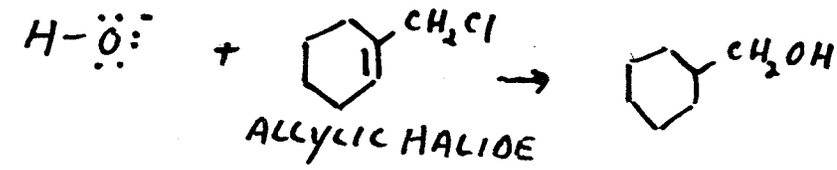
LECTURE NOTES CHAPTER 10 mm 2006

THE S_N2 MECHANISM IS WIDELY USED FOR SYNTHESIS

COMPETITION FROM ELIMINATIONS IS REDUCED BY MINIMIZING STERIC HINDRANCE AND MINIMIZING THE BASICITY OF THE NUCLEOPHILE

PREPARATION OF ALCOHOLS

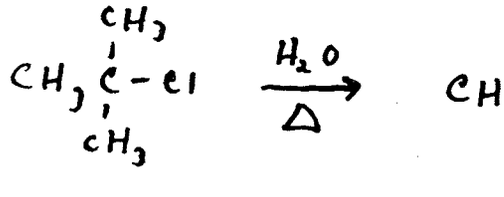
FROM ALKYL HALIDES + ^-OH OR H_2O



PRIMARY OR ALLYLIC/Be

TERTIARY SUBSTRATES REQUIRE S_N1

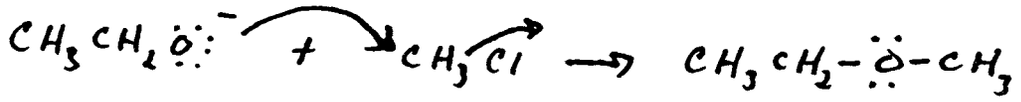
$^-:\ddot{O}H$ CAUSES E_2



CALLED "SOLVOLYSI

PREPARATION OF ETHERS - THE WILLIAMSON SYNTHESIS

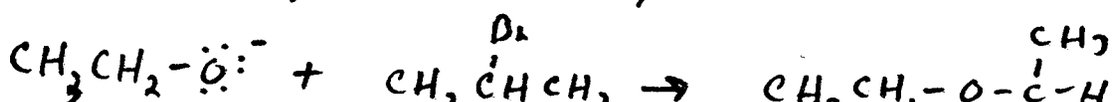
ALKOXIDE + ALKYL HALIDE → ETHER

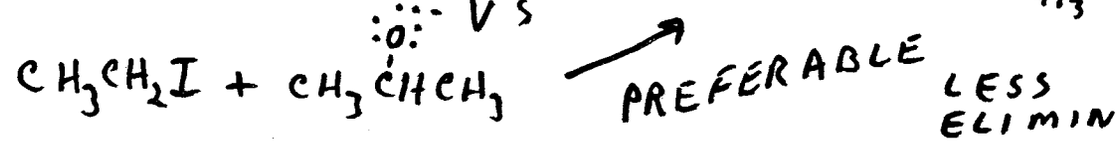


ALKOXIDES ARE MADE FROM ALCOHOLS + Na^0

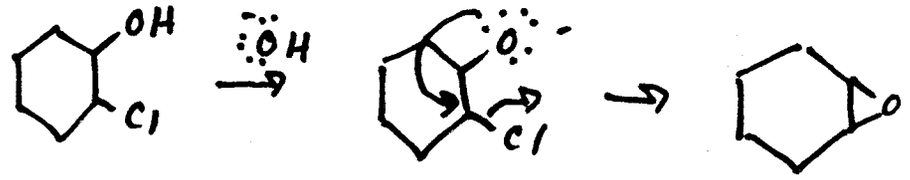
$$2\ CH_3OH + Na^0 \rightarrow 2\ CH_3\ddot{O}:^- + H_2$$

