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Silyl Phosphites. 15.[1] Reactions of Silyl Phosphites with α-Halo Carbonyl Compounds. Elucidation of the Mechanism of the Perkow Reaction and Related Reactions with Confirmed Experiments

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The reactions of silyl phosphites, i.e., tris(trimethylsilyl) phosphite (**1**), diethyl trimethylsilyl phosphite (**11**), and bis(trimethylsilyl) ethyl phosphite (**12**), with a variety of α-halo carbonyl compounds gave the 1:1 carbonyl addition products (**6, 13,** and **14**), enol phosphates (**5** and **26**), and/or 2-oxophosphonates (**4** and **25**). Substituents on the phosphites and the α-halo carbonyl compounds have influenced the product ratios. The results of these reactions strongly suggest that the Perkow reaction proceeds via an initial attack of phosphite on the carbonyl carbon of the α-halo carbonyl compound. Treatment of bis(trimethylsilyl) 1-[(trimethylsilyl)oxy]-2-halo phosphonates (**6**) with sodium methoxide in methanol followed by retrimethylsilylation gave bis(trimethylsilyl) 1,2-epoxy phosphonates (**17**), bis(trimethylsilyl) 2-oxo phosphonates (**4**), and bis(trimethylsilyl) methyl phosphate (**21**). On the other hand, diethyl 1-hydroxy-2-halo phosphonates (**22**) were converted by treatment with different bases to 1,2-epoxy phosphonates (**23**) predominantly in good yields. When some of tri-*n*-butyltin alkoxides were used as bases, enol phosphates (**26**) were obtained selectively. Several bis(trimethylsilyl) esters obtained in the above reactions were successfully converted to the corresponding monoanilinium salts in high yields by treatment with aniline-containing alcohols.

Introduction

In organophosphorus chemistry, it is well recognized that trialkyl phosphites react with α-halo carbonyl compounds to give enol phosphates (the Perkow reaction[2]) and/or 2-oxophosphonates (the Arbuzov reaction). Both reactions depend on the nature of the compounds and the conditions employed.[3] The enol phosphates obtained by the Perkow reaction can serve as useful synthetic intermediates for the synthesis of acetylenes[4] and olefins.[5] Several mechanistic elucidations on the Perkow reaction have appeared in a number of laboratories and there have been proposed some plausible mechanisms which involve an initial attack of the phosphorus on the halogen,[6] the carbonyl oxygen,[7] the α-carbon bound to the halogen,[8] or the carbonyl carbon.[9,10] The last proposal, originated independently by Allen and Johnson[9a] and by Kharash and Bengeldorf,[9b] seems to comply with all experimental data available. This mechanism has been also supported by the fact reported by Kirby[10] that the reaction of triethyl phosphite with α-haloacetones in the presence of alcohols or acetic acid gives diethyl 1-hydroxy-1-methyl-2-haloethylphosphonates along with the Perkow reaction products. Meanwhile, several kinetic studies on the Perkow reaction have appeared.[11-14] For example, Borowitz[11] described a reasonable mechanism of the Perkow reaction on the basis of the kinetic studies on the reaction of phenacyl halides with trialkyl phosphites. It involves initial attack of a trialkyl phosphite on the carbonyl carbon followed by a C$\rightarrow$O rearrangement of the dialkylphosphonyl group via a quasi-three-membered-ring transition state with concomitant elimination of alkyl halide. Gaydou[14a] has recently reported a systematic study of the Perkow reaction using various aromatic and aliphatic α-halo carbonyl compounds from the same point of view.

In this paper, we report a comprehensive study of the reaction of silyl phosphites with a variety of α-halo carbonyl compounds which helps clarify the mechanism of the Perkow reaction and describe some related reactions and new methods for the synthesis of a new class of unesterified phosphonic and phosphoric acid derivatives. A preliminary report of this work has already appeared.[15]

Results and Discussion

Preparation of Tris(trimethylsilyl) Phosphite. Tris(trimethylsilyl) phosphite (**1**) was first reported by Voronkov and Storik.[16] They prepared **1** in 39% yield by

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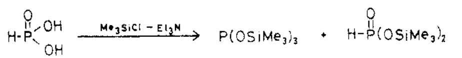
Table I. Reaction of Tris(trimethylsilyl) Phosphite (1) with α-Halo Carbonyl Compounds (3)[a]

	3				product, yield, %				
	R^1	R^2	R^3	X	4	5	6	9	bp, °C (mm)
a	H	H	CH_3	Cl			97		102-103 (0.18)
b	H	H	CH_3	Br			89		104-107 (0.25)
c	H	H	CH_3	OSO_2Me			92		143-146 (0.12)
d	CH_3	H	CH_3	Cl			92		109-110 (0.13)
e	CH_3		$(CH_2)_4$	Cl			82		87-110 (0.23)
f	CH_3	H	H	Cl			92		102-103 (0.45)
g	CH_3	CH_3	H	Cl			92		104-105 (0.30)
h	H	H	C_6H_5	Cl		74			134-135 (0.25)
i	H	H	C_6H_5	Br	14	61			80-126 (0.30)
j	H	H	4-BrC_6H_4	Cl	7	70			142-155 (0.19)
k	H	H	OEt	Cl	66				90-93 (0.10)
l	H	H	OEt	Br	84				92-97 (0.10)
m	H	H	COOEt	Cl		19	57		115-129 (0.31)
n	H	H	COOEt	Br		36	31		95-130 (0.35)
o	CH_3	H	$SiMe_3$	Br				68[b]	73-87 (0.19)

[a] All of the reactions were carried out in dry THF for 3 h except in the case of the reaction of 1 with 3k (under reflux) and the reaction of 1 with 3o (no solvent, 100 °C, 5 h). [b] Ratio of Z/E is 85/15.

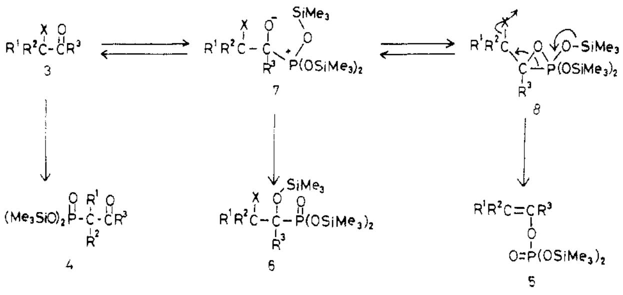
the reaction of phosphorus tribromide with ethyl trimethylsilyl ether in the presence of zinc chloride. Orlov[17] reported an alternative method by means of the silylation of phosphorous acid with trimethylsilyl chloride and triethylamine which provided 1 in 78% yield. The latter



method seemed to be accessible to us for the synthesis of 1 on a large scale. However, we have encountered great difficulty in purifying 1 from a mixture of 1 and bis(trimethylsilyl) phosphonate (2), usually present to an appreciable extent (20–30%).

In attempts to introduce the third silyl group into phosphorous acid, we have tested silylation in several solvents such as ether, benzene, tetrahydrofuran, and pyridine at room temperature or under reflux, but complete trimethylsilylation to give 1 was rather difficult. However, 2 was quite easily obtained in 91% yield by the silylation of phosphorous acid with 2 equiv each of trimethylsilyl chloride and triethylamine. It was expected that the final conversion of 2 to 1 was difficult compared with the exothermic bistrimethylsilylation of phosphorous acid to give 2 because the pK_a value of the H–P(O) group of 2 was estimated to be higher than that of diethyl phosphonate (pK_a = 13)[18] owing to the contribution of the two (trimethylsilyl)oxy groups as strong electron-donating groups. A similar situation was encountered in metalation of 2 with sodium in dry ether, while diethyl phosphonate underwent facile metalation with sodium to give a tervalent sodium salt.[19] The silylation of phosphorous acid in a mixed solvent of tetrahydrofuran–ether (6:1, v/v) under reflux for 6 h gave 1 with the best purity of 86% among the solvents employed. Compound 2 did not react with sodium at room temperature but at 140–150 °C the metalation proceeded with gentle evolution of hydrogen gas. At such temperatures, the simultaneous decomposition occurred and gave a mixture of 1 and 2 in the ratio of 2.4:1 (^{1}H NMR) after 20 h. Thus, treatment of a mixture of 1 and 2, obtained by the silylation of phosphorous acid with trimethylsilyl chloride in the presence of triethylamine, with an excess of sodium at 140–150 °C for 18 h gave 95–100% pure 1 in more than 82% overall yields. Analytically pure reagent 1 was readily obtained by repeated treatment with sodium if necessary. On the other hand, we found that 2 underwent facile silylation with diethyl(trimethylsilyl)amine at 145 °C for 7 h to give 93% pure 1 in 92% yield. Therefore, the two-step silylation of phosphorous acid via 2 is also available. However, the procedure involving the rough silylation of 1 followed by successive treatment with sodium is much more convenient for laboratory work.

Scheme I



Reaction of 1 with α-Halo Carbonyl Compounds. Substituent Effects of Alkyl Groups and Halogen of 3. The reaction of 1 with α-halo carbonyl compounds (3) was carried out in dry tetrahydrofuran at room temperature for 3 h except in the case of the reaction of 1 with ethyl haloacetate (3k and 3l) or with α-bromopropionylsilane (3o). These results are summarized in Tables I and II.

Table I reveals that the reaction of 1 with alkyl-substituted α-halo aldehydes and α-halo ketones uniformly gave neither 2-oxo phosphonates (4) nor enol phosphates (5) expected from the Arbuzov or Perkow reaction, but 1:1 carbonyl adducts (6). These results are of interest since the reaction of trialkyl phosphites with reactive ketones such as bromoacetone (3a) is known to give Arbuzov reaction products in preference to Perkow reaction products[9] while the reaction with α-chloro ketones[20] and α-halo aldehydes[8b,9a] usually gives the exclusive formation of Perkow reaction products. These results strongly suggest that the isolation of several carbonyl adducts described here indicates the trapping of the initially formed intermediate (7) discussed by Borowitz due to the rapid intramolecular rearrangement of a trimethylsilyl group of 7 to its oxygen via a five-membered transition state as described in Scheme I. Similar carbonyl addition reactions of silyl

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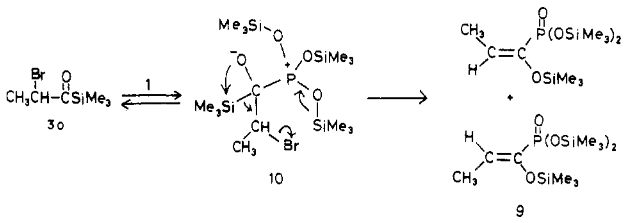
phosphites with simple aldehydes and ketones including α,β-unsaturated systems have appeared in a number of reports.[21]

On the other hand, the Arbuzov and/or Perkow reactions took place in the case of the reactions of **1** with phenacyl halides (**3h** and **3i**) having carbonyl groups substituted with aryl groups or with ethyl haloacetates (**3m** and **3n**) having carbonyl groups slightly deactivated with an ethoxy group. These results suggest that the Perkow reaction observed in the case of **3h**, **3i**, **3m**, and **3n** proceeds as a result of the predominant cleavage of the P–C bond of intermediate **8** in equilibrium with **7**. The equibria shown in Scheme I are affected by electron-withdrawing groups such as phenyl and ethoxycarbonyl groups. If R^3 is an electron-withdrawing group, the P–C bond of transition state **8** is easily cleaved because the carbanion formed as a result of the cleavage can be stabilized through delocalization of electrons. The effect of a substituent adjacent to the carbonyl group was clearly elucidated by the fact that, when *p*-bromophenacyl chloride (**3j**), having a stronger electron-withdrawing group, was used instead of **3i**, the ratio of the Perkow/Arbuzov reaction products increased from 4.4 to 10.0.

