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Sulfenyl Chlorides in Organophosphorus Chemistry, Recent Developments

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INTRODUCTION

About 35 years have passed since the discovery by Professor J. Michalski of the chlorination reaction of thiophosphates.* The reaction leads to P-sulfenylchlorides, compounds which extend the synthetic usefulness in a series of P, S-compounds. Up until now, the Polish chemists have continued to develop intensively the chemistry of phosphorus-containing sulfenyl chlorides.

Sulfenyl chlorides belong among the strongest electrophilic reagents. They are able to react with a variety of O-, N-, C-, S- and other nucleophilic centers in organic compounds [1]. Such reactions result in the introduction of an additional sulfur atom (N or P atoms are also introduced in the case of N- or P-sulfenyl chlorides), and this may lead to the introduction of new and potentially useful physiological properties into the compounds. Sulfenyl chlorides occupy a significant place in the chemistry of organophosphorus compounds [1], and a constantly increasing number of publications reflects the growing interest in this field. Additional information now available allows us to reveal new potentials of sulfenyl chlorides, including their application in those fields of organic chemistry where they have not been used earlier.

* J. Michalski, B. Lenard, *Rocz. Chem.*, *30*, 1956, 655.

IMPROVED METHODS OF SYNTHESIS OF P-SULFENYL CHLORIDES

Recent developments have led to improved methods of preparation of some types of sulfenyl chlorides. Thus, the Polish scientists have found [2] that the best approach to phosphorylsulfenyl chlorides (1 R = AlkO) is based, not on O,O,O-trialkyl thiophosphates (the Michalsky reaction), but on O,O-dialkyl-O-trimethylsilyl thiophosphates because the reactions of the latter with sulfuryl chlorides occur under mild conditions (at −20°C) and permit the preparation of pure sulfenyl chlorides without the necessity for additional purification.

$$R_2P(S)OSiMe_3 + SO_2Cl_2 \rightarrow R_2P(O)SCl + Me_3SiCl + SO_2$$

1

Similarly, on reaction of thiophosphinic acid silyl esters with chlorine or sulfuryl chloride under mild conditions, in contrast to analogous reactions with the alkyl esters of these acids, no phosphinyl chlorides are formed as by-products. Therefore, from the silyl esters, sulfenyl chlorides (1 R = Alk, Ar) are formed exclusively in quantitative yield [2].

Up to the present, thiophosphorylsulfenyl chlorides (**2**) were not readily available compounds. The only known method for their synthesis was based on the cleavage of the corresponding sulfenylamides with hydrogen chloride.

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$$(RO)_2P(S)SNR'_2 + 2\,HCl \rightarrow (RO)_2P(S)SCl + [R'_2NH_2]Cl$$

2

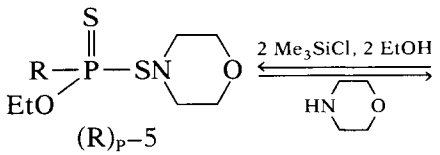
The method was improved by replacing hydrogen chloride with a trimethylchlorosilane-ethanol mixture, which permitted the preparation of pure thiophosphorylsulfenyl chlorides in quantitative yield.

By use of trimethylbromosilane, thiophosphorylsulfenyl bromides (**3**) [3] are easily obtained.

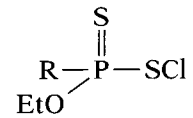
$$(RO)_2P(S)SNR'_2 + 2\,Me_3SiX \xrightarrow{2\,EtOH} (RO)_2P(S)SX + [R'_2NH_2]X + 2\,Me_3SiOEt$$

3 X = Cl, Br

An improved modification of sulfenylamide cleavage has been successfully applied to the synthesis of P-chiral thiophosphorylsulfenyl chlorides (**4**) [$(R)_P$–4 and $(S)_P$–4] from the corresponding stereoisomeric sulfenylmorpholides (**5**). Treatment of the stereoisomers (**4**) with morpholine leads to the original stereoisomeric sulfenylamides (**5**), in which the substitution of a chlorine atom proceeds with retention of configuration at phosphorus. This suggests that the cleavage and formation of the two-valent sulfur bonds to be synchronous processes, because by a prior dissociation of the sulfur-chlorine bond, racemization would have taken place [4].



