Solid Phase Phosphorus Reagents. Conversion of Alcohols to Alkyl Chlorides[1]

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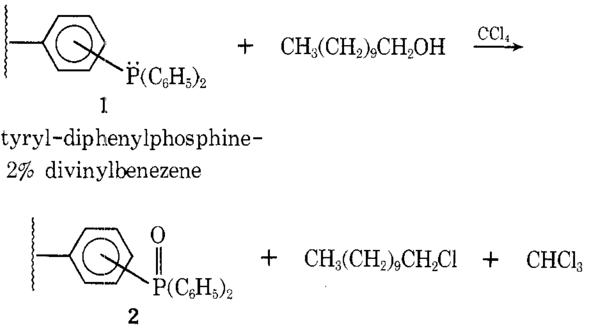
The reaction of triphenylphosphine with primary and secondary alcohols in carbon tetrachloride constitutes a mild and efficient method for conversion of the alcohols into the corresponding alkyl chlorides.[2]

We wish to describe a modification of the above reaction which requires only a filtration and evaporation process for product isolation. Our method is based upon the use of the polystyryl–diphenylphosphine resin **1** as the phosphorus reagent.[3,4] The convenience afforded by the use of **1** is demonstrated by the conversion of 1-undecanol to 1-chloroundecane. After heating a carbon tetrachloride solution of 1-undecanol for 2 hr at 80° in the presence of an excess of **1**, the oxidized phosphine polymer, **2**, was filtered. Solvent containing chloroform was then removed under reduced pressure, leaving a 99% isolated yield of 1-chloroundecane as a colorless liquid which was spectroscopically identical with an authentic sample.



Further examples of the use of **1** are illustrated in Table I. Heitz has recently reported that polymeric phosphine oxides similar to **2** can be readily reduced to the phosphine form with trichlorosilane.[5] We have found the reduction of **2** to **1** feasible using similar procedures.

The advantages of this method for the conversion of alcohols to alkyl chlorides lie in its simplicity, its ability to be carried out under neutral pH, and its facile regeneration of the polymer reagent.

Experimental Section[6]

General Methods. Unless stated otherwise, all reagents were obtained commercially and were used without further purification. Cross-linked polystyrene beads (2% divinylbenzene, 200–400 mesh) were obtained from Bio-Rad Laboratories and were used without further purification. Chlorodiphenylphosphine (Aldrich Chemical Co.) was distilled before use. Trichlorosilane (Aldrich Chemical Co.) was used without purification. Tetrahydrofuran and benzene were dried by distillation from sodium and benzophenone under a nitrogen atmosphere. Carbon tetrachloride (spectrophotometric grade, Aldrich Chemical Co.) was dried by passage through a short column of alumina. All glassware was oven dried (100°) prior to use. Elemental analyses were performed by Midwest Microlab, Indianapolis, Ind.

Bromination of Cross-Linked Polystyrene. Cross-linked polystyrene (2% divinylbenzene, 200–400 mesh) was brominated employing a procedure identical with that described by Relles.[4] Elemental analysis indicated that 71% of the phenyl rings contained bromine (Anal. Found: Br, 35.53).

Polystyryl–diphenylphosphine (1). Lithium wire (9.8 g, 1.4 mol, cut into 0.25-in. lengths) was placed in a 500-ml round-bottomed flask equipped with a No-Air stopper and a Teflon-coated magnetic stirring bar. The flask was thoroughly degassed under a stream of nitrogen and a dry solution of 100 g (0.55 mol) of chlorodiphenylphosphine in 250 ml of tetrahydrofuran was added via forced siphon through a stainless steel cannula under a nitrogen atmosphere. The mixture was stirred for 12 hr at room temperature, and the liquid phase was transferred via cannula into a 500-ml round-bottomed flask equipped with a No-Air stopper and Teflon-coated magnetic stirring bar which contained a degassed mixture of 50 g of 2% cross-linked brominated polystyrene (71% ring substitution) preswelled in 250 ml of tetrahydrofuran. The mixture was stirred for 24 hr at room temperature, hydrolyzed with degassed acetone–water (3:1), and filtered, and the resin was then washed with water, acetone, chloroform, benzene, and anhydrous ether. The polymer beads were dried under vacuum (6 hr, 100°, 0.05 mm). Elemental analysis indicated that 79% of the phenyl rings of the polymer backbone contained diphenylphosphine groups (Anal. Found: P, 9.87).[7,8]

General Procedure for Small-Scale Reactions. Procedures similar to that described for the conversion of 1-octanol to 1-chlorooctane were followed for all of the small-scale reactions described in Table I. A mixture of 65 mg (0.5 mmol) of 1-octanol, 200 mg (0.64 mmol of phosphorus) of **1**, 2 ml of carbon tetrachloride, and an internal standard were placed in a 5-ml round-bottomed flask equipped with a reflux condenser and a Teflon-coated magnetic stirring bar. The flask was maintained under a nitrogen atmosphere, and was placed in an oil bath (80°) for 2 hr, withdrawn, and cooled. The liquid phase was analyzed by GLC using a Carbowax on Chromosorb P column.