It is noted that, in the case of **3m** and **3n** having an ethoxycarbonyl group, an electron-withdrawing group, between phenyl and alkyl groups, both 1:1 carbonyl adducts (**6m** and **6n**) and enol phosphates (**5m**) were obtained. The ratio of **6**/**5** might depend on the ease of elimination of the halogen that assists the breaking of the P–C bond in the cyclic intermediate **8**. For instance, the ratios of **6**/**5** were 3.0 in the case of **3m** and 0.86 in the case of **3n**, respectively.

It seems impossible from the above explanations that **1** attacks the unreactive carbonyl carbon of α-haloacetates. In fact, only direct displacement reaction to give 2-oxo phosphonates took place. While bromoacetate (**3l**) underwent smooth reaction with **1** at room temperature to give **4l**, the reaction of chloroacetate (**3k**) with **1** required heating the mixture.

Next, we undertook the reaction of **1** with a newly synthesized α-halo carbonyl compound, α-bromoethyl trimethylsilyl ketone (**3o**).[22] The reaction did not take place at room temperature but proceeded at 100 °C for 5 h to give bis(trimethylsilyl) 1-[(trimethylsilyl)oxy]-2-methylvinylphosphate (**9**) in 63% yield as a mixture of *Z* and *E* isomers (85:15). In this case, the 1:1 carbonyl adduct (**6o**), enol phosphate (**5o**), and 2-oxo phosphonate (**4o**) were not obtained. A plausible mechanism for the formation of **9** is that the trimethylsilyl group attached to the carbonyl carbon migrates rapidly from carbon to oxygen in the initial intermediate (**10**) preferentially over nucleophilic attack of the negatively charged α-oxygen of the positively charged phosphorus and then β-elimination of the bromide ion occurs. This type of trialkylsilyl group migration from carbon to negatively charged oxygen has been well established by Brook's extensive studies where a number of examples have been shown.[23]



As one of the reasons why the reaction of **1** with alkyl-substituted α-halo aldehydes and ketones uniformly gives 1:1 carbonyl adducts, the inductive effect of three trimethylsilyloxy groups bound to the phosphorus could be also considered; the three (trimethylsilyl)oxy groups of intermediate **7** stabilize the phosphonium cation more effectively than the three alkoxy groups of trialkyl phosphites so that transfer of the trimethylsilyl group via a five-membered-ring transition state is favored over intramolecular attack of the negatively charged carbonyl oxygen on the phosphorus atom to form the cyclic intermediate (**8**). This view was evidently confirmed by the following substituent effect of silyl phosphites. It was expected that there was a borderline, in the reaction of silyl phosphites with **3**, which distinguished the carbonyl addition reaction from the Perkow and/or Arbuzov reactions. Therefore, the reaction of other silyl phosphites, i.e., diethyl trimethylsilyl phosphite (**11**) and bis(trimethylsilyl) ethyl phosphite (**12**), with several α-halo carbonyl compounds was undertaken. When the Arbuzov or Perkow reaction occurs in these reactions, trimethylsilyl bromide[24] simultaneously formed is expected to react further with the initial products to cause the ethyl esters, transformed partially into mono- or bistrimethylsilyl esters, to afford a complex mixture.

Therefore, the mixture was treated in situ, if necessary, with trimethylsilyl bromide and the products were characterized as the bis(trimethylsilyl) esters. We have previously reported that trimethylsilyl bromide did not react with bis(trimethylsilyl) enol phosphates.[25] Consequently, the reaction of **11** with **3a**, **3d**, and **3f** afforded exclusively 1:1 carbonyl adducts (**13a**, **13d**, and **13f**) as in the case of **1**. The reactions of **12** with **3a** and **3b** also gave 1:1 carbonyl adducts (**14a** and **14b**). Contrary to these results,

$(EtO)_2POSiMe_3$ **11** $EtOP(OSiMe_3)_2$ **12**

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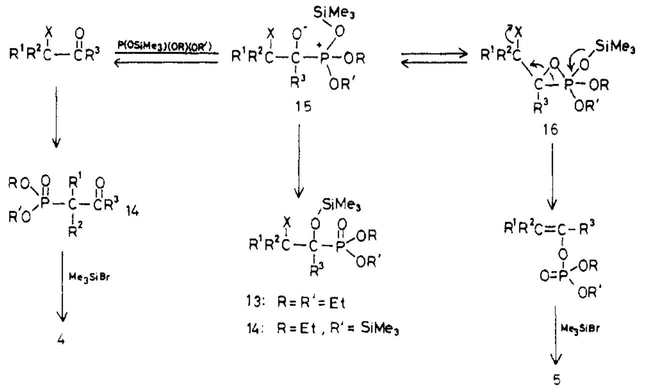
Table II. Elemental Analyses and Physical Data of Bis(trimethylsilyl) Enol Phosphates (5) and Bis(trimethylsilyl) 1-[(Trimethylsilyl)oxy]-2-halo Phosphonates (6)

		anal.		IR (NaCl)	
compd	formula	calcd	found	ν_{max}, cm^{-1}	^{1}H NMR (CDCl$_3$), δ
5h	$C_{14}H_{25}O_4PSi_2$	C, 48.81; H, 7.32	C, 48.81; H, 7.84	1629 1260	0.28 (s, 18 H, POSiCH$_3$), 5.22 (s, 1 H, C=CH), 5.27 (s, 1 H, C=CH), 7.23-7.48 (m, 3 H, Ar H), 7.52-7.72 (m, 2 H, Ar H)
5j	$C_{14}H_{24}O_4BrPSi_2$	C, 39.72; H, 5.71	C, 39.15; H, 5.90	1635	0.28 (s, 18 H, POSiCH$_3$), 4.93 (s, 1 H, C=CH), 4.98 (s, 1 H, C=CH), 7.15 (s, 4 H, Ar H)
5m[a]					0.32 (s, 18 H, POSiCH$_3$), 1.32 (t, 3 H, J_{H-H} = 7 Hz, CH$_3$), 4.27 (q, 2 H, J_{H-H} = 7 Hz, CH$_2$), 5.60 (t, 1 H, J_{P-H} = 2.5, J_{H-H} = 2.5 Hz, C=CH)
6a	$C_{12}H_{32}O_4ClPSi_3$	C, 36.86; H, 8.25	C, 36.63; H, 8.33	1258	0.23 (s, 9 H, SiCH$_3$), 0.33 (s, 18 H, POSiCH$_3$), 1.37 (d, 3 H, J_{P-H} = 16 Hz, CH$_3$), 3.58 (d, 2 H, J_{P-H} = 5 Hz, CH$_2$Cl)
6b	$C_{12}H_{32}O_4BrPSi_3$	C, 33.09; H, 7.41	C, 32.51; H, 7.54	1260	0.22 (s, 9 H, COSiCH$_3$), 0.33 (s, 18 H, POSiCH$_3$), 1.53 (d, 3 H, J_{P-H} = 16 Hz, CH$_3$), 3.63 (d, 2 H, J_{P-H} = 5 Hz, CH$_2$)
6c	$C_{13}H_{35}O_7PSSi_3$	C, 34.64; H, 7.83	C, 35.05; H, 8.45	1260	0.03 (s, 9 H, COSiCH$_3$), 0.15 (s, 18 H, POSiCH$_3$), 1.32 (d, 3 H, J_{P-H} = 17 Hz, CH$_3$), 2.88 (s, 3 H, SO$_2$CH$_3$), 4.12 (d, 2 H, J_{P-H} = 7 Hz, CH$_2$)
6d	$C_{13}H_{34}O_4ClPSi_3$	C, 38.5; H, 8.46	C, 37.85; H, 8.46	1260	0.23 (s, 9 H, COSiCH$_3$), 0.33 (s, 18 H, POSiCH$_3$), 1.48 (d, 3 H, J_{H-H} = 8 Hz, CH$_3$), 1.52 (d, 3 H, J_{P-H} = 17 Hz, PCCH$_3$), 4.13 (dq, 1 H, J_{P-H} = 7, J_{H-H} = 4 Hz, CHCl)
6e	$C_{16}H_{38}O_4ClPSi_3$	C, 43.17; H, 8.60	C, 43.07; H, 8.62	1254	0.23 (s, 9 H, COSiCH$_3$), 0.33 (s, 18 H, POSiCH$_3$), 1.43-2.50 (m, 8 H, (CH$_2$)$_4$), 1.63 (s, 3 H, CH$_3$)
6f	$C_{12}H_{32}O_4ClPSi_3$	C, 36.86; H, 8.25	C, 36.67; H, 8.15	1255	0.23 (s, 9 H, COSiCH$_3$), 0.33 (s, 18 H, POSiCH$_3$), 1.23, 1.32 (d, 3 H, J_{H-H} = 7 Hz, CH$_3$ of two diastereomers), 3.85 (dd, 1 H, J_{P-H} = 15, J_{H-H} = 7 Hz, PCH of one of two diastereomers), 4.50 (m, 1 H, PCCH)
6g	$C_{13}H_{34}O_4ClPSi_3$	C, 38.55; H, 8.46	C, 38.45; H, 8.61	1255	0.22 (s, 9 H, COSiCH$_3$), 0.32 (s, 18 H, POSiCH$_3$), 1.48 (s, 3 H, CH$_3$), 1.63 (s, 3 H, CH$_3$), 3.82 (d, 1 H, J_{P-H} = 10 Hz, PCH)
6m[a]					0.25 (s, 9 H, COSiCH$_3$), 0.30 (s, 18 H, POSiCH$_3$), 1.33 (t, 3 H, J_{H-H} = 7 Hz, CH$_3$), 3.53 (dd, 1 H, J_{P-H} = 11.6, J_{H-H} = 5.2 Hz, PCCH), 4.02 (dd, 1 H, J_{P-H} = 11.6, J_{H-H} = 3 Hz, PCCH)
6n[a]					0.26 (s, 9 H, COSiCH$_3$), 0.30 (s, 18 H, POSiCH$_3$), 1.33 (t, 3 H, J_{H-H} = 7 Hz, CH$_3$), 3.38 (dd, 1 H, J_{P-H} = 10.6, J_{H-H} = 5.7 Hz, PCCH), 4.07 (dd, 1 H, J_{P-H} = 10.6, J_{H-H} = 3.8 Hz, PCCH)

[a] These compounds could not be separated from other products simultaneously formed by repeated distillation.

the reaction of **11** with **3b** gave a mixture of Arbuzov and Perkow reaction products (**4b** and **5b**). The results are summarized in Table III. Thus, the borderline mentioned above was found to be betweeen the two reactions of **11** and **12** with **3b**. Another borderline to distinguish the carbonyl addition reaction from the Perkow or the Arbuzov reaction is marked with the line in Table IV which represents the summary of the reactions of silyl phosphites with α-haloacetones.



