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(36) When X = O an anion formation was so fast that additional heating was not necessary.
(37) When X = S, Se in some experiments, leading to phosphoryl compounds, dry CO_2 was bubbled through the reaction mixture at 90° for 2 hr.
(38) Sodium hydride did not react with **7** even in boiling dioxane as proved in a separate experiment.

Organophosphorus Compounds of Sulfur and Selenium. Stereochemistry of Oxidation of Thiono- and Selenophosphoryl Compounds with Hydrogen Peroxide

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The oxidation of 2-R-2-S(Se)-4-methyl-1,3,2-dioxaphosphorinanes with hydrogen peroxide to 2-oxo derivatives proceeds with net retention of configuration at the phosphorus atom. The same stereochemical course was observed in the case of enantiomeric *O*-ethyl-*O*-methyl ethylphosphonothionate. On the other hand, conversion of optically active phosphine sulfide into the corresponding oxide proceeds with inversion of configuration accompanied by racemization. In contrast the oxidation of enantiomeric phosphine selenide by hydrogen peroxide depends on the reaction conditions. Oxidation reactions of thio- and selenophosphoryl compounds with hydrogen peroxide are rationalized in terms of stability of pentacovalent intermediates, which depends on structure of reactants and reaction conditions.

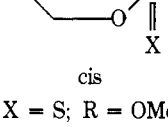
Better insight into the mechanism of oxidation of thio- and selenophosphoryl derivatives to their oxo analogues is of importance for stereochemical correlations, constructing new stereochemical cycles,[1] and better understanding of the metabolic pathways of some phosphoroorganic biocides which are known to involve PS → PO oxidation reactions.[2]

The stereochemistry of conversion of thiophosphoryl compounds into phosphoryl analogues has attracted attention in many research laboratories. It has been demonstrated that oxidizing agents such as potassium permanganate,[3] nitric acid,[4] dinitrogen tetroxide,[4] organic peracids,[5,6] ozone,[6] dimethyl sulfoxide,[7] and hydrogen peroxide[8] can smoothly oxidize thio- and selenophosphoryl compounds. The stereochemical course of the oxidation is dependent on the nature of oxidizing agent, reaction medium, and structure of thio- and selenophosphoryl moieties. Thus nitric acid oxidizes methylphenyl *n*-propylphosphine sulfide and *O*-ethyl-*O*-methyl ethylphosphonothionate with inversion of configuration,[4a] but retention was observed when diastereoisomeric 2-thiono-[4b] and 2-seleno-2-methoxy-4-methyl-1,3,2-dioxaphosphorinans[4c] were used as model compounds. Herriot has also demonstrated the reversal of stereochemistry in oxidation of diastereoisomeric *O*-menthyl methylphenylphosphinothionates by *m*-chloroperbenzoic acid.[5] Net retention was observed in neutral solvents. Addition of trifluoroacetic acid caused a dramatic change in stereochemistry and inversion was observed. The same relationship between stereochemistry and acidity of reaction medium was earlier reported from this laboratory for dinitrogen tetroxide oxidation of enantiomeric phosphine sulfide.[4a] However, dinitrogen tetroxide causes much racemization of the resulting phosphoryl compounds and determination of the particular reaction step responsible for this racemization must await further studies.[9]

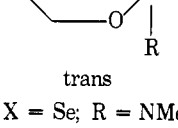
Hydrogen peroxide has also been used as an oxidizing agent[8] and oxidations of diastereoisomeric *O*-menthyl methylphenylphosphinothionate as well as optically active *O*-methyl *tert*-butylphenylphosphinothionate were described as fully stereospecific and proceeding with retention of configuration at phosphorus atom. This result seemed to be in disagreement with our preliminary findings on application of hydrogen peroxide for stereospecific PS → PO conversion. For this reason we undertook more detailed studies on this reaction employing various thio- and selenophosphoryl compounds and different reaction media.

Results

Diastereoisomeric 2-R-2-X-4-methyl-1,3,2-dioxaphosphorinanes (**1–6**), enantiomeric *O*-ethyl-*O*-methyl ethylphosphonates (**7, 8**), and thio, seleno, and oxo derivatives of

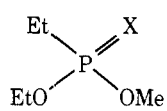


cis

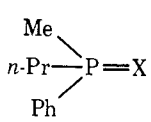


trans

1, X = S; R = OMe[4b,11]
2, X = Se; R = OMe[4c]
3, X = S; R = NMe_2[12]
4, X = Se; R = NMe_2[12]
5, X = O; R = OMe[13]
6, X = O; R = NMe_2[13]



7, X = S[14]
8, X = O[14]



9, X = S[3,15]
10, X = Se[4c]
11, X = O[3,15]

methylphenyl-*n*-propyl phosphine (**9–11**) were chosen as stereochemical models for our studies. Stereochemistry of these compounds has been well established. Information concerning models, reaction conditions (solvent, temperature, and time), and stereospecificities is collected in Tables I–IV.[10]

Table I
Oxidation of 2-R-2-X-4-Methyl-1,3,2-dioxaphosphorinanes with Hydrogen Peroxide

