KINETICS AND MECHANISM OF THE REACTION OF TRIALKYL PHOSPHITES WITH α-DIKETONES

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Preface

The present dissertation is the record of a series of kinetic studies on the reaction of trialkyl phosphites with α-diketones which have been carried out at Nagoya University under the direction of Professor Yoshiro Ogata during 1969-1972.

The major purpose of this study is to clarify the mechanism of the reaction of trialkyl phosphites with α-diketones, and to throw light upon many other reaction mechanisms of trivalent phosphorus compounds with carbonyl compounds, which are in general very complicated and as yet there is no consistency in the mechanistic interpretations.

The author wishes to express his heartiest gratitude to Professor Yoshiro Ogata for his kind guidance and encouragement throughout the course of this work, and he is heartfeltly grateful to Professor Saburo Inokawa of Shizuoka University for his kind supply of phosphites and his constant interest and many valuable advices for this work.

The author is sincerely grateful to Professor Yasuji Izawa of Mie University, Drs. Atsushi Kawasaki, Yasuhiko Sawaki, and Katsuhiko Takagi for their numerous instructive suggestions and discussions, and also to all other members of Professor Ogata's laboratory and his seniors, juniors, and fellows for their advices and supports. He is also thankful to Professor D. B. Denney of Rutgers University for his kind sending a copy of Dr. A. D. Litt's thesis, to Japan Electron Optics Laboratory Co., Ltd. for its kind measurement of the ^{31}P nmr spectra, and to Nippon Oil and

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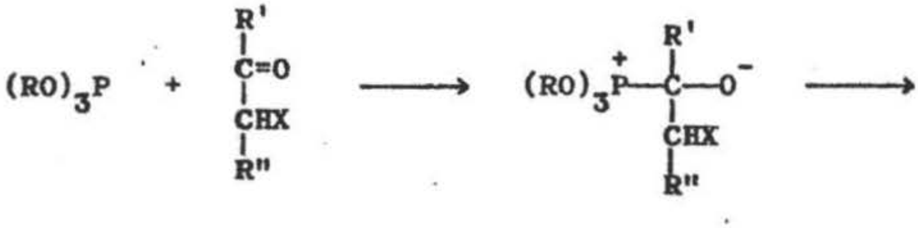
Chapter 1

INTRODUCTION

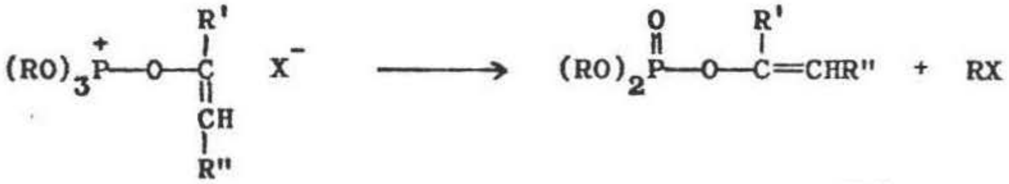
INTRODUCTION

The reaction of phosphorus compounds is often complicated because of their d-orbital and "softness", i.e., they sometimes react with nucleophilic trend, sometimes with electrophilic trend, and sometimes with radical trend.[1] The reaction of trivalent phosphorus compounds with some organic compounds which have X=Y bond (X is carbon or nitrogen atom and Y is oxygen or sulfur atom) is very interesting because of the variety of the mode of reaction of trivalent phosphorus compounds, i.e., carbophilicity, oxophilicity, thiophilicity, and halophilicity. The reaction mechanism of trivalent phosphorus compounds with carbonyl compounds cannot be explained straight forward from their products analysis, and it has more variety than that of nitrogen compounds with carbonyl compounds.[2]

For example, the reaction of phosphite with α-haloketones (Perkow reaction) produces enol phosphates, it has been considered to have four possible paths, i.e., attack of phosphorus atom on (i) α-carbon atom, (ii) halogen atom, (iii) carbonyl oxygen atom, and (iv) carbonyl carbon atom.[3] Many studies on the mechanism revealed that path iv is most probable one among these possible paths.[3,4]



