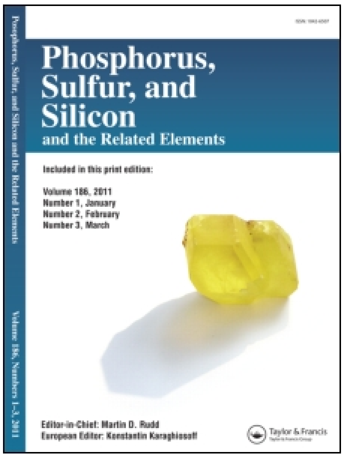

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New Chemistry and Stereochemistry of Organophosphorus Pseudohalogens

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NEW CHEMISTRY AND STEREOCHEMISTRY OF ORGANOPHOSPHORUS PSEUDOHALOGENS

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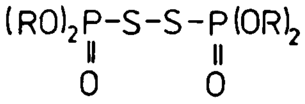
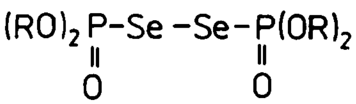
Abstract Synthesis, chemistry and stereochemistry of organophosphorus-sulfur(selenium)pseudohalogens are discussed and rationalized.

The term pseudohalogen was introduced in 1925 by Birckenbach and Kellermann as characteristic for some inorganic radicals, the physical and chemical properties of which resemble those of real halogens.[1,2] Cyanidate, cyanate, thiocyanate, selenocyanate, azide and azidodithiocarbonate are examples of radicals within this category. The term may be extended to include all types of compounds built up by combination in pairs of radicals formed by loss of one electron from a stable electronegatively charged group. The property of the halogens, which is mimicked by the pseudohalogens, is their ability to form interhalogen compounds. Thus formation of pseudohalogeno-halogen structures like Cl-SCN, Br-CN illustrates this property. Pseudohalogens can be compared with the halogens on the basis of their relative oxidizing power.

In 1947 the following types of phosphorus compounds were recognized by Norwegian chemist Olav Foss as the pseudohalogens on the basis of their redox potentials.[3,4]



$$(RO)_2\underset{\underset{O}{\|}}{P}-S-S-\underset{\underset{O}{\|}}{P}(OR)_2$$



$$(RO)_2\underset{\underset{O}{\|}}{P}-Se-Se-\underset{\underset{O}{\|}}{P}(OR)_2$$

R=alkyl

The redox potential of the system has been estimates as E°=-0.56 V

$$(RO)_2P(O)S^- \rightleftharpoons \frac{1}{2}\,[(RO)_2P(O)S]_2 + e$$

R = Me

in water solution which is close to that of involving elemental iodine.

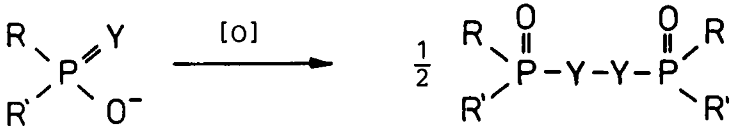
$$I^- \rightleftharpoons \frac{1}{2} I_2 + e \qquad E^\circ = 0.535\ V$$

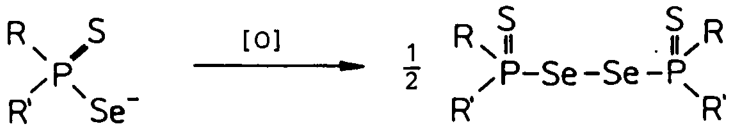
These organophosphorus pseudohalogens have disulfide or diselenide backbone bound to two electronegative phosphoryl groups and they resemble the classic pseudohalogen, thiocyanogen N≡C-S-S-C≡N.[5]

Compounds of the type $(RO)_2P(O)SCl$ representing pseudohalogenohalogens have been obtained for the first time in this laboratory.[6] Discovery of this class of compounds started a new chapter in chemistry and stereochemistry of organophosphorus-sulfur compounds.

Significant progress has been made recently in the field of organophosphorus-sulfur and selenium pseudohalogens. Due to improved methods they became readily available and easier to handle. The aim of this review is to show their wide applicability as reagents of choice in phosphorus and sulfur chemistry. New applications of this class of compounds in the organic synthesis will be also mentioned.

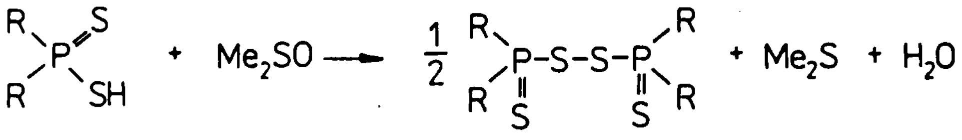
A usual method of preparing organophosphorus pseudohalogens is oxidation of the corresponding thio- or selenoacids salts. Iodine-water system is a most frequently used oxidition agent.[3] Oxidation of thioselenoacids leads exclusively to the diselenide structure.





1

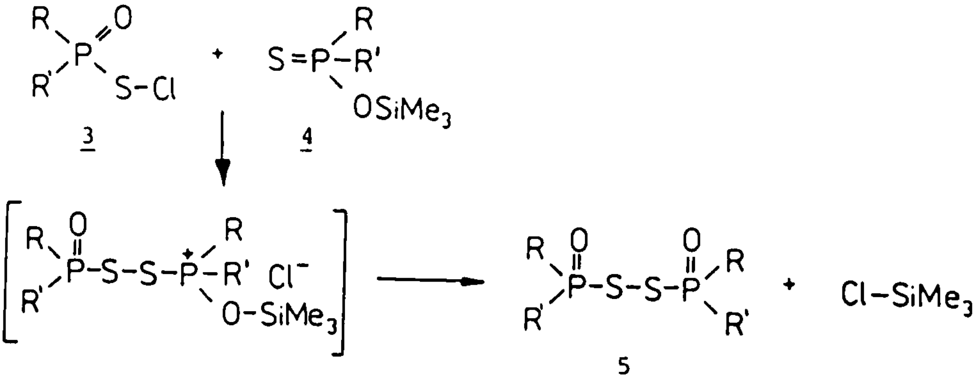
A very simple procedure for the preparation of bis-thiophosphoryl disulfides consists in oxidation of the corresponding phosphorus dithioacids by dimethylsulfoxide under mild conditions.[7]



2

Yields of these oxidations are moderate or good.

Highly efficient and more general method has been recently devised. Oxophosphoranesulfenyl chlorides 3, which chemistry is discussed in the other part of this review, react with trimethylsilylesters of monothioacids 4 to give high yield of the bis-phosphoryl disulfides 5.[8]

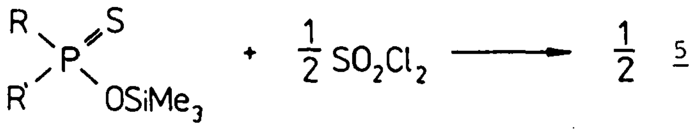


3

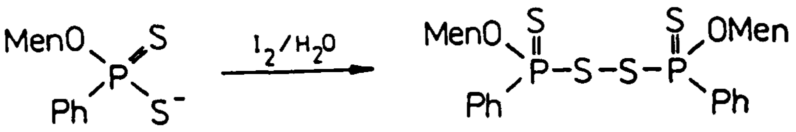
4

5

This reaction proceeds under mild conditions in dichloromethane solution and is also suitable for synthesis of disulfides 5 with different substituents at both phosphorus centers. Stability of the unsymmetrical disulfides is low since they tend to disproportionate. Oxophosphoranesulfenyl chlorides 3 are formed from the trimethylsilylester 4 by action of the elemental chlorine or sulfuryl chloride. Therefore symmetrically substituted disulfides can be prepared without isolation of the intermediate oxophosphoranesulfenyl chlorides 3.



A surprising case of stereospecific oxidation of prochiral dithioacid of phosphorus has been observed recently.[9]



6 $R_{(p)}, S_{(p)}$

7 $S_{(p)}$ $S_{(p)}$

m.p. 87-88°C

$[\alpha]_D^{20} = -54.3°$ (CHCl$_3$)

$\delta^{31}P$ 102.1 (CHCl$_3$)

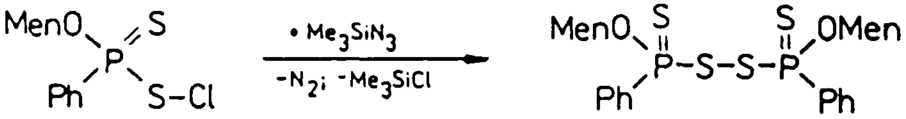
m.p. 153-154°C

$[\alpha]_D^{20} = +330.5°$ (C$_6$H$_6$)

$\delta^{31}P$ 86.9 (C$_6$D$_6$)

Men=L(-)menthyl

The disulfide 7 of the same configuration at P-centers has also been prepared from chiral R_P-L-menthoxyphenylthioxaphosphoranesulfenyl chloride 34 in reaction with trimethylsilylazide.



