Conversion of Acids into Acid Chlorides and Alcohols into Alkyl Chlorides Using a Polymer-supported Phosphine in Carbon Tetrachloride

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Summary Carboxylic acids can be converted into acid chlorides and alcohols into alkyl halides under neutral conditions by treatment with a polymer-supported phosphine in carbon tetrachloride, the reaction being largely worked up by filtration.

CARBOXYLIC acids react smoothly with Ph_3P in CCl_4 to give acid chlorides.[1] Alcohols react similarly to give alkyl chlorides[2] (see equation). As preparative methods these reactions have the attractive feature that the conditions are

$$\begin{array}{c} RCO_2H \\ \text{or} \\ ROH \end{array} + CCl_4 + Ph_3P \longrightarrow \begin{array}{c} RCOCl \\ \text{or} \\ RCl \end{array} + CHCl_3 + Ph_3P{=}O$$

essentially neutral; in particular no HCl is evolved. However, the separation of the products from Ph_3PO can present problems[3] if the products are not volatile or if the reaction has been carried out on only a small scale. Involatile alkyl halides may be separated by column chromatography but this is not possible with acid chlorides. We report that these separation problems can be overcome by using a polymer-supported Ph_3P. At the end of the reaction, filtration removes the excess and spent phosphine and leaves a solution of the product and any unchanged starting material.

TABLE 1. Conversion of acids into acid chlorides by treatment with phosphine resin (2 equiv.) in CCl_4 under reflux for 4 h

Acid	Yield of Derivative (%)	Derivative	Recovered acid (%)
n-Octanoic	63	Amide	7
Phenoxyacetic	50	Anilide	5
Stearic	82	Amide	13
Lithocholic acid acetate	82[a]	Methyl ester	13[b]
Cinnamic	77	*p*-Toluidide	5
Benzoic	90	*p*-Toluidide	3
α-Furoic	82	*p*-Toluidide	8
β-Naphthoic	84	Methyl ester	11

[a] 3 equiv. of phosphine used. [b] Not isolated. The figure given is the total recovery less the yield of ester.

The Ph_3P resin was prepared by brominating polystyrene crosslinked with 1% of divinylbenzene[4] and treating the product with lithium diphenylphosphide[5] The product generally contained (by elemental analysis) *ca.* 2·5 mmol of phosphine per gram (Ph_3P itself has 3·82 mmol/g). The results are summarised in Tables 1 and 2. Generally 1 or 2 mmol of substrate was treated with 2 mol equiv. of phosphine resin and at the end of the reaction period the polymer was removed by filtration. In the reactions with acids an i.r. spectrum of the filtrate was measured before it was treated with an amine or alcohol to afford a solid derivative. Some acid was always recovered and judging from the i.r. spectrum of the initial product this was largely due to the presence of some anhydride. Anhydride was also formed in similar small-scale reactions using monomeric phosphine. When the ultimate object is to prepare an amide this problem can be overcome by treating the acid with the reagent in the presence of the amine,[6] since then any anhydride reacts to give amide and acid, and the latter is recycled. Thus, treatment of phenoxyacetic acid and aniline with the phosphine resin in CCl_4 gave the anilide (57%), and benzoic acid and *p*-toluidine reacted similarly to give the toluidide (94%). It can be seen from the Tables that recoveries and yields were usually good even with substrates as large as steroids.

TABLE 2. Conversion of alcohols into alkyl chlorides by treatment with phosphine resin (2 equiv.) in CCl_4 under reflux

Alcohol	Reaction time (h)	Yield of chloride (%)	Recovered alcohol (%)
n-Octanol	1·5	98[a,b]	0
2-n-Butoxyethanol ..	1	94[a]	0
Benzyl alcohol ..	1	88[a]	0
Hexadecyl alcohol ..	2	98[c]	–
4-Hydroxymethyl-2,2-Dimethyl-1,3-dioxolan	6	78[a]	5
Cyclohexanol ..	5	40[a,d]	0
5β-Cholan-24-ol ..	2·5	78[e]	–

[a] By g.l.c. analysis. [b] From a reaction using 5 mmol of octanol octyl chloride was isolated in 76% yield by careful removal of the solvent and short-path distillation of the residue. [c] Chloride isolated as an oil, pure by g.l.c., with spectroscopic data (i.r., ^1H n.m.r.) identical with that of an authentic sample. [d] Cyclohexene (50%) was also formed. [e] Yield of recrystallised material m.p. 74—75 °C with satisfactory ^1H n.m.r. spectrum.

Relles and Schluenz[5] have recently reported a few examples of similar conversions using a Ph_3PCl_2 resin, but in these reactions molar quantities of HCl were produced.

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