The structures of the other five metabolites were determined by spectral analysis. Metabolite **2a**, oil, [α]D −8.3° (*c* 1.1, MeOH), was concluded to be (10*S*, 11*S*)-*cis,trans*-dihydroxyhomofarnesol, which is most probably the hydration product of the minor 2-cis substrate. **2a** might have come partly from the major 2-trans substrate by the action of a trans–cis isomerase, as was found in the metabolic course of epoxyfarnesol.[8] Metabolite **4b**, oil, [α]D −6.6° (*c* 0.2, MeOH), was identified as methyl (11*S*)-*trans,trans*-10-oxo-11-hydroxyhomofarnesoate, which was clearly an oxidation product of **3a** at C_{10}. Terminal oxidation of an allylic carboxylate in **3a** gave an alternate metabolite **5**, oil, [α]D −13.8° (*c* 0.7, MeOH), to which the structure (9*S*,10*S*)-*trans*-dihydroxyhomogeranylacetone was assigned. By a similar oxidation, **6a** was converted into (9*S*,10*R*)-*trans, cis*-epoxyhomogeranylacetone (**7**), oil, [α]D −27.9° (*c* 0.3, MeOH). Two-carbon degradation of **7** gave *trans-cis*-7,8-epoxy-4,8-dimethyl-dec-3-enoic acid (8a). Although the exact optical rotation of **8b** was not measured owing to its small value, the distinct negative sign in ORD indicated the absolute stereochemistry to be 7*S*,8*R*.

The seven metabolites may be placed in two groups by their structural characteristics, the first group (**2a**, **3a**, **4a**, **5**) having a glycollic moiety, and the second group, the epoxide-containing compounds (**6a**, **7**, **8a**). Metabolic conversion of the racemic substrate into these two groups of compounds could be reasonably explained by postulating two metabolic pathways. Namely, the glycollic compounds would be originally derived from the (+)-enantiomer of the substrate, (+)-**1**, which is hydrated enzymatically in the trans manner with nucleophillic attack at the C_{10} position. This hydration is essentially the same as in the case of (+)-epoxyfarnesol.[3] On the other hand, (−)-epoxy compounds would be derived from the (−)-enantiomer, (−)-**1**, the epoxy ring being resistant to hydration by the hydrase of the fungus. This difficulty for the fungus in hydrating (−)-**1** may be ascribed to the steric effect of an ethyl in place of the methyl group at the C_{11} position of (−)-epoxyfarnesol, which had been established to undergo cis hydration to produce optically minus glycol.[3] The juvenile hormone activity of the enantiomers, **6b** and **9**, should prove to be quite interesting, and the bioassay is under way.

(8) Y. Suzuki and S. Marumo, *Tetrahedron Lett.*, 5101 (1972).

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A Novel and Versatile Synthetic Reagent. The Monoalkyl Esters of Tetraalkylphosphorodiamidous Acid

Sir:

We wish to report the utility of alkyl esters of phosphorodiamidous acid (phosphorodiamidites) as a hitherto unrecognized class of convenient and versatile synthetic intermediates which may be utilized for the preparation of α,α-dichloroesters, α,α-dichlorophenyl alkanes, and trichloromethyl alkanes.[1]

The phosphorodiamidites, I, are conveniently synthesized from hexamethylphosphorus triamide (HMPT) by converting to the monochloro derivative,[2] II, followed by reaction of an ether solution of II with the appropriate alcohol in the presence of triethylamine as shown in eq 1. Compound II should be handled under

$$2P[NMe_2]_3 + PCl_3 \longrightarrow \underset{\text{II}}{3ClP[NMe_2]_2} \xrightarrow[\text{Et}_3\text{N}]{\text{ROH}} \underset{\text{I}}{[Me_2N]_2POR} \quad (1)$$

a dry nitrogen atmosphere as much as possible since it reacts rapidly with atmospheric moisture. *Caution:* II reacts explosively upon contact with water. The yields of I (based on HMPT) and boiling points are as follows: R = CH_3, 75%, bp 59–63° (40 Torr); R = Et, 77%, bp 42–43° (10 Torr); R = *i*-Pr, 66%, 61–62° (20 Torr); R = $PhCH_2$, 56%, 60–63° (0.01 Torr).[3]