$(R)_P$–5



$(R)_P$–4 R = menthyloxy

Analogously with $(S)_P$–4 and $(S)_P$–5.

The search for alternative methods of synthesis of thiophosphorylsulfenyl chlorides has continued. In particular, methods based on the corresponding disulfides were elaborated. They are similar to the well-known methods for the synthesis of the oxygen analogs. An additional study on the chlorinolysis of bis(di-iso-propoxythiophosphoryl)-disulfide (**6**) with an equivalent amount of chlorine in methylene chloride at −85°C has shown that the sulfenyl chloride (2a R = iso-Pr) is formed in 25–27% yield. The compound was identified by its ^{31}P NMR spectra, as well as by preparation of an adduct with cyclohexene. Together with the compound **2a**, the S-sulfenyl chloride (**7**), and the trisulfide (**8**) were detected by ^{31}P NMR spectroscopy of the mixture at −85°C. The major product of the disulfide (**6**) chlorinolysis is the thiophosphoryl chloride (**9**) (65–70%) which is evidently formed as a result of a further chlorination of the sulfenyl chloride **2a** [5].

$$(i\text{-}PrO)_2P(S)SSP(S)(OPr\text{-}i)_2 + Cl_2 \rightarrow 2\,(i\text{-}PrO)_2P(S)SCl$$

6 **2a**

$$\mathbf{2a} + Cl_2 \rightarrow [(i\text{-}PrO)_2P(S)\text{–}\overset{+}{S}Cl_2]Cl^- \xrightarrow[-SCl_2]{} (i\text{-}PrO)_2P(S)Cl$$

9

$(i\text{-}PrO)_2(S)SSCl$

7

$(i\text{-}PrO)_2P(S)SSSP(S)(OPr\text{-}i)_2$

8

The reaction between silyl esters (**10**) and chlorine was found to lead to thiophosphorylsulfenyl chlorides (**11**) in low yields. However, on replacing chlorine by sulfuryl chloride fluoride, these sulfenyl chlorides are obtained in better but still moderate yields [6].

$$RR'P(S)SSiMe_3 \xrightarrow[[SO_2ClF]]{Cl_2} RR'P(S)SCl$$

10 **11**

In contrast to the use of chlorine, bromine reacts with an equivalent amount of bis(thiophosphoryl)disulfides at low temperatures to yield thiophosphorylsulfenyl bromides but not thiophosphoryl bromides. A method for the preparation of thiophosphorylsulfenyl chlorides (**2**) from their bromide analogs has been developed [7]. It relies on the transformation of sulfenyl bromides into methylsulfenates (yield 70–80%) upon the action of methanol and a stoichiometric amount of 2,6-lutidine (a worse yield being obtained with pyridine or triethylamine) at room temperature, followed by reaction of the sulfenates with trimethylchlorosilane at room temperature, which gives sulfenyl chlorides (**2**) in quantitative yield. The transformation of sulfenyl bromides into sulfenyl chlorides can be carried out as a one-pot process [6].

$$[(RO)_2P(S)S]_2 \xrightarrow[-10\text{--}-80°C]{Br_2} (RO)_2P(S)SBr \quad 100\%$$

$$\xrightarrow[20°C]{MeOH/2,6\text{-lutidine}} (RO)_2P(S)SOMe \quad 70\text{–}80\%$$

$$\xrightarrow[\sim 20°C]{Me_3SiCl,\ CH_2Cl_2} (RO)_2P(S)SCl \quad 100\%$$

The search for a general method of P-sulfenyl and P-selenyl halide synthesis has led to a discovery of a new procedure based on treatment of mixed anhydrides of thio or selenophosphoric acids and

acetic acid with an appropriate halogen. The reaction occurs at low temperature in a neutral medium and gives phosphoryl- and thiophosphorylsulfenyl halides (and the corresponding selenyl halides as well) in almost quantitative yields. This procedure provides more pure and more stable products then other methods [6].