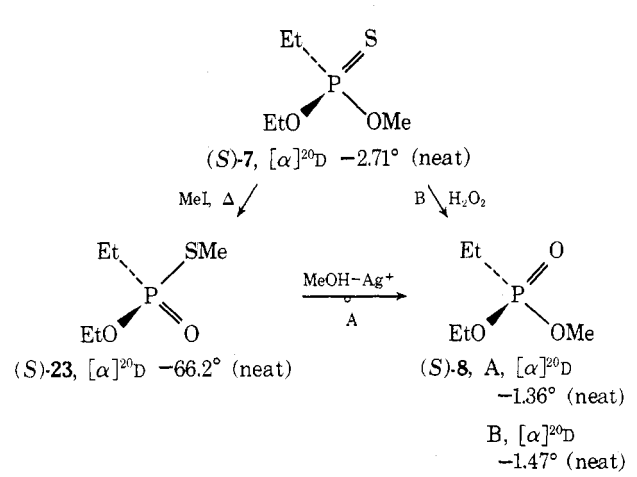
Expt	Starting material: Compd	Starting material: Isomer ratio	Reaction conditions	Product: Compd	Product: Yield, %	Product: Isomer ratio
1	1	6% cis 94% trans	Boiling methanol, 1 hr	5	70	20% cis 80% trans
2	1	86% cis 14% trans	Boiling acetone, 2 hr	5	65	75% cis 25% trans
3	3	90% cis 10% trans	Boiling nitromethane, 30 min	6	62	75% cis 25% trans
4	2	4% cis 96% trans	Methanol, 20°, 30 min	5	85	4% cis 96% trans
5	2	88% cis 12% trans	Acetone, 20°, 30 min	5	82	86% cis 14% trans
6	4	85% cis 15% trans	Acetone, 20°, 30 min	6	83	85% cis 15% trans

Table II
Oxidation of Optically Active *O*-Ethyl-*O*-methyl Ethylphosphonothionate (7) with Hydrogen Peroxide

Expt	$[\alpha]^{20}D$ (neat) of 7, deg	Reaction conditions	Yield of 8, %	$[\alpha]^{20}D$ (neat) of 8, deg
1	−2.71	Boiling methanol, 15 min	85	−1.35
2	−2.71	Boiling dioxane, 15 min	82	−1.47
3	−2.71	Boiling nitromethane, 15 min	78	−0.96

Inspection of Table I reveals that conversion of dioxaphosphorinanyl derivatives (1–4) to corresponding 2-oxo compounds (5, 6) proceeds with overall retention of configuration at phosphorus, but in the case of 2-thiono derivatives (1, 3) the products are partly epimerized (expt 1–3). Oxidation of 2-seleno derivatives (2, 4, expt 4–6) proceeds faster under milder conditions. Yields and stereospecificities are higher than those for 2-thiono compounds. Retention of configuration at phosphorus atom has also been found during oxidation of optically active phosphonothioate (7) (see Table II). Although the optical purity of 7 as well as the resulting *O*-ethyl-*O*-methyl ethylphosphonate (8) has not been precisely determined, on the basis of stereochemical correlations summarized in a form of the podal, three-reaction cycle, containing one ligand, metathesis (see Scheme I) we assume that the stereospecificity of oxidation is rather high.[16]

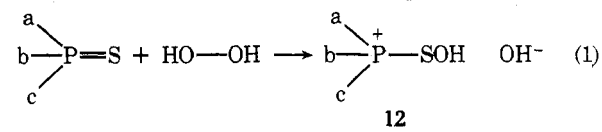
Scheme I



However, oxidation of the sulfide 9 with hydrogen peroxide is accompanied with net inversion of configuration at phosphorus atom, but the resulting methylphenyl-*n*-propylphosphine oxide (11) is highly racemized (Table III). Variations of solvents and temperature did not increase the stereospecificity of investigated reactions. Higher stereospecificity was achieved in oxidation of the optically active phosphine selenide 10. The stereochemistry of this reaction distinctly depends on reaction conditions (see Table IV). When the process was carried out in primary alcohols such as methanol or ethanol, net retention was noted (expt 9–12). Other solvents such as acetone, pyridine, dioxane, nitromethane, *tert*-butyl alcohol, or water (reaction in a heterogenic medium) gave product 11 with inverted configuration (expt 1–8). The same stereochemical course was observed when reaction was carried out in methanol containing 10% trifluoroacetic acid (expt 13). It is of interest to note that in the nitromethane solution (expt 5, 6) the stereospecificity of the reaction does not depend on the reaction temperature. However, when the reaction was carried out in ethanol, the increase of the temperature (expt 9–11) improves its stereospecificity.

Discussion

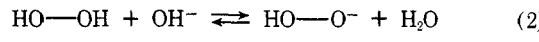
Taking into account the high stereospecificity of oxidation of chiral phosphinothionates[8] and structure- and solvent-dependent stereochemistry of oxidation of compounds under investigation the following rationale can be proposed. We assume that the first step in the reaction of thio(seleno)phosphoryl compounds with hydrogen peroxide, by analogy with other heterolytic reactions of peroxy compound with nucleophiles,[17] is the nucleophilic attack of sulfur (selenium) on the oxygen atom of hydrogen peroxide molecule with formation of ion pair 12 (eq 1).[18]



(1)

12

This is supported by the fact of higher reactivity of selenophosphoryl compounds than that of corresponding thio derivatives toward electrophilic reagents owing to higher polarizability of the selenium atom than that of sulfur. Also the fact that the oxidation of selenide 10 does not occur in the presence of strong base (5% NaOH solution) supports electrophilic activity of H_2O_2 molecule. The nucleophilic attack on anionic species 13 (coming from the equilibrium 2) seems unlikely.



