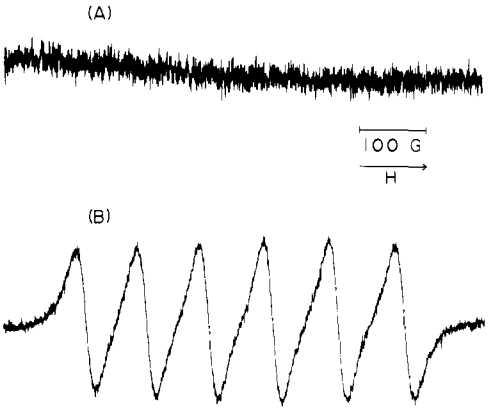

Figure 1. ESR spectra of the native enzyme (A) and the denaturated enzyme (B) at 20 °C. Sample B was obtained by mixing sample A (0.5 mM; 0.2 mL) in water with HCl (1.0 M; 0.05 mL) and then heating to 100 °C for 3 min.

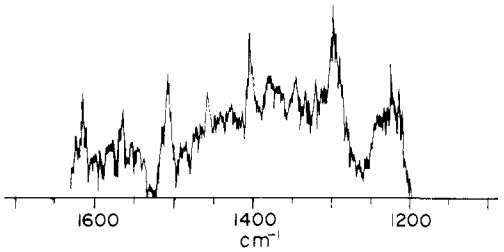

Figure 2. Resonance Raman spectrum of Mn-containing acid phosphatase. The sample concentration was 0.5 mM, and the spectrum was measured at pH 6.8 and 4 °C. Instrumental conditions were as follows: excitation, 514.5-nm line of Ar^+ laser; power, 20 mW at a sample point; time constant, 16 s; slit width, 200 μm; scan speed, 10 cm^{-1}/min.

excited by the 5145-Å line of an argon ion laser and was recorded on a JEOL-400 D Raman spectrometer equipped with a HTV-R 649 photomultiplier. The native enzyme exhibited prominent Raman lines at 1230, 1298, 1508, and 1620 cm^{-1}. These appear to be in resonance with the visible band and are probably due to internal vibrations of the coordinated amino acid residue. Repeated experiments established that these Raman bands are indeed reproducible. The four Raman lines of the Mn–enzyme complex resemble those of the Fe(III) complexes of transferrin (1174, 1288, 1508, and 1613 cm^{-1}),[9] protocatechuate 3,4-dioxygenase (1177, 1265, 1505, and 1605 cm^{-1}),[11] and *p*-cresol (1180, 1222, 1488, and 1618 cm^{-1}).[11] In these Fe(III) complexes, the four characteristic Raman lines have been assigned to vibrations of the coordinated phenolate anion. On the basis of the chemical similarity between Fe(III) and Mn(III) ions, the present Raman spectrum of the Mn–enzyme complex is interpretable in terms of the internal vibration of a coordinated tyrosine phenolate anion. Indeed, the amino acid composition of the violet enzyme revealed an abundance of tyrosine residues.

Sulfhydryl coordination was strongly suggested by the results of our *p*-chloromercuribenzoate binding study on the Mn-containing enzyme.[12] Mn(III) complexes of mercaptoamine and mercaptocarboxylate such as cysteamine, cysteine, and mercaptoacetic acid give intense absorption bands (ϵ 10^3–10^4) in the range of 480–670 nm. Both tyrosine(O) → Mn(III) and cysteine(S) → Mn(III) charge transfers may contribute to the intense 515-nm band of this Mn–enzyme complex. A Raman line due to Mn(III)–S(cysteine) stretching modes would be expected to appear near 350 cm^{-1} [13,14] but was not detected under our experimental condition because of the fluorescence of the sample.

In conclusion, the Mn-containing acid phosphatase is a classic example of tightly bound Mn(III). One of the characteristics of this Mn–enzyme complex is the intense charge-transfer band seen at 515 nm. The resonance Raman evidence indicates the coordination of a tyrosine phenolate anion to the Mn(III) active site. Investigations on the Mn chromophore of the acid phosphatase are under way.

Acknowledgment. Gratitude is due to Dr. S. Fujimoto for pertinent advice on the enzyme preparation, Dr. T. Kitagawa for resonance Raman measurements, and M. Ohara for comments on the manuscript. This study was supported in part by a grant from the Ministry of Education, Science, and Culture, Japan.