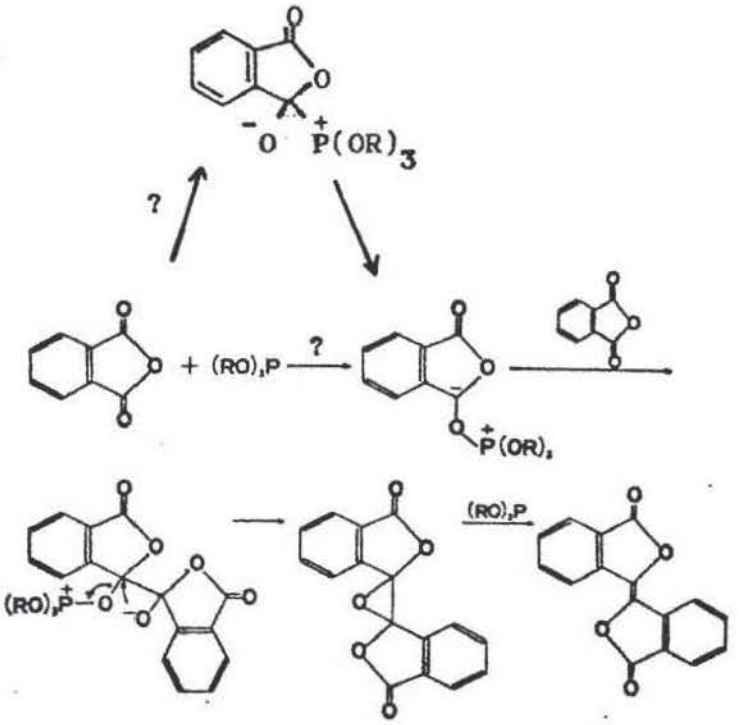
$$(RO)_3P + \begin{array}{c} R' \\ | \\ C{=}O \\ | \\ CHX \\ | \\ R'' \end{array} \longrightarrow (RO)_3\overset{+}{P}-\begin{array}{c} R' \\ | \\ C \\ | \\ CHX \\ | \\ R'' \end{array}-O^- \longrightarrow$$



$$(RO)_3\overset{+}{P}-O-\underset{\underset{R''}{|}}{\overset{\overset{R'}{|}}{C}}{=}CH\ X^- \longrightarrow (RO)_2\overset{\overset{O}{\|}}{P}-O-\overset{\overset{R'}{|}}{C}{=}CHR'' + RX$$

(1)

The reaction of trialkyl phosphite with phthalic anhydride is known to give 3,3'-diphthalyl. This reaction may proceed via epoxide intermediate.[3] The first step may involve a nucleophilic attack of phosphorus atom either on a carbonyl carbon atom or an oxygen atom, this is as yet obscure.

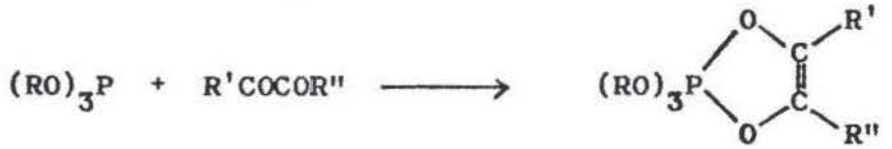


(2)

The reaction of nitro or nitroso compounds with phosphites was reported to proceed via a nucleophilic attack of phosphorus atom on oxygen atom, on the basis of kinetic study and the product analysis.[5]