As far as α-chloro carbonyl compounds were concerned, substituent effects of silyl phosphite were not so significant that the Perkow reaction did not occur and the equilibrium between **15** and **16** was likely to exist in favor of **15**. The remarkable change in reaction mode between the reactions of **11** and **12** with **3b** suggests strongly that the net positive charge on the phosphorus is one of the important factors to determine the reaction course. The difference between the reactions of **11** with **3a** and **3b** can be explained as follows. In the case of the reaction of **11** with **3b**, the normal Perkow reaction was induced owing to the superior leaving ability of bromine to that of chlorine in intermediate **16**.

Reactions of 1:1 Carbonyl Adducts. 1,2-Epoxy phosphonic acids are of great interest in connection with a naturally occuring unesterified epoxyalkylphosphonate, phosphonomycin,[26] which acts as a wide-spectrum antibiotic. The transformation of 1-[(trimethylsilyl)oxy]-2-halo phosphonates to 1,2-epoxy phosphonates was attempted. First, we attempted the thermal conversion of **6a** into bis(trimethylsilyl) 1,2-epoxypropylphosphonate (**17f**) in the presence of various Lewis acids. However, all attempts

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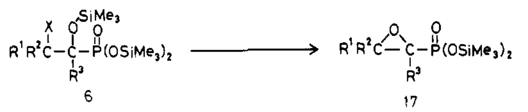
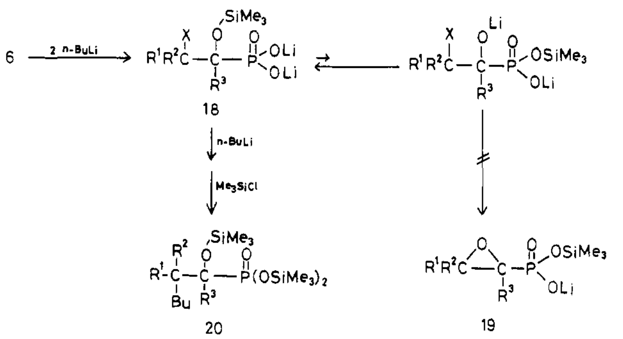
(26) (a) D. Hedlin, E. O. Stapley, M. Jackson, H. Wallick, A. K. Miller, F. J. Wolt, T. W. Muller; L. Chaiet, F. M. Kahan, E. L. Foltz, H. B. Woodruft, J. M. Mata, S. Hernandez, and S. Mochales, *Science*, 166, 122 (1969); (b) B. G. Christensen, W. J. Leanza, T. R. Beattie, A. A. Patchett., B. H. Arison, R. E. Ormond, F. A. Kuehl, Jr., G. A. Schonberg, and O. Jardetzky, *ibid.*, 166, 123 (1969).

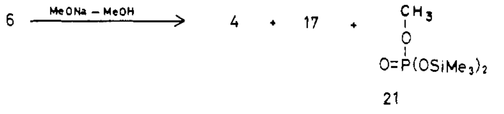


failed. For example, heating **6f** at 200 °C in the presence of stannyl(IV) chloride caused the reverse reaction of decomposition into **1** and **3f**.

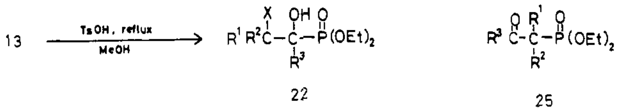
It is known that trimethylsilyl enol ethers can be converted to metal enolates[27] by treatment with alkyllithium reagents. When a dilithium salt (**18**) is formed by addition of 2 equiv of *n*-BuLi to **6**, a ring-closure reaction to give an epoxy phosphonate (**19**) may be possible if migration of the trimethylsilyl group at the β-position to the phosphonyl oxygen occurs. However, treatment of **6a** with 2.1 equiv of *n*-BuLi followed by retrimethylsilylation gave only the starting material. Treatment of **6a** with 3 equiv of *n*-BuLi did not afford **17a**, but β-butylated phosphonates (**20**) were obtained.

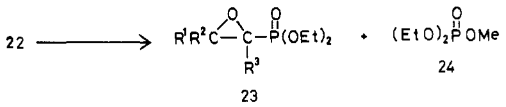


Next, we chose sodium methoxide as a milder base for the silicon–metal exchange. When **6a** was treated with 3 equiv of sodium methoxide in methanol at −78 °C for 3 h and the mixture was treated with 3 equiv of trimethylsilyl chloride for 3 h, a mixture of **17a** and bis(trimethylsilyl) 2-oxopropylphosphonate (**4a**) was obtained in 52% and 27% yields, respectively. Similar reactions using several 1:1 carbonyl adducts were carried out under various conditions. The conditions and results are summarized in Table V and VI. In some cases, bis(trimethylsilyl) methyl phosphate (**21**) was obtained as a byproduct as shown in Table V. Mechanisms of the formation of the products like **4** and **21** are not easily elucidated.



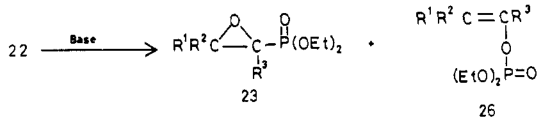
Next, we examined the reactions of diethyl esters of 1-hydroxy-2-halo phosphonates with several bases in order to observe the electronic effect in reaction mode between the esterified and unesterified 1-hydroxy-2-halo phosphonates. Some reports[28] on the conversion of dialkyl 1-hydroxy-2-halo phosphonates by treatment with bases to dialkyl 1,2-epoxy phosphonates have already appeared. We have independently examined the reaction of several diethyl 1-hydroxy-2-halophosphonates (**22**) with sodium methoxide in methanol. The latter phosphonates **22** were prepared in high yields by treatment of diethyl 1-[(trimethylsilyl)oxy]-2-halo phosphonates (**13**) with a catalytic amount of *p*-toluenesulfonic acid in methanol under reflux (see Table VII). In the reaction of **22** with sodium methoxide, the isolated products were diethyl 1,2-epoxy phosphonates (**23**) and diethyl methyl phosphate (**24**) as shown in Table VIII. Diethyl 2-oxo phosphonates (**25**) were not detected.





Tables V and VIII show that **24** was formed in 16% yield in the case of **22a** but **21** was not formed in the reactions of **6a** with sodium methoxide. This result suggests that the electron-rich phosphorus atom of the dissociated $P(O)(O^-)_2$ group is attacked by the negatively charged alcoholic α-oxygen with more difficulty than that of the neutral $P(O)(OEt)_2$ group.[29]

In connection with the mechanism of the Perkow reaction, we have examined the reaction of diethyl 1-hydroxy-2-halo phosphonates (**22**) with several bases other than sodium methoxide. The results are summarized in Table VII. When **22a** was treated with *t*-BuOK in *tert*-butyl alcohol, epoxy phosphonate **23a** was mainly obtained with a small amount of enol phosphate **26a**. On the other hand, treatment of **22a**, **22d**, and **22f** with *n*-BuLi in ether gave epoxy phosphonates as the sole products.



In contrast with these results, when tri-*n*-butyltin methoxide was chosen as the base, the reaction did not give epoxy phosphonates but enol phosphates and **24** were obtained (Table IX). In order to avoid the reaction to form **24**, tri-*n*-butyltin *tert*-butoxide was employed. Thus, treatment of **3a**, **3d**, and **3f** with the latter agent gave enol phosphates **26a**, **26d**, and **26f** in 73%, 69%, and 50% yields, respectively. The use of (tri-*n*-butylstannyl)diethylamine in place of the alkoxides resulted in a poorer yield of **26a** from the reaction with **3a**. Highly selective formation of **26** by means of the tin reagents might be explained as follows. After the stannylation of the α-hydroxy group, the tributylstannyl group plays the role of a weak Lewis acid[30] coordinating with the neighboring oxygen of the O═P bond so that the positively charged phosphorus atom tends to be attacked by the α-oxygen of the O–Sn bond to form a three-membered-ring interme-

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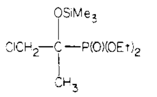
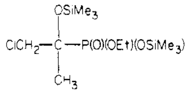
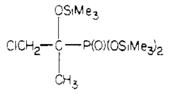
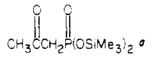
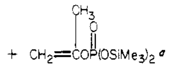
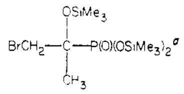
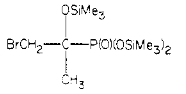
[27] H. O. House, "Modern Synthetic Reactions", Benjamin, Menlo Park, CA, 1972, pp 565–570.