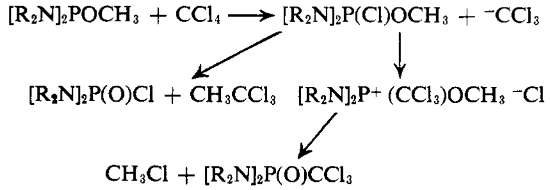
Upon addition of I (R = CH_3) to carbon tetrachloride even at 0° a very exothermic, almost explosive, reaction ensues yielding the products shown in eq 2.

$$[R_2N]_2POCH_3 + CCl_4 \longrightarrow \underset{\text{III}}{[R_2N]_2P(O)Cl} + \underset{\text{IV}}{[R_2N]_2P(O)CCl_3} + CH_3Cl + CH_3CCl_3 \quad (2)$$

The products, with the exception of IV, were identified by comparison of nmr spectra and chromatographs with those of authentic compounds. Compound III was independently synthesized by treatment of a benzene solution saturated with chlorine with I. The yield of methyl chloride (15%) and 1,1,1-trichloroethane (85%) were determined by nmr using toluene as an internal standard. At high temperatures proportionately more methyl chloride was formed. A similar reaction of I (R = $PhCH_2$) yielded benzyl chloride (7%) and 1,1,1-trichloro-2-phenylethane (73%) although the reaction was considerably less exothermic.

We feel these results are best explained on the basis of the mechanism shown in Scheme I. The enchanced reactivity of I over the corresponding trialkylphosphites, which give no detectable reaction at room temperature, is presumably due to an increase in the nucleophilicity of phosphorus in this system. Dialkoxy compounds, $[R_2N]P[OCH_3]_2$ (V), react only slowly at room temperature.

Scheme I



The reactions of phosphites with carbon tetrachloride have recently been reinvestigated by Cadogan and coworkers[5] who concluded that, in the absence of light

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(1) Presented in part at the 167th National Meeting of the American Chemical Society, Los Angeles, Calif., April 1974.

(2) H. Noth and H. J. Vetter, *Chem. Ber.*, **94**, 1505 (1961).

(3) An alternative method of synthesis of these compounds, the direct combination of hexamethylphosphorus triamide and alcohol,[4] was found to yield mixtures of amidites, diamidites, and phosphites which could not be conveniently separated.

(4) D. Houalla, M. Sanchez and R. Wolf, *Bull. Soc. Chim. Fr.*, 2368 (1965).

(5) R. E. Atkinson and J. I. G. Cadogan, *J. Chem. Soc., B*, 138 (1969).

and free radical initiators, the reaction proceeds *via* the heterolytic mechanism shown in Scheme II. In the

Scheme II

$$(EtO)_3P + CCl_4 \xrightarrow{80^\circ} (EtO)_3P^+CCl_3 + Cl^- \longrightarrow EtCl + (EtO)_2P(O)CCl_3$$

phosphorodiamidite system we favor a nucleophilic attack of phosphorus on halogen rather than on the central carbon.[6] In addition to the preponderance of product presumably derived from the trichloromethyl anion (which was not observed in the phosphite reaction) the following observations support this contention. No detectable reaction occurs when I is mixed with chloroform or methylene chloride even after several hours at 40°. These compounds should be more susceptible to nucleophilic attack at carbon by the phosphorus since the steric demands are reduced. These observations are, however, in accord with attack at halogen since increasing the number of halogens should stabilize the resulting carbanion by an inductive effect.

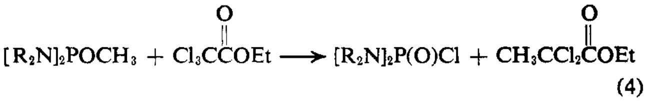
Although a radical pathway may not be rigorously excluded, we detect no products, such as hexachloroethane, which would be expected if a radical process were operative. In addition, no CIDNP signals were observed when the reaction was carried out in the probe of a nmr spectrometer.

In order to investigate the generality of the reaction we have utilized some other polyhaloalkanes. Trichloroethane fails to react, but 1,1,1-trichlorotoluene reacts slowly with I (R = CH_3) to give excellent yields (>80% isolated) of 1,1-dichloro-1-phenylethane (eq 3).