$$RR'P(S)YC(O)Me + X_2 \rightarrow RR'P(Y)SX + MeC(O)X$$

X = Cl, Br: Y = 0, S

NOVEL REACTIONS OF P-SULFENYL CHLORIDES

Phosphorylsulfenyl chlorides, being strong electrophilic reagents, undergo reaction with isobutyraldehyde and alkyl isopropyl ketones at 5°C in methylene chloride to give the α-C-phosphorylated products of the structure (**12**) in good yields. These substances display fungicidal activity [8].

$$(RO)_2P(O)SCl + Me_2CHC(O)R' \rightarrow (RO)_2P(0)SCMe_2C(O)R'$$

12

R = Alk, CH = CCl_2; R' = H, Alk

The reaction of phosphorylsulfenyl chlorides with silyl enol ethers at low temperature in methylene chloride proceeds regioselectively giving only one product in good yield, S-(β-oxoalkyl)-O,O-dialkylthiophosphates. These types of compounds exhibit biological activity of potential interest and may be intermediates in the conversion of carbonyl compounds to olefins. Moreover, in the case of rigid cyclic structures, for example, the silyl enol ether of 4-*tert*-butyl cyclohexanone, the reaction with phosphorylsulfenyl chlorides proceeds in a stereoselective manner, with a significant prevalence of one diastereoisomer in the products (in the above example, the trans:cis ratio was 77:23; the pure trans-diastereoisomer was isolated by column chromatography) [9].

$$RC(O)CH_2R' \xrightarrow[Et_3N]{Me_3SiCl} RC(OSiMe_3)=CHR' \xrightarrow{(R''O)_2P(O)SCl} RC(O)CH(R')SP(O)(OR'')_2$$

56–100%

Similar to other diazoalkanes, diazoacetic ester reacts with phosphorylsulfenyl chlorides with nitrogen evolution and subsequent 1,1-addition of the sulfenyl chloride to the methylene group. In this way, O,O-dialkyl-S-ethoxycarbonylchloromethyl thiophosphates were obtained. They are effective inhibitors of carboxylesterase [10].

$$(RO)_2P(O)SCl + N_2CHCOOEt \xrightarrow[\text{ether, } -25^\circ C]{-N_2} (RO)_2P(O)SCH(Cl)COOEt$$

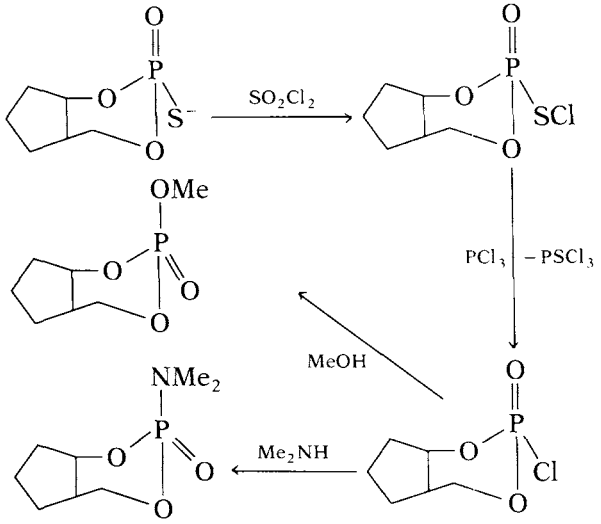
82–95%

Dimethoxyphosphorylsulfenyl chloride reacts with trimethyl-(p-vinylbenzyl)stannane at both reactive centers. Moreover, the second reaction step is faster than the first one, because only a 1:2 adduct is obtained in a high yield, irrespective of the ratio of the reagents, the temperature (from −70 to 20°C) and the nature of the solvent. Substitution of the stannyl group in the initially formed adduct by the phosphonate results from a successive elimination-addition reaction [11].

$$Me_3SnCH_2C_6H_4C{=}CH_2 \xrightarrow{(MeO)_2P(O)SCl} [Me_3SnCH_2{-}C_6H_4{-}CHClCH_2SP(O)(OMe)_2 \xrightarrow{-Me_3SnCl} CH_2{=}C_6H_4{=}CHCH_2SP(O)(OMe)_2] \xrightarrow{(MeO)_2P(O)SCl} (MeO)_2P(O)SCH_2C_6H_4CHCH_2SP(O)(OMe)_2$$

87% (Cl)

Bicyclic P-sulfenyl chlorides are known to react with phosphorus trichloride by abstracting sulfur to ultimately give thiophosphoryl trichloride and chlorophosphates. The ability of the thiophosphoryl chloride to react with phosphorus trichloride regio- and stereoselectivity has been used in the preparation of pure stereoisomeric phosphates and amidophosphates belonging to the bicyclo[4,3,0]nonane series that has been chosen as a model of cyclic nucleotides [12].