GIVEN A CHOICE, USE 1° ALKYL HALIDE





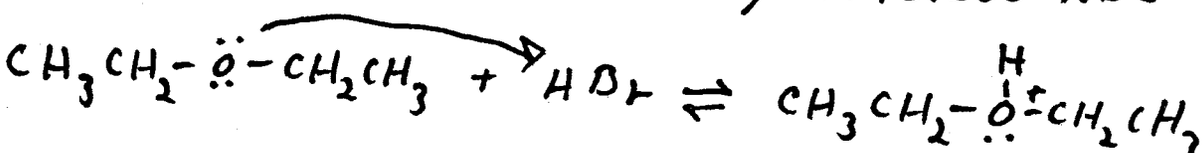
EPOXIDES ARE INTERNAL ETHERS

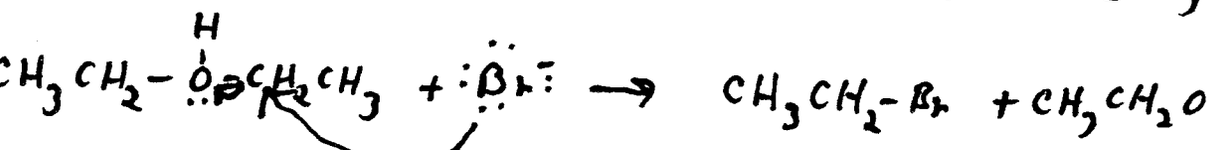


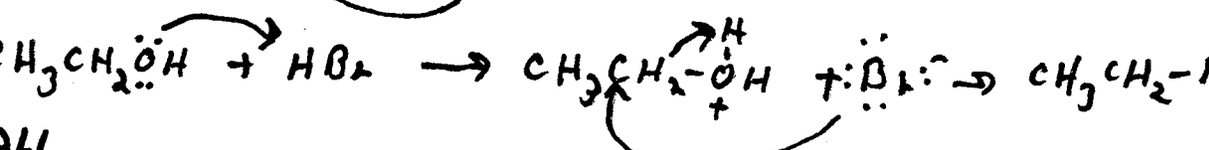
ETHER CLEAVAGE

ETHERS ARE CLEAVED BY HI

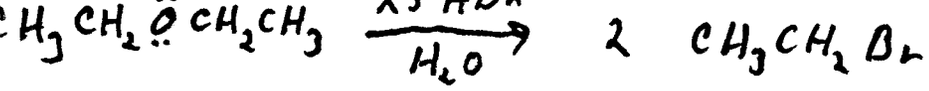
THE PROTONATED ETHER IS SUBJECT TO NUCLEOPHILIC ATTACK. ALKYL HALIDES RESULT



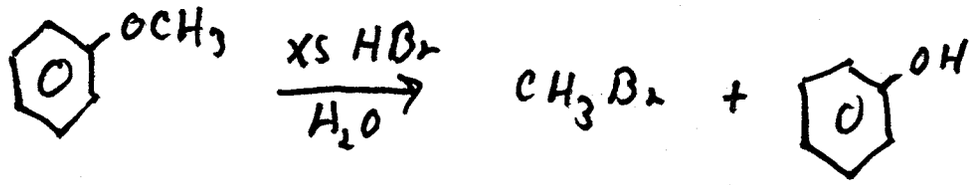




OVERALL



IF ONE ALKYL GROUP IS AROMATIC, PHENOL IS THE PRODUCT

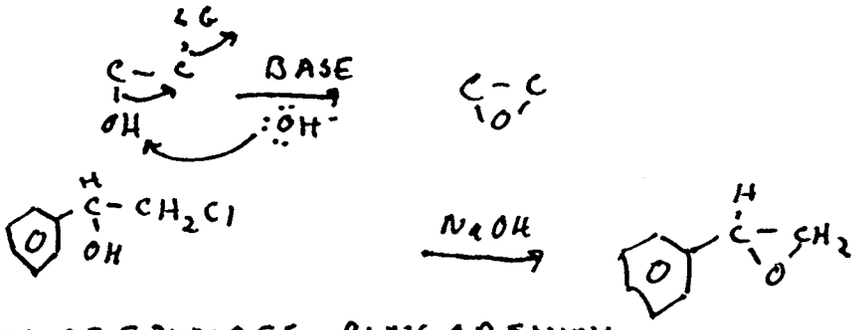


EPOXIDES REACT IN THE SAME WAY

THE EPOXIDE RING IS STRAINED

AND IS EASILY OPENED BY ANY NUCLEOPHILE

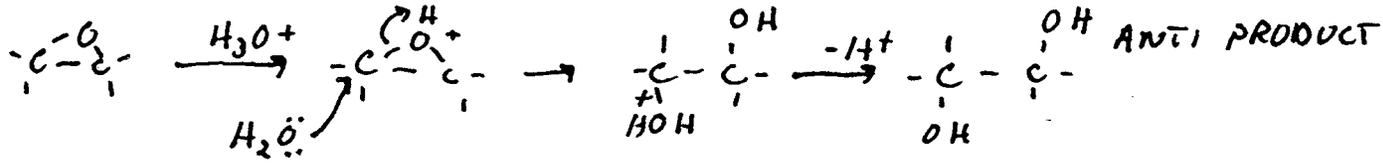
EPOXIDES MAY BE MADE BY INTERNAL S_N2



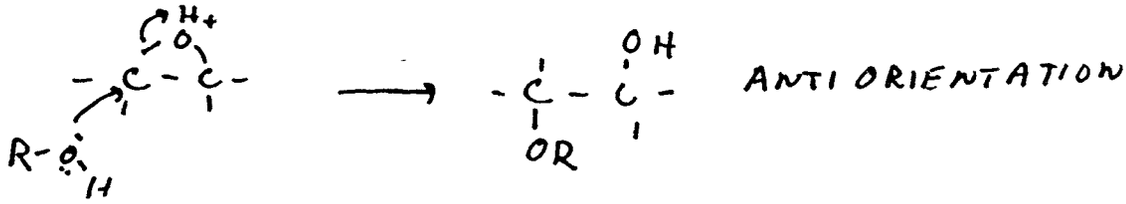
REACTIONS OF EPOXIDES - RING OPENING

ACID CATALYSED

- IN H_2O THE PROTONATED EPOXIDE IS SUBJECT TO S_N2 ATTACK

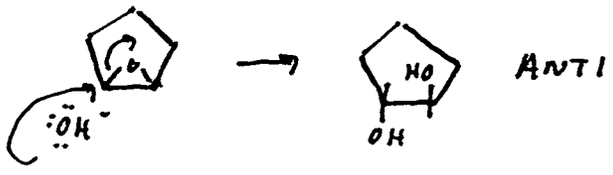