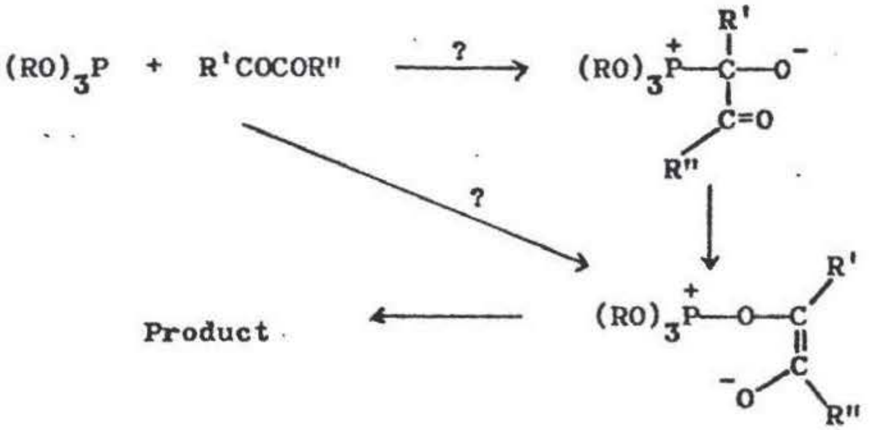
$$\mathrm{ArN{=}O} + \mathrm{P(OEt)_3} \longrightarrow \mathrm{Ar\overset{-}{N}O\overset{+}{P}(OEt)_3} \longrightarrow \mathrm{Ar\overset{-}{N}\!:} + \mathrm{O{=}P(OEt)_3} \qquad (3)$$

Kukhtin et al. reported the reaction of α-diketone with phosphite in 1958.[6] The studies on the reaction of chloranil with trivalent phosphorus compounds was done by Ramirez et al. They proceeded with their studies onto the reaction of α-diketones with trivalent phosphorus compound.[7] The unique reaction was extensively researched by them and an extensive amount of literature concerning the reaction of trialkyl phosphite with α-diketone has been reported in the last decade.[8] The structure of the product was confirmed by the chemical and physical methods, e.g., hydrolysis, ^{31}P nmr, ^{1}H nmr, ir, and X-ray analysis, to be a 1:1 adduct having a pentacovalent phosphorus atom.[9]



(4)

The reaction has been thought to involve an attack of phosphorus atom either on a carbonyl carbon atom or an oxygen atom,[1,10] however, few studies on the reaction mechanism has been reported.[11]



(5)

The author wished to clarify the reaction mechanism, and he began to study it kinetically. First, he studied by the ordinary kinetic procedure, then gradually he proceeded with his studies to get the more direct evidence of the mechanism proposed by him.

Chapter 2 describes the general kinetic studies on the reaction of trialkyl phosphites with benzil, where the effects of temperature, solvents, acid, and base will be shown. The successive two chapters (Chapters 3 and 4) deal with the substituent effects in benzil and phosphite, respectively. Chapter 5 shows the kinetic results of the reaction of trimethyl phosphite with aliphatic α-diketones, which are correlated with Taft's equation. The next chapter (Chapter 6) will reveal the strain effect and twist angle effect in cyclic α-diketones. Appendixes A and B deal with the kinetic studies on the autoxidation of trivalent phosphorus compounds.

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Chapter 2

KINETICS OF THE REACTION OF TRIALKYL PHOSPHITES WITH BENZIL

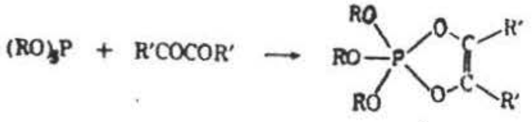
2 KINETICS OF THE REACTION OF TRIALKYL PHOSPHITES WITH BENZIL[1]

2.1 Summary

The reaction of trialkyl phosphites with benzil to form a cyclic adduct (**1**) has been studied kinetically in anhydrous dioxane and benzene. The rate is expressed as $v = k[(RO)_3P][PhCOCOPh]$. An Arrhenius plot gives the values of 9.90 kcal mol^{-1} and -35.5 eu for the activation energy and entropy, respectively. The rate constant increases with increasing dielectric constant of solvent. In a benzene solution the rate constant increases with an increasing amount of added organic acid (e.g., acetic acid) and decreases with an increasing amount of added triethylamine. The plot of k vs. [acid] or [base] gives a straight line at low concentrations. The reactivity of trialkyl phosphites is affected by alkyl groups in the order of Me < sec-Bu < Et < i-Pr. A mechanism involving a nucleophilic attack of the phosphorus atom on the carbonyl carbon is postulated and discussed.