(2)

13

The apparent acidic catalysis (see expt 7, Table III) can be also rationalized in terms of enhanced electrophilicity of protonated species 14.

Table III
Oxidation of Optically Active Methylphenyl-*n*-propylphosphine Sulfide (9) with Hydrogen Peroxide

Expt	$[\alpha]^{20}D$ of 9 (methanol), deg	Reaction conditions	Yield of oxo compd (11), %	$[\alpha]^{20}D$ of 11 (methanol), deg	Stereospecificity[a]
1	−8.25	Boiling acetone, 20 min	82	+3.5	42.5% of inv
2	−8.25	Boiling methanol, 20 min	80	+1.8	22.0% of inv
3	−8.25	Boiling ethanol, 20 min	75	+1.3	16.0% of inv
4	−8.25	Boiling nitromethane, 10 min	74	+1.35	16.5% of inv
5	−8.25	Boiling dioxane, 10 min	68	+0.85	10.3% of inv
6	−8.25	Boiling pyridine, 60 min	69	+1.8	22.0% of inv
7	−8.25	10% CF_3COOH in dioxane, 50°, 10 min	72	+5.3	64.0% of inv

[a] The stereospecificity was calculated on the basis of specific rotations $[\alpha]^{20}D \pm 20°$ (methanol) given by Mislow[27] for 9 and 11.

Table IV
Oxidation of Optically Active Methylphenyl-*n*-propylphosphine Selenide (10) with Hydrogen Peroxide

Expt	$[\alpha]^{20}D$ of 10 (methanol), deg	Reaction conditions	Yield of oxo compd (11), %	$[\alpha]^{20}D$ of 11 (methanol), deg	Stereospecificity[a]
1	−15.2	Acetone, 20°, 10 min	85	+8.1	52.0% of inv
2	−14.4	Dioxane, 20°, 10 min	74	+7.0	47.5% of inv
3	−15.2	Pyridine, 20°, 20 min	78	+4.3	28.0% of inv
4	−14.9	*tert*-Butyl alcohol, 30°, 10 min	81	+7.95	51.0% of inv
5	+19.4	Nitromethane, 20°, 10 min	76	−11.3	57.0% of inv
6	−15.6	Nitromethane, −20°, 30 min	82	+9.6	59.0% of inv
7	−15.2	10% CF_3COOH in dioxane, 20°, 10 min	85	+5.8	37.0% of inv
8[b]	−14.5	H_2O, 20°, 10 min	90	+12.5	83.0% of inv
9	−14.4	Ethanol, 20°, 10 min	80	−5.2	35.5% of ret
10	−15.6	Ethanol, −25°, 30 min	78	−0.5	3.1% of ret
11	−15.6	Boiling ethanol, 5 min	75	−10.55	65.0% of ret
12	−15.2	Methanol, 20°, 10 min	82	−8.4	54.0% of ret
13	−15.2	10% CF_3COOH in methanol, 20°, 10 min	85	+5.8	37.0% of inv

[a] The value ±19.8° of specific rotation $[\alpha]^{20}D$ (methanol) of 10[4c] served as a base of calculation of the stereospecificity of oxidation. [b] The reaction was performed by addition of fine powdered 10 into 30% H_2O_2.

$$HO{-}OH + H^+ \rightleftharpoons HO{-}\overset{+}{O}\begin{matrix}H\\H\end{matrix} \quad (3)$$

14

The next step cannot be deprotonation of 12 by OH^- (eq 4a) because resulting intermediate 15 should decompose

$$\begin{matrix}a\\b{-}P{=}S{=}O\\c\end{matrix} + H_2O \quad (4a)$$

15

$$12 \xrightarrow{a,\ b} \begin{matrix}a\\b{-}P:\\c\end{matrix} + [S(OH)_2] \quad (4b)$$

with retention of configuration at phosphorus.[5] Displacement by OH^- at sulfur is also unlikely (eq 4b) because the intermediate P^{III} compound with at least one P–OR bond should readily hydrolyze in reaction conditions or act with H_2O_2 to give product with retained configuration.[3] Absence of hydrolysis products as well as inversion in the case of oxidation of phosphine sulfide (see Table III) rules out this possibility.

The most probable course of events seems to be, by analogy to base-catalyzed hydrolysis of alkoxy- and alkylthiophosphonium salts,[8,15] an attack of hydroxyl anion on phosphorus atom with formation of the pentacovalent intermediate 16. The mode of attack strongly depends on the environment of phosphorus atom. When a, b, c are alkyl or aryl ligands, the attack of OH^- is most likely to be directed on the a, b, c face of the tetrahedron along the axis of the P–S bond (eq 5).

$$\begin{matrix}a\\b{-}\overset{+}{P}{-}SOH\\c\end{matrix} \quad OH^- \longrightarrow \left[\begin{matrix}a\\HO{-}P{-}SOH\\b\quad c\end{matrix}\right] \longrightarrow$$

12 16a

$$\begin{matrix}a\\O{=}P{-}b\\c\end{matrix} + S + H_2O \quad (5)$$

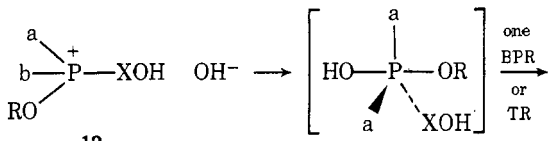
11

The five-coordinate intermediate 16a formed has the most apicophilic[19] groups (e.g., OH and SOH) in axial positions and should decompose giving elemental sulfur[20] and phosphine oxide 11 with inverted configuration. An experimental proof of net inversion at phosphorus atom during phosphine sulfide 9 oxidation has been documented (Table III).

