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A rapid, mild procedure for the preparation of alkyl chlorides and bromides

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Primary and secondary alkyl chlorides have been conveniently prepared by the reaction of tri-*n*-octylphosphine with carbon tetrachloride solutions of the corresponding alcohols. This rapid, high yield reaction proceeds with inversion of configuration. By using carbon tetrabromide the method has been extended to the synthesis of alkyl bromides.

[4]

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The formation of ylid **1** ($\mathbf{R} = C_6H_5$) and triphenylphosphine dihalide (**2**) from the interaction of triphenylphosphine with carbon tetrahalides (eq. [1]) was simultaneously and independently discovered by Rabinowitz and Marcus (1) and Ramirez and co-workers (2). An ionic

[1]
$$2 R_3 P + CX_4 \rightarrow R_3 P = CX_2 + R_3 PX_2$$
$$X = Cl, Br \qquad 1 \qquad 2$$

mechanism involving nucleophilic displacement on halogen has been invoked (3) to account for the formation of these products (eqs. [2] and [3]).

$$\begin{bmatrix} 2 \end{bmatrix} R_{3}P : \stackrel{+}{+} X \stackrel{\frown}{-} C X_{3} \rightarrow R_{3}P X \bar{C} X_{3} \rightarrow R_{3}P \bar{C} X_{3} \bar{X}$$

$$3 \qquad 4$$

$$\begin{bmatrix} 3 \end{bmatrix} R_{3}P : \stackrel{+}{+} X \stackrel{\frown}{-} C P R_{3}\bar{X} \rightarrow R_{3}P = C X_{2} + R_{3}P X_{2}$$

$$\downarrow$$

Ylids of structure 1 ($R = C_6H_5$) possess considerable synthetic potential since they provide a route to otherwise difficultly accessible 1,1-dihaloalkenes on reaction with carbonyl compounds (1, 2, 4). Reagents of the type R_3PX_2 ($R = C_6H_5$ or $n-C_4H_9$) have been demonstrated to permit the conversion of alcohols to alkyl halides to proceed generally without complication of elimination or rearrangement (5, 6); in addition, they convert phenols to aryl halides (6, 7) without formation of position isomers.

The present study arose out of a consideration that intermediates of structure 3 (or 4) could be trapped by reaction with alcohols to provide 5 (or 6), e.g.

$$R_3 \stackrel{+}{P} X \overline{C} X_3 + R'OH \rightarrow R_3 \stackrel{+}{P} X \overline{O}R' \rightarrow R_3 \stackrel{+}{P} OR' \overline{X} + HCX_3$$

5 6

The anticipated collapse of 6 to alkyl halide and tertiary phosphine oxide finds ample analogy in a related study (8).

$$R_3 \overline{P}OR' \overline{X} \rightarrow R'X + R_3 PO$$

Accordingly, we have found that phosphines smoothly convert alcohols to chlorides (eq. [5]).

[5]
$$R_3P + R'OH + CCl_4 \rightarrow R'Cl + R_3PO + HCCl_3$$

where $R = n \cdot C_8H_{17}$ or C_6H_5

Using tri-*n*-octylphosphine (TOP) and primary alcohols, conversions are of the order 90–100% in favorable cases. Triphenylphosphine may also be used at longer reaction times.¹ Although no attempts at optimization have been made, we find that this facile transformation is conveniently accomplished (for chlorides) by adding a slight excess over one mole equivalent of TOP to a solution of alcohol in carbon tetrachloride as solvent. A vigorous reaction ensues which is complete, in the case of primary alcohols, in ca. 5 min. The product is readily isolated by standard methods of distillation and chromatography (cf. Experimental).

Typical results are the formation of n-C₅H₁₁Cl (94%), C₆H₅CH₂Cl (100%), n-C₈H₁₇Cl (93%), and C₆H₅CH₂CH₂Cl (66%).²

Secondary alcohols also react. Thus, after ca. 5 min reaction time, *sec*-butyl chloride and 2-chlorooctane were formed in 60% and 80% yields, respectively, from the corresponding alcohols. When (+)-2-octanol was subjected to this reaction, (-)-2-chlorooctane was obtained in 90% optical purity, a result consistent with a bimolecular displacement process accompanied by a Walden inversion in the product determining step (eq. [4]).

