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The reaction of hydrogen chloride with primary alcohols, which occurs slowly and in poor yields in water, has been found to give good yields of alkyl chlorides in 30–45 min at 70–85 $^{\circ}$ C in the solvent hexamethylphosphoric triamide. 2-Octanol and neopentyl alcohol required longer reaction periods. Neopentyl chloride was formed without contamination by rearrangement products.

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La réaction de l'acide chlorhydrique avec les alcools primaires, qui se produit lentement et avec de faibles rendements dans l'eau, conduit à des bons rendements en chlorure d'alkyle en 30-45 min, à 70-85 °C, dans le HMPT comme solvant. L'octanol-2 et l'alcool néopentylique demandent des périodes de réaction plus longues. Le chlorure de néopentyle se forme sans contamination par des produits de réarrangement.

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The much greater reactivity of aqueous hydriodic acid compared with hydrochloric acid toward primary alcohols is usually attributed to the greater nucleophilicity of iodide ion (vs. chloride). Both acids are sufficiently strong to protonate alcohols extensively, but the subsequent $S_N 2$ displacement of water from the protonated alcohol occurs readily only with iodide. For this reason the conversion of primary alcohols to chlorides with hydrochloric acid usually requires quite high temperatures and the addition of large amounts of zinc chloride, or poor yields are the result (1).

It has occurred to us that the reaction rate could be increased by making use of the greater nucleophilicity of chloride ion in dipolar aprotic solvents compared with protonic solvents (2). We have chosen to examine hexamethylphosphoric triamide (HMPT), because it is moderately resistant to acid attack (3), and the products of such attack by hydrogen chloride are readily separated from alkyl chlorides.

The reaction is carried out at 50-85 °C using a 35-37% (by weight) solution of hydrogen

chloride in HMPT. Within 30 min the alcohol is essentially undetectable by gas chromatography. Yields given in Table 1 are based on isolated products.

The reaction appears to be a convenient method giving very good yields, for the conversion of primary alcohols to the corresponding chloride. The mechanism may involve direct attack of chloride ion on a protonated alcohol:

$$\begin{array}{ccc} H^+ & + & Cl^- \\ \text{RCH}_2\text{OH} & \rightleftarrows & \text{RCH}_2\text{OH}_2 & \rightarrow & \text{RCH}_2\text{Cl} + H_2\text{O} \\ & & S_N^2 \end{array}$$

but the intervention of a reagent containing a phosphorus-chloride bond (formed by the reaction of hydrogen chloride with HMPT) cannot at present be ruled out.

When optically active 2-octanol was used as substrate, the resulting 2-chlorooctane was racemized, probably by repeated displacement of chloride from the initially formed product by the chloride ion in the reaction mixture. No conclusions can therefore be drawn concerning the mechanism of hydroxyl replacement.

Experimental

The reagent is prepared by slowly passing hydrogen chloride gas from a commercial cylinder into HMPT. The mixture is allowed to warm somewhat to prevent crystal-

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FUCHS AND COLE: SYNTHESIS IN HMPT

| Product | b.p. (°C) | i.r.(C–Cl, cm ⁻¹) | Reaction temperature (°C) | Yield (%) | | | |
|----------------------------------|--------------------|-------------------------------|---------------------------|-----------|--|--|--|
| -Chlorohexane | 130–133 | 650, 704 | 75–85 | 76 | | | |
| I-Chlorooctane | 120-123 (137 Torr) | 654, 790 | 7585 | 87 | | | |
| 2-Chlorooctane* | 115 (140 Torr) | 672 | 75-87 | 89 | | | |
| I-Chlorobutane | 74–78 | 653, 709 | 70–80 | 74 | | | |
| Neopentyl chloride† | 80-85 | 714, 900 | 71-80 | 65 | | | |
| <i>n</i> -Methoxybenzyl chloride | 116 (10 Torr)‡ | 680 | 50-65 | 87 | | | |

| TABLE 1 | Reaction of | alcohols | with hydrogen | chloride in | HMPT |
|----------|-------------|----------|---------------|-------------|------------|
| IADLC I. | Reaction of | alconois | with nyulogon | cinoriae m | T T TATA T |

*When the temperature was raised to 100 °C the crude product of 2-chlorooctane showed (by g.c.) large amounts of 2-octene and unchanged 2-octanol. *Although unchanged neopentyl alcohol was detected in the pentane extract, a g.c. analysis showed no traces of products of rearrangement. A number of other cases of neopentyl displacement in HMPT without rearrangement have recently been reported (6), although these reactions were not under acidic conditions. Neopentyl chloride has been prepared from the alcohol in two steps (53% overall yield) via neopentyl tosylate, and in unstated yield by the reaction of the alcohol with triphenylphosphine and carbon tetrachloride (6). ‡Reported (4, 5) 55 °C at 0.3 Torr, 124 °C at 13 Torr.

lization, but is maintained below 115 °C. Above this temperature an exothermic reaction occurs resulting in solvent decomposition. Gas flow is continued until the composition reaches 35-37% hydrogen chloride by weight. Smaller concentrations of hydrogen chloride lead to incomplete conversion, as do molar ratios (HCl:ROH) appreciably less than 10.

1-Chlorohexane was prepared by mixing 4.2 g (39 mmol) of 1-hexanol with 40 g of the HMPT HCl reagent and heating on the steam bath for 45 min. The mixture was diluted with 50 ml of ice and water and was extracted twice with 40 ml of hexane. The organic layer was washed with sodium bicarbonate solution and with water, dried with magnesium sulfate, and filtered. Hexane was removed on a rotary evaporator and the residue of 1chlorohexane was distilled at 130-133 °C (lit. (1) 131-134 °C) to give 3.59 g (76% yield). The identity of the product was confirmed by comparison of the g.c. retention time and i.r. spectrum with those of an authentic sample.

1- and 2-chlorooctanes, 1-chlorobutane, m-methoxybenzyl chloride, and neopentyl chloride were prepared by a procedure similar to that described for the preparation of 1-chlorohexane.

When hydrogen fluoride replaced hydrogen chloride in the reactions described above, no trace of alkyl fluoride was found.

Further studies are required before the stereochemical and mechanistic details of this reaction can be more fully understood.

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