[28] (a) B. A. Arbuzov, V. S. Vinogradova, and N. A. Polezhaeva, *Dokl. Akad Nauk SSSR*, **111**, 107 (1956); *Chem. Abstr.*, **51**, 8001 (1957); (b) V. S. Abramov and A. S. Kapustima, *Zh. Obshch. Khim.*, **27**, 1012 (1957); *Chem. Abstr.*, **52**, 3667 (1958); (c) A. N. Pudovik and L. G. Biktimirova, *Zh. Obshch. Khim.*, **27**, 1708 (1957); *Chem. Abstr.*, **52**, 3714 (1958); (d) P. A. Kirpichnikov, A. S. Kapustina, and G. N. Tokareva, *Tr. Kazan. Khim.-Teknol. Inst.*, **33**, 188 (1964); *Chem. Abstr.*, **66**, 2619 (1967); (e) V. S. Abramov and R. N. Savintseva, *Khim. Org. Soedin. Fosfora*, 129 (1967); *Chem. Abstr.*, **69**, 67465 (1968); (f) T. A. Guseva, L. M. Kozlova, I. M. Shermorgorn, *Zh. Obsh. Khim.*, **43**, 292 (1973); *Chem. Abstr.*, **78**, 159754 (1973); (g) E. E. Nifant'ev, A. I. Zavalishina, S. F. Sorokina, A. A. Borisenko, *Zh. Obshch. Khim.*, **46**, 471 (1976); *Chem. Abstr.*, **85**, 45907 (1976). For a comprehensive review of 1,2-epoxy phosphonates see the following: (h) D. Redmore, *Chem. Rev.*, **71**, 315 (1971).

[29] L. D. Freedman and G. O. Doak, *Chem. Rev.*, **57**, 479 (1957).

[30] (a) R. M. Munavu, H. H. Szmant, *J. Org. Chem.*, **41**, 1832 (1976); (b) M. A. Nashed, L. Anderson, *Tetrahedron Lett.*, 3503 (1976); (c) *Carbohydr. Res.*, **56**, 325 (1977); (d) T. Ogawa, M. Matsui, *ibid.*, **56**, C 1 (1977).

Table III. Reaction of Silyl Phosphites (1, 11, and 12) with α-Haloacetones (3a and 3b)

α-haloacetone	silyl phosphite	product	% yield	bp, °C (mm)
$ClCH_2C(O)CH_3$ **3a**	$P(OEt)_2(OSiMe_3)$ **11**	 $\mathrm{ClCH_2C(OSiMe_3)(CH_3){-}P(O)(OEt)_2}$ **13a**	86	103-110 (0.65)
	$P(OEt)(OSiMe_3)_2$ **12**	 $\mathrm{ClCH_2C(OSiMe_3)(CH_3){-}P(O)(OEt)(OSiMe_3)}$ **14a**	76	103-105 (1.0)
	$P(OSiMe_3)_3$ **1**	 $\mathrm{ClCH_2C(OSiMe_3)(CH_3){-}P(O)(OSiMe_3)_2}$ **6a**	96	105-106 (2.0)
$BrCH_2C(O)CH_3$ **3b**	$P(OEt)_2(OSiMe_3)$	 $\mathrm{CH_3C(O)CH_2P(O)(OSiMe_3)_2}$ [a] **4a**	24	70-100 (1.25)
		 $+\ \mathrm{CH_2{=}C(CH_3)OP(O)(OSiMe_3)_2}$ [a] **5a**	65	
	$P(OEt)(OSiMe_3)_2$	 $\mathrm{BrCH_2C(OSiMe_3)(CH_3){-}P(O)(OSiMe_3)_2}$ [a] **6b**	67	110-115 (0.40)
	$P(OSiMe_3)_3$	 $\mathrm{BrCH_2C(OSiMe_3)(CH_3){-}P(O)(OSiMe_3)_2}$ **6b**	91	101-104 (0.20)

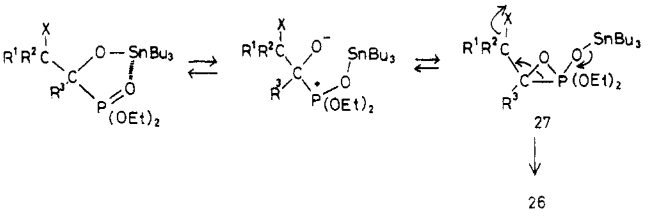
[a] After the reaction the mixture was treated with trimethylsilyl bromide and the products were isolated as the bis(trimethylsilyl) esters.

Table IV. Reaction Mode of Silyl Phosphites and Triethyl Phosphite with α-Haloacetones[a]

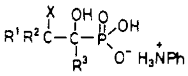
	$(EtO)_3P$	$(EtO)_2POSiMe_3$	$EtOP(OSiMe_3)_2$	$P(OSiMe_3)_3$
$ClCH_2C(O)CH_3$	Arb < Per	Add	Add	Add
$BrCH_2C(O)CH_3$	Arb ≃ Per	Arb < Per	Add	Add

[a] Add, Arb, and Per refer to 1:1 carbonyl addition reaction, the Arbuzov reaction, and the Perkow reaction, respectively.

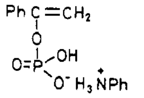
diate (**27**) which induces the activation of the O=P bond; i.e., the generation of the positively charged phosphorus atom is essential for the Perkow reaction.



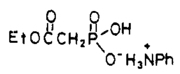
Preparation of Unesterified New Phosphonic and Phosphoric Acid Derivatives. The trimethylsilyl groups of trimethylsilyl esters of organophosphorus oxy acids are feasibly removed by addition of water or alcohols to give the unesterified acids.[31] Therefore, all bis(trimethylsilyl) esters obtained through the present study were treated with aniline-containing alcohols.[25,32] Treatment of 1:1 carbonyl adducts **6a**, **6b**, and **6f** with 3 equiv of ethanol and 2 equiv of aniline in dry ether gave monoanilinium salts (**28a**, **28b**, and **28f**) as the precipitates, although pure products were not obtained from **4c**, **4d**, and **4g** because of the difficult separation from simultaneously formed byproducts. In a similar manner, bis(trimethylsilyl) 1-phenylvinyl phosphate (**5h**) was converted to the mono-


$\mathrm{R^1R^2C(X){-}C(OH)(R^3){-}P(O)(OH)O^-\ H_3\overset{+}{N}Ph}$

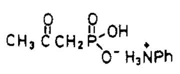
28


$\mathrm{PhC({=}CH_2){-}O{-}P(O)(OH)O^-\ H_3\overset{+}{N}Ph}$

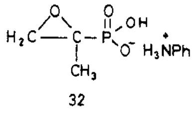
29


$\mathrm{EtOC(O)CH_2P(O)(OH)O^-\ H_3\overset{+}{N}Ph}$

30


$\mathrm{CH_3C(O)CH_2P(O)(OH)O^-\ H_3\overset{+}{N}Ph}$

31



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(31) R. Rabinowitz, J. Org. Chem., 28 2975 (1963).

(32) (a) T. Hata, H. Mori, and M. Sekine, Chem. Lett., 1431 (1977). (b) M. Sekine and T. Hata, J. Chem. Soc., Chem. Commun., 285 (1978).

Table V. Treatment of 1:1 Carbonyl Adducts (6) with MeONa-MeOH Followed by Retrimethylsilylation

entry no.		6				method[a]	temp, °C	time, h		products, yield, %			bp, °C (mm)
		R^1	R^2	R^3	X			MeONa	Me_3SiCl	4	17	21	
1	a	H	H	CH_3	Cl	A	−78	3	3	27	52		68–77 (0.1–0.12)
2						A	r.t.[c]	18	5	16	47		79–83 (0.45–0.38)
3						B	r.t.	7	14	67			79 (0.23)
4	b	H	H	CH_3	Br	A	−78	3	3	79			76–77 (0.15)
5						B	r.t.	17	19	79			73–79 (0.25–0.29)
6	c	H	H	CH_3	MsO[b]	A	−78	3	3	42	23		74–76 (0.24)
7	d	CH_3	H	CH_3	Cl	A	−78	3	3	35			73–74 (0.09)
8						A	r.t.	21	16	16		10	42–64 (0.28–0.22)
9						B	r.t.	21	17	14		10	49–63 (0.18–0.13)
10	f	CH_3	H	H	Cl	A	−78	3	3	23		27	69–74 (0.63–0.45)
11						A	r.t.	13	3	25		19	67–74 (0.50–0.37)
12						B	r.t.	3	18	33		28	68–73 (0.25–0.18)
13	g	CH_3	CH_3	H	Cl	A	−78	3	3	12	6	12	58–66 (0.22–0.32)
14						A	r.t.	8	14	8	4	9	61–66 (0.43–0.50)

[a] A: Sodium methoxide in methanol was added to 1:1 carbonyl adducts in THF. B: 1:1 Carbonyl adducts in THF were added to sodium methoxide in methanol. [b] MsO refers to CH_3SO_2O. [c] r.t. = room temperature.

Table VI. Elemental Analyses and NMR Data of Bis(trimethylsilyl) β-Oxo Phosphonates (4) and Bis(trimethylsilyl) 1,2-Epoxy Phosphonates (17)

compd	formula	anal.		IR (NaCl) ν_{max}, cm^{-1}	^{1}H NMR ($CDCl_3$), δ
		calcd	found		
4a	$C_9H_{23}O_4PSi_2$	C, 38.28; H, 8.21	C, 39.24; H, 8.55	1730, 1255	0.17 (s, 18 H, $POSiCH_3$), 2.13 (s, 3 H, CH_3), 2.83 (d, 2 H, J_{P-H} = 24 Hz, PCH)
4d	$C_{10}H_{25}O_4PSi_2$	C, 40.52; H, 8.50	C, 40.57; H, 9.02	1732, 1255	0.13 (s, 18 H, $POSiCH_3$), 1.13 (dd, 3 H, J_{P-H} = 7 Hz, CH_3), 2.15 (s, 3 H, $CH_3C(O)$), 2.97 (dq, 1 H, J_{P-H} = 27, J_{H-H} = 7 Hz, PCH)
4f[a]					0.17 (s, 18 H, $POSiCH_3$), 1.18 (dd, 3 H, J_{P-H} = 18, J_{H-H} = 7 Hz, CH_3), 2.82 (ddq, 1 H, J_{P-H} = 28, J_{H-H} = 2 Hz, PCH), 9.23 (s, 1 H, C(O)H)
4g[a]					0.20 (s, 18 H, $POSiCH_3$), 1.18 (d, 6 H, J_{P-H} = 17 Hz, CH_3), 9.12 (d, 1 H, J_{P-H} = 1.5 Hz, C(O)H)
17a	$C_9H_{23}O_4PSi_2$	C, 38.28;[b] H, 8.21	C, 38.05; H, 8.44	1255, 1220	0.17 (s, 18 H, $POSiCH_3$), 1.35 (d, 3 H, J_{P-H} = 12 Hz, CH_3), 2.48 (t, 1 H, J_{P-H} = 5, J_{H-H} = 5 Hz, OCH), 2.92 (t, 1 H, J_{P-H} = 5, J_{H-H} = 5 Hz, OCH)
17g[a]					0.20 (s, 18 H, $POSiCH_3$), 1.43 (d, 3 H, J_{P-H} = 2 Hz, CH_3), 1.53 (s, 3 H, CH_3)

[a] These compounds could not be separated from other products simultaneously formed by repeated distillation. [b] The 52:27 mixture of **17a** and **4a** was analyzed (see Table V) because both compounds have the same formula.