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(12) The binding of *p*-chloromercuribenzoate strongly inhibited the phosphatase activity and was concomitant with the loss of the violet color. The SH determination with the Ellman reagent showed that no free sulfhydryl groups were detected in the native enzyme, but 1 mol of SH/mol of enzyme was detected in the denaturated and Mn-removed enzyme.

(13) In iron–sulfur proteins, the Raman line near 350 cm^{-1} has been assigned to the Fe(III)–S stretching modes: (a) Long, T. V.; Loeher, T. M.; Alkins, J. R.; Lovenberg, W. J. *J. Am. Chem. Soc.* **1971**, *93*, 1809–1811. (b) Tang, S.-P. W.; Spiro, T. G.; Autanaitis, C.; Moss, T. H.; Holm, R. H.; Herskovitz, T.; Mortenson, L. E. *Biochem. Biophys. Res. Commun.* **1975**, *62*, 1–6.

(14) In the IR spectrum of the tris(*N*,*N*-diethylcarbamdithioato)manganese(III) complex, the Mn(III)–S band at ca. 370 cm^{-1} is extremely broad: Healy, P. C.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1972**, 1883–1887.

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Stereochemistry of Chlorinolysis of the Phosphorus–Sulfur Bond in Thioloesters of Organic Phosphorus Thio Acids. Reaction of *S*-Methyl *tert*-(Butylphenylphosphino)thiolate with Halogens and Sulfuryl Chloride

Sir:

The reaction of organic phosphorus thioloesters with halogenating agents has been known for 20 years.[1] This reaction has been shown to proceed via different pathways, depending on the reaction medium. The reaction in nonaqueous solvents has been applied successfully in the synthesis of optically active 4-coordinated phosphorus compounds.[2] However, interpretation of the accumulated experimental facts on the basis of a frequently used scheme (Scheme I) leads to inconsistencies. Scheme I consists of electrophilic attack of the halogen on the sulfur atom with formation of the corresponding chlorosulfonium salt **2** (step a), which subsequently decomposes by nucleophilic attack of the halide anion on the phosphorus atom (step b).

The aim of this investigation was to examine the stereochemical course of the chlorinolysis reaction of organic phosphorus thioloesters by using a model which, due to the presence of a sterically crowded phosphorus atom, should reduce the rate of any intermediate step involving nucleophilic displacement at the reaction center, thus allowing the possibility to detect intermediates by spectroscopy.

It could be expected on the basis of Scheme I that halogenolysis of **1** (R = *t*-Bu; R′ = Ph; R″ = CH_3) should occur with inversion of configuration at the phosphorus atom, considering the preferences (apicophilicity vs. apicophobicity) of the groups bonded to phosphorus in an intermediate trigonal bipyramid. Contrary to this prediction, retention of configuration was observed[3] and

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(3) Retention of configuration is also observed on models not containing a sterically large *t*-Bu group at phosphorus.[2a,d]

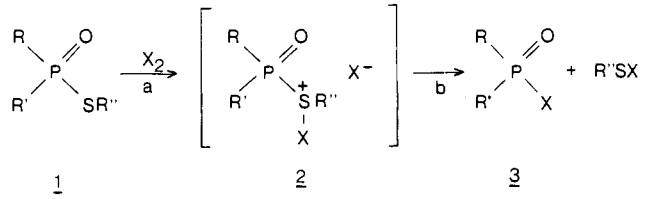
0002-7863/80/1502-6582$01.00/0

Table I

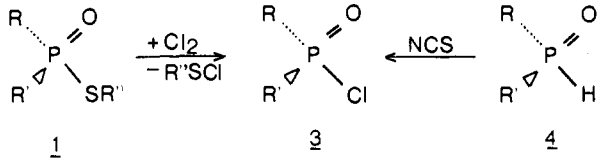
t-BuPhP(O)SCH_3		*t*-BuPhP(O)Cl				
$[\alpha]^{25}_D$,[a] deg	op,[b] %	$[\alpha]^{25}_D$,[a] deg	op,[b] %	optical yields of reaction, %	reaction solvent	chlorinating agent
−106.9	66	−30.6	61	92	benzene	SO_2Cl_2
+107.3	66	+28.5	57	86	benzene	SO_2Cl_2
−131.9	81	−20.2	40	49	CH_2Cl_2	SO_2Cl_2
+154.0	95	+40.6	81	85	CCl_4	Cl_2
−148.2	91	−20.0	40	43	CH_2Cl_2/CCl_4 (5:1)	Cl_2