34 $R_{(p)}$

7 $S_{(p)}$ $S_{(p)}$

$[\alpha]_D^{20} = -129.3°$ (C$_6$H$_6$)

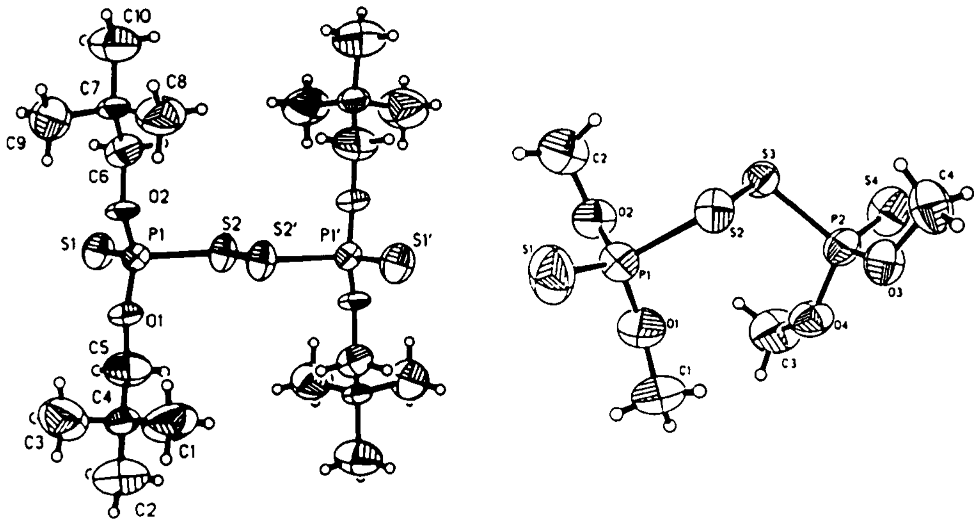
$\delta^{31}P$ 83.1 (hexane)

m.p. 153-154°C

$[\alpha]_D^{20} = +330.5°$ (C$_6$H$_6$)

$\delta^{31}P$ 86.9 (C$_6$P$_6$)

The bis-(O-L-menthylphenylthiophosphonyl)disulfide 7 became a new source of chiral organophosphorus-sulfur compounds of defined configuration at the P-center. The absolute configuration S_P at both phosphorus atoms has been established by X-ray crystallography.[9] Conformation and length of the disulfide bonds are very important in relation to the secondary structure of proteins. Despite many efforts to rationalize the structural properties of the disulfide bond some problems are still a subject for considerable discussions. The most challenging question is the relationship between S-S bond length and torsional angle of C-S-S-C unit. In globular proteins, packing requirements may result in torsional angle that is very substantially different from the widely accepted value of about 90° for L-cysteine aqueous media. Bis(dialkoxythiophosphoryl)disulfides 2a,b proved to be very convenient models for studies of nature of the disulfide bond. The X-ray and solid state NMR studies showed that conformations with torsional angle in the range 100 - 180° are common for the P-S-S-P unit. Furthermore it has been established that the relationship between disulfide bond length and the torsional angle is extremely accurate with those reported for similar C-S-S-C backbone.[10] Structures of disulfides 2a,b are exemplified on Figure 1.



2a 2b

FIGURE 1 Structures of the disulfides 2

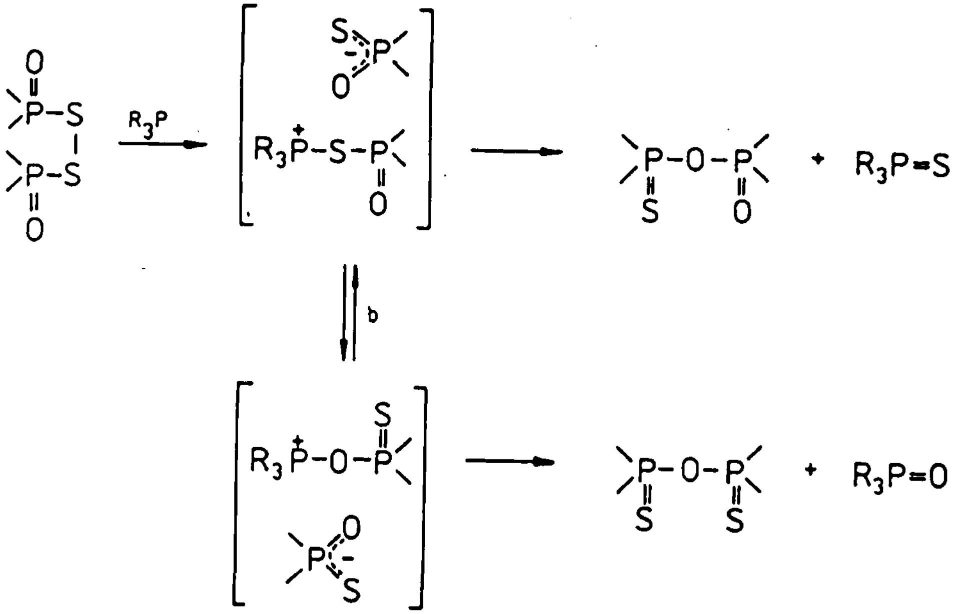
a. bis(dineopenthoxythiophosphoryl)disulfide, torsion angle 180°

b. bis(dimethoxythiophosphoryl)disulfide, torsion angle 105°

Organophosphorus pseudohalogens containing reactive disulfide or diselenide unit exhibit strong sulfur or selenium kationoid properties. The S-S or Se-Se bonds are very readily cleft by nucleophiles due to generation of a stable monothioacid (or selenoacid) anions. Reactions with tricoordinate phosphorus compounds are of special interest.

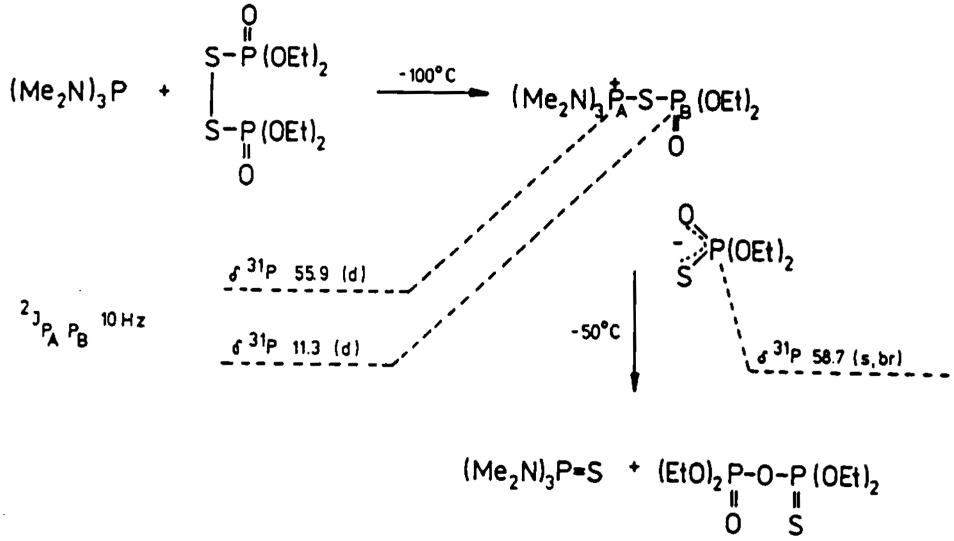
Such reactions can be classified as desulfurization, deselenization and deoxygenation processes, and they result in the formation of various useful products. The general pattern of the reaction is illustrated on the Scheme 1.

SCHEME 1



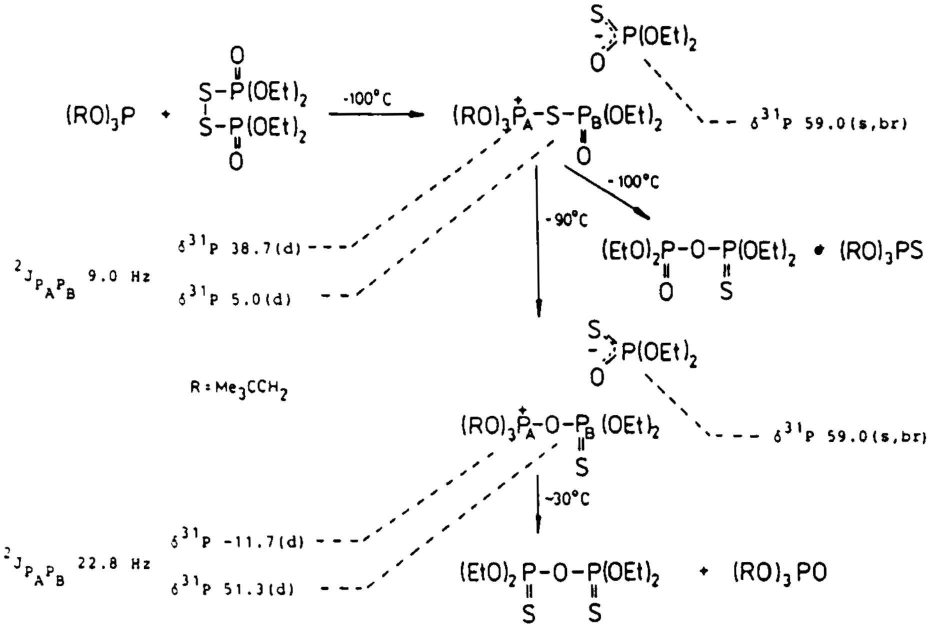
The reaction with diselenides takes similar course. This scheme is adequate for the substituents R which do not undergo dealkylation. Additional products are observed when alkoxy group is attached to the phosphonium center. These products have their origin in nucleophilic attack of thioacid counterion on the alkoxy group. When tris(dimethylamino)phosphine was used selective desulfurization (or deselenization) took place. In this case the thermally labile phosphonium intermediates containing P-S-P or P-Se-P bridges decompose via the nucleophilic attack of the counterion on the phosphoryl center.

SCHEME 2



One sulfur (selenium atom is removed as a part of the leaving group. As a consequence the thiophosphorotriamidate and unsymmetrical monothiopyrophosphate are formed. The structure of the $>\overset{+}{P}$-S-P(O)< intermediate has been firmly established by ^{31}P NMR spectroscopy.

