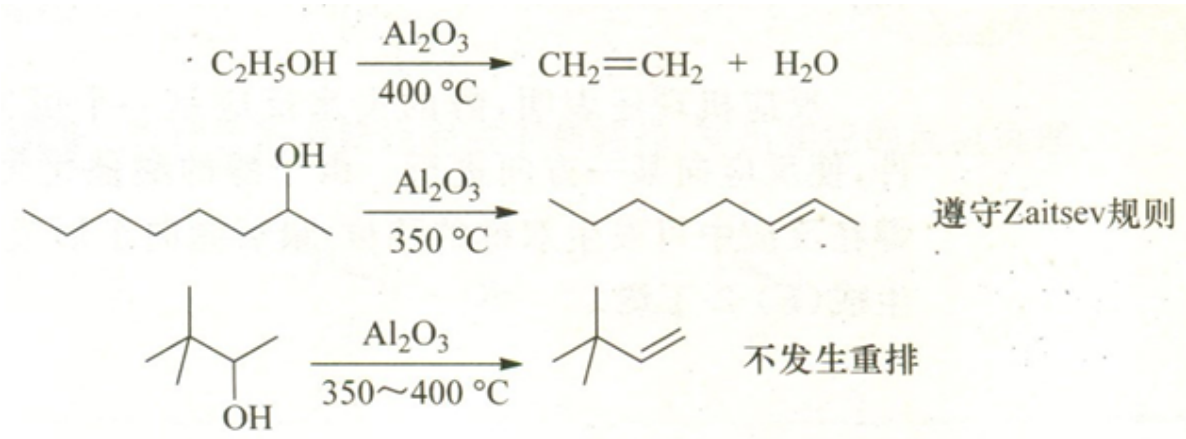


Since then, 4 methods for converting alcohols into halogenated hydrocarbons have been completed.

#PartII:Elimination of alcohol

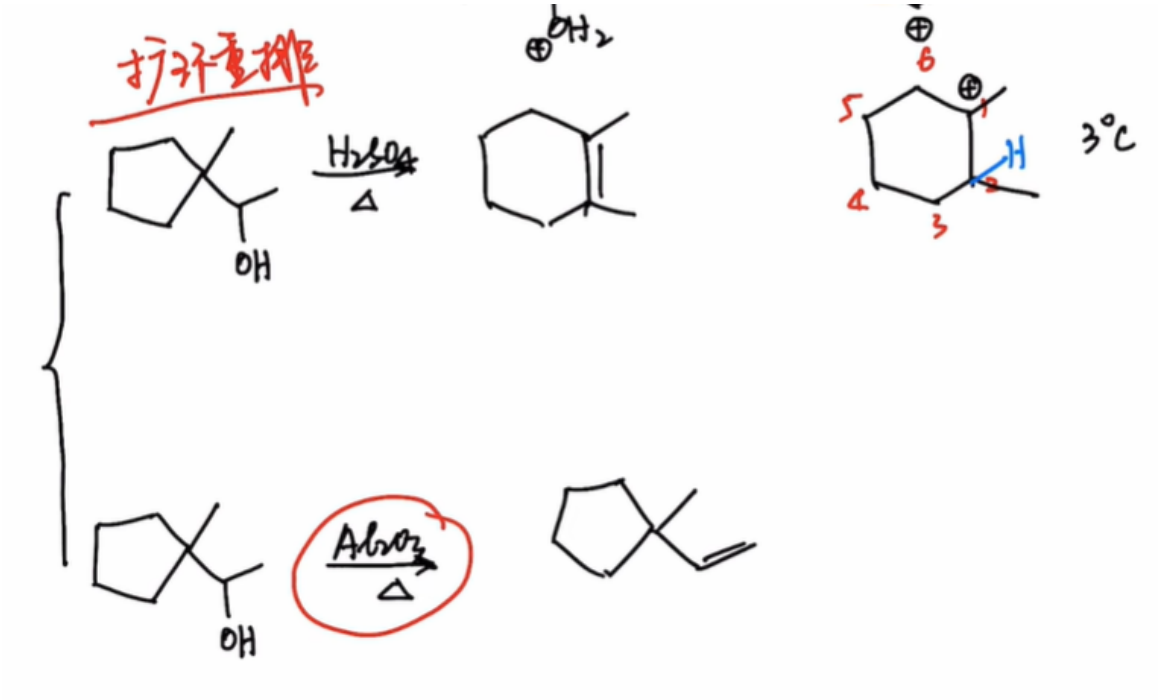
1. Protonation of hydroxyl group
2. Formation of carbocation
3. *Possible rearrangement
4. $$\text{Elimination into olefins}\begin{cases}\text{Stereoselectivity}\begin{cases}Z,\\E\end{cases}\\\text{Regional selectivity}\begin{cases}Zaitsev,\\Hoffmann\end{cases}\end{cases}$$

In industry, commonly used alcohols are dehydrated on the surface of alumina or silicate at 350~400°C. This reaction does not cause rearrangement**.



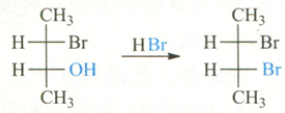
Ring expansion rearrangement

Generally speaking, for carbocations, six-membered rings have less tension and are more stable than five-membered rings.



Practice

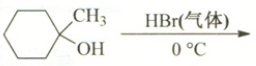
习题 7-11 请为下述反应提出合理的反应机理。

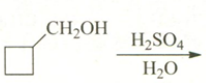


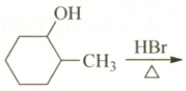
(i) 赤型 (2*R*, 3*S*)-3-溴-2-丁醇　　(ii) 内消旋

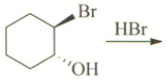
习题 7-12 完成下列反应，并提出合理的反应机理。

(i) $(CH_3CH_2)_3CCH_2OH \xrightarrow[H_2SO_4,\ \triangle]{HBr}$

(ii) 

(iii) 

(iv) 

(v) 

习题 7-13 预测下列两组醇与氢溴酸进行 S_N1 反应的相对速率。

(i) $CH_2{=}CH{-}CH_2OH$　　$O_2N{-}CH{=}CH{-}CH_2OH$　　$CH_3O{-}CH{=}CH{-}CH_2OH$

(ii) $CH_2{=}CHCH_2CH_2OH$　　$CH_2{=}CHCH_2OH$　　$CH_2{=}CHCHCH_3$ (OH)

习题 7-14 2-环丁基-2-丙醇与 HCl 反应得 1,1-二甲基-2-氯环戊烷；2-环丙基-2-丙醇与 HCl 反应得 2-环丙基-2-氯丙烷，而不是 1,1-二甲基-2-氯环丁烷。请提出一个合理的解释。