- IN R-OH THE NUCLEOPHILE IS THE ALCOHOL

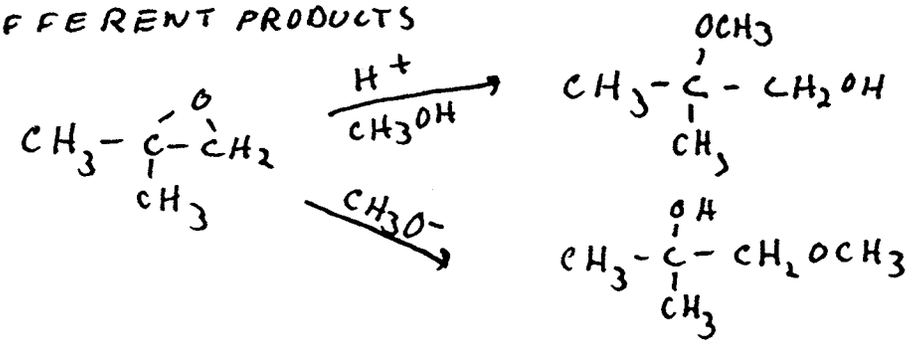


BASE CATALYSED

IN SIMPLE EPOXIDES, A BASE LIKE OH^- DOES A NUCLEOPHILIC ATTACK AND OPENS THE RING



BUT IN UNSYMMETRICAL EPOXIDES, ACID AND BASE CATALYSED REACTIONS GIVE DIFFERENT PRODUCTS



S_N2 BY WEAK NUCLEOPHILE ON MOST ELECTROPHILIC CARBON

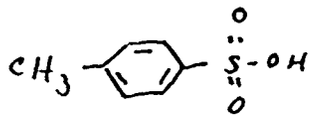
S_N2 ON LESS HINDERED SUBSTRATE

ALCOHOLS CAN ONLY BE SUBSTITUTED UNDER ACIDIC CONDITIONS

TOSYLATES OFFER A WAY AROUND THIS PROBLEM

THE TOSYLATE GROUP IS AN EXCELLENT LEAVING GROUP, AND ITS COMPATIBLE WITH STRONGLY BASIC NUCLEOPHILES

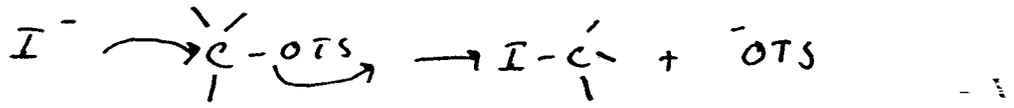
TOSYLATE

PARA-TOLUENE SULFONIC ACID 

TOSYLATES ARE MADE FROM ALCOHOLS

$$R\text{-}OH \xrightarrow[\text{PYRIDINE}]{TsCl} R\text{-}OTs$$

AS OUR BEST LEAVING GROUP, THE TOSYLATE ANION IS RESONANCE STABILIZED AND HAS 3 OXYGENS TO CARRY THE MINUS CHARGE