SCHEME 3

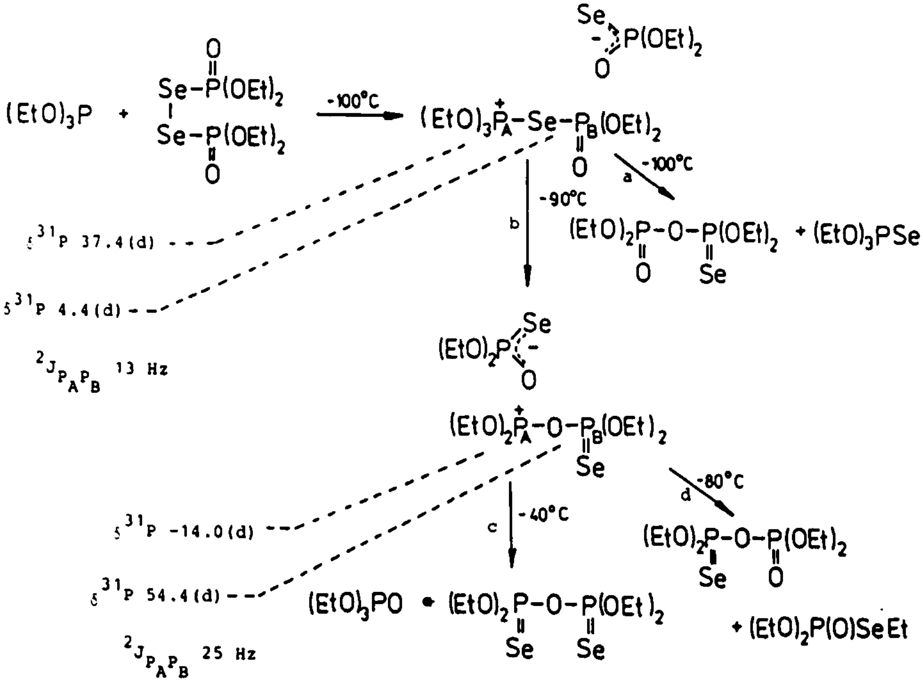


The chemical shifts, multiplicity of spectral terms and relatively low coupling constant between phosphorus atoms of P-S-P unit are in agreement with the proposed structure.

An example of the reaction involving both desulfurization and deoxygenation pathways is the one between bis(diethoxyphosphoryl)disulfide and trineopentyl phosphite.

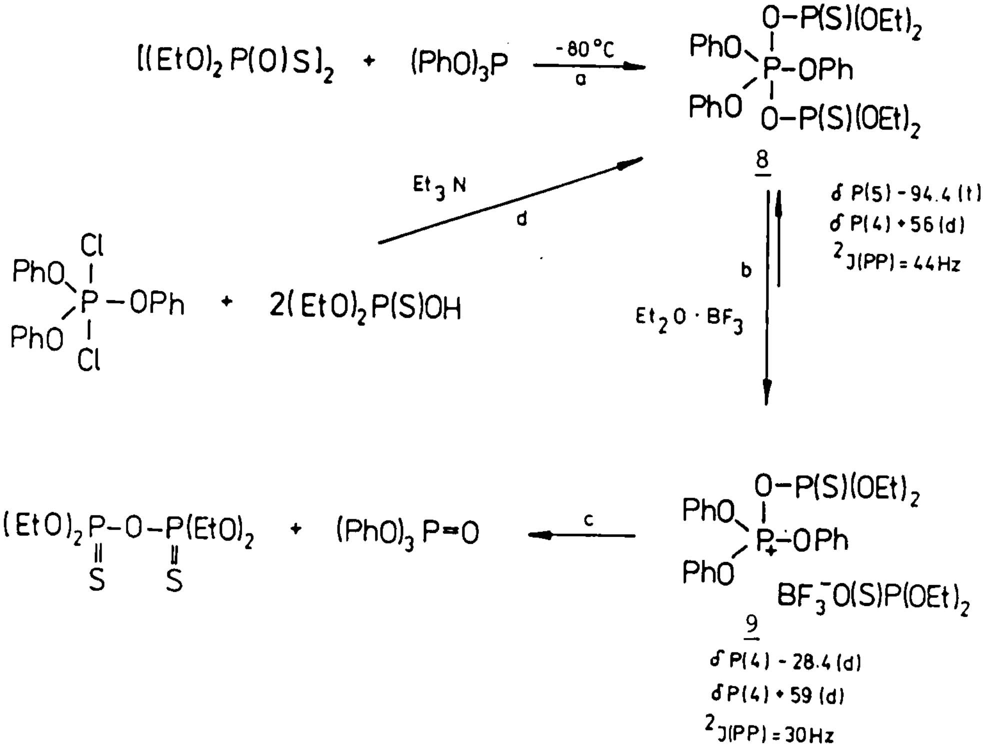
The neopentoxy group is known to resist dealkylation, which explains relative simplicity of the Scheme 3. When tricoordinate substrates have alkoxy groups prone to dealkylation the reaction pathway is more complex. The additional products, which have their origin in dealkylations of the intermediate phosphonium structures are formed. This is illustrated on the Scheme 4 in the case of the reaction between bis(diethoxyphosphoryl)selenide and triethylphosphite.

SCHEME 4



The intermediate compound with one five coordinate phosphorus central atom and two adjacent four coordinate phosphorus atoms linked by the oxygen bridge has been demonstrated in the reaction between bis(diethoxyphosphoryl)disulfide and triphenylphosphite.

SCHEME 5

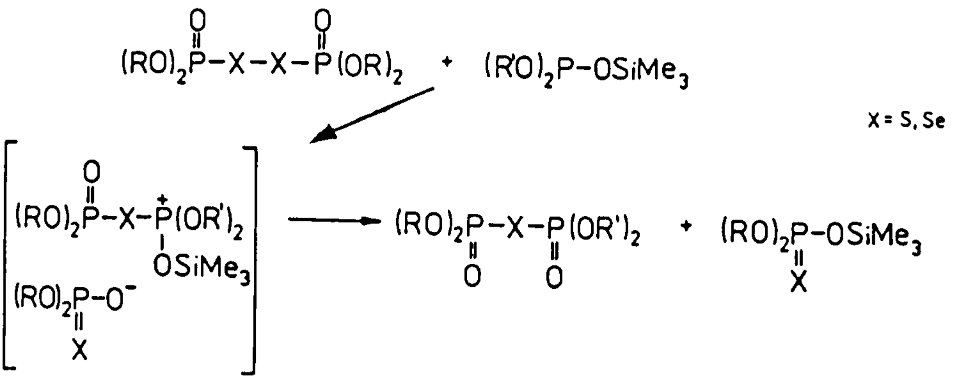


Upfield chemical shifts observed for the compound 8 and independent synthesis of 8 from the dichlorotriphenoxyphosphorane (step d) indicate the pentacoordinate nature of 8. These data, however, do not give an unambigous answer concerning the position of ligands in the trigonal bipyramidal structure involved. When phosphorane 8 was treated at -80°C with an excess of boron fluoride etherate, a well known trap for nucleophiles, the ^{31}P NMR spectra confirmed the presence of the starting phosphorane and the phosphonium salt 9. After several minutes, when the temperature was raised to -60°C, the phosphonium salt was the only observable species. Such a result suggests the existance of an equilibrium between 8 and 9. The subsequent decomposition of the phosphorane 8 occurs, giving the deoxygenation products via the phosphonium salt 9 (steps b and c).

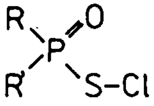
The ^{31}P NMR spectroscopy data gave an unambigous evidence that the key intermediates in the desulfurization, deselenization and deoxygenation processes are the phosphonium salts $>\overset{+}{P}-S-P(O)<$ and

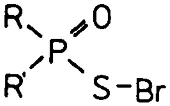
$>\overset{+}{P}\text{-Se-P(O)}<$ containing P-S-P or P-Se-P bridges, respectively. Such salts have the electrophilic centers at the phosphoryl and at the phosphonium phosphorus atoms. Depending on the electronic and steric features of substituents at both phosphorus atoms and on the reaction conditions, the nucleophilic attack of the counterion may occur on the phosphoryl or the phosphonium center or on both centers. Therefore, the reaction selectivity depends on the relative rates of nucleophilic displacement at both phosphorus atoms. The mechanistic schemes presented above are in full agreement with stereochemical studies using optically active, diastereomeric tetra- and tricoordinate phosphorus model compounds.[11-13]

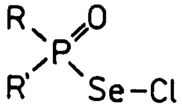
The course of the reaction between bis-phosphoryl disulfides and diselenides is strikingly changed when trialkylphosphites are replaced by those containing trimethylsilyloxy group. In such reaction, fully chemoselective attack of phosphorothioic (or phosphoroselenoic) counter anion on silicon center in the intermediate phosphonium salt is observed. Consequently sym- thiopyrophosphates and sym- selenopyrophosphates are formed in excellent yield.[14]

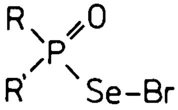


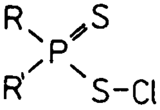
The oxophosphoranesulfenyl chlorides RR'P(O)SCl were obtained a relatively long time ago, but only recently more efficient methods of their preparation have been available. Following phosphorus pseudohalogenohalogens have recently become relatively readily accessible with an aid of methods worked out in our Laboratory.

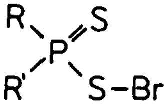


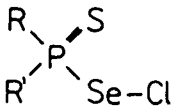


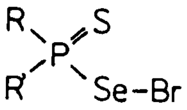


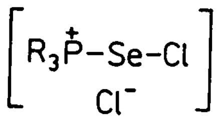








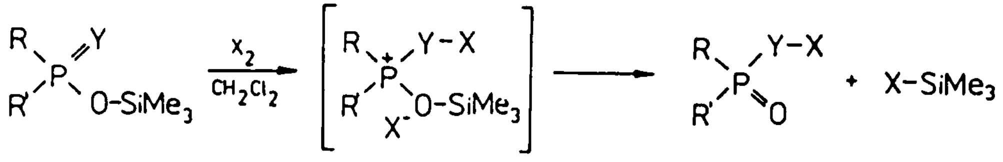




$$\left[R_3\overset{+}{P}-Se-Cl\quad Cl^-\right]$$

Although these compounds differ in stability, they can be prepared in solution in high purity and immediatly used for further transformations. Many systems mentioned contain chiral center at the phosphorus atom can be obtained in pure enantiomeric or diastereoizomeric forms.

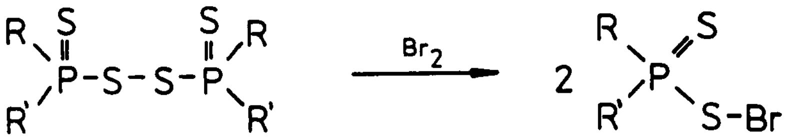
The oxophosphoranesulfenyl and selenyl halides can be prepared from the trimethylsilylesters of the parent thio- or selenoacids in high yield and purity.[8]



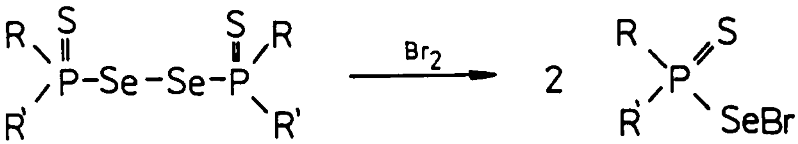
X = Cl, Br

Y = S, Se

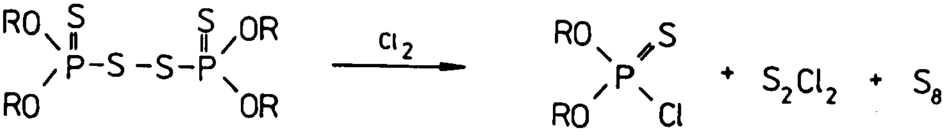
The pseudohalogeno-halogens derived from phosphorus dithioacids have become available in pure form only recently. Thioxaphosphoranesulfenyl bromides can be readily obtained from the corresponding disulfides by reaction with the elemental bromine.[15,16]



In similar way relatively stable thioxaphosphoraneselenyl bromides can also be prepared.[17]

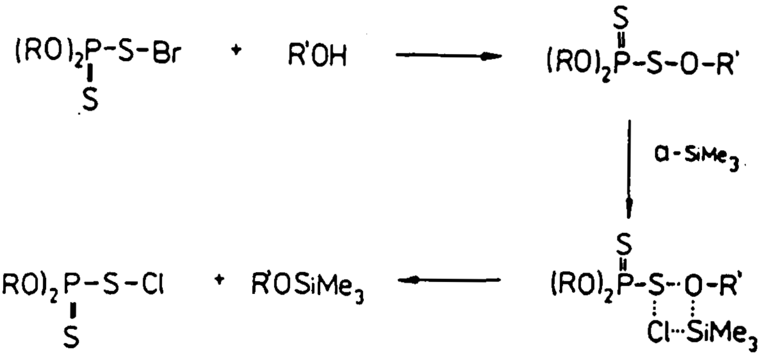


It seems somewhat surprising that the reaction of disulfides derived from dithioacids with elemental chlorine or other chlorinating reagents proceeds in a different way in contrast to that with elemental bromine.[18,19]



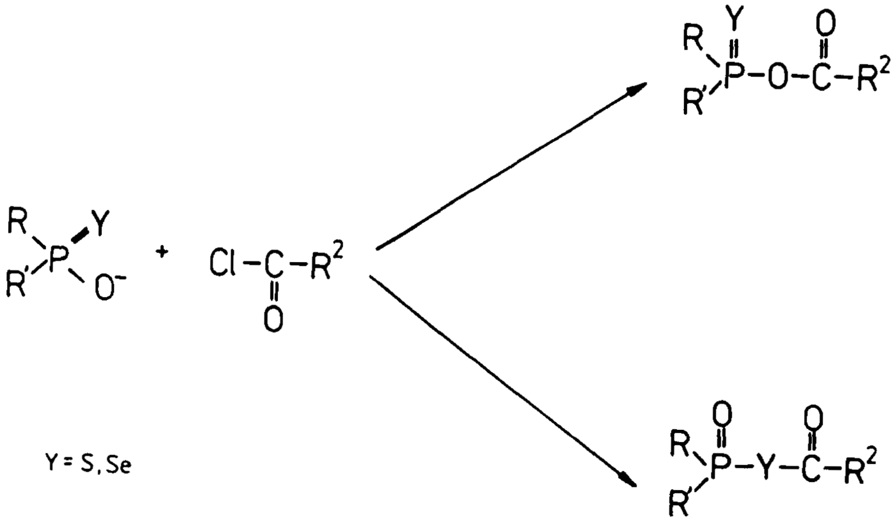
This difference has its origin in the fast reaction between intermediate thioxaphosphoranesulfenyl chloride 10 and elemental chlorine and other chlorinating species involved in the reaction.

Thioxaphosphoranesulfenyl chlorides 10 can be obtained from the corresponding bromides by the two steps procedure. The bromide is converted by reaction with methanol in the presence of a suitable tertiary amine into sulfenate ester which is allowed to react with trimethylsilyl chloride. This transformation can be performed as one-flask procedure without isolation of the sulfenate ester.[16] This interesting reaction between sulfenyl ester and trimethylsilyl chloride seems to proceed via four center transition state and is geared by high affinity of the silicon center towards oxygen. This reaction is analogous to that described by Harp et al. for simple organic sulfenates.[20]



10

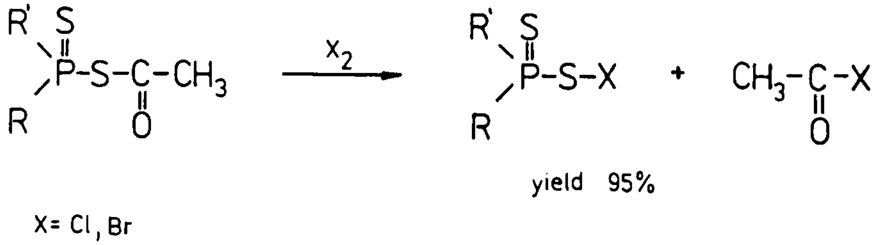
More general synthesis of phosphorus pseudohalogenohalogens is based on mixed anhydrides of thiophosphorus (or selenophosphorus) acids and carboxylic acids.[21] These anhydrides can be prepared by condensation of the corresponding thio- or selenoacids with acyl halides in the presence of a base. Due to the ambident character of anions, two izomeric anhydrides are formed.



An interesting case of an ambident anion is that derived from thioselenoacids. Its acylation also leads to the mixture of two izomeric anhydrides. The structure of the anhydrides can be unambigously assigned by ^{31}P NMR chemical shifts and $^2J(^{31}P^{77}Se)$ coupling constants. A more convenient method leading to the pure anhydrides is the reaction of free phosphorus thio- or selenoacids with ketene.[22] This method is exemplified by reaction between phosphorus dithioacids and ketene (Scheme 6).[23]

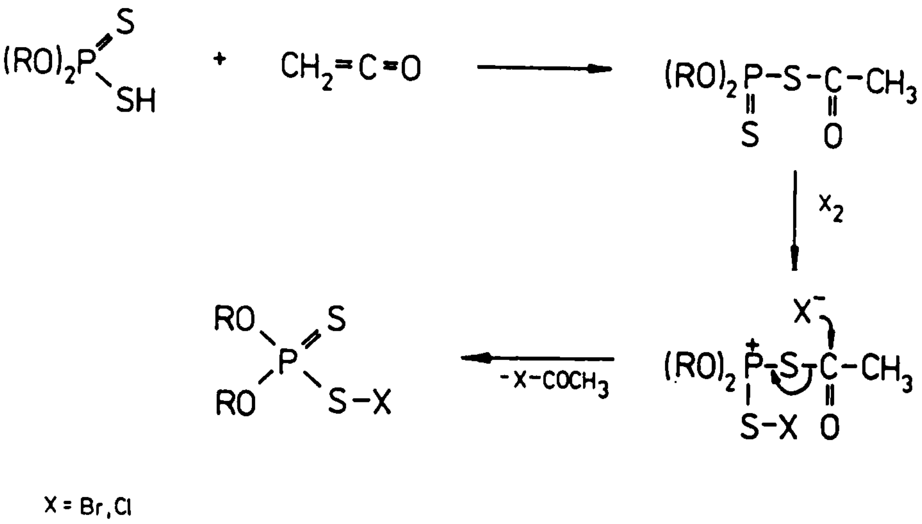
The same reaction with monothioacids leads to O-bridged anhydrides >P(S)-O-CO-. In the case of thioselenoacids >P(Se)SH two izomeric anhydrides >P(S)-Se-CO- and >P(Se)-S-CO-, identical with those prepared by acylation with acyl halides, are formed.

Both types of anhydrides, containing oxygen or sulfur (selenium) bridge react with elemental bromine and chlorine to give the sulfenyl and selenyl halides in good yield.