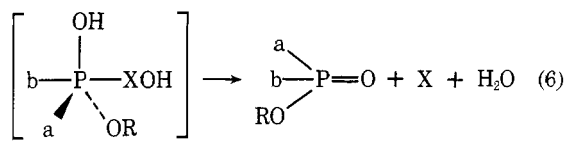
It has to be emphasized that the product 11 as well as other products, 5, 6 and 8, are stereochemically stable under the reaction conditions, indicating that any loss in the stereospecificity at phosphorus atom must have occurred prior to product formation. Although net inversion during oxidation of 9 was noticed, it seems to be reasonable to accept that the pseudorotation process of intermediate 16a is responsible for partial racemization.

In those cases, when at least one alkoxy group is attached to phosphorus in thio- or selenophosphoryl molecule, an attack of hydroxyl anion on electrophilic phosphorus center

is expected along the P–O axis from the opposite side to the most apicophilic[19] oxo ligand. This leads to formation of an intermediate **16b** in which the attacking group is in



12 **16b**



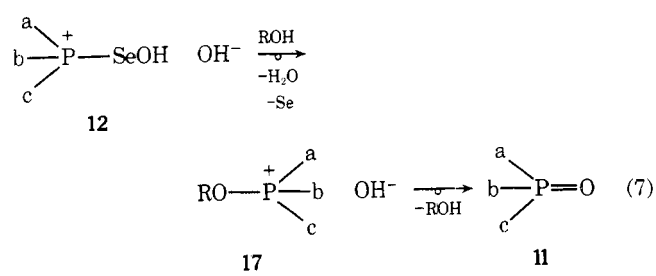
16c

X = S, Se

an axial and the leaving group in an equatorial position. Since the leaving group is required to reach the apical position in an intermediate of type trigonal bipyramid, one permutational isomerization can satisfy this condition, which in consequence leads to retention of configuration at phosphorus atom.

The approach presented above explains the stereochemical results listed in Tables I and II as well as those reported by Trippett,[8] and is in harmony with well-documented mechanistic considerations of base-catalyzed hydrolysis of alkoxy(alkylthio)phosphonium salts.[8] Observed partial epimerization in the case of cyclic thionophosphates **1** and thionoamidates **3** may be due to the subsequent pseudorotation process of intermediate **16c.** In the case of corresponding selenophosphoryl compounds (**2, 4**) such an intermediate is considerably less stable and its subsequent pseudorotation seems to be unlikely. An increase of the stereospecificity of oxidation of compounds **2** and **4** (see Table I) was indeed observed.

The summary of results concerning the oxidation of phosphine selenide **10,** presented in Table IV, requires special comment. Inversion observed, when the reaction was performed in solvents such as acetone, nitromethane, dioxane, pyridine, or *tert*-butyl alcohol, can be explained in the same manner as the oxidation of sulfide **9** (see eq 5). Higher stereospecificity may be due to the lower stability of the pentacovalent species of type **16a** for the selenium analogue and its faster decomposition to the products. Temperature has no effect on the stereospecificity of the oxidation process (compare expt 5 and 6, Table IV) carried out in the solvents mentioned above. Even more surprising results were noted when oxidation was performed in primary alcohol as reaction medium (Table IV, expt 9–13). Observed in this case net retention of configuration at phosphorus may be explained by assumption of direct assistance of solvent in the reaction mechanism. The intermediate ion pair **12** (see eq 1) can be attacked by solvent molecule with formation of the alkoxyphosphonium salt **17** of



12 **17** **11**

inverted configuration (eq 7) in the manner described in eq 5 for oxidation of sulfide **9.** The lack of influence of the less nucleophilic and sterically hindered *tert*-butyl alcohol on the stereospecificity of the whole process speaks in favor of this explanation. A similar effect of lowering of nucleophilicity of alcohol was achieved by addition of trifluoroacetic acid to the reaction medium (expt 13, Table IV) where once again net inversion was observed. Similar considerable influence of primary alcohol on the stereochemistry of oxidation of methylphenyl-*n*-propyl phosphine with *tert*-butyl hypochlorite was earlier reported by Denney and Hanifin.[21] Striking dependence of the stereospecificity of oxidation of **10** with H_2O_2 on the temperature in those cases when the reaction was carried out in ethanol as a solvent (Table IV, expt 9–11) is of special interest. This fact may be rationalized by the assumption that influence of primary alcohol discussed above on reaction mechanism (eq 7) is more efficient at higher temperatures. At the lower temperatures direct influence of alcohol on the reaction mechanism can be less important and the inversion mechanism (eq 5) has to be considered. This is supported by the fact that sulfides **9** even in methanol solution are oxidized with net inversion owing to higher stability of the P–S bond as compared to the P–Se one, and contribution of solvent to the stereospecificity of the whole process can be neglected. As an alternative explanation of the influence of temperature on oxidation of selenide **10** in primary alcohol solution the pseudorotation of intermediate **16** may be considered because of its longer life-time at −20°. However, these various reaction paths cannot be distinguished at the present time.