HAVING THE TOSYLATE GROUP FAVORS SUBSTITUTION OVER ELIMINATION ALTHOUGH ELIMINATIONS ARE STILL POSSIBLE

S_N2 Reactions of Tosylate Esters

R—OTs	+	$^-$OH (hydroxide)	⟶	R—OH (alcohol)	+	$^-$OTs
R—OTs	+	$^-$C≡N (cyanide)	⟶	R—C≡N (nitrile)	+	$^-$OTs
R—OTs	+	Br^- (halide)	⟶	R—Br (alkyl halide)	+	$^-$OTs
R—OTs	+	R′—O$^-$ (alkoxide)	⟶	R—O—R′ (ether)	+	$^-$OTs
R—OTs	+	:NH_3 (ammonia)	⟶	R—NH_3^+ $^-$OTs (amine salt)		
R—OTs	+	$LiAlH_4$ (LAH)	⟶	R—H (alkane)	+	$^-$OTs

:DUCTION OF ALCOHOLS $R\text{-}OH \rightarrow R\text{-}H$

TOSYLATES ARE REDUCED BY $LiAlH_4$

$$R\text{-}OH \xrightarrow[\text{PYRIDINE}]{TsCl} R\text{-}OTs \xrightarrow{LiAlH_4} R\text{-}H$$

EACTIONS WITH HCl AND HBr

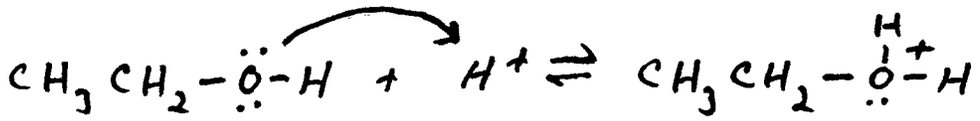
THESE STRONG ACIDS PROTONATE ALCOHOLS, MAKING A GOOD LEAVING GROUP

$$R\text{-}OH \overset{HBr}{\rightleftharpoons} R\text{-}\overset{+}{\underset{H}{O}}H \xrightarrow[S_N2 \text{ OR } S_N1]{Br^-} R\text{-}Br$$