The mechanistic explanation of this reaction is similar to that involving interaction of elemental halogen with trimethylsilyl esters of the corresponding thio- and selenoacids. In the intermediate phosphonium salt the carbonyl group is a site of preferentional attack by the counter ion, namely Br$^-$ or Cl$^-$.

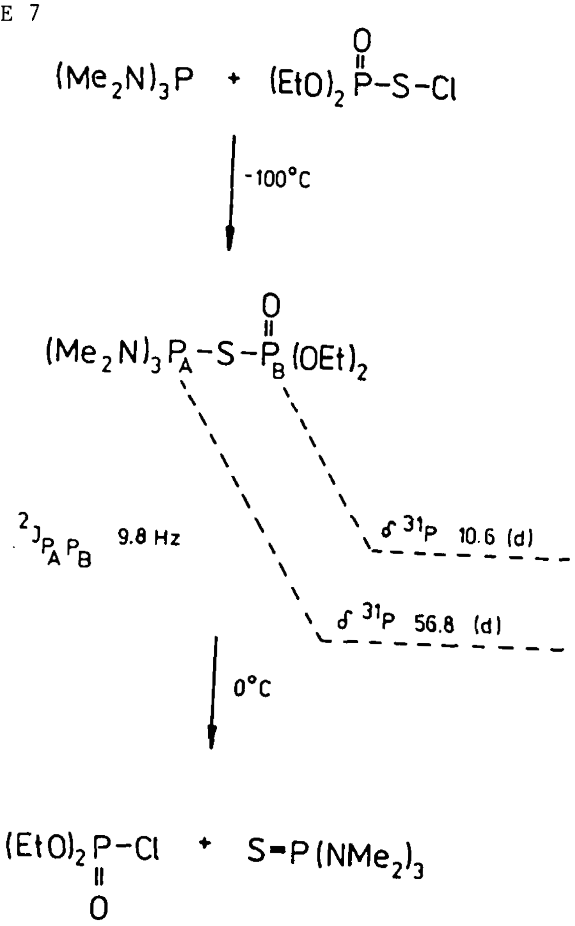
SCHEME 6



Pseudohalogeno-halogens are versatile thio- and selenophosphorylating reagents containing kationoid dicoordinate sulfur or selenium atoms attached to the tetracoordinate phosphorus center. The addition to ethylenic systems, aromatic substitution and reactions with C, O, S, N, P nucleophiles are to be mentioned.[11,16,24-26]

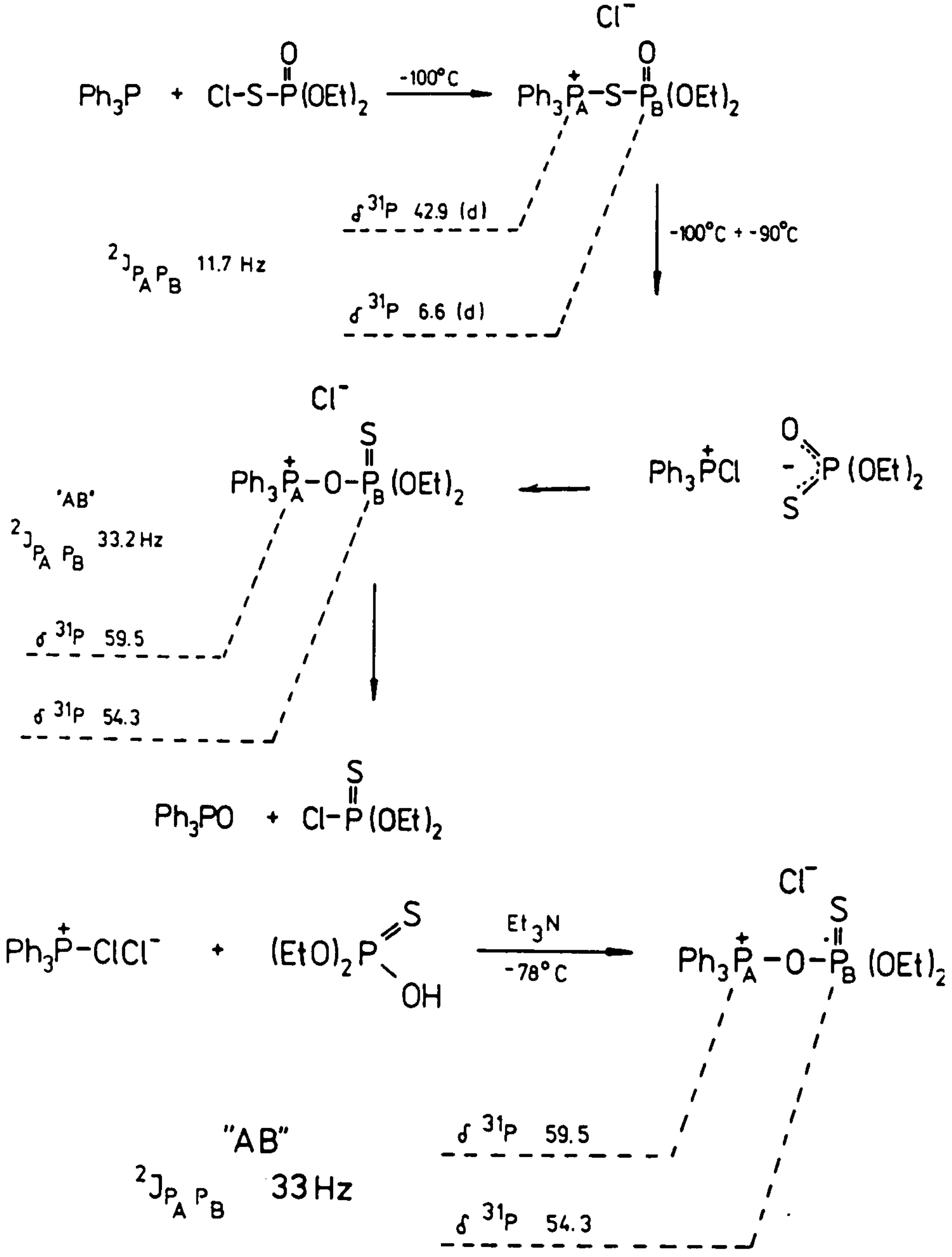
Special attention was paid to the reactions of pseudohalogeno-halogens with tricoordinate phosphorus compounds. They react in a manner similar to phosphorus pseudohalogens containing disulfide and diselenide units. Three main reaction pathways are observed: desulfurization (or deselenylation), deoxygenation and in case of trialkylphosphites also dealkylation.[11,27-30]
Chemoselective desulfurization is observed in the reaction between tris(dimethylamino)phosphine and diethoxyoxophosphoranesulfenyl chloride (Scheme 7).

SCHEME 7

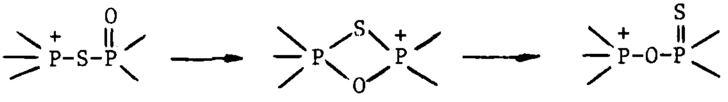


Similar reaction with triphenyl phosphine (Scheme 8) proceeds via deoxygenation pathway involving izomerization of the intermediate phosphonium salt $>\overset{+}{P}-S-P(O)<$ into the $>\overset{+}{P}-O-P(S)<$. In this case an independent synthesis of the oxygen bridged intermediate fully confirms the observed sequence of events.

SCHEME 8



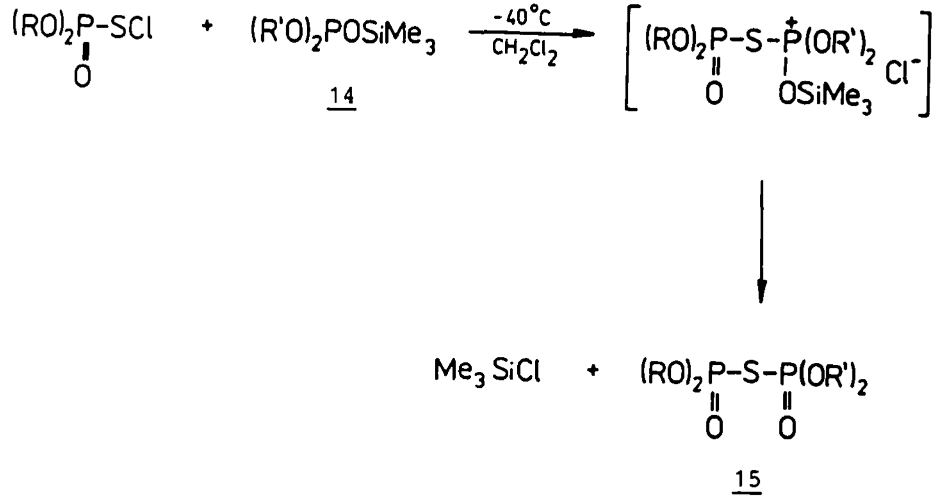
The mode of izomerization shown on the Scheme 8 consists of nucleophilic attack of the chloride anion on the phosphonium phosphorus atom and subsequent recombination of the ion pair formed according to "hard-hard" centers interaction. However, the conversion of the sulfur bridged intermediate 11 into the oxygen bridged one 12 through a cyclic complex 13 cannot be excluded.



11 13 12

The cyclic intermediate is even more likely to be involved when ligands, which have stabilizing effect on the pentacoordinate phosphorus structure, are present.