The incursion of a competing olefin-forming elimination process renders this method of

¹Recently, and concurrent with the present work, a similar study has been reported (10) using triphenyl-phosphine.

²Analysis by gas-liquid partition chromatography.

limited value for the preparation of tertiary chlorides. For example, t-butanol gave only 13-15% t-butyl chloride, and isobutylene was detected by gas-liquid partition chromatography (g.l.p.c.).

Bromides may also be prepared by this method but in this case the ratio of reagents is ROH: TOP:CBr₄ = 1:2:2. Diethyl ether is a suitable solvent. In this manner n-C5H11Br (97%) and $C_6H_5CH_2Br$ (96%)² were formed after ca. 5 min reaction time.

In view of the mild conditions employed and good yields obtained, this method offers considerable promise as a synthetic tool.

Experimental

All melting and boiling points are uncorrected. The alcohols, chlorides, and bromides were commercially available materials whose homogeneity was established by g.l.p.c., using an Aerograph A90-P3 instrument equipped with a thermal conductivity detector. Infrared spectra were recorded on a Perkin-Elmer model 421 spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Varian A-60 analytical spectrometer using tetramethylsilane as internal standard.

All conversions of alcohol to alkyl chloride were accomplished by a procedure similar to that employed for the preparation of 1-chlorooctane which is described in detail. Bromides were prepared by the method described for the synthesis of 1-bromopentane.

Preparation of 1-Chlorooctane

To a magnetically-stirred solution of 1-octanol (10.0 mmoles) in 20 ml carbon tetrachloride was added tri-noctylphosphine (10.5 mmoles). An exothermic reaction ensued. (In larger scale runs it is recommended that the reaction be moderated by a cooling bath.) Approximately 5 min after complete addition of the phosphine an aliquot was analyzed by g.l.p.c. (5 ft \times 1/4 in. FFAP on Chromosorb W column operated at 140°, helium flow 55 ml/min). No octanol was present, but a new peak appeared, and was shown to be 1-chlorooctane by comparison of retention time with that of an authentic sample. The yield³ (as determined by g.l.p.c.) was 94%. By operating at a column temperature of 50° and helium flow of 25 ml/min, the peaks due to carbon tetrachloride and chloroform could be resolved but the yield of the latter was not determined.

Chloroform and carbon tetrachloride were distilled through a 25 cm Vigreaux column and the residue was chromatographed on BDH alumina. The pentane eluate

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was concentrated and distilled to give an 88% yield of pure 1-chlorooctane.4

Isolation of Tri-n-octylphosphine Oxide

The above-described experiment was duplicated, and after ca. 5 min reaction time the crude mixture was distilled to remove all material boiling up to ca. 184°. The residue was triturated with pentane and cooled to -78° . The resulting solid was filtered, washed with cold pentane, and dried. In this manner there was obtained 3.55 g (92%) of solid, m.p. 48-52° (lit. (9) m.p. 48-54°), $\nu_{\rm max}$ (Nujol) 1138 cm⁻¹ (PO). The nuclear magnetic resonance spectrum (CDCl₃) showed absorption for 9 protons as a multiplet centered at τ 9.1 (CH₃) and 42 protons with absorption from ca. τ 8.0–8.92 (CH₂).

Preparation of 1-Bromopentane

Tri-n-octylphosphine (20 mmoles) was added to a magnetically-stirred solution of 1-pentanol (10 mmoles) and carbon tetrabromide (20 mmoles) in 20 ml anhydrous ether. An immediate exothermic reaction took place and the initially colorless mixture turned yellow. Five minutes after complete addition of the phosphine an aliquot was analyzed by g.l.p.c.; the yield of 1-bromopentane was 97%. The mixture was worked up in a manner identical to that described for 1-chlorooctane, and upon distillation there was obtained an 80% yield of 1-bromopentane.⁴ Since no special precautions were taken to minimize handling losses this yield can doubtless be improved.

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⁴The structures of all synthetic materials were secured by comparison of physical properties with those of authentic samples.

³Under otherwise identical conditions, the yield of 1-chlorooctane was 47 % after 5 min reaction time employing triphenylphosphine.