2.2 Introduction

The reaction of trialkyl phosphites with α-diketones such as biacetyl and benzil was first reported by Kukhtin, et al.[2] Ramirez, et al.,[3,4] have postulated a cyclic structure (**1**) for the 1:1 addition product (2,2,2-trialkoxy-1,3,2-dioxaphosphole) of trialkyl phosphite with an α-diketone, which was found to be an effective insecticide.[5]



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(1)

However, no report is available on the mechanism of this reaction. This chapter deals with a kinetic study of the reaction of trialkyl phosphite with benzil (R' = phenyl). The rate was measured spectrophotometrically to clarify the effects of acid, base, and solvent and also structural effects on the rate. The mechanism for the reaction will be discussed on the basis of these findings.

2.3 Results

Rate Law. The reaction of trialkyl phosphite with benzil (neat) is irreversible and proceeds almost to completion within 15 min. The reaction rate in dioxane and benzene was measured by means of ultraviolet spectrophotometry of produced 2,2,2-trialkoxy-4,5-diphenyl-1,3,2-dioxaphosphole (**1**, R' = Ph). The ultraviolet spectra of **1** is shown in Figure 1. The structure was confirmed by ir and nmr spectra[3b,d,6] as described in the Experimental Section.

The rate of reaction 1 was measured in dioxane; the

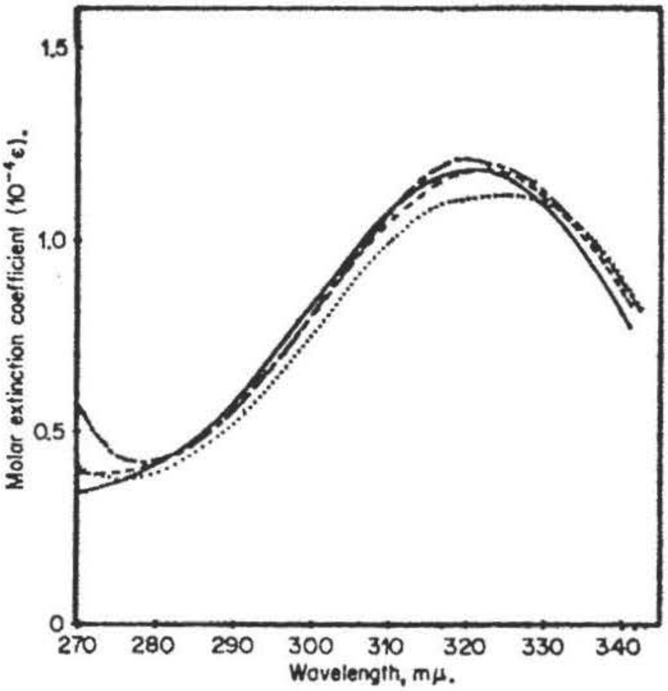


Figure 1. The ultraviolet spectra of **1** from $(RO)_3P$ and PhCOCOPh in n-hexane: ——, R = Me; ---, R = Et; ···, R = i-Pr; –·–, R = sec-Bu.

kinetic data obtained are listed in Table I. The rate law is expressed as eq 2. The k value is fairly constant up to 70-80% conversion.

$$v = k[\text{trialkyl phosphite}][\text{benzil}] \qquad (2)$$

Temperature Effect. The rate was measured in dioxane at various temperatures. The second-order rate constants (10^3 k, $M^{-1}sec^{-1}$) were 2.95 at 15.0°, 3.76 at 20.0°, 4.83 at 25.0°, and 6.64 at 30.0°. The plot of log k vs. 1/T afforded a good straight line, which gave the values of 9.90 kcal mol^{-1} and -35.5 eu at 25.0° by least square calculation for the energy and entropy of activation, respectively.