In contrast to the reaction of P-sulfenyl chlorides with trialkyl phosphites which follows several pathways [1], the reaction of phosphoryl- and thio-

phosphorylsulfenyl chlorides with O,O-dialkyl-O-trimethylsilyl phosphites proceeds unambiguously to abstract the trimethylsilyl group. In the case of phosphorylsulfenyl chlorides, the reaction occurs at −40°C and gives symmetrical thiopyrophosphates in yields > 95%. Only symmetrical thiopyrophosphates with bulky substituents at phosphorus can be isolated in the analogous reaction with trialkyl phosphites. In other cases, the initially formed symmetrical thiopyrophosphate readily isomerizes into the unsymmetrical isomer. However, in the reactions with monosilylated phosphites, no isomerization of the compounds, even those with lower alkoxy groups, occurs [13, 14].

$$(RO)_2P(O)SCl + (R'O)_2POSiMe_3 \xrightarrow[-40°C]{CH_2Cl_2} [(RO)_2\overset{+}{P}(O)S\overset{+}{P}(OR')_2OSiMe_3]Cl^- \xrightarrow{-Me_3SiCl}$$

$$(RO)_2P(O)SP(O)(OR')_2 \not\longrightarrow (RO)_2P(S)OP(O)(OR')_2$$

R = R′ = Me, Et, i-Pr, Me_3CCH_2;
$R_2 = R'_2 = CH_2CMe_2CH_2$;
$R = Me_3CCH_2$, $R'_2 = CH_2CMe_2CH_2$

REACTIONS OF N-SULFENYL CHLORIDES WITH ORGANOPHOSPHORUS COMPOUNDS

The recent discovery, that introduction of a group containing an N—S bond to the nitrogen atom in carbamic acid derivatives, ureas, or amido(thio)phosphates decreases their toxicity in mammals, stimulated an interest in the study of reactions of N-sulfenyl chlorides with the types of compounds mentioned above. In this connection, a study on the reactions of aminosulfenyl chlorides (diethylamino- and N-piperidinosulfenyl chlorides) with arylhydrazides of phosphoric and thiophosphoric acids was performed. It was found that these compounds always react regiospecifically. However, with hydrazidophosphates and hydrazidothiophosphates, the reaction proceeds at different nitrogen centers. Thus, the arylhydrazides of diethylphosphoric acid react in the usual manner for acylation reactions of arylhydrazidophosphates and give the products of substitution at the β-nitrogen.

$$(EtO)_2P(O)NHNHAr + R_2NSCl \xrightarrow{Et_3N}$$

Ar = Ph, m-$CF_3C_6H_4$

$$(EtO)_2P(O)NHN(Ar)SNR_2$$

29–88%

On the other hand, arylhydrazides of diethyl- and diphenylthiophosphoric acids react with N-sulfenyl chlorides in a more complicated fashion, producing products of substitution at the α-nitrogen, presumably as a result of an attack of a "soft" electrophile at a "soft" thiophosphoryl sulfur, with subsequent migration of a dialkylamino group to a neighboring nitrogen atom [15].

$$(RO)_2P(S)NHNHAr + R'_2NSCl \xrightarrow{Et_3N} [(RO)_2\overset{+}{P}{=}NNHAr]\rightarrow \underset{SSNR'_2}{|}$$

$$(RO)_2P(S)N(NHAr)SNR'_2$$

100%

Bis(O,O-dialkylthiophosphoryl)trisulfides and O,O-dialkylthiophosphoryl isothiocyanate were obtained in high yields by the reaction between dichlormethyleniminosulfenyl chloride and the sodium or ammonium salts of O,O-dialkyldithiophosphoric acids in a molar ratio of 1:3. The formation of the products was accounted for by the substitution of all the chlorine atoms in the sulfenyl chloride, followed by the migration of a phosphorus-containing group from carbon to nitrogen and the fragmentation of the resulting intermediate compound.