[a] All optical rotation measurements were done in benzene (*c*, 0.01–0.05 g/l mL) on a Perkin-Elmer-141 polarimeter. [b] Determinations of optical purities were based on the assumption that 3 with $[\alpha]^{23}_D$ +49.8° (highest known value[12]) is optically pure; for 1, the value of ca. (±)162.6° was estimated from the $[\alpha]_D$ of optically pure acid, *t*-BuPhP(S)OH[12].

Scheme I



Scheme II

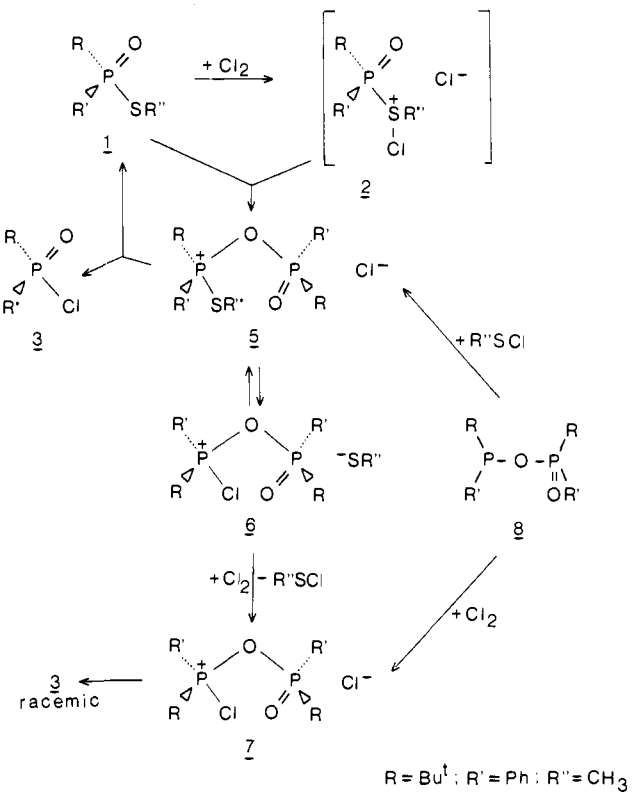


R = Bu^t; R' = Ph; R'' = CH_3;
NCS = N-chlorosuccinimide

in some cases accompanied by racemization independent of the reaction conditions.[4] Evidence of retention was obtained from comparison of the reaction product **3** with that prepared by chlorination of optically active *tert*-butylphenylphosphine oxide **4**, which has been shown[5] to undergo chlorination with retention of configuration at phosphorus (Scheme II). ^{31}P FT NMR studies[6] in methylene chloride or toluene in the temperature range −80 to +20 °C, using equimolar amounts of **1** and chlorinating agent, led to the detection of intermediate products containing two phosphorus atoms bonded through an oxygen bridge. These results are fully consistent with the mechanism proposed in Scheme III.

The first step, which could not be detected spectroscopically, leads to the formation of the chlorosulfonium salt **2**. This salt reacts with a second molecule of the starting phosphinothiolate **1**, giving the oxygen-bridged intermediate **5**,[7] which can exist in equilibrium with the isomeric salt **6** by means of ligand exchange at the phosphonium center. The salt **6**[8] then undergoes reaction

Scheme III



R = Bu^t; R' = Ph; R'' = CH_3

with chlorine, subsequently forming **7**, which slowly decomposes into final product **3**. The salt **5** also breaks down to form equivalent amounts of phosphinochloridate **3** and substrate **1**. Evidence supporting this reaction mechanism is based on ^{31}P NMR spectroscopy and on the independent synthesis of the transient salts **5**, **6**, and **7** by the reaction of bis[(*tert*-butylphenyl)phosphino]phosphinic anhydride **8**[9] with elemental chlorine and methanesulfenyl chloride, respectively. The ^{31}P NMR spectra of salts **5** and **7**, arising from enantiomerically pure **1**, contain a characteristic doublet of doublets due to spin–spin coupling between two nonequivalent ^{31}P atoms. The multiplicity of signals was doubled in the case of racemic **1** due to the presence of the diastereoisomeric pairs of salts **5**–**7**. The chemical shifts of the salts **5**–**7** for the phosphonium nuclei in the ^{31}P NMR spectra were in the range 103–114 ppm while those for the phosphoryl groups were between 50 and 69 ppm. The coupling constants $^2J_{P^+O-P^{IV}}$ were between 41 and 47 Hz.