Solvent Effect. The rate was measured at 25.0° in various solvents, and is shown in Table II. In acetone and cyclohexanone, the rate constant is small in spite of relatively high dielectric constant. In the other solvents, the rate constant increases with increasing dielectric constant, but in protic solvents, such as methanol, it is abnormally large.

Effect of Added Acid. When organic acids are added in a benzene solution of the reaction mixture at 25.0°, the rate constant increases as shown in Table III. The plot of k vs. [acetic acid] afforded a good straight line with a slope of +0.306 at low acetic acid concentration ($0-5.80 \times 10^{-3}$ M) as expressed in eq 3. Hammett's acidity

$$k = 6.83 \times 10^{-3} + 0.306[\text{AcOH}] \qquad (3)$$

function (H_0) cannot be measured because of the low acidity of this system. An increase of the acidity of acetic acid by the substitution of chlorine atoms results in an increase of rate constant (Table III).

Table I. Typical Second-Order Rate Constants for the Reaction of Trimethyl Phosphite with Benzil in Dioxane at 25.0°

PhCOCOPh, (M)	$(MeO)_3P$, (M)	10^3k, ($M^{-1}sec^{-1}$)
0.0250	0.0250	4.70
0.0500	0.0500	4.83
0.100	0.100	4.85

__Effect__ __of__ __Added__ __Base__. The addition of some tertiary amines to a benzene solution of the reaction mixture results in a decrease of the rate constant as shown in Table IV. The plot of k vs. [triethylamine] afforded a straight line with a slope of -1.16 at low concentration of triethylamine, and fits eq 4, whereas the addition of dimethylaniline has virtually no effect on k.

$$k = 6.83 \times 10^{-3} - 1.16[Et_3N] \qquad (4)$$

__Effect__ __of__ __Substituents__. The effect of changing alkyl group of trialkyl phosphite was studied for the reaction with benzil in dioxane, and is shown in Table V. In general, the rate increases in the order of Me < sec-Bu < Et < i-Pr, which corresponds to an increase of nucleophilicity of phosphites. But steric effect is also operating with bulky alkyl phosphite, e.g., tri-sec-butyl

Table II. Solvent Effect on the Reaction of Trimethyl Phosphite with Benzil at 25.0° (Initial Concentration [$(MeO)_3P$] = [PhCOCOPh] = 0.0500 M)

Solvent	Dielectric constant	10^3k, ($M^{-1}sec^{-1}$)
n-Hexane [a]	1.89	4.90
Dioxane	2.21	4.83
Benzene	2.28	6.83
Anisole	4.33	6.48
Chlorobenzene	4.65	7.67
Cyclohexanone	18.3	7.22
Acetone	20.7	3.27
Methanol [b]	32.6	158
Acetonitrile	37.5	13.4

[a] Initial concentration [$(MeO)_3P$] = [PhCOCOPh] = 0.0400 M.

[b] Initial concentration [$(MeO)_3P$] = [PhCOCOPh] = 0.00250 M.

Table III. Effect of Organic Acid on the Reaction of Trimethyl Phosphite with Benzil in Benzene at 25.0° (Initial Concentration [$(MeO)_3P$] = [PhCOCOPh] = 0.0500 M)

Acid (pK_a)	Acid concentration, (10^{-3} M)	10^3 k, ($M^{-1}sec^{-1}$)
CH_3COOH (4.76)	0	6.83
	1.45	7.22
	2.90	7.59
	4.35	8.16
	5.80	8.59
	14.5	9.57
	29.0	9.88
	54.0	12.7
$CH_2ClCOOH$ (2.87)	0.255	6.94
	0.510	7.88
	1.02	9.91
CCl_3COOH (0.635)	0.207	6.84
	0.414	7.85