Table VII. Preparation of Diethyl 1-Hydroxy-2-halo Phosphonates (**22**) from Diethyl 1-[(Trimethylsilyl)oxy]-2-halo Phosphonates (**13**)

	13				% yield of **22**
	R^1	R^2	R^3	X	
a	H	H	CH_3	Cl	100
d	CH_3	H	CH_3	Cl	80[a]
f	CH_3	H	H	Cl	94[b]

[a] The NMR spectrum of **22d** suggests the exclusive formation of one diastereomer. [b] The NMR spectrum of **22f** shows two diastereomeric methyl groups (CH_3CCP) at 1.46 and 1.48 ppm in the ratio of ca. 1:1.

anilinium salt (**29**) of the free acid in 81% yield. On the other hand, the monoanilinium salt (**30**) of (carboethoxy)methylphosphonic acid was obtained from **4k** in 94% yield. Bis(trimethylsilyl) 2-oxopropylphosphonate (**4a**) derived from **6a** was also successfully converted to the monoanilinium salt (**31**) of the free acid. Finally, from a 52:27 mixture of **17a**/**4a**, monoanilinium 1-methyl-1,2-epoxyethylphosphonate (**32**) was separated and isolated in 58% yield.

We believe that the above method involving alcoholysis of silyl esters followed by neutralization with aniline would be useful for the preparation of relatively unstable organophosphorus oxy acids, especially, biologically important phosphate esters.

Conclusion

The mechanism of the Perkow reaction has been debated by the product distributions of the Perkow and Arbuzov reaction products. Studies on the Perkow reaction using silyl phosphites made us consider more concretely where the initial attack of the phosphite molecule occurred, since these reactions gave 1:1 carbonyl addition products under mild conditions and the Perkow and Arbuzov reactions occurred under certain conditions. The present study should be emphasized by the introduction of a trimethylsilyl group in phosphite molecules. This is because the silyl group is easily transferred to the negatively charged oxygen atom owing to the strong affinity of silicon for oxygen. Reactive carbanions or oxygen anions often have been trapped with trimethylsilyl chloride in carbanion chemistry and the methodology has proved to be a quite useful tool for grasping unstable reactive intermediates.[27] Our results described here suggest strongly the conceivable but more direct evidence for the initial attack of the phosphite molecule on the carbonyl carbon in the Perkow reaction. Substituent effects of α-halo carbonyl compounds and phosphite residues showed the importance of the electronic circumstance of the α-carbon

Table VIII. Reaction of Diethyl 1-Hydroxy-2-halo Phosphonates (22) with Bases

	22						products, yield, %		
	R^1	R^2	R^3	base	temp, °C	time, h	23	24	26
a	H	H	CH_3	MeONa	r.t.^{e}	2	54	16	0
d	CH_3	H	CH_3	MeONa	r.t.	2	69^a	31	0
f	CH_3	H	H	MeONa	r.t.	2	56^b	16	0
a	H	H	CH_3	*t*-BuOK	r.t.	2	61		4
d	CH_3	H	CH_3	*t*-BuOK	r.t.	2	74^a		0
f	CH_3	H	H	*t*-BuOK	r.t.	2	47^c		0
a	H	H	CH_3	*n*-BuLi	−78 ⟶ r.t.	1 + 16	81		0
d	CH_3	H	CH_3	*n*-BuLi	−78 ⟶ r.t.	1 + 17	87^a		0
f	CH_3	H	H	*n*-BuLi	−78 ⟶ r.t.	1 + 17	65^d		0

[a] *Z* and *E* isomers could not be resolved in their NMR spectra. [b] The ratio of *Z*/*E* is 29/71. [c] The ratio of *Z*/*E* is 34/66. 34% of **22f** was recovered. [d] The ratio of *Z*/*E* is 31/69. [e] r.t. = room temperature.

Table IX. Reaction of Diethyl 1-Hydroxy-2-halo Phosphonates (22) with Tri-*n*-butyltin Alkoxides or Amide

	22					products, yield, %	
	R^1	R^2	R^3	base	time, h	26	24
a	H	H	CH_3	*n*-Bu_3SnOMe	8	33	21
a	H	H	CH_3	*n*-Bu_3SnNEt_2	8	34	
a	H	H	CH_3	*n*-Bu_3SnO-*t*-Bu	6	73	
d	H	CH_3	CH_3	*n*-Bu_3SnOMe	8	47	32
d	H	CH_3	CH_3	*n*-Bu_3SnO-*t*-Bu	6	69	
f	CH_3	H	H	*n*-Bu_3SnOMe	8	37	
f	CH_3	H	H	*n*-Bu_3SnO-*t*-Bu	6	50	

and phosphoryl center for determination of the reaction mode and for distinguishing the Perkow and Arbuzov reactions from the 1:1 carbonyl addition reaction. We could find the clear borderlines for discrimination of the above three reactions and all experimental data are available for the explanation of the reactions between α-halo carbonyl compounds and phosphites.

Experimental Section

General Procedures. NMR spectra were measured at 60 MHz on a Hitachi R24-B spectrophotometer with tetramethylsilane as an internal standard unless otherwise specified. Infrared spectra were recorded on a Hitachi Model EPI-G3 spectrophotometer. All melting points were recorded on a Thomas-Hoover capillary melting-point apparatus and are uncorrected.

Tetrahydrofuran (THF) was purified as follows. Commercial THF was distilled over sodium wire after reflux for 6 h, redistilled over sodium hydroxide after reflux for 6 h, and finally purified by distillation from sodium benzophenone ketyl. Benzene was distilled and stored over sodium wire. Methanol was treated with magnesium under reflux, distilled, and stored over molecular sieves. Trimethylsilyl chloride, purchased from Japan Silicon Co., was purified by distillation from calcium hydride.

Tris(trimethylsilyl) Phosphite. A. Commercially available phosphorous acid (40 g, 0.463 mol) with a purity of 95% was rendered anhydrous by being dissolved in tetrahydrofuran (200 mL) followed by repeated coevaporation with dry benzene (3 × 200 mL) and the dry acid was dissolved in a mixture of dry THF (400 mL) and dry ether (1.6 L). To the solution was added trimethylsilyl chloride (166 g, 1.528 mol), and then triethylamine (155 g, 1.528 mol) was added dropwise at room temperature over a period of 1 h. The mixture was kept under reflux for 6 h and cooled to room temperature. The precipitate of triethylamine hydrochloride was filtered off and washed with dry ether (200 mL). The filtrate and washings were concentrated by a rotary evaporator and the residue was distilled under reduced pressure to give 1 [131 g, purity of 86 wt %, 90–92 °C (20 mmHg)] contaminated with 2. The crude product was heated with sodium (3 g, 0.130 mol) at 140–150 °C for 18 h and distillation of the mixture gave pure 1 (118 g, 82%): bp 90–92 °C (20 mm); NMR (C_6H_6) δ 0.20 (s, 27 H, $SiCH_3$). Anal. Calcd for $C_9H_{27}O_3PSi_3$: C, 36.21; H, 9.12. Found C, 36.01; H, 9.04.

B. A mixture of 2 (56.59 g, 0.25 mol) and diethyl(trimethylsilyl)amine (39.97 g, 0.275 mol) was placed in a flask equipped with a Dimroth condenser, on the top of which a distillation apparatus was attached. All outlets were excluded from moisture by an argon balloon and P_4O_{10}. The mixture was refluxed at a bath temperature of 125 °C. After the mixture was heated for 7 h, distillation gave diethylamine (16.76 g, 92%, bp 52–53 °C) and the silylamine (4.25 g, bp 40–48 °C (18 mm)). The NMR spectrum of the residue showed the presence of 1 and 2 in the ratio of 93:7. The residue was treated with sodium (3.25 g) at 140 °C for 13 h to give pure 1 (67.5 g, 91%), bp 83–84 °C (16 mm).

Bis(trimethylsilyl) Phosphonate (2). Phosphorous acid with a purity of 95% (40 g, 0.463 mol) was rendered anhydrous in the same manner as described before. The dry acid was dissolved in dry THF (300 mL) with vigorous stirring and trimethylsilyl chloride (101 g, 0.926 mol) in dry ether (1.5 L) was added to the solution. Triethylamine (94 g, 0.926 mmol) was then added dropwise at room temperature whereby the solution was gently refluxed. After the addition was complete, the mixture was refluxed for 2.5 h and then cooled to room temperature. The precipitate of triethylamine hydrochloride was filtered off and washed with dry ether (200 mL). The filtrate and washings were evaporated and the residual oil was distilled under reduced pressure to afford 2 (97 g, 93%): bp 77–79 °C (10 mm); NMR ($CDCl_3$) δ 0.17 (s, 18 H, $SiCH_3$), 6.75 (d, 1 H, J_{P-H} = 700 Hz, H-P). Anal. Calcd for $C_6H_{19}O_3PSi_2$: C, 31.84; H, 8.46. Found: C, 32.08; H, 8.50.

Disproportionation Reaction of 2 with Sodium. Sodium (1.93 g, 84 mmol) was added to 2 (15.85 g, 70 mmol). The mixture was heated at 140–150 °C for 20 h and then distilled under reduced pressure to afford a mixture (8.63 g) of 1 (22 mmol) and 2 (9.1 mmol).

Treatment of the Residue of the Disproportionation Reaction with Trimethylsilyl Chloride. To a mixture of 1 (4.72 g, 15.82 mmol) and 2 (9.17 g, 40.5 mmol) was added sodium (0.79 g, 34.4 mmol) and the mixture was heated at 140–150 °C for 23 h. The volatile phosphorus compounds were distilled under reduced pressure. The resulting white residue was treated with trimethylsilyl chloride (3.84 g, 35.4 mmol) in dry THF (20 mL) with vigorous stirring at room temperature for 3 h. After removal of the solvent in vacuo, distillation of the residue gave 2 (3.38 g, 87%), bp 46–56 °C (0.26 mm).

General Procedure for the Reaction of 1 with α-Halo Carbonyl Compounds. To a solution of an appropriate α-halo carbonyl compound (20 mmol) in dry THF was added 1 (21 mmol) at room temperature over a period of 15 min. After being stirred for 3 h, the mixture was distilled and the products were identified by their NMR spectra and elemental analyses. The results are summarized in Table I.