The reaction mechanism demonstrated provides the possibility of an unambiguous interpretation of the reaction stereochemistry. The reaction between **1** and **2** occurs with inversion of configuration at the phosphoryl center and with retention at the phosphonium center. The decomposition of the salt **5** into phosphi-

(4) I.e., in three solvents, benzene, tetrachloromethane, and methylene chloride. It is of interest to note that this reaction can be induced to proceed with inversion in methylene chloride solution with the addition of mercuric chloride.

(5) Michalski, J.; Skrzypczyński, Z. *J. Chem. Soc., Chem. Commun.* **1977**, 66.

(6) ^{31}P NMR spectra were recorded on a Jeol JNM-FX-60 FT NMR instrument at 24.2 MHz, chemical shifts to low field from 85% H_3PO_4 being positive.

(7) Additional support of this interpretation can be found in the behavior of bromine in this reaction. The salt **5** with Br^- instead of Cl^- was observed to be stable even at room temperature due to the fact that bromide, being a poorer nucleophile than chloride toward phosphorus, was not capable of attacking the phosphoryl center. Moreover, the ligand exchange leading to the bromine analogue of salt **7** was not observed for the same reason.

(8) This salt cannot be detected in the presence of chlorinating agents; however, it has been observed during the reaction of methanesulfenyl chloride with the anhydride **8**.

(9) ^{31}P NMR data for the diastereomeric mixture of anhydride **8**. **8a**: $\delta_{P(III)}$ 129.2 (d), $\delta_{P(IV)}$ 49.8 (d), $J_{P(III)-O-P(IV)}$ = 8 Hz. **8b**: $\delta_{P(III)}$ 126.7 (d), $\delta_{P(IV)}$ 48.6 (d), $J_{P(III)-O-P(IV)}$ = 18 Hz.

nochloridate **3** and starting phosphinothiolate **1** involves a second inversion at the phosphoryl center which consequentially results in retention of configuration. Racemization, instead, arises from the decomposition of the salt **7**, which leads to one molecule with unchanged configuration and another that is inverted.

It is interesting to note that in the case of the reaction involving nearly complete retention of configuration, namely, chlorination with sulfuryl chloride in toluene, only traces of the salt **7** are observed. In contrast, when the chlorinating agent was elemental chlorine in methylene chloride, the amount of the salt **7** observed was considerably greater, and at the same time appreciable racemization took place. Specific rotations and optical yields for chlorination reactions performed at 0 °C are included in Table I.

Participation of transient species containing two phosphorus atoms was also demonstrated in other types of organic phosphorus thioloesters and will be a topic of future publications.

This communication resolves the problem of the reaction mechanism of halogenolysis of the phosphorus–sulfur bond in 4-coordinated organophosphorus compounds via the combined results of the stereochemical investigations and the structural studies accomplished by ^{31}P NMR spectroscopy of the reaction intermediates. Another important aspect of this paper is the demonstrated facile formation of the P–O–P system by nucleophilic attack of phosphoryl oxygen on the 4-coordinated phosphorus center. This result confirms the reaction schemes proposed earlier for a number of reactions, important from the synthetic point of view of the organophosphorus compounds[10] and polymers.[11]

Acknowledgment. This work was supported by the Polish Academy of Sciences (Project MR.I.12).

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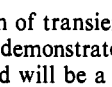
Received March 25, 1980

Arene–Metal Complexes in Organic Synthesis: Addition to Styrene-Type Ligands

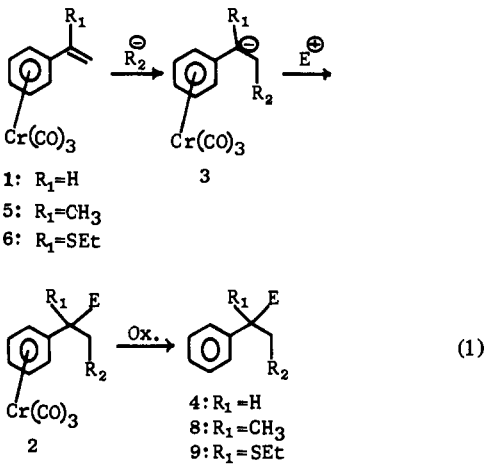
Sir:

The special reactivity of arene rings coordinated to transition metals has been developed into useful synthesis methodology.[1] An important effect is the electron-accepting power of the chromium tricarbonyl unit, which promotes nucleophilic addition to the arene ring in arene–$Cr(CO)_3$ complexes[2] and strongly increases the kinetic acidity of benzylic hydrogens.[3] Complexes of η^6-styrene with $Cr(CO)_3$ have been known for many years,[4] and it was recognized early that nucleophilic addition to the β position of an η^6-styrene ligand would generate the stabilized benzyl anion (e.g., **1**).[5] However, the yields of products attributed to addition of phenyllithium (30%) and methyllithium (7%) appear to have discouraged development of this process. No simple benzyl anion coordinated to $Cr(CO)_3$ has been prepared by addition to styrene or by any other route.[6] We are interested in the scope and limitations of the reaction because (a) it allows conversion of a simple arene complex (e.g., **1**) into a more elaborate one (e.g., **2**), (b) it may allow isolation and study of the coordinated benzyl anion (e.g., **3**),[6] and (c) overall, two new carbon–carbon bonds (e.g., in **4**) could be formed, depending on the choice of nucleophile and electrophile in the reaction. We report that a variety of nucleophiles, electrophiles, and styrene-type ligands participate smoothly in the conversion represented. In the prototype example, 2-lithio-2-methylpropionitrile added to η^6-styrenechromium tricarbonyl slowly at −30 °C in THF, and quenching with ammo-

Table I. Addition of Carbon Anions to Styrene–$Cr(CO)_3$ Derivatives

entry	complex	anion unit, R_2	electrophile	product(s), yield,[a] %
1	1	$-C(CH_3)_2CN$	H^+	4: E = H, 92
2	1	$-C(CH_3)_2CN$	CH_3I	4: E = CH_3, 82
3	1	$-C(CH_3)_2CN$	CH_3COCl	4: E = $COCH_3$, 71
4	1	$-(CH_3)_2CO_2$-*t*-Bu	H^+	4: E = H, 73
5	1	$-C(CN)(OR)CH_3$[c]	H^+	4: E = H, 75[b]
6	5	$-C(CH_3)_2CN$	H^+	8: E = H, 34
7	5	$-C(CN)(OR)CH_3$[c]	H^+	8: E = H, 62[b]
8	6	$-C(CH_3)_2CN$	H^+	9: E = H, 62
9	6	$-C(CH_3)_2CN$	PhSSPh	9: E = SPh, 59[d]
10	6	$-C(CN)(OR)CH_3$	H^+	9: E = H, 81[b,e]
11	6		H^+	9: E = H, 41
12	6	$-C_4H_9$	H^+	9: E = H, 61
13	6	-Ph	H^+	9: E = H, 84
14	6	$-CH_3$	H^+	9: E = H, 60
15	7	$-C(CH_3)_2CN$	H^+	12, 100
16	7	$-C(CH_3)_2CN$	CH_3I	14, 75
17	7	$-C(CH_3)_2CN$	PhCOCl	15, 32

[a] The yield refers to isolated product after oxidation of the inter-intermediate complexes. [b] The product has $R_2 = COCH_3$, obtained after hydrolysis of the cyanohydrin acetal; see: G. Stork and L. Maldonado, *J. Am. Chem. Soc.*, 93, 5286 (1971). [c] R = $CH(CH_3)OCH_2CH_3$. [d] Characterized as the hydrolysis product of the bisthioketal. [e] The product is 4-phenyl-3-buten-2-one obtained after hydrolysis of the cyanohydrin acetal and base-promoted elimination of the ethylthio group.



1: R_1=H
5: R_1=CH_3
6: R_1=SEt

3

2

4: R_1=H
8: R_1=CH_3
9: R_1=SEt

(1)

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(6) Related species have been characterized, but simple benzyl anions on $Cr(CO)_3$ have not been observed directly. For related examples, see: J. F. Helling and W. A. Hendrickson, *J. Organomet. Chem.*, **141**, 99 (1977). For species such as **3** as transient intermediates, see ref 3.

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