Table IV. Effect of Base on the Reaction of Trimethyl Phosphite with Benzil in Benzene at 25.0° (Initial Concentration [$(MeO)_3P$] = [PhCOCOPh] = 0.0500 M)

Base (pK_a)	Base concentration, (10^{-3} M)	10^3 k, ($M^{-1}sec^{-1}$)
Et_3N (10.9)	0	6.83
	0.597	5.77
	1.19	5.35
	1.79	4.89
	2.39	4.08
	11.9	2.16
	23.9	1.52
$PhNMe_2$ (4.64)	1.32	6.90
	2.64	6.81
	26.4	6.84

Table V. Substituent Effect on the Reaction of Trialkyl Phosphite with Benzil in Dioxane at 25.0°

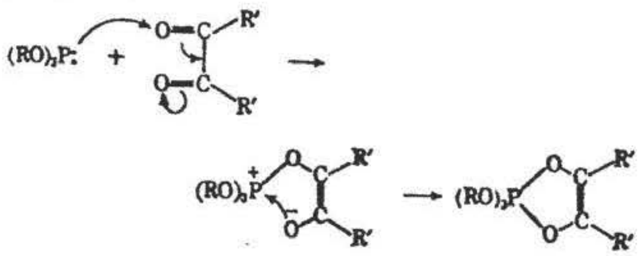
R of $(RO)_3P$	10^3 k, ($M^{-1}sec^{-1}$)
Me	4.83
Et	11.3
i-Pr	18.5
sec-Bu	9.19

phosphite, its rate constant being smaller than expected.

2.4 Discussion

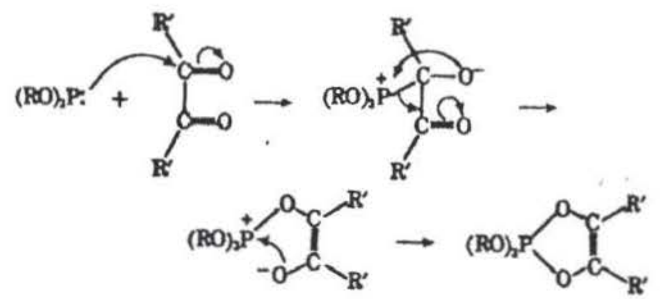
A mechanism postulated by Ramirez, et al., involes a nucleophilic attack of phosphorus atom on carbonyl oxygen[7,8] followed by cyclization of the formed zwitterion as shown in mechanism A.

Mechanism A



Another mechanism involves a nucleophilic attack of phosphorus atom on carbonyl carbon[2a,9] followed by rearrangement[10] and then cyclization as formulated in mechanism B.

Mechanism B



In view of rate eq 2, each molecule of trialkyl phosphite and benzil should participate in the rate-determining step. The value of 9.90 kcal mol^{-1} for activation energy and the value of -35.5 eu for activation entropy are usual for the addition reaction of carbonyl compounds.[11] The low value of activation energy shows that in the rate-determining step no large energy is needed and hence it involves probably no C-P bond fission.[12] The large negative entropy of activation reflects a high degree of orientation and/or a rigid structure in the transition state, and this negative value is consistent with a reaction of neutral molecules via polarized transition states to yield ions.[13] Diels-Alder reactions in general exhibit entropies of activation not more than -30 eu;[14] hence the Diels-Alder-type mechanism is unlikely for this reaction.