Diethyl Trimethylsilyl Phosphite (11, DTSP). Sodium (13.8 g, 0.6 mmol) was added to dry ether (250 mL) and diethyl phosphonate (69 g, 0.5 mol) was added dropwise to the ethereal solution at 10 °C whereby an exothermic reaction occurred. After evolution of hydrogen gas almost ceased, the mixture was heated under reflux for an additional 30 min. Trimethylsilyl chloride (65.2 g, 0.6 mol) was then added slowly at 10 °C over a period of 1 h. After the addition the mixture was stirred at room temperature for 1.5 h. The solvent was removed and the residual liquid was distilled under reduced pressure to afford **11** (95.7 g, 91%), bp 66 °C (15 mm) [lit.[33] bp 60–62 °C (11 mm)].

Typical Procedure for the Reaction of 11 with α-Chloro Carbonyl Compounds. To a solution of α-chloroacetone (**3a**) was added dropwise **11** (29.6 g, 0.14 mol) at room temperature. The mixture (11.5 g, 0.12 mol) was stirred at room temperature for 6 h. After removal of the solvent, distillation of the residual liquid gave **13a** (32.5 g, 86%): bp 103–110 °C (0.65 mm); NMR ($CDCl_3$) δ 0.1 (s, 9 H, $SiCH_3$), 1.15 (t, 6 H, $J = 6$ Hz, CH_2CH_3), 1.40 (d, 3 H, $J = 6$ Hz, PCH_3), 3.06 (d, 2 H, $PCCH_2$), 4.00 (m, 4 H, $J_{P-H} = 2$, $J_{H-H} = 6$ Hz, $POCH_2$). Anal. Calcd for $C_{10}H_{24}O_4ClPSi$: C, 39.67; H, 7.99. Found: C, 39.47; H, 7.70.

Diethyl 1-[(trimethylsilyl)oxy]-1-methyl-2-chloropropylphosphonate (13d): NMR (CCl_4) δ 0.17 (s, 9 H, $SiCH_3$), 1.27 (t, 6 H, $J_{H-H} = 6$ Hz, CH_2CH_3), 1.57 (d, 3 H, $J_{H-H} = 6$ Hz, $PCCCH_3$), 1.57 (d, 3 H, $J_{P-H} = 16$ Hz, $PCCH_3$), 4.00 (m, 5 H, OCH_2 and ClCH). Anal. Calcd for $C_{11}H_{26}O_4ClPSi$: C, 41.70; H, 8.27. Found: C, 40.96; H, 8.14.

Diethyl 1-[(trimethylsilyl)oxy]-2-chloropropylphosphonate (13f): NMR (CCl_4) δ 0.10 (s, 9 H, $SiCH_3$), 1.21 (t, 6 H, $J_{H-H} = 7$ Hz, CH_2CH_3), 1.46, 1.48 (d, 3 H, $J_{H-H} = 7$ Hz, $PCCCH_3$ of two diastereomers), 4.03 (m, 6 H, OCH_2, ClCH, and PCH). Anal. Calcd for $C_{10}H_{24}O_4ClPSi$: C, 39.67; H, 7.99. Found: C, 39.61; H, 8.03.

Reaction of 11 with α-Bromoacetone (3b). To a solution of **3b** (4.27 g, 31.1 mmol) in dry benzene (30 mL) was added **11** (7.19 g, 34.1 mmol) and the mixture was stirred at room temperature for 5 h. The solvent was then removed in vacuo and the residue was treated with trimethylsilyl bromide (9 mL, 62.2 mmol) at room temperature. After 2 h, the mixture was distilled to afford a mixture of **4a** (24%) and **5a** (65%) (7.0 g, 70–100 °C (1.25 mm)).

Ethyl Bis(trimethylsilyl) Phosphite (12). Concentrated ammonium hydroxide (50 mL) was added to diethyl phosphonate (30 mL, 0.24 mol) whereupon an exothermic took place. The mixture was set aside at room temperature for 1 h and then concentrated to dryness by rotary evaporator. The resulting white solid was rendered anhydrous by repeated coevaporation with dry benzene (100 mL) and then with dry pyridine (2 × 100 mL) and further treated with hexamethyldisilazane (70 mL, 0.33 mol) under reflux for 4 h. Distillation of the mixture afforded **12** (42.0 g, 71%): bp 79–82 °C (20 mm); ^{31}P NMR (C_6H_6) δ −117.8; ^1H NMR ($CDCl_3$) δ 0.17 (s, 18 H), 1.17 (t, 3 H, CH_3), 3.73 (m, 2 H, CH_2). Anal. Calcd for $C_8H_{23}O_3PSi_2$: C, 37.77; H, 9.11. Found: C, 38.14; H, 9.14.

Ethyl Trimethylsilyl 1-[(Trimethylsilyl)oxy]-1-methyl-2-chloroethylphosphonate (14a). To a solution of **3a** (2.53 g, 27 mmol) in dry benzene (20 mL) was added **12** (7.31 g, 29 mmol) at room temperature. After being stirred for 5 h, distillation of the mixture gave **14a** (7.10 g, 76%): bp 103–105 °C (1 mm); NMR (CCl_4) δ 0.02 (s, 9 H, $SiCH_3$), 0.27 (s, 9 H, $SiCH_3$), 1.27 (t, 3 H, $J_{H-H} = 3$ Hz, CH_2CH_3), 1.30 (d, 3 H, $J_{P-H} = 15$ Hz, $PCCH_3$), 3.63 (d, 2 H, $J_{P-H} = 5$ Hz, $ClCH_2$), 4.07 (m, 2 H, OCH_2). Anal. Calcd for $C_{11}H_{28}O_4ClPSi_2$: C, 38.08; H, 8.13. Found: C, 38.28; H, 7.82.

Bis(trimethylsilyl) 1-(Trimethylsiloxy)-1-methyl-2-bromoethylphosphonate (6b). To a solution of **3b** (7.16 g, 52 mmol) in dry benzene (50 mL) was added dropwise **12** (14.4 g, 57 mmol) at room temperature. The mixture was stirred at room temperature for 5 h. The solvent was then removed in vacuo and the residue was treated with trimethylsilyl bromide (7.5 mL, 52 mmol) at room temperature. After 2 h, the mixture was distilled to afford **6b** (1.52 g, 67%), bp 110–115.5 °C (0.4 mm).

Treatment of 6f with Lewis Acids. A mixture of **6f** (2.09 g, 5.34 mmol) and stannic chloride (0.128 g, 0.837 mmol) was heated at 110 °C. After 5.5 h the NMR spectrum of the mixture showed that **6f** still remained. The mixture was further heated at 250 °C whereupon thermal decomposition took place. The products were collected by using a distillation apparatus as the thermal decomposition proceeded. The NMR spectrum of the distillate showed the presence of a considerable amount of **3f**. Similar results were obtained by use of zinc chloride, aluminium chloride, and aluminum oxide.

Treatment of 6a with n-Butyllithium. To a solution of **6a** (2.50 g, 6.39 mmol) in dry THF (10 mL) was added dropwise 0.702 M *n*-butyllithium (13.5 mL, 19.23 mmol) in hexane over a period of 20 min at −78 °C. After the addition, it was warmed to room temperature and stirred for 1 h. To the solution was added trimethylsilyl chloride (2.08 g, 19.15 mmol) and the solvent was removed in vacuo. The residue was distilled to afford a 1:2 mixture of **6a** and bis(trimethylsilyl) 1-(trimethylsiloxy)-1-methyl-hexylphosphonate (**20a**) [(1.225 g, 98–116 °C (0.07–0.09 mm)]. The latter product was characterized by its typical NMR pattern of the *n*-pentyl group [δ 0.8–1.9 (m, 11 H)] and α-methyl protons [δ 1.27 (d, 3 H, $J_{P-H} = 18$ Hz)].

General Procedure for Reaction of 6 with Sodium Methoxide. A. To a solution of an appropriate 1:1 carbonyl adduct **6** (10 mmol) in dry THF (10 mL) was added sodium methoxide (30 mmol) in dry methanol (30 mL) dropwise at −78 °C or at room temperature over a period of 40 min. After the addition, the mixture was stirred for an additional 3–21 h at room temperature whereupon a white solid was precipitated. The solvents were then removed in vacuo and the residue was treated with trimethylsilyl chloride (3.58 g, 33 mmol) in dry THF (30 mL) at room temperature. After the mixture was stirred for 3–14 h, distillation gave the products. The reaction conditions and the products are listed in Table V.

B. To a solution of sodium methoxide (30 mmol) in dry methanol (30 mL) was added an appropriate 1:1 carbonyl adduct **6** (10 mmol) dropwise at room temperature over a period of 40 min. After the same workup as described in A, the products listed in Table V were obtained.

Reaction of 1 with α-Bromoethyl Trimethylsilyl Ketone (3o). α-Bromoethyl trimethylsilyl ketone **3o**[22] (1.94 g, 9.28 mmol) and **1** (3.24 g, 10.85 mmol) were mixed and the mixture was heated at 100 C. After 5 h, the resulting mixture was distilled to afford a mixture of 2.23 g (68%) of *Z* and *E* isomers of bis(trimethylsilyl) 1-[(trimethylsilyl)oxy]-2-methylvinylphosphonate (**9**) in the ratio of 85:15: bp 73–87 °C (0.19 mm); NMR ($CDCl_3$) for (*Z*)-**9** δ 0.13 (s, 9 H, $COSiCH_3$), 0.20 (s, 18 H, $POSiCH_3$), 1.52 (dd, 3 H, $J_{P-H} = 7$, $J_{H-H} = 3$ Hz, $C{=}CCH_3$), 5.67 (dq, 1 H, $J_{P-H} = 11$, $J_{H-H} = 7$ Hz, $C{=}CH$); NMR ($CDCl_3$) for (*E*)-**9** δ 0.13 (s, 9 H, $COSiCH_3$), 0.20 (s, 18 H, $POSiCH_3$), 1.85 (dd, $J_{P-H} = 7$, $J_{H-H} = 7$ Hz, $C{=}CCH_3$) (the vinyl proton could not be resolved; only part of the proton appears as a quartet having $J_{H-H} = 7$ Hz at 5.04 ppm and the other part is hidden behind the vinyl proton of the *Z* isomer); IR(NaCl) for *Z* and *E* isomers 1645 (C=C), 1255 (P=O), 1025, 850, 760 cm^{-1}. The configuration of the two isomers was determined based on the assignment of the vinyl proton of diethyl 1-[(trimethylsilyl)oxy]vinylphosphonate reported by Novikova.[21c]

Reaction of 6a with Sodium Methoxide in the Presence of Propionaldehyde. To a solution of sodium methoxide (prepared from 0.88 g (38.2 mmol) of sodium) in methanol (30 mL) was added a mixture of **6a** (5.0 g, 12.75 mmol) and propionaldehyde (0.740 g, 12.75 mmol) over a period of 7 min. After the mixture was stirred at room temperature for 5 h, the solvent was removed in vacuo and the residue was treated with trimethylsilyl chloride (4.57 g, 42.1 mmol) in dry THF (30 mL) with vigorous stirring for 15 h. The solvent was then removed in vacuo and the residual oil was distilled under reduced pressure to afford a fraction [91–94 °C (0.65–0.8 mm)] containing **4a** (30%) and **17a** (25%).