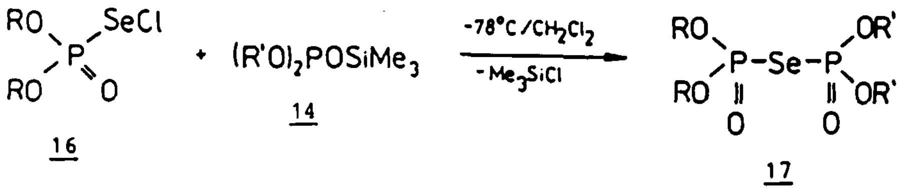
We have found that course of the reaction between oxophosphoranesulfenyl chlorides and tricoordinate phosphorus compounds could be noticeably changed using dialkyl trimethylsilyl phosphites 14. The only products observed are the sym- monothiopyrophosphates 15 resulting from the attack of a chloride ion on a silicon atom in the intermediate phosphonium salt.[31,32]



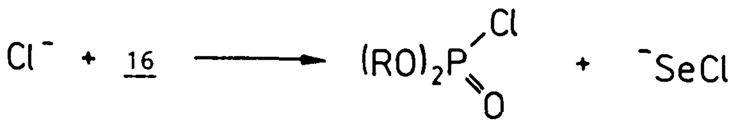
14

15

The sym- monoselenopyrophosphates 17 are effectively synthesized from trimethylsilylphosphites and the oxophosphoraneselenyl chlorides 16.[32,33]



The chlorides 16 decompose rapidly even below -40°C by a chain reaction involving nucleophilic displacement at the phosphoryl centre by chloride anion.



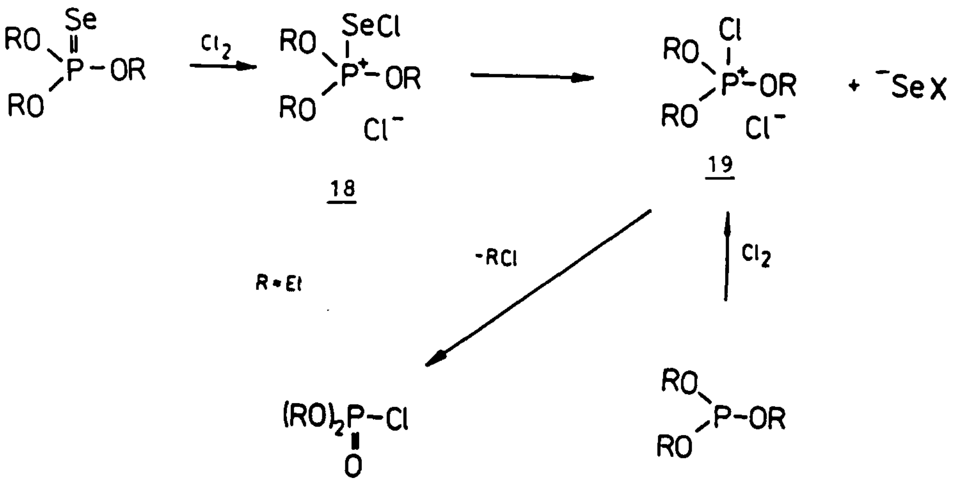
$$Cl^- + \underline{16} \longrightarrow (RO)_2P(O)Cl + {}^-SeCl$$

$$x\,(\bar{S}eCl) \longrightarrow Se_x + x\,Cl^-$$

The SeCl group is very readily displaced at both phosphoryl and phosphonium centres. The phosphonium intermediates 18 and 19 are observed at -78°C by ^{31}P NMR spectroscopy when elemental chlorine is allowed to react with the trialkylselenonophosphate.

The structure of the phosphonium salt has been confirmed by its independent synthesis via Arbuzov reaction between triethyl phosphite and elemental chlorine (Scheme 9).

SCHEME 9

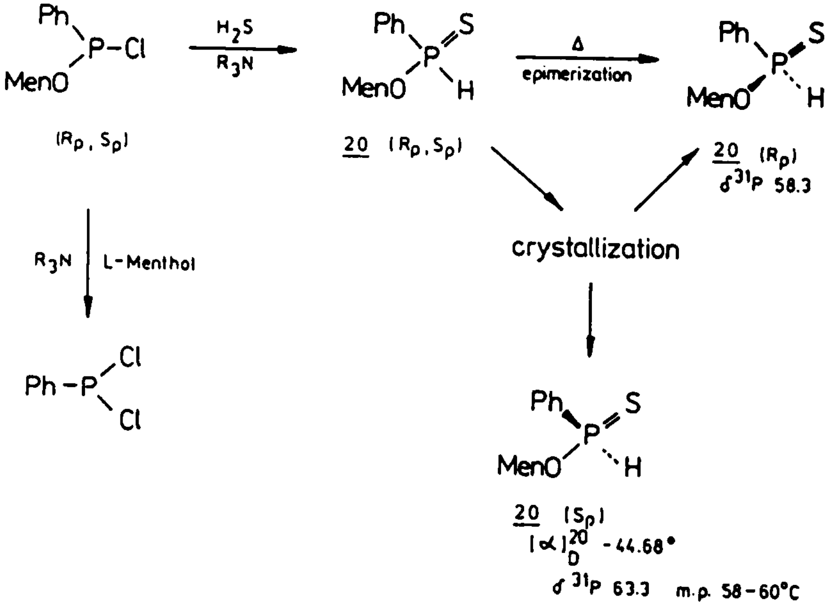


It is of interest to note that compounds of the general formula $[(RO)_3\overset{+}{P}\text{-SeCl}]Cl^-$ are stable enough to be applied as useful synthetic reagents. Their application will be demonstrated in the other part of this review.

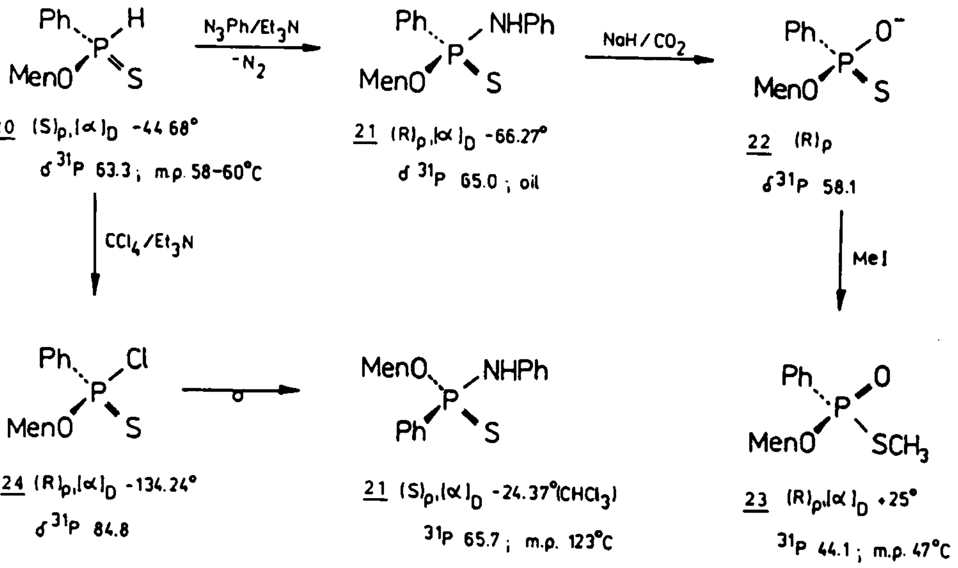
Special attention was focused on P-chiral thioxaphosphoranesulfenyl derivatives of general formula RR'P(S)SX in hope that they can be used as a new tool in stereochemistry of phosphorus and sulfur compounds.[9,21]

P-chiral thioxaphosphoranesulfenyl chlorides containing L-menthoxy group as an auxiliary source of chirality were synthesized by the following strategy. The L-menthoxyphenylchlorophosphine was prepared from L-menthol and phenyldichlorophosphine and without purification allowed to react with the hydrogen sulfide. This sequence of reactions produced the expected L-menthylphenylhydrogen thiophosphonate as a mixture of $(R)_P$ and $(S)_P$ diastereoizomers which can be separated into crystalline $(S)_P$ 20 izomer and an oily residue with the $(R)_P$ 20 as main component.

More detailed studies revealed that $(R)_P$ izomer rearranges thermally or under influence of acids into the mixture of both izomers. This property allows full conversion of the reaction product into the single diastereoizomer $(S)_P$ 20.



Absolute configuration at the phosphorus atom and the high optical purity of the hydrogen phosphonate $(S)_P$ 20 were established by combination of chemical correlations and X-ray crystallography. The thiophosphonate $(S)_P$ 20 was transformed by Staudinger type reaction into the phosphoroamidate $(R)_P$ followed by 21, Wadsworth, Emmons and Stec procedure leading to the salt of phosphonothioic acid $(R)_P$ 22.[34] The latter was converted into the phosphonothiolate $(R)_P$ 23 of the known absolute configuration.[35] All these reactions proceed with retention of configuration at the phosphorus center and without ligand methathesis.