$$Cl_2C{=}NSCl + 3\,MSP(S)(OR)_2 \xrightarrow[20°C]{acetone}$$

$$\left[\begin{array}{l}(RO)_2P(S)S\\ \qquad\qquad\diagdown\\ \qquad\qquad C{=}NSSP(S)(OR)_2\\ \qquad\qquad\diagup\\ (RO)_2P(S)S\end{array}\right] \rightarrow$$

$$\left[(RO)_2\overset{S}{\overset{\|}{P}}-S-\overset{S}{\overset{\|}{C}}-\underset{\underset{P(S)(OR)_2}{|}}{\overset{SSP(S)(OR)_2}{\overset{|}{N}}}\right] \rightarrow$$

$$(RO)_2P(S)SSSP(S)(OR)_2 +$$

73–81%

$$(RO)_2P(S)NCS$$

68–71%

R = Et, Pr, ^{i}Pr; M = Na, NH_4

With an equimolar ratio of the reactants, the initial reaction probably takes place only at the sulfenyl chloride group to yield eventually the O,O-dialkylthiophosphoryl chloride, sulfur and $[ClCN]_3$.

$$Cl_2C{=}NSCl + MSP(S)(OR)_2 \rightarrow [Cl_2C{=}NSSP(S)(OR)_2] - [ClCN]_3 +$$

$$+ (RO)_2P(S)Cl + S$$

Similar results were obtained with free O,O-dialkyldithiophosphoric acids [16].

REACTIONS OF C-SULFENYL CHLORIDES WITH ORGANOPHOSPHORUS COMPOUNDS

Reactions of Trivalent Phosphorus Compounds

Reaction of C-sulfenyl chlorides with alkyl or silyl phosphites *via* an Arbuzov type reaction scheme has been used as an intermediate stage in the synthesis of phospholipid thioanalogs, for example, thiophosphatidilcholine (**13**). It has been shown that the reaction of 1,2-di(stearoyloxy)propyl-3-sulfenyl chloride (**14**), which was obtained *via* chlorinolysis and used without isolation, with cyclic phosphites (**15**) can proceed in two directions: 1) the desirable one (pathway A) with survival of the ring and formation of thiophosphate (**16**) which can react with water-free trimethylamine to yield thiophosphatidilcholine (**13**), and 2) opening of the ring in the intermediate quasiphosphonium salt (**17**) (pathway B). The ratio of the products formed is determined by the nature of the exocyclic substituent in the phosphite (**15**); in the case of the methoxy group, a 2:1 mixture of products of the two pathways is produced (^{31}P NMR spectral data), while the reaction between sulfenyl chloride (**14**) and phosphite (15, R = Me_3Si) leads exclusively to the thiophosphate (**16**) [17].

Studying the interaction of alkyl(tetraethyldiamido)-phosphites with propylsulfenyl chloride, Gasisov, Sal'keeva and Chugunov [18] have substantiated the earlier suggestion that the reactions of such compounds proceed *via* the Arbuzov reaction scheme and excluded the halogenophilic attack of sulfenyl chloride by the trivalent phosphorus atom.

$$(Et_2N)_2POR + PrSCl \xrightarrow[-RCl]{} (Et_2N)_2P(O)SPr$$

R = Et, tert-Bu

It has been shown [19] that, in the reaction of p-nitrophenylsulfenyl chloride with dialkyl vinyl- and dialkyl ethynylphosphonites having two reactive centers capable of an easy reaction with sulfenyl chlorides (i.e., the trivalent phosphorus atom and the unsaturated carbon-carbon bond) the former is more reactive. Unsaturated bonds are not susceptible to attack in benzene at a temperature below 30°C, and O-alkyl-S-p-nitrophenyl esters of α,β-unsaturated thiophosphonic acids are formed in a high yield.