Experimental Section

All solvents and commercial reagents were purified by the conventional method and distilled before use. NMR spectra were recorded on a Jeol C-60H instrument at 60 MHz observing frequency for ^1H and 24.3 MHz for ^{31}P nuclei. Chemical shifts were referred to internal Me_4Si (^1H NMR) and external H_3PO_4 (^{31}P NMR). Negative values were reported for compounds absorbing at lower fields than H_3PO_4. Heteronuclear Spin Decoupler JNM-SD-HC was used for chemical shift determination and integrations. GLC analyses were conducted with a Varian Aerograph 1520. Optical activity measurements were made with a Perkin-Elmer 141 photopolarimeter in methanol as a solvent (unless specified otherwise). Products purities were determined from integrated ^1H and ^{31}P NMR spectra and GLC analyses. Highly concentrated H_2O_2 solutions (80–90%, measured by manganometric titration) were obtained by careful evaporation of commercial 30% reagent under reduced pressure.

I. Starting Materials. 2-Chloro-4-methyl-1,3,2-dioxaphosphorinane (18) was prepared from 1,3-butanediol and PCl_3 in CH_2Cl_2 according to the Lucas[22] procedure.

***cis*-2-Methoxy-4-methyl-1,3,2-dioxaphosphorinane (19a)** was prepared from chlorophosphite **18** and methanol in the presence of 5% molar excess of triethylamine in ether at −20°: bp 44° (5 mmHg); $n^{21}D$ = 1.4480; yield 70% [lit.[11b] bp 20–22° (0.05 mmHg), $n^{21}D$ = 1.4468]. In repeated experiments the content of **19a** (δ_{31P} −132.6 ppm) in **19** was found to be in a range of 85–96%.

***trans*-2-Methoxy-4-methyl-1,3,2-dioxaphosphorinane (19b)** was obtained from **19a** by addition of a catalytic amount of benzene saturated with HCl and subsequent distillation: bp 65° (30 mmHg), $n^{20}D$ = 1.4418 (lit.[11b] bp 90–92° (60 mmHg), $n^{21}D$ = 1.4481. Prepared samples of **19** contained 94–100% of **19b** (δ_{31P} −129.5 ppm).

***cis*-2-Methoxy-2-thiono-4-methyl-1,3,2-dioxaphosphorinane (1a)** was obtained in 83% yield by addition of elemental sulfur to **19** (containing 90% of **19a**) at 5° in benzene, bp 68–70° (0.02 mmHg), $n^{20}D$ = 1.4892 [lit.[11b] bp 78–80° (0.3 mmHg), $n^{20}D$ = 1.4902]. The product contained 86% of **1a** (δ_{31P} −65.0 ppm) and 14% of **1b** (δ_{31P} −63.4 ppm).

***trans*-2-Methoxy-2-thiono-4-methyl-1,3,2-dioxaphosphorinane (1b)** was prepared in 85% yield by addition of elemental sulfur to **19** (containing 96% of **19b**) in benzene, bp 74–76° (0.02 mmHg), $n^{20}D$ = 1.4942 [lit.[11b] bp 76–80° (0.03 mmHg), $n^{22}D$ = 1.4913]. The product consisted of a mixture of **1a** and **1b** in the ratio 6:94, respectively.

***cis*-2-Methoxy-2-seleno-4-methyl-1,3,2-dioxaphosphori-**

nane (2a) was synthesized in 79% yield from **19** (**19a:b** 90:10) and elemental selenium at 5° in benzene, bp 85–87° (0.1 mmHg), $n^{20}D$ = 1.5216 (Anal. Calcd for $C_5H_{11}O_3PSe$: C, 26.22; H, 4.84; P, 13.53. Found: C, 26.32; H, 4.97; P, 13.41). GLC and ^{31}P NMR analysis revealed the presence of **2a** (88%, $\delta_{^{31}P}$ −68.5 ppm, $^1J_{P-Se}$ = 941 Hz) and **2b** (12%, $\delta_{^{31}P}$ −67.2 ppm). ^1H NMR ($CDCl_3$) δ_{CH_3} 1.41 ppm, $^3J_{HCCH_3}$ = 6.4 Hz, $^4J_{POCCH_3}$ = 2.2 Hz, δ_{OCH_3} 3.80 ppm, $^3J_{POCH_3}$ = 15.0 Hz.

***trans*-2-Methoxy-2-seleno-4-methyl-1,3,2-dioxaphosphorinane (2b)** was prepared in 81% yield by addition of elemental selenium to **19** (96% of **19b**) in benzene, bp 100–102° (0.2 mmHg), $n^{20}D$ = 1.5268 (Anal. Found: C, 26.30; H, 4.86; P, 13.28). GLC and ^{31}P NMR analysis showed the presence of **2a** (4%, $\delta_{^{31}P}$ −68.5 ppm) and **2b** (96%, $\delta_{^{31}P}$ −67.2 ppm, $^1J_{P-Se}$ = 978 Hz). ^1H NMR ($CDCl_3$) δ_{CH_3} 1.41 ppm, $^3J_{HCCH_3}$ = 6.4 Hz, $^4J_{POCCH_3}$ = 2.2 Hz, δ_{OCH_3} 3.70 ppm, $^3J_{POCH_3}$ = 14.5 Hz.