Conversion of 1-Undecanol to 1-Chloroundecane. A mixture of 3.10 g (18 mmol) of 1-undecanol, 10.0 g (32 mmol of phosphorus) of **1**, and 50 ml of carbon tetrachloride was placed in a 100-ml round-bottomed flask equipped with a reflux condenser and a Teflon-coated magnetic stirring bar. The flask was maintained under a nitrogen atmosphere and was placed in an oil bath (80°) for 2 hr, withdrawn, cooled to room temperature, and filtered. The resin was washed with 75 ml of carbon tetrachloride and the combined filtrate was concentrated by rotary evaporation, leaving a colorless liquid which was found to be 1-chloroundecane (3.42 g, 99%) having NMR and ir spectra indistinguishable from those of an authentic sample.

Regeneration of 1 from 2. Polymer **2** (5.0 g, 16 mmol of phosphorus) was placed in a 100-ml round-bottomed flask equipped with a No-Air stopper and Teflon-coated magnetic stirring bar. A solution of trichlorosilane (13.0 g, 96 mmol) in 20 ml of benzene was added to the flask via syringe followed by 7.2 g (71 mmol) of triethylamine while stirring in an ice–water bath. The flask was fitted with a reflux condenser and heated for 170 hr at 80°. The mixture was filtered and the beads were washed successively with benzene and tetrahydrofuran. The beads were then added to 250 ml of

Table I
Conversion of Alcohols to Alkyl Chlorides[a]

Alcohol	Registry no.	Alkyl Chloride	Registry no.	Yield,[b] %
1-Decanol	112-30-1	1-Chlorodecane	1002-69-3	89
1-Undecanol	112-42-5	1-Chloroundecane	2473-03-2	80 (99)[c]
1-Dodecanol	112-53-8	1-Chlorododecane	112-52-7	71
1-Octanol	111-87-5	1-Chlorooctane	111-85-3	90
Benzyl alcohol	100-51-6	Benzyl chloride	100-44-7	99
Cyclohexanol	108-93-0	Chlorocyclohexane	542-18-7	60
Cycloheptanol	502-41-0	Chlorocycloheptane	2453-46-5	92

[a] Unless noted otherwise, reactions were carried out using procedures similar to that described for the chlorination of 1-octanol. [b] Yields based on the alcohol were obtained by GLC. [c] Isolated yield from a large-scale reaction.

a 20% sodium hydroxide solution, stirred for 4 hr at room temperature, filtered, and added to 500 ml of 0.5 *N* sodium hydroxide in tetrahydrofuran. After stirring for an additional 4 hr, the resin was filtered, washed with tetrahydrofuran, and dried under vacuum (6 hr, 100°, 0.1 mm). Reaction of regenerated **1** with 1-undecanol using the small-scale procedure produced a 76% yield of 1-chloroundecane.

Acknowledgment. We are grateful to Professor Heitz for communicating valuable experimental procedures to us prior to publication.

Registry No.—Polystyrene, 9003-53-6; chlorodiphenylphosphine, 1079-66-9.

References and Notes

(1) Supported by the Research Corporation, the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Marquette University Committee on Research.

(2) J. B. Lee and T. J. Nolan, *Can. J. Chem.* **44**, 1331 (1966); J. Hooz and S. S. H. Gilani, *ibid.*, **46**, 86 (1968).

(3) Similar solid-phase techniques have been successfully applied to Wittig reagents for the facile removal of triphenylphosphine oxide: W. Heitz and R. Michels, *Angew. Chem., Int. Ed. Engl.* **11**, 298 (1972); S. V. McKinley and J. V. Rakshys, Jr., *J. Chem. Soc., Chem. Commun.*, 134 (1972); F. Camps, J. Castells, J. Font, and F. Vela, *Tetrahedron Lett.*, 1715 (1971).

(4) Relles has recently reported the preparation of certain polymer-supported trisubstituted phosphine dichlorides. Although such reagents are capable of converting alcohols to alkyl chlorides, they necessarily liberate hydrogen chloride: H. M. Relles and R. W. Schluenz, *J. Am. Chem. Soc.*, **96**, 6469 (1974).

(5) W. Heitz and R. Michels, *Justus Liebigs Ann. Chem.*, 227 (1973).

(6) All ^{1}H NMR spectra were recorded using a Varian A-60 spectrometer. Product mixtures were analyzed by GLC on a Hewlett-Packard Model 5711A flame ionization instrument.

(7) Phosphorus analyses for such samples were usually high and were not lowered by extensive washing.

(8) In order to determine the number of reactive phosphine sites along the polymer backbone, we treated **1** with 2 equiv of benzyl alcohol (based upon phosphorus content) using the procedure described for the small-scale reactions. Analysis of the benzyl chloride produced indicated that 100% of the phosphorus present was active in the halogenation reaction.

Oxygenated α-Methylene-γ-butyrolactones[1]

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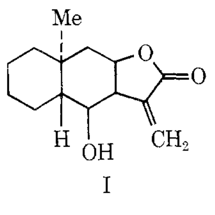
Synthetic efforts to date[3] have concentrated on the construction of α-methylene-γ-butyrolactones with almost no attention being devoted to the homoallylic oxygenated α-methylene-γ-butyrolactones. Two recent publications have reported syntheses of the oxygenated α-methylene lactones I[4] and II.[5] Interest in such oxygenated α-methylene lactones stems from recent studies[6] which have demonstrated that the presence of a lipophilic, conjugated ester or halo ester situated homoallylic to the exocyclic double bond of many naturally occurring α-methylene-γ-butyrolactones contributes to the enhancement of cytotoxic activity. Such oxygenated α-methylene lactone structural types are commonly found fused to six-, seven-, and ten-membered rings.[3]



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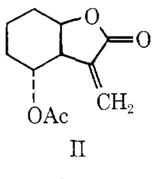
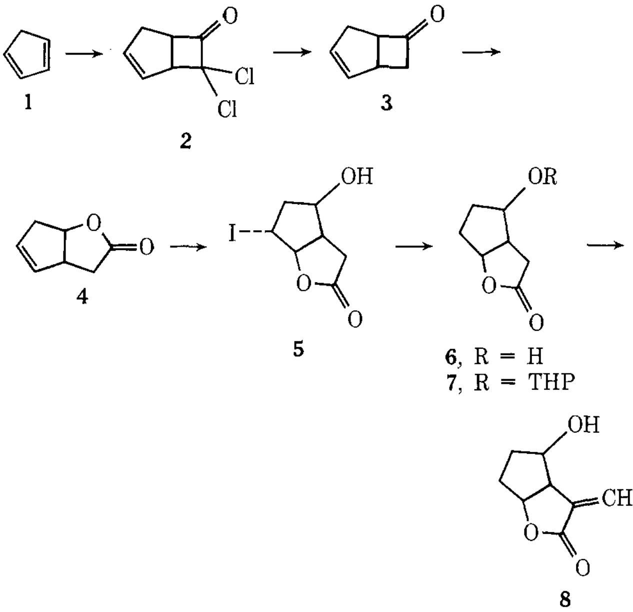


II

We wish to detail here a method for the construction of oxygenated α-methylene-γ-butyrolactones fused to five- and six-membered rings of type I. The method is applicable to other ring systems as well.[7] As illustrated in Scheme I, the approach involves the position-specific addition of dichloroketene[8] to an appropriate diene followed by dechlorination. Baeyer–Villiger oxidation results in formation of an olefinic γ-butyrolactone, which when subjected to the conditions of saponification and subsequent iodolactonization results in formation of the oxygenated γ-butyrolactone structural unit. Deiodination is cleanly carried out on the free hydroxy lactone followed by methylenation of the γ-lactone ring.

Scheme I



Addition of dichloroketene to cyclopentadiene followed by dechlorination and Baeyer–Villiger oxidation as previously described[9] results in the formation of the bicyclic lactone **4**. Saponification of **4** in water followed by neutralization with carbon dioxide and treatment with potassium triiodide at 5° causes iodolactonization with formation of **5** (95%). Deiodination of **5** using tributyltin hydride (initiation with azobisisobutyronitrile) in benzene at an elevated temperature affords hydroxy lactone **6** (91%). Protection of the free hydroxyl of **6** as its tetrahydropyranyl ether **7** followed by methylenation employing the α-hydroxymethylation procedure for lactone enolates[10] produces the oxygenated α-methylene-γ-butyrolactone **8**. During the elimination (anhydrous pyridine, ca. 130°) of the mesylate derived from the hydroxymethylated derivative of lactone **7**, simultaneous formation of the α-methylene unit and cleavage of the tetrahydropyranyl ether occur.[11]

Scheme II