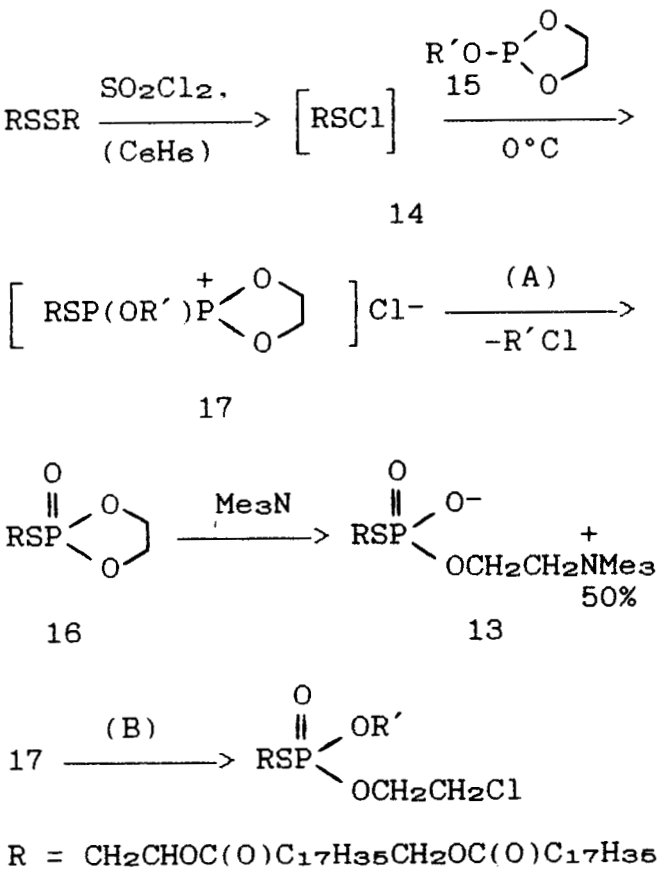
$$(RO)_2PCR'{=}CH_2 + 4\text{-}NO_2C_6H_4SCl \rightarrow RO(CH_2{=}CR')P(O)SC_6H_4NO_2\text{-}4$$

88–92%

$$(EtO)_2PC{\equiv}CPh + 4\text{-}NO_2C_6H_4SCl \rightarrow EtO(PhC{\equiv}C)P(O)SC_6H_4NO_2\text{-}4$$

87%

FIGURE 1



The analogous reaction of ethoxyethynyldi-(tert-butyl)phosphine occurs even at −100°C and phosphoranylydeneketene is obtained in 95% yield. At higher temperatures it dimerizes to give several dimers [20].

$$t\text{-}Bu_2PC{\equiv}COEt + EtSCl \xrightarrow[ether]{-100°C}$$
$$[t\text{-}Bu_2\overset{+}{P}(SEt){-}C{\equiv}C{-}OEt\ Cl^-] \xrightarrow[-EtCl]{}$$
$$t\text{-}Bu_2P(SEt){=}C{=}C{=}O$$

S,S-Diethyl trichloromethyldithiophosphonite reacts exothermically with ethylsulfenyl chloride at room temperature with trichloromethyl group abstraction and yields quantitatively triethyl thiophosphite and carbon tetrachloride [21].

$$(EtS)_2PCCl_3 + EtSCl \rightarrow (EtS)_3P + CCl_4$$

No reaction between the products, $(EtS)_3P$ and CCl_4, occurs at room temperature, but at 140°C they react in a 2:1 molar ratio to give a mixture of products, including diethyl trichloromethyldithiophosphonite, as has been shown previously. An equilibrium has been suggested to be formed in a mixture of the trithiophosphonite and carbon tetrachloride, which is shifted to the right as the sulfenyl chloride reacts with a second trithiophosphite molecule [1].

$$(RS)_3P + CCl_4 \leftrightarrows (RS)_2PCCl_3 + RSCl$$

$$(RS)_3P + RSCl \begin{cases} \rightarrow (RS)_2PCl + RSSR \\ \rightarrow (RS)_3P{=}S + RCl \end{cases}$$

The equilibrium can be shifted more readily by an addition of two equivalents of amine: a reaction occurs even at 80°C in acetonitrile or dimethoxyethane [21].