20 $(S)_P$, $[\alpha]_D$ -44.68°
$\delta\,^{31}P$ 63.3; m.p. 58-60°C

21 $(R)_P$, $[\alpha]_D$ -66.27°
$\delta\,^{31}P$ 65.0; oil

22 $(R)_P$
$\delta\,^{31}P$ 58.1

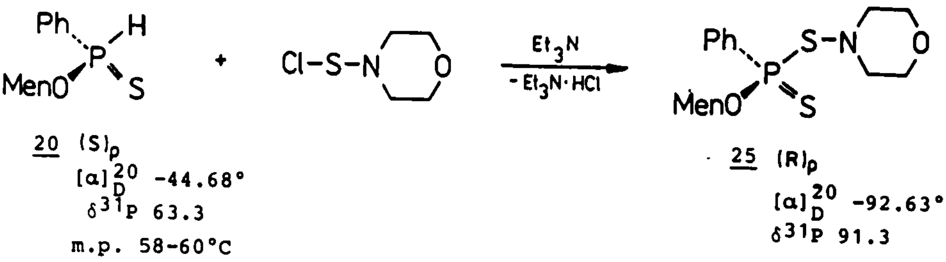
24 $(R)_P$, $[\alpha]_D$ -134.24°
$\delta\,^{31}P$ 84.8

21 $(S)_P$, $[\alpha]_D$ -24.37°$(CHCl_3)$
^{31}P 65.7; m.p. 123°C

23 $(R)_P$, $[\alpha]_D$ +25°
^{31}P 44.1; m.p. 47°C

The crystalline anilidate $(S)_P$ 21 can be also obtained by chlorination of the hydrogenthiophosphonate $(S)_P$ 20 with carbon tetrachloride in the presence of triethylamine leading to the phosphonochloridate $(R)_P$ 24 followed by reaction of the latter with aniline. The first of these reactions proceeds with retention of configuration at P-center, the second, being a typical nucleophilic displacement, with the inversion of configuration yielding the anilidate $(S)_P$ 21 of opposite configuration to that obtained by Staudinger reaction.

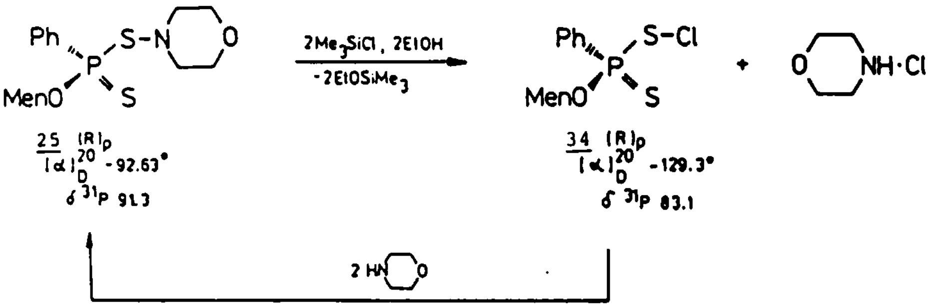
The hydrogenthiophosphonate $(S)_P$ 20 was allowed to react with morpholine sulfenyl chloride to yield the corresponding thioxaphosphoranesulfenyl morpholidate $(R)_P$ 25 in almost quantitative yield and full stereoselectivity.[9]



20 (S)$_P$
$[\alpha]_D^{20}$ −44.68°
$\delta^{31}P$ 63.3
m.p. 58-60°C

25 (R)$_P$
$[\alpha]_D^{20}$ −92.63°
$\delta^{31}P$ 91.3

L-menthoxyphenylthioxaphosphoranesulfenyl chloride (R)$_P$ 34 was prepared from the morpholidate (R)$_P$ 25 by reaction with hydrogen chlorine. Conversion of thioxaphosphoranesulfenamidates into the corresponding sulfenyl chloride in reaction with hydrogen chloride was described by Almasi.[36] This reaction when performed according to the Almasi procedure by blowing excess of hydrogen chloride into a solution of thioxasulfenamide gives fair yield (40-60%) of the sulfenyl chlorides contaminated with a spectrum of other products. This method when applied to the pure diastereoizomeric sulfenamides causes full loss of stereochemical identity at the chiral phosphorus center and leads to 1:1 mixture of the corresponding diastereoizomers. The thioxaphosphoranesulfenyl chlorides have been obtained in excellent yield, only when thioxaphosphoranesulfenamides were allowed to react with hydrogen chloride produced in situ from trimethylsilyl chloride and ethanol.[37] This procedure was applied to synthesize pure diastereoizomeric L-menthoxyphenylthioxaphosphoranesulfenyl chloride (R)$_P$ 34.



25 (R)$_P$
$[\alpha]_D^{20}$ −92.63°
$\delta^{31}P$ 91.3

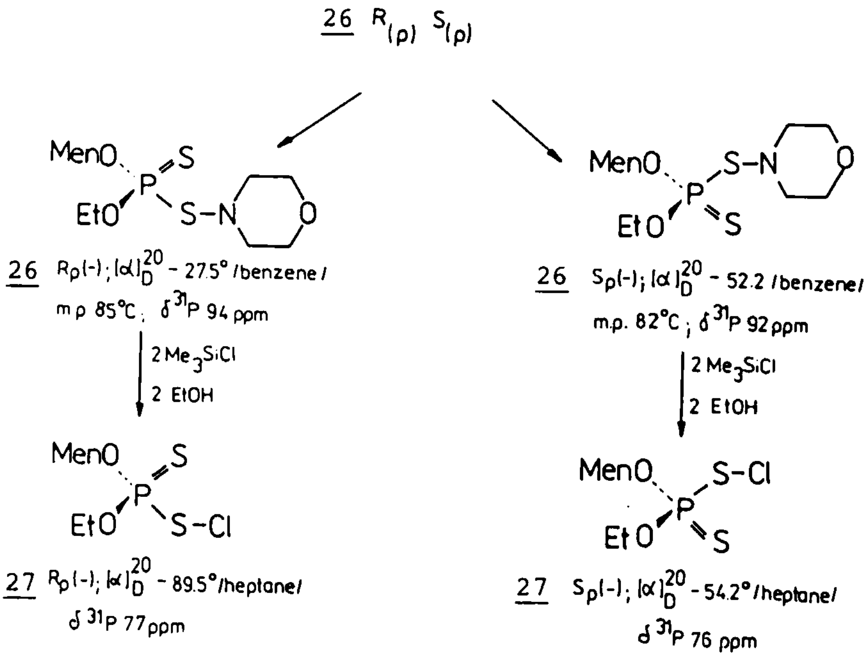
34 (R)$_P$
$[\alpha]_D^{20}$ −129.3°
$\delta^{31}P$ 83.1

Our failure to prepare the pure (S)$_P$ 34 diastereoizomer has its origin in lack of the suitable starting materials. The already mentioned L(−)menthylphenylhydrogen phosphonate (R)$_P$ 20 is not available.

We also failed to separate the sulfenamides 25 into the diastereoizomers. The purity of the $(R)_P$ 34 was established by ^{31}P NMR spectroscopy and its stereospecific conversion into the starting sulfenamide $(R)_P$ 25.

Having in mind the application of thioxaphosphoranesulfenyl chlorides as stereochemical probes it was advantageous to find out models which can be prepared in both diastereoizomeric forms $(R)_P$ and $(S)_P$. This goal was achieved in the case of L-menthoxyethoxyoxophosphoranesulfenyl chlorides $(R)_P$ 27 and $(S)_P$ 27, which were synthesized by similar strategy.

Crude ethyl L-menthylphosphorochloridite was converted into ethyl-L-menthyl hydrogenthiophosphonate and afterwards into the mixture of diastereoizomeric sulfenamides $(R)_P$, $(S)_P$ 26. This mixture was separated into the pure diastereoizomers by crystallization from absolute ethanol. Their purity and absolute configuration was established by ^{31}P NMR and X-ray spectroscopy.



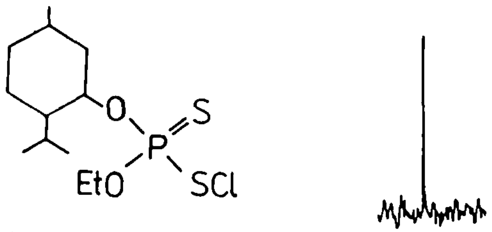
26 $R_p(-)$; $[\alpha]_D^{20}$ $-27.5°$ /benzene/ m.p. 85°C; $\delta\,^{31}P$ 94 ppm

26 $S_p(-)$; $[\alpha]_D^{20}$ -52.2 /benzene/ m.p. 82°C; $\delta\,^{31}P$ 92 ppm

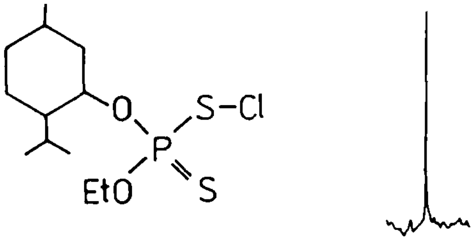
27 $R_p(-)$; $[\alpha]_D^{20}$ $-89.5°$/heptane/ $\delta\,^{31}P$ 77 ppm

27 $S_p(-)$; $[\alpha]_D^{20}$ $-54.2°$/heptane/ $\delta\,^{31}P$ 76 ppm

Full stereoselectivity of the reaction between sulfenamides $(R)_P$ 26 and $(S)_P$ 26 and hydrogen chloride was confirmed by reconversion of the sulfenyl chlorides $(R)_P$ 27 and $(S)_P$ 27 formed into the original sulfenamides.[38] Diastereoizomeric purity of the sulfenyl chlorides can be conveniently estimated by ^{31}P NMR spectroscopy.



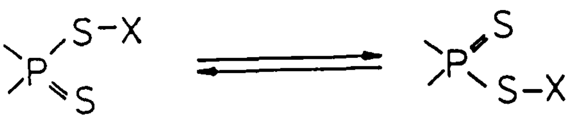
$(1R,2S,5R)_c$ $(R)_p$

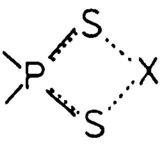


$(1R,2S,5R)_c$ $(S)_p$

$(R+S)_p$

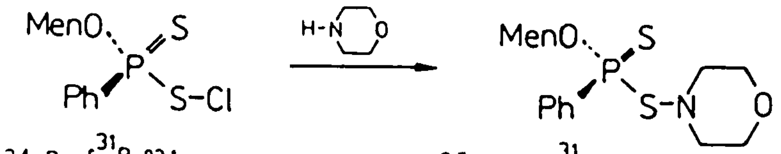
Successful stereoselective synthesis of configurationally stable sulfenyl chlorides demonstrates an absence of halotropy and excludes symmetrical structure in which the chloride atom is bound to both sulfur atoms since this type of structure is achiral.





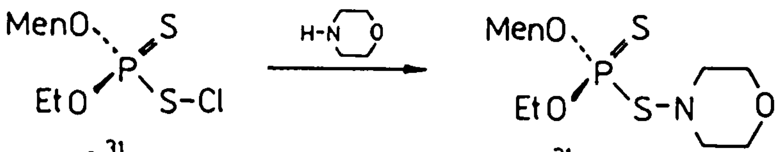
Thioxaphosphoranesulfenyl chlorides RR'P(S)SCl are very reactive towards a spectrum of nucleophiles. Their chemical behaviour is similar to other compounds of dicoordinate sulfur of the general formula R-S-X, where X is a good leaving group. The previous mechanistic studies on the nucleophilic displacement at a dicoordinate sulphur atom based on kinetics and free energy correlations have led to the general belief that such substitutions normally entail a trigonal bipyramidal intermediate (or transition state) in which the entering and leaving groups occupy and apical position.[40]

P-chiral sulfenyl chlorides 34, 27 can be employed as a stereochemical probe for displacement reactions occuring at dicoordinate sulfur in this type of compounds. Only these processes at sulfur center in which bond formation and bond breaking proceed in dissociative manner either ionic or radical should result in loss of the stereochemical identity at the chiral phosphorus center. In contrast synchronous S_N2 and addition-elimination processes should proceed with retained stereochemical identity at the phosphorus center.
To illustrate this, reactions of the P-chiral sulfenyl chlorides $(R)_P$ 34, $(R)_P$ 27 and $(S)_P$ 27 with secondary amines such as morpholine and dicyclohexylamine were investigated.[39]



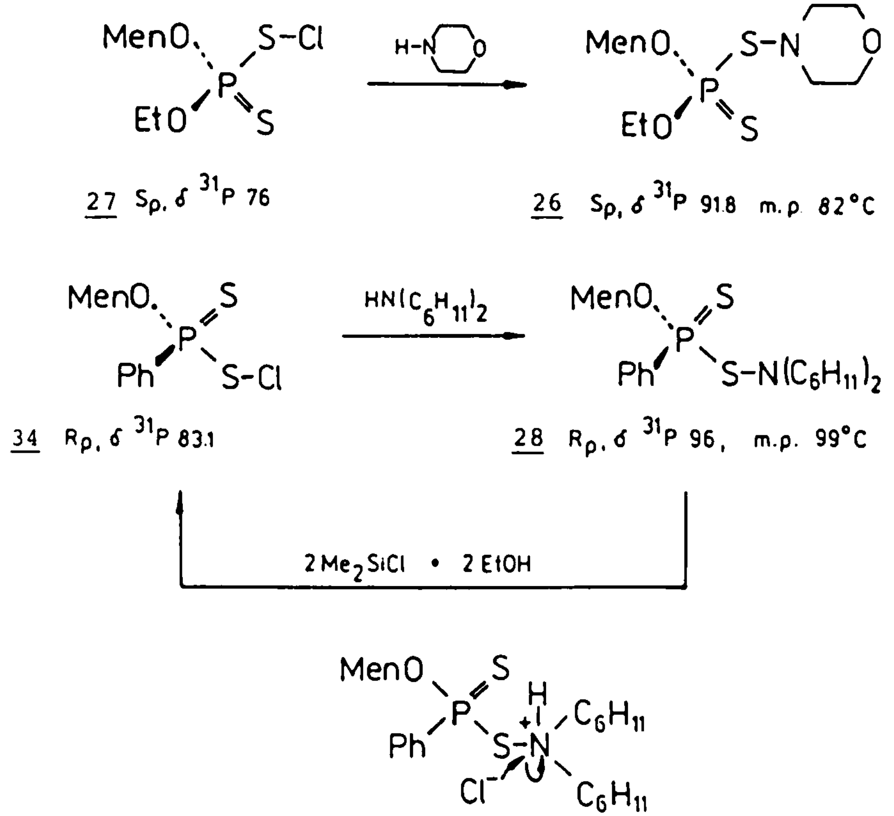
34 R_P, δ ^{31}P 83.1

25 R_P, δ ^{31}P 91.3
one diastereoisomer



27 R_P, δ ^{31}P 77

26 R_P, δ ^{31}P 94, m.p. 85°C



27 S_P, δ ^{31}P 76

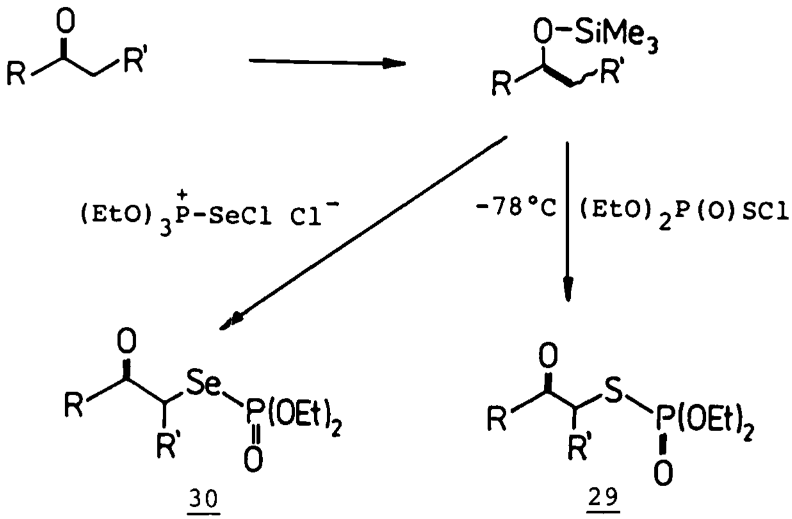
26 S_P, δ ^{31}P 91.8 m.p. 82°C

34 R_P, δ ^{31}P 83.1

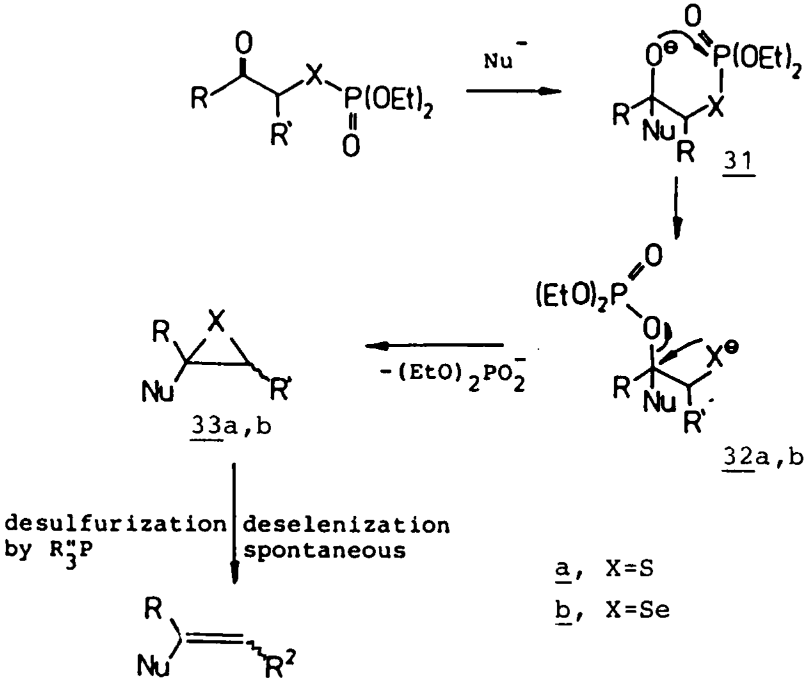
28 R_P, δ ^{31}P 96, m.p. 99°C

All these displacement reactions with secondary amines proceed with almost complete stereoselectivity at the chiral phosphorus center. These observations speak against any kind of dissociative mechanism and corroborate with mechanistic views derived from kinetic studies. This statement is also valid for the reaction of sulfenamides $(R)_P$ 25, $(R)_P$ 26 and $(S)_P$ 26 with hydrogen chloride which also proceed with very high stereoselectivity.

Organophosphorus pseudohalogeno-halogens have been recently successfully employed as a key reagent in the novel strategy of olefin synthesis. It has been found that readily available silyl enol ethers react with organophosphorus sulfenyl and selenyl halides to give β-oxo-alkyl thio- 29 and selenophosphates 30 in excellent yield.[41]



Compounds of the type 29 and 30 can be transformed by addition of nucleophilic reagents to the carbonyl group into the corresponding oxyanion 31 which undergo intramolecular transphorylation. The nucleophilic displacement at the phosphorus center leads to thiolates 32a, selenoates 32b which in turn undergo intermolecular displacement at carbon center with formation of the corresponding episulfides or episelenides 33a,b.



The episelenides decompose spontaneously to olefines while the episulfides require trialkyl phosphite or triphenyl phosphine as desulfurization reagents. Noteworthy this new olefination strategy leads preferentially to Z-olefines (Nu=H) and functionalized Z-olefines [Nu=CN,P(O)R_2].[42-44]

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