Reaction of 6a with Sodium Methoxide in the Presence of Diphenyl Disulfide. Diphenyl disulfide (2.78 g, 12.75 mmol) was dissolved in dry THF (10 mL). To the solution was added sodium methoxide (prepared from 0.88 g (38.2 mmol) of sodium) in methanol (40 mL). Then, **6a** (5.00 g, 12.75 mmol) was added dropwise at room temperature over a period of 30 min to the resulting solution. After the mixture was stirred at room temperature for 8 h, the solvent was removed in vacuo and the residue was treated with trimethylsilyl chloride (4.57 g, 42.1 mmol) at room temperature for 15 h. TLC (Avicel plate) of the reaction mixture showed no formation of bis(trimethylsilyl) *S*-phenyl phosphorothioate.

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[33] E. F. Bugerenko, E. A. Chernyshev, and E. M. Popov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1391 (1966); *Chem. Abstr.*, **66**, 76078 (1967).

Removal of Trimethylsilyl Group from 13. Typical Procedure. The adduct **13a** (11.0 g, 36 mmol) was treated with methanol (120 mL) and water (12 mL) in the presence of *p*-toluenesulfonic acid monohydrate (50 mg) at 60 °C. After the mixture was heated for 1.5 h, water (100 mL) was added and the mixture was extracted with methylene chloride (3 × 100 mL). The organic layers were dried over Na_2SO_4 and the solvent was removed in vacuo. The residue was chromatographed on silica gel (CCl_4–Et_2O) to afford **22a**[28a] (100%): mp 42–43 °C; NMR (CCl_4) δ 1.36 (t, 6 H, J_{H-H} = 6 Hz, CH_2CH_3), 1.40 (d, 3 H, J_{P-H} = 15 Hz, $PCCH_3$), 3.69 (m, 2 H, $ClCH_2$), 4.18 (m, 4 H, J_{H-H} = 7 Hz, CH_2CH_3), 5.13 (s, 1 H, OH).

Diethyl 1-hydroxy-1-methyl-2-chloropropylphosphonate (22d): NMR ($CDCl_3$) δ 1.33 (t, 6 H, J_{H-H} = 7 Hz, CH_2CH_3), 1.53 (d, 3 H, J_{P-H} = 21 Hz, $PCCH_3$), 1.63 (d, 3 H, J_{H-H} = 7 Hz, $PCCH_3$), 3.67 (d, 1 H, J_{P-H} = 8.4 Hz, OH), 4.20 (m, 4 H, CH_2CH_3), 4.27 (m, 1 H, ClCH).

Diethyl 1-hydroxy-2-chloropropylphosphonate (22f): NMR (CCl_4) δ 1.33 (t, 6 H, J_{H-H} = 7 Hz, CH_2CH_3), 1.53 (d, 3 H, J_{H-H} = 7 Hz, $PCCCH_3$), 3.82–4.50 (m, 8 H, CH_2CH_3, ClCH, and PCH), 5.22 and 5.63 (t, 1 H, J_{P-H} = J_{H-H} = 8.4 Hz, OH).

Typical Procedure for Reaction of Diethyl 1-Hydroxy-2-chloroalkylphosphonates (22) with Sodium Methoxide. To a solution of diethyl 1-hydroxy-1-methyl-2-chloroethylphosphonate (**22a**; 3.78 g, 16.4 mmol) was added dropwise in methanol (5 mL) sodium methoxide, prepared from sodium (0.4 g, 17.4 mmol) in methanol (10 mL), at room temperature and the mixture was stirred for 2 h. The reaction mixture was quenched with 1 M ammonium chloride (20 mL) and extracted with methylene chloride (3 × 20 mL). After the mixture was dried over Na_2SO_4, the solvent was removed in vacuo and the residue was chromatographed on silica gel (hexane–ether) to afford a mixture (2.16 g) of **23a**[34] (54%) and **24** (16%). **23a**: NMR (CCl_4) δ 1.40 (t, 6 H, J_{H-H} = 6 Hz, CH_2CH_3), 1.43 (d, 3 H, J_{P-H} = 10 Hz, $PCCH_3$), 2.58 (t, 1 H, J_{H-H} = 5, J_{P-H} = 5 Hz, OCH), 3.00 (t, 1 H, J_{H-H} = J_{P-H} = 5 Hz, OCH), 4.12 (m, 4 H, J_{H-H} = 7 Hz, CH_2CH_3); IR (NaCl) 1260 (P=O), 1217 cm^{-1}.

Diethyl 1-methyl-1,2-epoxypropylphosphonate (23d):[35] NMR (CCl_4) δ 1.33 (m, 12 H, CH_2CH_3, $PCCH_3$, and $PCCCH_3$), 3.20 (q, 1 H, J_{H-H} = 6.3 Hz, OCH), 4.06 (m, 4 H, CH_2CH_3).

Diethyl 1,2-epoxypropylphosphonate (23f):[35] NMR (CCl_4) for *E* isomer δ 1.33 (t, 6 H, CH_2CH_3), 1.47 (d, 3 H, $OCCH_3$), 2.57 (dd, 1 H, J_{P-H} = 30, J_{H-H} = 2 Hz, PCH), 3.17 (m, 1 H, OCH), 4.07 (m, 4 H, CH_2CH_3); NMR (CCl_4) for *Z* isomer 1.33 (t, 6 H, CH_2CH_3), 1.50 (d, 3 H, J_{H-H} = 2.6 Hz, $OCCH_3$), 2.68 (dd, 1 H, J_{P-H} = 26, J_{H-H} = 4.8 Hz, PCH), 3.15 (m, 1 H, OCH), 4.10 (m, 4 H, CH_2CH_3).

Typical Procedure for Reaction of Diethyl 1-Hydroxy-2-chloroalkylphosphonate (22) with Potassium *tert*-Butoxide. To a solution of **22a** (2.429 g, 10 mmol) in dry *tert*-butyl alcohol (20 mL) was added potassium *tert*-butoxide (1.32 g, 12 mmol) at room temperature and the mixture was stirred for 2 h. After being quenched with 1 M ammonium chloride, the mixture was extracted with methylene chloride (3 × 20 mL), dried over Na_2SO_4, and evaporated to dryness. The residue was chromatographed on silica gel (hexane–ether) to afford **23a** (1.69 g, 61%) and **26a**[9a] (0.081 g, 4%). **26a**: NMR (CCl_4) δ 1.33 (t, 6 H, J_{H-H} = 7 Hz, CH_2CH_3), 1.90 (s, 3 H, $C{=}CCH_3$), 4.06 (m, 4 H, CH_2CH_3), 4.34 (m, 1 H, *trans*-vinyl H to P), 4.63 (m, 1 H, *cis*-vinyl H to P).

General Procedure for Reaction of Diethyl 1-Hydroxy-2-chloroalkylphosphonate (22) with *n*-Butyllithium. To a solution of **22a** (1.724 g, 7.48 mmol) in dry ether (15 mL) was added dropwise 0.525 M *n*-butyllithium in hexane (4.0 mL, 7.62 mmol) at −30 °C. The reaction mixture was stirred at −30 °C for 1 h and then at room temperature for 16 h. After being quenched with 1 M ammonium chloride (20 mL) the mixture was extracted with methylene chloride (3 × 20 mL). The extracts were collected and dried over sodium sulfate. After removal of the solvent in vacuo, the residue was chromatographed on silica gel (*n*-hexane–ether) to afford **23a** (1.18 g, 81%).

Typical Procedure for Reaction of Diethyl 1-Hydroxy-2-chloroalkylphosphonate (22) with *n*-Butyltin Methoxide. To a solution of **22a** (2.35 g, 10 mmol) in dry toluene (20 mL) was added tri-*n*-butyltin methoxide (3.92 g, 12 mmol). The mixture was heated under reflux for 8 h. After removal of the solvent, the mixture was treated with 1 M ammonium chloride, extracted with methylene chloride (3 × 20 mL), and dried over Na_2SO_4. The solvent was removed in vacuo and the residue was chromatographed as described before to afford a mixture (0.98 g) of **26a** (33%) and **24** (21%).

Diethyl 1,2-dimethylvinylphosphonate (26d):[36] NMR (CCl_4) δ 1.30 (t, 6 H, J_{H-H} = 6 Hz, CH_2CH_3), 1.57 (d, 3 H, $CH_3C{=}C$), 1.83 (s, 3 H, CH_3COP), 4.33 (m, 4 H, CH_2CH_3), 5.17 (m, 1 H, $C{=}CH$).

Diethyl 2-methylvinylphosphate (26f):[14b] NMR (CCl_4) δ 1.30 (t, 6 H, J_{H-H} = 6 Hz, CH_2CH_3), 1.53 (d, 3 H, J_{H-H} = 10 Hz, $CH_3C{=}C$), 4.03 (m, 4 H, CH_2CH_3), 5.33 (m, 1 H, $HCCH_3$), 6.30 (m, 1 H, POCH).

Typical Procedure for Reaction of 22 with Tri-*n*-butyltin *tert*-Butoxide. To a solution of **22a** (0.614 g, 2.6 mmol) in dry toluene (5 mL) was added tri-*n*-butyltin *tert*-butoxide (1.076 g, 3.0 mmol). The mixture was heated under reflux for 6 h. After the mixture cooled to room temperature, the solvent was removed in vacuo and the residue was treated with 1 M ammonium chloride (20 mL), extracted with methylene chloride (3 × 20 mL), and dried over Na_2SO_4. After removal of the solvent, the residue was chromatographed (hexane–ether) to afford **26a** (0.378 g, 73%).

Reaction of 22a with (Tri-*n*-butylstannyl)diethylamine. To a solution of **22a** (2.381 g, 10 mmol) in dry toluene (20 mL) was added (tri-*n*-butylstannyl)diethylamine (4.49 g, 12.4 mmol). The mixture was heated under reflux for 8 h. After removal of the solvent, the residue was treated with 1 M ammonium chloride (20 mL), extracted with methylene chloride (3 × 20 mL), and dried over sodium sulfate. The solvent was removal in vacuo and the residual oil was chromatographed (hexane–ether) to afford **26a** (0.66 g, 34%).