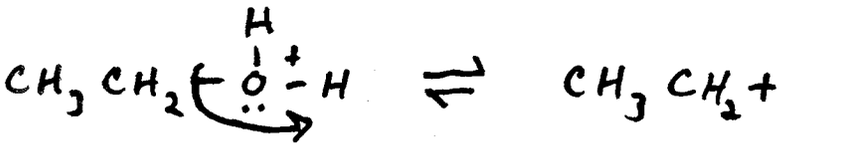
DEHYDRATION OF ALCOHOLS TO FORM ALKENES

$$CH_3CH_2OH \xrightleftharpoons{H_2SO_4} CH_2=CH_2 + H_2O$$

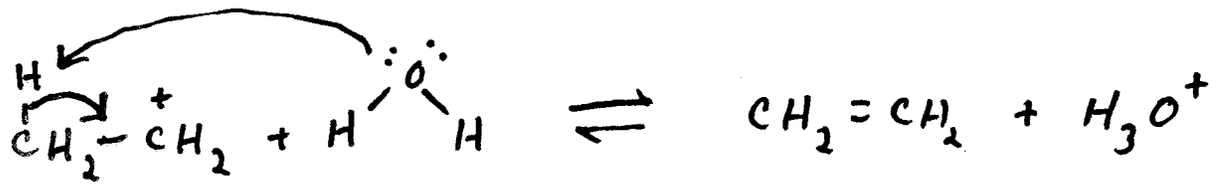
1) PROTONATION



2) LOSS OF H_2O, CATION FORMATION



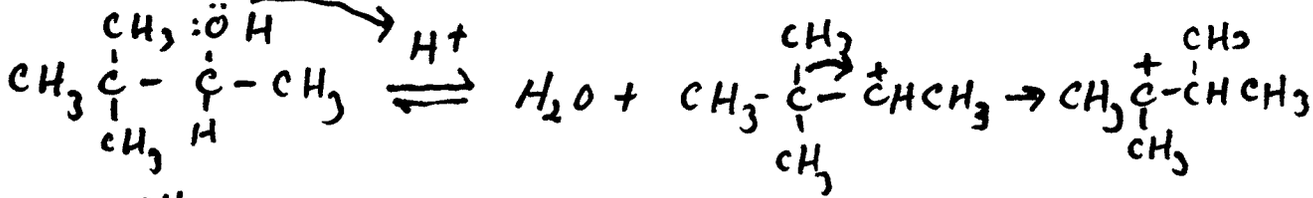
3) CARBOCATION ELIMINATES A PROTON H^+

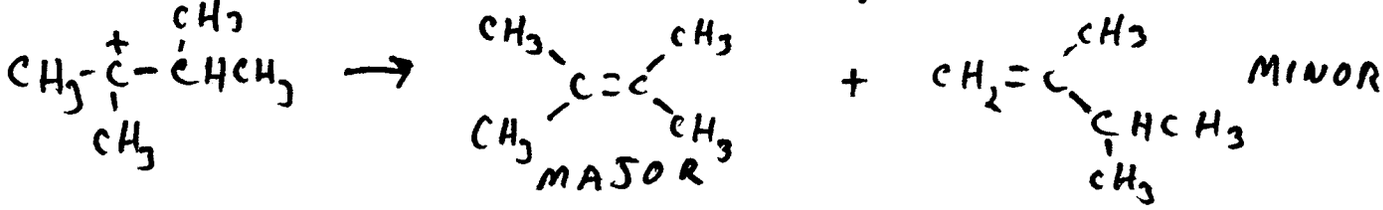


COMPLETELY REVERSIBLE, ALKENES CAN BE HYDRATED

$$CH_2=CH_2 \xrightleftharpoons{H_3O^+} CH_3CH_2OH + H^+$$

REARRANGEMENTS ARE LIKELY IN DEHYDRATIONS





CHAPTER 10

DRAW STRUCTURES FOR S_N2, S_N1, E_2, E_1 PRODUCTS — 33, 36, 40

GET THE STEREOCHEMISTRY OF EACH MECHANISM — 43, 55-58; 42, 44, 46

USE THESE REACTIONS FOR SYNTHESIS — 41, 47, 54