2-Dimethylamino-4-methyl-1,3,2-dioxaphosphorinane (20) was synthesized from chlorophosphite (**18**) and dimethylamine in benzene at 10°, bp 75° (20 mmHg), $n^{20}D$ = 1.4652, yield 71% (lit.[12] bp 71° (13 mmHg), $n^{20}D$ = 1.4650). The ^{31}P NMR analysis revealed the presence of *cis*-**20** (80%, $\delta_{^{31}P}$ −143.4 ppm) and trans isomer (20%, $\delta_{^{31}P}$ −139.2 ppm).

2-Dimethylamino-2-thiono-4-methyl-1,3,2-dioxaphosphorinane (3) was obtained in 83% yield by addition of elemental sulfur to **20** in benzene, bp 92–93° (0.3 mmHg), $n^{23}D$ = 1.5000 (Anal. Calcd for $C_6H_{14}O_2NPS$: C, 36.90; H, 7.23; N, 7.18; P, 15.87. Found: C, 37.43; H, 7.40; N, 7.52; P, 16.20). The ^{31}P and ^1H NMR analysis ($CDCl_3$) showed the presence of 90% *cis*-**3** ($\delta_{^{31}P}$ −73.5 ppm, δ_{NCH_3} 2.80 ppm, $^3J_{PNCH_3}$ = 11.3 Hz) and 10% of *trans*-**3** ($\delta_{^{31}P}$ −73.0 ppm, δ_{NCH_3} 2.50 ppm, $^3J_{PNCH_3}$ = 13.3 Hz). The product had solidified during the storage in the refrigerator. Its recrystallization from ether–hexane let us obtain pure *cis*-**3**, mp 37–38°. Anal. Found: C, 37.07; H, 7.25; N, 7.28; P, 15.83).

2-Dimethylamino-2-seleno-4-methyl-1,3,2-dioxaphosphorinane (4) was prepared in 79% yield from **20** and elemental selenium in benzene solution, bp 88–90° (0.2 mmHg), $n^{22}D$ = 1.5302 (Anal. Calcd for $C_6H_{14}O_2NPSe$: C, 29.75; H, 5.82;N, 5.78; P, 12.79. Found: C, 30.06; H, 6.10; N, 6.05; P, 1308). The ^{31}P and ^1H NMR analysis (benzene) revealed the presence of *cis*-**4** (85%, $\delta_{^{31}P}$ −79.0 ppm, $^1J_{P-Se}$ = 930 Hz, δ_{NCH_3} = 2.70 ppm, $^3J_{PNCH_3}$ = 12.0 Hz) and *trans*-**4** (15%, $\delta_{^{31}P}$ −79.8 ppm, $^1J_{P-Se}$ = 960 Hz, δ_{NCH_3} 2.30 ppm, $^3J_{PNCH_3}$ = 14.0 Hz). The product had solidified during the storage at room temperature. Its recrystallization from ether–hexane gave pure *cis*-**4**, mp 51–52° (Anal. Found: C, 29.84; H, 6.05; N, 5.98; P, 13.03).

***O*-Ethyl ethylphosphonothioic acid (21)** [bp 57–59° (0.08 mmHg), $n^{20}D$ = 1.4907] was obtained and resolved into optical antipodes according to Aaron et al.[23]

***O*-Ethyl ethylphosphonochloridothionate (22)** [bp 20° (0.05 mmHg), $n^{23}D$ = 1.4912, $[\alpha]^{20}D$ −65.8° (neat)] was prepared by chlorination of thio acid **21** [$[\alpha]^{20}D$ = −14.2° (neat)] with PCl_5 according to the procedure given by Michalski and Mikołajczyk.[24]

***O*-Ethyl-*O*-methyl ethylphosphonothionate (7)** [bp 46° (3 mmHg), $n^{20}D$ = 1.4662, $[\alpha]^{20}D$ = −2.71° (neat), $\delta_{^{31}P}$ −102.5 ppm)] was prepared by the reaction of **22** [$[\alpha]^{20}D$ = −65.8° (neat)] with sodium methoxide.[16]

***O*-Ethyl-*S*-methyl ethylphosphonothiolate (23)** [bp 62° (2 mmHg), $n^{22}D$ = 1.4776, $[\alpha]^{20}D$ = −66.2° (neat), $\delta_{^{31}P}$ −61.5 ppm] was synthesized from **7** [$[\alpha]^{20}D$ = −2.71° (neat)] by the reaction with methyl iodide under Pishschimuka reaction conditions.[16]

***O*-Ethyl-*O*-methyl ethylphosphonate (8)** [bp 50° (2.5 mmHg), $n^{20}D$ = 1.4129, $[\alpha]^{20}D$ = −1.36° (neat), $\delta_{^{31}P}$ −34.5 ppm] was prepared by methanolysis of **23** [$[\alpha]^{20}D$ = −66.2° (neat)] in the presence of silver nitrate according to the procedure described by Stec.[16]

Optically active methylphenyl-*n*-propylphosphine (24) was prepared by alkaline hydrolysis of diastereoisomeric benzylmethylphenyl-*n*-propylphosphonium dibenzoyl hydrogen tartrates[3,25] followed by reduction with $SiHCl_3$–Et_3N of the resulting phosphine oxide **11**:[26] bp 70° (1 mmHg); $n^{22}D$ = 1.5448; $\delta_{^{31}P}$ +37.6 ppm (benzene); δ_{CH_3} 1.26 ppm ($CDCl_3$), $^2J_{PCH_3}$ = 3.0 Hz [lit.[3] bp 73–74° (0.7 mmHg)].