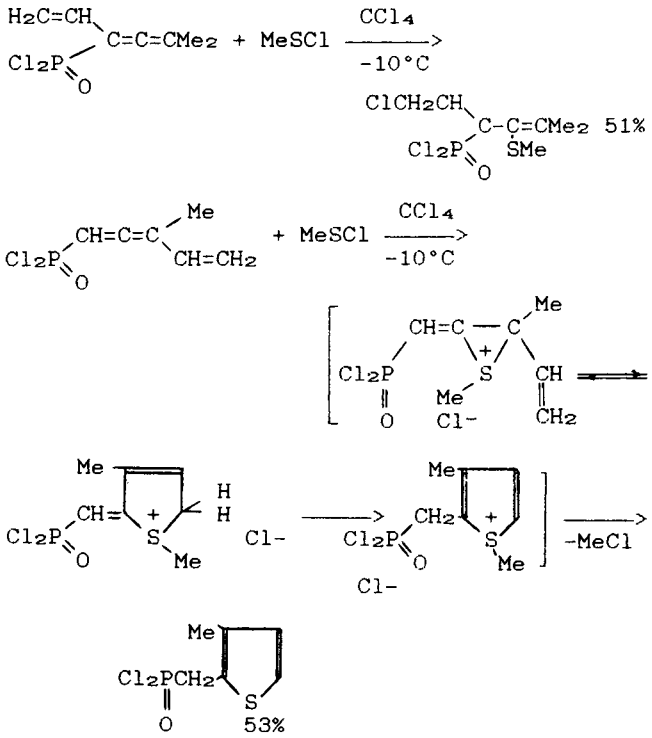
$$(EtS)_3P + CCl_4 + 2\,RNH_2 \rightarrow$$
$$(EtS)_2PCCl_3 + EtSNHR + [\overset{+}{R}NH_3]Cl^-$$
$$R = Et, Pr$$

The reaction of phenylsulfenyl chloride with P-phenyl-C-dimethylaminophosphene has been used for the determination of the direction of P—C bond polarization in this phosphene. These very active compounds react exothermically in the molar ratio 1:2, and the main products have been isolated and identified as bis(phenylthio)phenylphosphine and dimethyl(dichloromethyl)amine; i.e., addition of the PhS-group occurs at the phosphorus atom of the phosphene [22].

$$PhP{=}CHNMe_2 + PhSCl \xrightarrow{MeCN,\ 0°C}$$
$$PhP(SPh)_2 + Cl_2CHNMe_2$$
$$47\% \qquad 73\%$$

Reactions with Pentavalent Phosphorus Compounds

An investigation of the dependence of the course of the reactions between sulfenyl chlorides and allenylphosphonic acid derivatives on the nature of the substituents at the phosphorus and the carbon atoms in the allene system and in the sulfenyl chlorides is now in progress. In particular, it has been shown that, in the reaction of methylsulfenyl chloride with allenylphosphonyl dichloride having a vinyl substituent at the C-1 atom, a product of 1,4-addition to the conjugated double bond system is formed, while the analogous compound with a vinyl group at the 3-position gives 2-dichlorophosphorylmethylthiophene derivatives [23].



In contrast to the dialkyl esters of 3,3-disubstituted allenylphosphonic acids which form with methylsulfenyl chloride a mixture of cyclic and acyclic products, dimethyl(3-methylbuta-1,2-dienyl)-phosphine oxide gives only a 1,2-oxaphosphonium salt both with this sulfenyl chloride and with a series of other electrophilic reagents [24].

$$Me_2P(O)CH{=}C{=}CMe_2 \xrightarrow[CCl_4,0°C]{MeSCl}$$
$$Me_2P(O)CH{=}\overset{+}{C}CMe_2\ Cl^- \rightarrow Me_2P^+(O)(Me)(SMe)\ Me\ Cl^-$$
$$MeS \qquad\qquad 90\%$$

