The most common methods for converting 1º- and 2º-alcohols to the corresponding chloro and bromo alkanes (i.e. replacement of the hydroxyl group) are treatments with thionyl chloride and phosphorus tribromide, respectively. These reagents are generally preferred over the use of concentrated HX due to the harsh acidity of these hydrohalic acids and the carbocation rearrangements associated with their use.

Synthetic organic chemists, when they want to convert an alcohol into a better leaving group, have several methods to choose from. One common strategy is to convert the alcohol into an alkyl chloride or bromide, using thionyl chloride or phosphorus tribromide:

\[
\begin{align*}
\text{OH} & \quad + \quad \text{Cl-SOCl}_2 \quad \xrightarrow{\text{Pyr}} \quad \text{Cl} \quad + \quad \text{SO}_2 \quad (g) \\
\end{align*}
\]

\[
\begin{align*}
3 \quad \text{OH} & \quad + \quad \text{PBr}_3 \quad \xrightarrow{} \quad 3 \quad \text{Br} \quad + \quad \text{H}_3\text{PO}_4 \\
\end{align*}
\]

**Drawbacks to using \((\text{PBr}_3\)) and \((\text{SOCl}_2))**

Despite their general usefulness, phosphorous tribromide and thionyl chloride have shortcomings. Hindered 1º- and 2º-alcohols react sluggishly with the former, and may form rearrangement products, as noted in the following equation.

Below, an abbreviated mechanism for the reaction is displayed. The initially formed trialkylphosphite ester may be isolated if the HBr byproduct is scavenged by base. In the presence of HBr a series of acid-base and Sn2 reactions take place, along with the transient formation of carbocation intermediates. Rearrangement (pink arrows) of the carbocations leads to isomeric products.

Reaction of thionyl chloride with chiral 2º-alcohols has been observed to proceed with either inversion or retention. In the presence of a base such as pyridine, the intermediate chlorosulfite ester reacts to form an "pyridinium" salt, which undergoes a relatively clean Sn2 reaction to the inverted chloride. In ether and similar solvents the chlorosulfite reacts with retention of configuration, presumably by way of a tight or intimate ion pair. This is classified as an Sni reaction (nucleophilic substitution internal). The carbocation partner in the ion pair may also rearrange. These reactions
are illustrated by the following equations. An alternative explanation for the retention of configuration, involving an initial solvent molecule displacement of the chlorosulfite group (as SO$_2$ and chloride anion), followed by chloride ion displacement of the solvent moiety, has been suggested. In this case, two inversions lead to retention.

**Example 1: Conversion of Alcohols to Alkyl Chlorides**

\[
\text{OH} \quad \xrightarrow{\text{SOCl}_2} \quad \text{Cl} \quad + \text{HCl} + \text{SO}_2
\]

There’s one important thing to note here: see the stereochemistry? It’s been inverted.* (white lie alert – see below) That’s an important difference between \(\text{SOCl}_2\) and \(\text{TsCl}\), which leaves the stereochemistry alone. We’ll get to the root cause of that in a moment, but in the meantime, can you think of a mechanism which results in inversion of configuration at carbon?

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**Formation of Alkyl Chlorides**

Since the reaction proceeds through a backside attack (\((S\_N2)\)), there is inversion of configuration at the carbon

The mechanism for formation of acid chlorides from carboxylic acids is similar. The conversion of carboxylic acids to acid chlorides is similar, but proceeds through a \([1,2]\)-addition of chloride ion to the carbonyl carbon followed by \([1,2]\)-elimination to give the acid chloride, \(\text{SO}_2\) and \(\text{HCl}\)

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**Formation of Alkyl Bromides**

The PBr$_3$ reaction is thought to involve two successive \(S\_N2\)-like steps:
Notice that these reactions result in inversion of stereochemistry in the resulting alkyl halide.

Contributors