Methylphenyl-*n*-propylphosphine sulfide (9) ($[\alpha]^{20}D$ = −8.25°) was prepared by addition of elemental sulfur to **24** [$[\tau]^{20}D$ = −8.05° (toluene)];[3,15] mp 65–75°; $\delta_{^{31}P}$ −37.3 ppm (benzene); δ_{CH_3} 2.12 ppm ($CDCl_3$), $^2J_{PCH_3}$ = 12.7 Hz.

Methylphenyl-*n*-propylphosphine selenide (10) ($[\alpha]^{20}D$ = −15.2°) was obtained by addition of elemental selenium to **24** [$[\alpha]^{20}D$ = −15.0° (toluene)];[4c] mp 60–70°; $\delta_{^{31}P}$ −25.3 ppm (benzene); δ_{CH_3} 2.15 ppm ($CDCl_3$); $^2J_{PCH_3}$ = 12.7 Hz (Anal. Calcd for $C_{10}H_{17}PSe$: C, 49.00; H, 6.17; P, 12.63. Found: C, 49.22; H, 5.94; P, 12.42).

II. Oxidation of 1 with Hydrogen Peroxide. A. Hydrogen peroxide (2 ml) was added to a solution of **1** (3.64 g, 0.02 mol, **1a:b** 6:94) in methanol (20 ml). The mixture was refluxed for 1 hr, cooled, and evaporated. The residue was shaken with water and the resulting elemental sulfur was filtered off. The filtrate was extracted with $CHCl_3$ (5 × 10 ml). Combined $CHCl_3$ solutions were dried over $MgSO_4$ and evaporated. The residue was distilled, yielding 2.3 g (70%) of **5**, bp 115° (1.0 mmHg), $n^{22}D$ = 1.4388 [lit.[13] bp 90° (0.8 mmHg), $n^{20}D$ = 1.4365]. GLC and ^{31}P NMR analysis (neat) revealed the presence of **5a** (20%, $\delta_{^{31}P}$ +5.2 ppm) and **5b** (80%, $\delta_{^{31}P}$ +6.5 ppm).

B. The same procedure as in expt IIa performed in boiling acetone yielded from **1** (containing 86% of **1a** and 14% of **1b**) **5** containing 25% of **5a** and 75% of **5b** with overall yield 65%, bp 103–105° (0.6 mmHg), $n^{21}D$ = 1.4382 [lit.[13] bp 80–95° (0.5 mmHg), $n^{20}D$ = 1.4390].

III. Oxidation of 2 with Hydrogen Peroxide. A. Hydrogen peroxide (1 ml) was added dropwise, with stirring at 20°, to a solution of **2** (4.6 g, 0.02 mol, **2a:b** 4:96) in methanol (20 ml). An exothermic reaction was accompanied with precipitation of red selenium. Stirring at room temperature was continued for 20 min and the resulting selenium was filtered off. The filtrate was evaporated and the residue was distilled, yielding 2.8 g (85%) of **5**, bp 110° (0.8 mmHg), $n^{20}D$ = 1.4368. GLC and ^{31}P NMR analysis (neat) revealed the presence of **5a** (4%, $\delta_{^{31}P}$ +5.2 ppm) and **5b** (96%, $\delta_{^{31}P}$ +6.5 ppm).

B. The same procedure performed with **2** (containing 88% of **2a** and 12% of **2b**) in acetone yielded 82% of **5** (86% of **5a** and 14% of **5b**), bp 90° (0.3 mmHg), $n^{21}D$ = 1.4352.

IV. Oxidation of 3 with Hydrogen Peroxide. The procedure described in section II was performed with **3** (90% cis and 10% trans) in boiling nitromethane. The resulting phosphonoamidate **6** [bp 80° (0.3 mmHg), $n^{22}D$ = 1.4540, yield 62%] contained as the major component the cis isomer (75%, $\delta_{^{31}P}$ −12.3 ppm) contaminated with the trans isomer (25%, $\delta_{^{31}P}$ −6.4 ppm) [lit.[13] $\delta_{^{31}P}$ (*cis*-**6**) −7.5 ppm, $\delta_{^{31}P}$ (*trans*-**6**) −4.5 ppm].

V. Oxidation of 4 with Hydrogen Peroxide. The reaction was performed, as in section III, in acetone solution. Starting from the mixture of 85% of *cis*-**4** and 15% of *trans*-**4**, **6** was obtained with the same isomer ratio, bp 85° (0.4 mmHg), $n^{20}D$ = 1.4526, yield 81%.

VI. Oxidation of Phosphine Sulfide 9 with H_2O_2. General Procedure. Hydrogen peroxide (2 ml) was added to a solution of **9** (0.4 g, 0.002 mol) in appropriate solvent (20 ml). The solution was heated under reflux for 10–60 min. Solvent was removed under reduced pressure and the residue was dissolved in water (20 ml). The precipitated elemental sulfur was filtered off and the product **11** extracted with $CHCl_3$ and purified by distillation, bp 120° (0.6 mmHg), $\delta_{^{31}P}$ −32.5 ppm (benzene). The distillate had solidified in the form of white, extremely hygroscopic crystals, mp 55–58°, yield 70–80%.