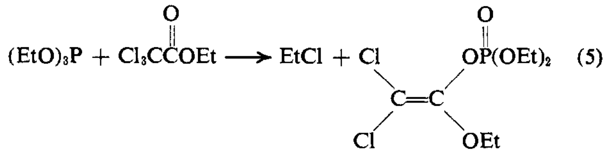
$$ROP[NMe_2]_2 + PhCCl_3 \longrightarrow RCCl_2Ph + [Me_2N]_2P(O)Cl \quad (3)$$

Approximately 2 hr is required for the reaction to go to completion when run at room temperature. This compound was identified by comparison with an authentic sample synthesized by treatment of acetophenone with phosphorus pentachloride. A similar reaction with I (R = $PhCH_2$) yielded 83% of 1,1-dichloro-1,2-diphenylethane and ~5% of benzyl chloride. The possibility of resonance stabilization of the α,α-dichlorobenzyl anion apparently enhances the reactivity of the trichlorotoluene as compared to that of the trichloro alkanes. Since 1,1-dichloro-1-phenyl alkanes should be readily hydrolyzed to the corresponding ketones, this reaction may prove to be of considerable synthetic utility. It is also interesting to note that the dichlorodiphenylethane is a possible precursor of diphenylacetylene, which is not conveniently synthesized by other means.[8] This method may allow a novel and convenient synthesis which, depending upon the availability of the appropriate benzyl alcohol, would yield substituted diphenylacetylenes.

A reaction of I (R = CH_3) with ethyl trichloroacetate yields 89% of ethyl 2,2-dichloropropanoate (eq 4). A 95% yield of ethyl 2,2-dichloro-3-phenylpropanoate was observed upon reaction of I (R = $PhCH_2$) with ethyl trichloroacetate. Only trace amounts of the alkyl halide (methyl chloride and benzyl chloride, respectively) are observed in these experiments. Surprisingly, we see no evidence for the vinyl phosphate analog normally observed in reactions between trivalent phosphorous compounds and α-halocarbonyl compounds (Perkow reaction)[9] (eq 5). The reaction observed is best rationalized by involving a nucleophilic attack of phosphorus on one of the α-halogens of ethyl trichloroacetate generating a phosphonium ion and the resonance stabilized anion, VI, followed by alkylation of the anion and formation of the phosphoryl bond (Scheme III).

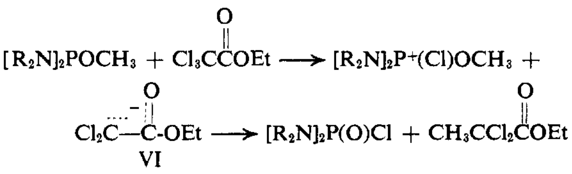


$$[R_2N]_2POCH_3 + Cl_3C\overset{O}{\overset{\|}{C}}OEt \longrightarrow [R_2N]_2P(O)Cl + CH_3CCl_2\overset{O}{\overset{\|}{C}}OEt \quad (4)$$



$$(EtO)_3P + Cl_3C\overset{O}{\overset{\|}{C}}OEt \longrightarrow EtCl + (Cl)_2C{=}C(OEt)OP(O)(OEt)_2 \quad (5)$$

Scheme III



$$[R_2N]_2POCH_3 + Cl_3C\overset{O}{\overset{\|}{C}}OEt \longrightarrow [R_2N]_2P^+(Cl)OCH_3 + \underset{\text{VI}}{Cl_2C\cdots\overset{O}{\overset{\|}{C}}\text{-}OEt} \longrightarrow [R_2N]_2P(O)Cl + CH_3CCl_2\overset{O}{\overset{\|}{C}}OEt$$

We are currently extending our investigation to include a wide variety of phosphorodiamidites and also other polyhalogen compounds. The results of these studies will be published in a subsequent paper.

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(6) This proposal has previously been suggested by Miller[7] to rationalize the reactions of trialkyl phosphites with carbon tetrachloride.

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(8) R. H. Mitchell, *J. Chem. Soc., Chem. Commun.*, 955 (1974).

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Do S$_N$2 Reactions Go through Ion Pairs? The Isotope Effect Criterion[1]

Sir:

It has been suggested[2f] that S$_N$2 reactions[3] go through ion pairs[2] and that in borderline[3] solvolyses the competing S$_N$1 and S$_N$2 processes occur through common intermediates. This suggestion has been criticized recently.[4–8]

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(1) Research sponsored by the U. S. Atomic Energy Commission under contract with the Union Carbide Corporation.

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(3) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp 315, 353, 360.

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(6) A. R. Stein, *J. Org. Chem.*, **38**, 4022 (1973).

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