Both chromatographic and NMR spectroscopic studies of the reaction between γ-unsubstituted allenylphosphonates (18, R′ = H) and C-sulfenyl chlorides have revealed for the first time that, not only the above mentioned 2-organylthio-3-chloroprop-1-enyl phosphonates (**19**), but also substantial amounts of the prop-2-enyl isomer (**20**) and small amounts of 2-alkoxy-2-oxo-4-organylthio-1,2-oxaphosphol-3-ens (21) are formed. Under the same conditions 3-monoalkyl substituted allenylphosphonates (18, R′ = Alk) give oxaphospholenes (**21**) as the major products, along with phosphonates (**19**) and 2-organylthio-1-chloroprop-2-enylphosphonates (**22**). In addition, in the reaction with phenylsulfenyl chloride, cyclization to the oxaphospholene (**21**) prevails, while in the reaction with alkylsulfenyl chlorides, the phosphonates (**19**) and oxaphospholenes (**21**) are formed in comparable amounts [25].

$$(RO)_2P(O)CH{=}C{=}CHR' + R^2SCl$$

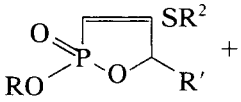
18

$$(RO)_2P(O)CH{=}C(SR^2){-}CH(R')Cl +$$

19

$$(RO)_2P(O)CH_2C(SR^2){=}C(R')Cl +$$

20



$$+(RO)_2P(O)CH(Cl)C(SR^2)CHR'$$

21 **22**

Reactions with Pentavalent Phosphorus Compounds Occurring in a Side Chain

On treatment of the ethyl ester or diethylamide of diethoxyphosphorylacetic acid with sodium hydride in tetrahydrofuran and then with phenylsulfenyl chloride, disubstitution at the methylene group resulting in α,α-bisphenylthio derivatives (60–70% yield) takes place as in the case of the nitrile of this acid studied earlier.

$$(EtO)_2P(O)CH_2C(O)R + 2\ PhSCl \xrightarrow[20°C]{NaH} (EtO)_2P(O)C(SPh)_2C(O)R$$

$R = OEt, NEt_2$

These compounds do not react in the presence of acids. In the absence of a base, diethylamide gives only monosubstituted products.

$$(EtO)_2P(O)CH_2C(O)NEt_2 + PhSCl \rightarrow (EtO)_2P(O)CH(SPh)C(O)NEt_2$$

68.5%

The chloroanhydride of diethoxyphosphorylacetic acid reacts analogously with phenylsulfenyl chloride in the absence of a solvent to form 2-diethoxyphosphoryl-2-phenylthioacetic acid or its methyl ester in 50% yield after treatment with water or methanol [26].

$$(EtO)_2P(O)CH_2COCl$$

1. PhSCl
2. H_2O → $(EtO)_2P(O)CH(SPh)COOH$

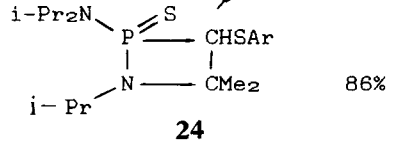
1. PhSCl
2. MeOH → $(EtO)_2P(O)CH(SPh)COOMe$

To prepare 1,2-azaphosphetanes with an arylthio group in the 3-position, reactions of p-tolylsulfenyl chloride with silylated diazamethylthiophosphonate or a phosphorus ylide having a proton in the methylene group were utilized. In the first case, the carbene (**23**) is formed as a result of dinitrogen evolution occurring in benzene at room temperature. The carbene further cyclizes to 1-isopropyl-2-diisopropylamino-3-(p-tolythio)- 4,4-dimethyl-1,2-azaphosphetane (**24**). The same carbene presumably arises on photochemical elimination of triphenylphosphine from the ylide (25) initially formed in the second case, as has been revealed by the final result, i.e., formation of the same 1,2-azaphosphetane (**24**) [27].

$$(i\text{-}Pr_2N)_2P(S)CSiMe_3 + ArSCl \rightarrow [(i\text{-}Pr_2N)_2P(S)CSAr] + Me_3SiCl + N_2$$

Ar = 4-MeC_6H_4

23



86%

24

$$Ph_3P{=}CHP(S)(N\text{-}i\text{-}Pr_2)_2 \xrightarrow[0°C]{ArSCl,\ toluene} Ph_3P{=}C(SAr)P(S)(N\text{-}i\text{-}Pr_2)_2$$

86%

25

$$\xrightarrow[-Ph_3P]{benzene,\ h\nu,\ 0°C} \mathbf{23} \longrightarrow \mathbf{24}$$

78%

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