The form used for describing preparations is: substrate reagent

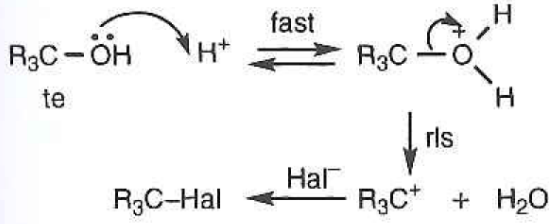
## 1 ROH

**a HHal** / 20° (room temp) or Δ if necessary

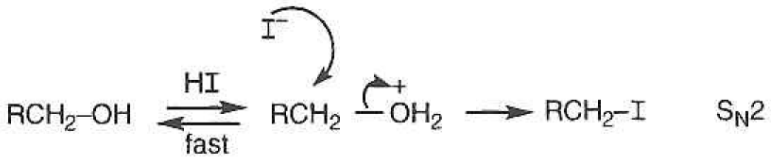
$ROH + HHal \longrightarrow RHal + H_2O$

concentrated aqueous acids

| | | HCl | HBr | HI |
|---|---|---|---|---|
| ROH | te | *yes* | *yes* | *yes* |
| | se | *no* | *yes (slow)* | *yes* |
| | pm | *no* | *no* | *yes* |




$S_N1$



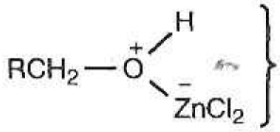

$S_N2$

but not with $Cl^-$ or $Br^-$ (weaker $Nu^-$, **1.11Ge**)

Potency of HHal increased by using e.g.

'dry' HBr (no $H_2O$) reaction potentially reversible, absence of $H_2O$ drives reaction

'dry' HBr / sq $H_2SO_4$ increases amount of protonated alcohol (sq = small quantity)

$HCl / ZnCl_2$ forms  better $L^-$ than $H_2O$



**b P–Hal reagents** driving force is formation of very strong PO double bond

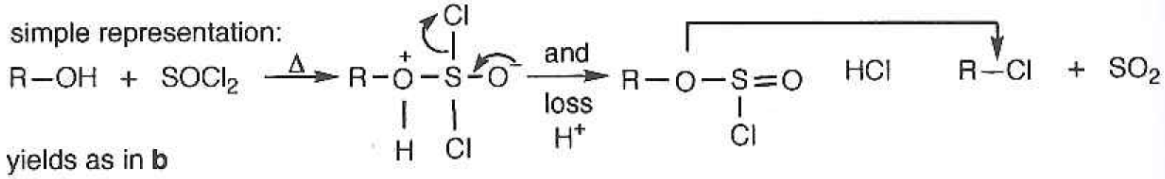
yields pm > se > te ◄---- tend to give elimination

$PHal_3$ (Cl, Br, I) or mixtures P / $Br_2$, P / $I_2$ $PBr_3$ / / 10° is good method

several modern developments e.g. $PPh_3 / Br_2$, $PPh_3 / CCl_4$

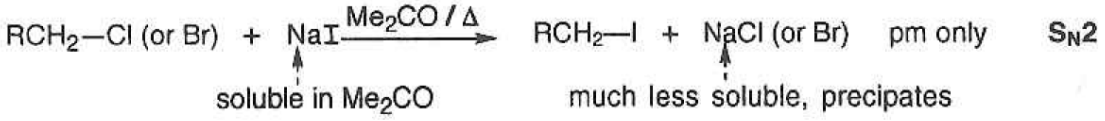
**c $SOCl_2$ (thionyl chloride)**

simple representation:



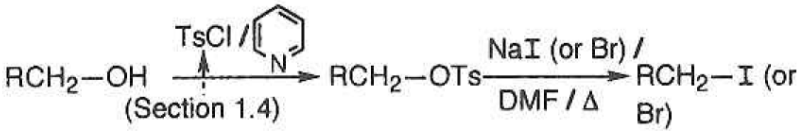

yields as in **b**

## 3 RHal (i.e. from halides obtained by the other methods given here)




direction contrary to expectation from nucleophilicities in aprotic solvents (Section 1.13); reaction driven by precipitation of NaCl (or Br)

useful development:



## 2.1Re

**1 With $Nu^-$** Yields pm—good, se—modest, te—poor

Δ unless stated otherwise

**a** **R–Hal** $\xrightarrow[\text{EtOH}]{\text{KOH / } H_2O \text{ /}}$ R–OH *alcohols*

to dissolve RHal

**b** **R–Hal** $\xrightarrow{Na^+\ ^-O-R^1}$ R–O–$R^1$ *ethers*

R and R′ may be identical or different; highest yields with both pm

**c** **R–Hal** $\xrightarrow[Et_2O]{R^1-CO-OAg \text{ /}}$ R–O–CO–$R^1$ *esters*

**d** **R–Hal** $\xrightarrow{K^+\ SH^- \text{ / EtOH}}$ R–SH *thiols* (vile smell)

**e** **R–Hal** $\xrightarrow{K^+\ ^-SR^1 \text{ / EtOH}}$ R–S–$R^1$ *thioethers* (vile smell)

**f** **R–Hal** $\xrightarrow{H-N\langle}$ R–N$\langle$ *amines*

e.g. Me–Br + $NH_3$ → $MeNH_2$

**g** **R–Hal** $\xrightarrow{R^1_3N}$ R–$\overset{+}{N}R^1_3$ $Hal^-$ *quaternary ammonium salts*

**h** **R–Hal** $\xrightarrow{R^1_3P}$ R–$\overset{+}{P}R^1_3$ $Hal^-$ *phosphonium salts*

**i** **R–Hal** $\xrightarrow[\text{(sodium azide)}]{NaN_3 \text{ / MeOH}}$ R–$N_3$ *azides*

see notes about **i**,**j** and **k** at bottom of this scheme

**j** **R–Hal** $\xrightarrow{NaNO_2 \text{ / DMF / } 20°}$

more convenient than $AgNO_2$ / $Et_2O$

→ R–$N^+(=O)O^-$ *nitro compounds* major product

→ R–O–N=O *nitrite esters* minor product

**k** **R–Hal** $\xrightarrow[\text{EtOH or in DMSO}]{\text{NaCN in } H_2O \text{ /}}$ R–C≡N *nitriles* ~90%

Et–I $\xrightarrow[\text{no solvent}]{AgCN}$ Et–$\overset{+}{N}$≡$\overset{-}{C}$ *isonitrile* (50%) (vile smell)

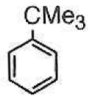
AgCN reaction is complex, reliable results not available for many R–Hal; not general Pr of R–NC

**l** **R–Hal** $\xrightarrow{\overset{-}{C}\equiv C-R^1}$ R–C≡C–$R^1$ *disubstituted alkynes*

**m** **R–Hal** $\xrightarrow{CH_3-CO-\overset{-}{C}H-CO_2Et}$ $CH_3$–CO–CH(R)–$CO_2Et$

**n** **R–Hal** $\xrightarrow{\overset{-}{C}H(CO_2Et)_2}$ R–CH($CO_2Et$)$_2$

**o** **R–Hal** $\xrightarrow{Li\overset{-}{C}uR^1_2}$ R–$R^1$ **4.2Pr2c**

**p** **R–Hal** $\xrightarrow{ArH \text{ / } AlCl_3}$ R–Ar e.g. $\xrightarrow[AlCl_3]{Me_3C-Cl \text{ /}}$ 


Friedel–Crafts reaction, mechanism different from others here, range of R–Hal can be used