Typical Procedure for Synthesis of Monoanilinium Salts of 1-Hydroxy-2-haloalkylphosphonates (28). To a solution of aniline (1.25 mL, 13.7 mmol) and ethanol (1.2 mL, 20.6 mmol) in dry THF (10 mL) was added dropwise **3f** (2.4 g, 6.14 mmol) in dry THF (5 mL) at 0 °C over a 10-min period. After the mixture was stirred at room temperature overnight, a precipitate was collected by filtration, washed with dry THF (5 mL), and dried over P_4O_{10} to afford **28f** (1.44 g, 87%), mp 126–127 °C. Anal. Calcd for $C_9H_{15}ClNO_4P$: C, 40.38; H, 5.64; N, 5.11. Found: C, 40.39; H, 5.65; N, 5.23.

Monoanilinium salt of 1-hydroxy-1-methyl-2-chloroethylphosphonic acid (28a): mp 156–157 °C. Anal. Calcd for $C_9H_{15}ClNO_4P$: C, 40.05; H, 5.48; N, 5.03. Found: C, 40.39; H, 5.65; N, 5.23.

Monoanilinium salt of 1-hydroxy-1-methyl-2-bromoethylphosphonic acid (28b): mp 141–143 °C. Anal. Calcd for $C_9H_{15}BrNO_4P$: C, 34.53; H, 4.78; N, 4.30. Found: C, 34.64; H, 4.84; N, 4.49.

Monoanilinium 1-Phenylvinylphosphate (29). To a mixture of ethanol (2.0 mL, 34.3 mmol) and aniline (0.754 g, 8.10 mmol) in dry THF (5 mL) was added dropwise at 0 °C **6h** (2.35 g, 6.82 mmol) in dry THF (5 mL) over a period of 15 min. A white precipitate immediately was separated and after stirring for 2.5 h it was collected by filtration, washed with dry THF (5 mL), and dried over P_4O_{10} to afford **29** (1.62 g, 84%), mp 179–180 °C. Anal. Calcd for $C_{14}H_{16}NO_4P$: C, 57.34; H, 5.50; N, 4.78. Found: C, 56.52; H, 5.62; N, 4.88.

Monoanilinium Salt of (Carboethoxy)methylphosphonate (30). To a mixture of ethanol (2.0 mL, 34.3 mmol) and aniline (0.891 g, 9.57 mmol) in dry ether (14 mL) was added dropwise **4k** (2.47 g, 7.91 mmol) in dry ether (6 mL) at 0 °C over a period of 5 min. After the mixture was stirred at room temperature for 1.5 h, the resulting white precipitate was collected by filtration, washed with dry ether (10 mL), and dried over P_4O_{10} to afford **30** (1.95 g, 94%), mp 136–137 °C. Anal. Calcd for $C_{10}H_{16}NO_5P$: C, 46.07; H, 6.20; N, 5.21. Found: 45.98; H, 6.18; N, 5.36.

Monoanilinium Salt of 2-Oxopropylphosphonate (31). To a mixture of methanol (1.0 mL, 24.8 mmol) and aniline (0.866 g, 9.29 mmol) in dry ether (25 mL) was added dropwise **4a** (2.15 g,

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7.61 mmol) at 0 °C over a period of 10 min. After the mixture was stirred at room temperature for 3.5 h, the resulting white precipitate was collected, washed with dry ether (20 mL), and dried over P_4O_{10} to afford **31** (1.48 g, 84%): mp 104–105 °C; IR (KBr) 1705 (C=O), 1495, 1250 cm^{-1}. Anal. Calcd for $C_9H_{14}O_4NP$: C, 46.76; H, 6.10; N, 6.06. Found: C, 46.70; H, 7; H, 6.06; N, 5.97.

Monoanilinium Salt of 1,2-Epoxy-1-methylethylphosphonate (32). To a mixture of methanol (0.503 g, 15.70 mmol) and aniline (0.736 g, 7.90 mmol) in dry ether (25 mL) was added dropwise with stirring at 0 °C a mixture of **17a** (1.34 g, 4.95 mmol) and **4a** (0.46 g, 1.65 mmol), obtained in the previous experiment, in dry ether (5 mL) over a period of 10 min. After the mixture was stirred at room temperature for 3 h, the resulting white precipitate was collected by filtration, washed with dry ether (10 mL), and dried over P_4O_{10} to afford crude product, which was further recrystallized from ethanol (21 mL) to afford an analytical sample of **32** (0.662 g, 58%): mp 126–127 °C; IR (KBr) 1459, 1220, 850, 745 cm^{-1}. Anal. Calcd for $C_9H_{14}O_4NP\cdot0.5H_2O$: C, 45.86; H, 6.21; N, 5.95. Found: C, 45.95; H, 6.04; N, 5.96.

Registry No. 1, 1795-31-9; **2**, 3663-52-3; **3a**, 78-95-5; **3b**, 598-31-2; **3c**, 23479-35-8; **3d**, 4091-39-8; **3e**, 10409-46-8; **3f**, 683-50-1; **3g**, 917-93-1; **3h**, 532-27-4; **3i**, 70-11-1; **3j**, 4209-02-3; **3k**, 105-39-5; **3l**, 105-36-2; **3m**, 65868-37-3; **3n**, 70-23-5; **3o**, 76600-03-8; **4a**, 68064-25-5; **4d**, 68064-26-6; **4f**, 76600-04-9; **4g**, 76600-05-0; **4i**, 65868-38-4; **4j**, 65868-39-5; **4k**, 65868-40-8; **5a**, 57222-19-2; **5h**, 57222-17-0; **5j**, 65868-41-9; **5m**, 65868-42-0; **6a**, 65868-43-1; **6b**, 65868-44-2; **6c**, 65868-45-3; **6d**, 65868-46-4; **6e**, 65868-47-5; **6f**, 65868-48-6; **6g**, 65868-49-7; **6m**, 65868-50-0; **6n**, 66119-35-5; (*E*)-**9**, 76600-06-1; (*Z*)-**9**, 76600-07-2; **11**, 13716-45-5; **12**, 39059-59-1; **13a**, 76600-08-3; **13d**, 76600-09-4; **13f**, 76600-10-7; **14a**, 76600-11-8; **17a**, 65868-51-1; **17g**, 76600-12-9; **20a**, 76613-01-9; **21d**, 76600-13-0; **21f**, 76600-14-1; **21g**, 76600-15-2; **22a**, 73519-29-6; **22d**, 76291-02-6; **22f** (isomer 1), 76600-16-3; **22f** (isomer 2), 76600-17-4; **23a**, 1445-84-7; **23d**, 17151-59-6; *cis*-**23f**, 25030-59-5; *trans*-**23f**, 66187-63-1; **24**, 867-17-4; **26a**, 5954-28-9; **26d**, 76600-18-5; **26f**, 34600-14-1; **28a**, 65868-53-3; **28b**, 65868-55-5; **28f**, 65868-57-7; **29**, 70334-78-0; **30**, 65868-58-8; **31**, 76600-19-6; **32**, 65868-60-2.

Aromatic Oxidation with Peroxydiphosphate Catalyzed by Metal Ions[1]

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Aqueous potassium peroxydiphosphate brings about aromatic ring hydroxylation of benzene and toluene in modest yields in the presence of suitable metal ion oxidants, notably cupric ion. The acidity function ($-H_0$) of the reaction solution for the optimum conditions is −1.5–0, i.e., 0.05–1 M H^+, on the basis of a plot of total product yield vs. $-H_0$. The selectivity of ring hydroxylation increases with decreasing acidity of the aqueous solution and with increasing concentration of Cu^{2+}. But the reverse is true for the total product yield under these conditions. Our observations are consistent with a scheme by which the radical $H_2PO_4\cdot$ oxidizes the aromatic to a radical cation, similar to the mechanism suggested for aromatic hydroxylation by sulfate radical $SO_4^{-}\cdot$.

The reactions of phosphate radicals ($H_2PO_4\cdot$, $HPO_4^{-}\cdot$, $PO_4^{2-}\cdot$) with organic compounds in an aqueous solution have been extensively studied, where the rate constants for the consumption of radicals were measured[2-7] and the radical species produced during these reactions were identified.[7-11] Furthermore, the oxidation powers of phosphate radicals were measured for hydrogen atom abstraction and compared with those of $SO_4^{-}\cdot$ and $HO\cdot$.[12] But no information is available on the products formed by the reactions of these phosphate radicals with organic compounds.

The aromatic hydroxylation using radicals derived from Fenton's reagent (Fe^{2+}–H_2O_2) and peroxydisulfate (Fe^{2+}–$S_2O_8^{2-}$) has been studied. The latter reaction proceeds probably by a mechanism involving an electron transfer from the aromatics to sulfate radical, i.e., to form the radical cation of the aromatics.[13,14]

Table I. Hydroxylation of Benzene with Peroxydiphosphate at 25 °C[a]

		% yield	
$[H^+]$, M	$-H_0$[b]	PhOH	PhPh[c]
8.18	2.16	4.0	
5.45	1.25	12.3	trace
3.48	0.78	18.7	3.9
1.82	0.26	18.5	24.8
1.00	−0.13	16.1	42.0
0.87	−0.17	19.1	36.9
0.46	−0.50	9.2	53.1
0.33	−0.81	10.3	45.4
0.087	−1.19	9.1	47.1
0.050	−1.43	3.0	28.4
0.020	−1.72	0.1	8.3
0.010	−2.04	-	5.0

[a] All runs were conducted by addition of 0.05 M Fe^{2+} to a two-phase system containing 1.06×10^{-2} M $H_2P_2O_8^{2-}$ and 0.5 M substrate at 25 ± 1 °C. Yields are based on $H_2P_2O_8^{2-}$ used. [b] Hammett acidity function.[d] [c] Based on $2C_6H_6 \longrightarrow C_{12}H_{10}$. [d] C. H. Rochester, "Acidity Functions", Academic Press, London, 1970.

On the other hand, the mechanism for the reactions of aromatic compounds with phosphate radicals is not definitive; i.e., Maruthamuthu et al. reported that there is no direct oxidative electron transfer from aromatic compounds to phosphate radicals in view of ESR studies[11] on one hand, but they reported that the substituent effect suggests an one-electron transfer from the aromatic ring to $H_2PO_4\cdot$ on the other.[6] Furthermore, no information about products in these reactions is obtained as stated above.

In the present paper, the reaction of aromatic compounds with phosphate radical derived by the reaction of

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