CHEM 203

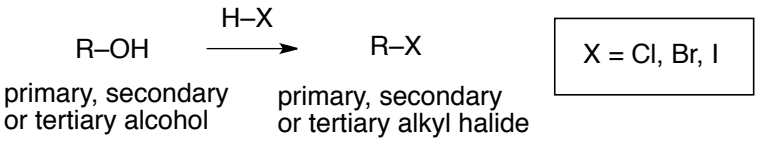
Topics Discussed on Nov. 20

Principle: protonation of alcohols transforms the OH group into an incipient molecule of H_2O, which is the conjugate base of a strong Bronsted acid, H_3O^+ (pKa ≈ –2). So, H_2O can function as a leaving group in S_N2/S_N1 or E2/E1 reactions (cf. the case of ethers; notes of Nov. 16)

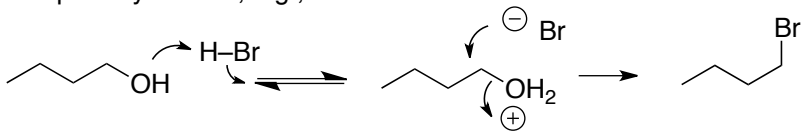
> **Note**: the OH group *per se* cannot function as a leaving group in S_N2/S_N1 or E2/E1 reactions, because then it would have to leave as HO^-, which is the conjugate base of the weak acid, H_2O (pKa≈16). Recall that only conjugate bases of strong acids (pKa<0) can function as leaving groups in such reactions (notes of Oct. 28).

Reactions in which a protonated alcohol undergoes nucleophilic substitution of H_2O:

Reactions of alcohols with H–X: formation of alkyl halides:

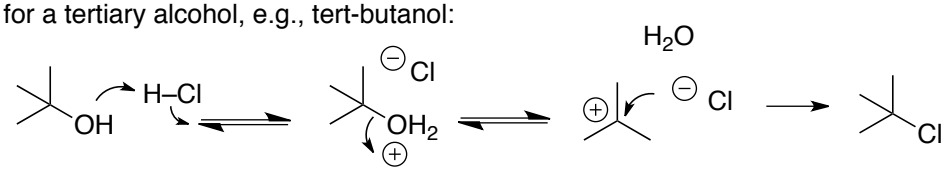


for a primary alcohol, e.g., 1-butanol:



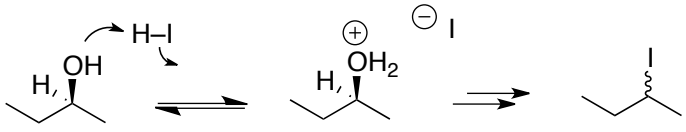
primary: backside readily accessible
⇨ reacts by S_N2 mechanism

for a tertiary alcohol, e.g., tert-butanol:



tertiary: backside inaccessible
⇨ reacts by S_N1 mechanism

for a secondary alcohol, e.g., (*S*)-2-butanol:



alkyl halide may forms with partial erosion of stereochemical purity

secondary: backside fairly accessible
⇨ tends to react partly by S_N2 and partly by S_N1 mechanism: precise extent of S_N2 / S_N1 reactivity depends on structure and conditions

Principle: alkyl halides are best prepared from alcohols

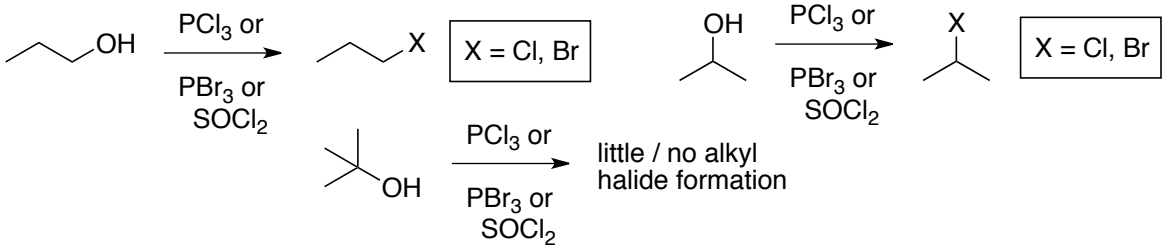
Potential usefulness of halogenation reagents that might permit the conversion of secondary alcohols into secondary halides in a stereochemically unequivocal manner (= 100% inversion or 100% retention of configuration)

Phosphorus and sulfur halides that convert alcohols to alkyl halides in a stereochemically clean manner: phosphorus trichloride / tribromide (PCl_3, PBr_3), thionyl chloride ($SOCl_2$)

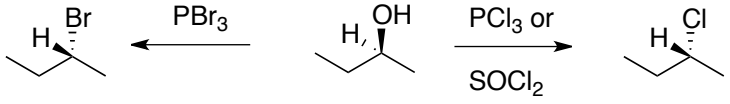
Electrophilic character of the above reagents and facile reaction thereof with nucleophiles

Principle: the above reagents rely on the **nucleophilic** properties of the OH group to achieve conversion of alcohols into alkyl halides

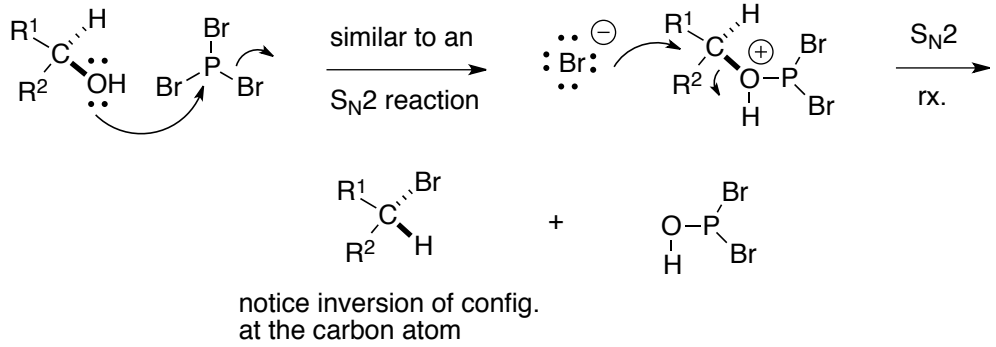
Principle: only primary and secondary alcohols are sufficiently nucleophilic to react with the above reagents. The OH group of tertiary alcohols is poorly nucleophilic due to steric hindrance:



Inversion of configuration during the reaction of secondary alcohols with the above reagents:



Probable mechanism of the conversion of primary / secondary alcohols to alkyl bromides with, e.g., PBr_3 (PCl_3 reacts in the same fashion):



notice inversion of config.
at the carbon atom

note: $HO–PBr_2$ still posseses P–Br bonds, so it may undergo a 2nd and a 3rd round of the same reaction, ultimately producing phosphorous acid, $P(OH)_3$

Probable mechanism of the conversion of primary and secondary alcohols into alkyl chlorides with $SOCl_2$: