

A Mechanistic Investigation of the Todd Reaction

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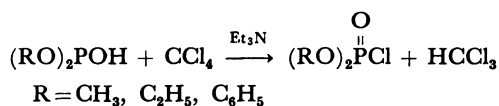
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Synopsis. The Todd reaction, involving formation of a dialkyl phosphorochloridate by reaction of a dialkyl phosphonate with tetrachloromethane under basic conditions, has been determined to involve the intermediacy of the trichloromethanide anion.

The Todd reaction, a synthetically valuable method for the preparation of dialkyl phosphoramidates¹⁾ and dialkyl phosphorochloridates,²⁾ was the subject of early kinetic investigations by Steinberg.³⁾ On the basis of the kinetic data, several possible mechanisms for the reaction were proposed, two of these involving the intermediacy of the trichloromethanide anion. We have now obtained direct evidence for the intermediacy of this species in the Todd reaction under carefully defined conditions, giving foundation for a detailed mechanism.

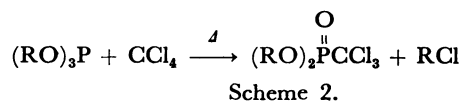
The chemistry of the trichloromethanide anion has become quite well known since the postulation of its intermediacy in the Todd reaction. Hine⁴⁾ first gained positive data for the dissociation of the trichloromethanide anion into chloride ion and dichlorocarbene during the hydrolysis of chloroform. It was later noted that dichlorocarbene so produced could add to olefins.⁵⁾ Should the Todd reaction proceed through a route involving the trichloromethanide anion, it would be anticipated that dichlorocarbene would be produced which is capable of being trapped.

The formation of dialkyl (or diaryl) phosphorochloridate in the Todd reaction occurs with near violent rapidity upon addition of small amounts of base (amine) to a mixture of dialkyl (or diaryl) phosphonate and tetrachloromethane as shown in Scheme 1.



Scheme 1.

We have confirmed and extended several earlier observations³⁾ regarding this reaction: 1) In the absence of base, no reaction occurs, even with prolonged heating. 2) The reaction is not influenced by the presence of free radical initiators or inhibitors. 3) The only phosphorus-containing side products are those as reported by Steinberg,³⁾ the hypophosphate and pyrophosphate, resulting from further reaction of the initially generated dialkyl (diaryl) phosphorochloridate; under GLC analysis using either thermal conductivity or hydrogen flame detection capable of detecting products at amounts less than 0.1 % conversion, no formation of the dialkyl trichloromethylphosphonate could be observed. This material is easily formed in an Arbuzov-type reaction with a trialkyl phosphite as shown in Scheme 2. 4) The reaction may be accom-



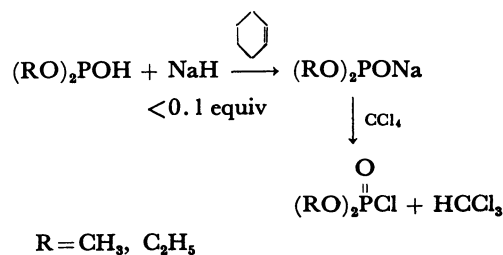
plished in the presence or absence of solvent, which simply serves to moderate the reaction.

The general procedure for performing and analyzing reactions involved placement of the dialkyl (diaryl) phosphonate (0.1 mol) with the solvent (if any) and a weighed amount of a suitable inert standard (for quantitative GLC analysis) in a reaction flask equipped with a dropping funnel, reflux condenser, and magnetic stirrer. If amine were used as base, an equivalent amount (0.1 mol) was then added; if the sodium salt of the dialkyl phosphonate were used, sodium or sodium hydride was added with stirring until all had reacted. Tetrachloromethane was then added dropwise at ambient temperature, and stirring continued for 2 h.

An immediate analysis was made using GLC to determine quantitatively chloroform generated, and to note the presence of the phosphorochloridate using one of the following columns: (a) 5' × 1/4" 1.5 % OV-101 on Chrom GHP, (b) 5' × 1/4" 30 % SE-30 on Chromosorb W, or (c) 5' × 1/4" 20 % Apiezon L on Chromosorb W. As the phosphorochloridates underwent significant decomposition under the analytical conditions, the reaction mixture was then treated with an excess of abs ethanol and triethylamine for conversion of the phosphorochloridate to the phosphate. A further chromatographic analysis was then made to determine the yield of the phosphate, and by inference the phosphorochloridate (*minimal* yield). The phosphate was also isolated from the reaction mixture and its structure was confirmed by ¹H-NMR analysis (Varian EM-360).

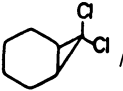
In all attempts using a tertiary amine to initiate the reaction and cyclohexene as solvent or cosolvent, the reaction proceeded "normally" yielding only the products found in the absence of solvent. It had been anticipated that cyclohexene would serve to trap any dichlorocarbene which would result from trichloromethanide decomposition.

Attempts using a less than one equivalent amount of preformed anion of dialkyl phosphonate produced similar results (Scheme 3). When a small amount of anion was generated by addition of sodium hydride



Scheme 3.

TABLE 1.

Starting Materials			Product Yields		
R	Base	Solvent	CHCl ₃ /%	(RO) ₂ P(O)Cl/%	 /%
CH ₃	Et ₃ N ^{a)}	Toluene	69.0	63.6	—
C ₂ H ₅	Et ₃ N ^{a)}	Toluene	63.9	61.0	—
C ₆ H ₅	Et ₃ N ^{a)}	Toluene	57.9	48.2	—
CH ₃	Et ₃ N ^{a)}	Cyclohexene	70.6	67.3	0 ^{e)}
C ₂ H ₅	Et ₃ N ^{b)}	Cyclohexene	69.8	61.5	0 ^{e)}
C ₆ H ₅	Et ₃ N ^{a)}	Cyclohexene	60.3	51.8	0 ^{e)}
C ₂ H ₅	Na ^{b)}	Cyclohexene	53.1	42.1	0 ^{e)}
C ₂ H ₅	NaH ^{c)}	Cyclohexene	71.4	62.7	0 ^{e)}
CH ₃	NaH ^{d)}	THF	40.6	29.2	—
CH ₃	NaH ^{d)}	Cyclohexene	31.7	48.2	22.6

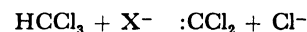
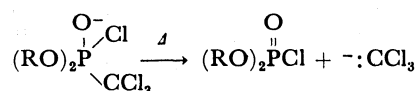
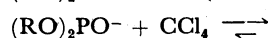
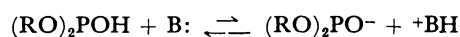
a) Equiv amounts of base, CCl₄, and dialkyl (diaryl) phosphonate. b) Preformed anion with 0.1 equiv Na; Yields based on 0.5 equiv CCl₄. c) Preformed anion with 0.015 equiv NaH; Yields based on CCl₄ as limiting reagent. d) Preformed anion with 1.0 equiv NaH. e) Below detectable limits.

and to this was added tetrachloromethane, rapid reaction ensued generating phosphorochloridate and chloroform with an average conversion of 60 % based on tetrachloromethane.

This result could be observed in the absence of solvent or in the presence of varying amounts of several solvent systems (tetrahydrofuran, toluene, cyclohexene). Again, with cyclohexene no trapping of dichlorocarbene could be noted using GLC techniques.

Finally the reaction was performed by the conversion of the entire amount of dialkyl phosphonate to the anion form using sodium hydride. To this system in cyclohexene was added an equivalent amount of tetrachloromethane. Analysis of the reaction mixture showed the formation of dialkyl phosphorochloridate along with 7,7-dichloronorcaradiene, the product of dichlorocarbene addition to cyclohexene, with an average 50 % conversion. Typical results are illustrated in Table 1.

The verification of the intermediacy of the trichloromethanide anion along with prior data regarding the phosphorus stereochemistry (retention) for this type of reaction^{6,7)} supports the overall mechanism as illustrated in Scheme 4. In the presence of any proton source the trichloromethanide anion accepts a proton with extreme rapidity precluding decomposition to dichlorocarbene. In the absence of any such proton source, the resultant trichloromethanide anion leads to products derived from dichlorocarbene.



Scheme 4.

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