VII. Oxidation of Phosphine Selenide 10 with H_2O_2. General Procedure. Hydrogen peroxide (0.022 mol) was added dropwise, with stirring and external cooling, to a solution of **10** (0.5 g, 0.002 mol) in appropriate solvent (20 ml). An exothermic reaction, accompanied with precipitation of red selenium, was observed. Stirring at room temperature was continued for 10–20 min and the resulting elemental selenium was filtered off. The filtrate was evaporated and the residue was distilled, yielding 75–90% of phosphine oxide **11**, bp 120° (0.6 mmHg), mp 55–58°, $\delta_{^{31}P}$ −32.5 ppm (benzene).

VIII. Oxidation of Thionophosphonate 7 with Hydrogen Peroxide. To a solution of **7** [3.36 g, 0.02 mol, $[\alpha]^{20}D$ = −2.71° (neat)] in dioxane (30 ml) was added hydrogen peroxide (2 ml, 90%). The solution was gently heated until an exothermic reaction took place. Heating under reflux was continued for the next 10 min and the mixture was evaporated and dissolved in water (20 ml). The resulting elemental sulfur was filtered off and the filtrate was extracted with $CHCl_3$ (8 × 10 ml). Combined $CHCl_3$ solutions were dried over $MgSO_4$ and evaporated. The residue was distilled, giving 2.5 g (82%) of **8**, bp 54° (3 mmHg), $n^{20}D$ = 1.4148, $[\alpha]^{20}D$ = −1.47° (neat).

Registry No.—**1a**, 23168-88-9; **1b**, 23168-89-0; **2a**, 33996-01-9; **2b**, 33996-02-0; *cis*-**3**, 40986-08-1; *trans*-**3**, 40986-07-0; *cis*-**4**, 57215-11-9; *trans*-**4**, 40986-11-6; **5a**, 33996-04-2; **5b**, 33996-03-1; *cis*-**6**, 41158-21-8; *trans*-**6**, 41158-20-7; **7**, 5152-73-8; **8**, 31660-62-5; **9**, 13153-91-8; (*S*)-(−)-**10**, 34641-79-7; (*R*)-(+)-**10**, 33995-97-0;

(S)-(−)-11, 1515-99-7; (R)-(+)-11, 17170-48-8; (±)-11, 2328-23-6; 18, 6362-87-4; 19a, 7735-85-5; 19b, 7735-81-1; cis-20, 40781-04-2; trans-20, 40781-03-1; 21, 4789-36-0; 22, 4789-37-1; 23, 20698-84-4; 24, 13153-89-4; sodium methoxide, 124-41-4; benzylmethylphenyl-n-propylphosphonium dibenzoyl hydrogen tartrate isomer 1, 57215-13-1; benzylmethylphenyl-n-propylphosphonium dibenzoyl hydrogen tartrate isomer 2, 57215-15-3; hydrogen peroxide, 7722-84-1.

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1-Vinylcycloalkenes in the McCormack Cycloaddition with Phosphonous Dihalides. Stereochemistry of Some Resulting Bicyclic Phospholene Oxides[1]

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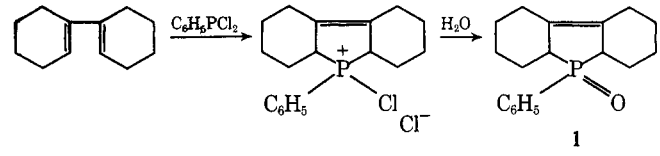
1-Vinylcyclohexene condenses at 25° with methylphosphonous dichloride. Hydrolysis of the cycloadduct gives the 3-phospholene oxide with a tetramethylene group at the 2,3 positions. The product consists of a mixture of stereoisomers (72% trans, 28% cis); their structures were assigned with the aid of ^{13}C, ^{31}P, and ^{1}H NMR spectral relations. 1-Vinylcyclohexenes containing bromine or chlorine on the α-vinyl carbon also participate smoothly in the cycloaddition. A new type of diene, containing a 2-trimethylsiloxy group, was used in the cycloaddition; 1-acetylcyclohexene gave such a siloxy diene with $LiN(i\text{-}Pr)_2$ and $(CH_3)_3SiCl$, and on hydrolysis of the cycloadduct formed with CH_3PCl_2 there was obtained a 3-keto phospholane derivative. The 4-vinyl derivative of 1,2-dihydronaphthalene also participated readily in the cycloaddition, giving a tricyclic phospholene oxide derivative. Two examples of further utilization of the bicyclic phospholene oxides are provided, namely, P-deoxygenation to the bicyclic phosphines and hydrogenation of the double bond to perhydrophosphindole derivatives.

The cycloaddition of conjugated dienes and trivalent phosphorus halides, first described by McCormack,[2] has proved to be an excellent route to derivatives of the phospholene ring system. To the present, however, this reaction has been used primarily to form monocyclic structures, although it has far greater potential through extension to the synthesis of multicyclic structures. McCormack did report[2] the use of 1,1′-biscyclohexenyl in the reaction with phenylphosphonous dichloride to form a tricyclic adduct which on hydrolysis gave phospholene oxide **1**, and the same compound was later obtained by other workers.[3] Phosphorus trichloride also adds to this diene.[4] Bridged phospholene



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oxides (**2**) can be obtained by cycloaddition with cycloheptadienes.[5]

1-Vinyl cyclic alkenes are readily obtainable dienes, and should serve as valuable precursors of bicyclic phospholene derivatives. Thus, with 1-vinylcyclohexene, members of the hexahydrophosphindole family would be formed. While