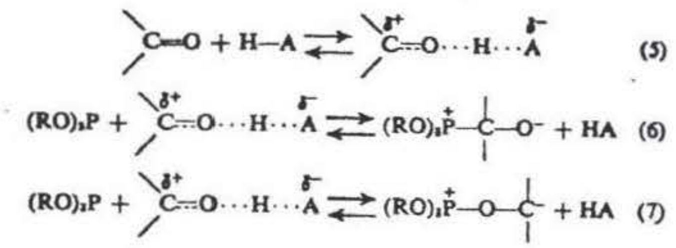
The solvent effect shows that the rate constant increases with increasing dielectric constant except in some solvents (Table II). As the solvent is changed from n-hexane (ε 1.89) to acetonitrile (ε 37.5) the rate increases by a factor of 2.8. The reaction via a charge-separated complex should be facilitated by an increase of the solvent polarity[15] (e.g., the quaternization of pyridine with ethyl iodide shows a solvent dependence in a factor of ca. 10^3).[16] The poor dependence of this rate on the solvent polarity may be explaind as follows: 2p-3d π bonding of oxygen and phosphorus atoms[17] may lead to some dispersal of the positive charge on a phosphorus atom, and the transition state is most likely in the form of an intimate ion pair in which there is a minimal separation of charge.[18] The small rate constant observed in the reaction in acetone or cyclohexane may be explained by the solvation effect involving a polarizable carbonyl group which retards the reaction. A marked increase of rate in protic solvents such as methanol is probably due to its action as an acid having $pK_a = 16.7$. The catalysis of methanol for the reaction of α-halo ketones with trivalent phosphorus compounds is known.[19]

No appropriate data are available on the basicity of trialkyl phosphites. Taft's σ^* value[20] predicts that the nucleophilicity of phosphite seems to be in the order of $(MeO)_3P < (EtO)_3P < (i\text{-}PrO)_3P < (sec\text{-}BuO)_3P$. This ρ^*-σ^* correlation is successful for pK_a of aliphatic phosphine,[21] and with aromatic phosphonic[22] and phosphinic acids,[23] the correlation between pK_a of acids and Hammett's σ parameter is very good. The observed reactivity order of the present reaction, i.e., $(MeO)_3P < (EtO)_3P < (i\text{-}PrO)_3P$, is in agreement with the nucleophilicity of phosphite. Thus it is probable that the reaction involves a nucleophilic attack of phosphorus atom on carbonyl group in the rate-determining step.[18] The k value for (sec-BuO)$_3$P is smaller than expected.

Mark, et al., have explained the reactivity of (t-BuO)$_3$P by the inductive and steric effects of alkyl groups.[24] When Taft's equation is applied to this reaction, the k value for (i-PrO)$_3$P is also somewhat smaller than calculated. These facts imply that the steric hindrance is operating with (i-PrO)$_3$P and (sec-BuO)$_3$P.

Acids catalyze this reaction. At low concentration of added acetic acid, the plot of k vs. [acetic acid] gives a straight line, while at higher concentration of added acetic acid (above 0.0145 M) it approaches a limiting value, and at the same time the rate law begins to deviate from the second-order plot. As reported by Ramirez,[25] the deviation may be due to the acid-catalyzed hydrolysis followed by further reactions of the 1:1 adduct (see Experimental Section).

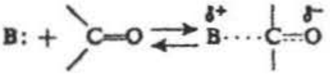
Acetic acid at such a low concentration in benzene solution cannot change the color of an indicator,[26] but ultraviolet spectra afforded evidence for the presence of hydrogen bonding to benzil (see Experimental Section). Because of the first-order dependence on [AcOH], benzil may be hydrogen bonded with one molecule of acetic acid, which activates the carbonyl group for the nucleophilic attack of trialkyl phosphite as follows.



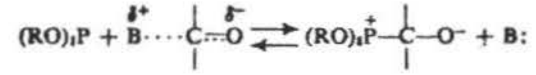
Since the nucleophilic attack of phosphorus atom on carbonyl carbon in the reaction of α-halo ketone with trialkyl phosphite is catalyzed by acetic acid,[19a,27] eq 7 is less probable. Chloroacetic and trichloroacetic acids are more effective catalysts in this reaction, because they are more acidic and thus more effective in forming a hydrogen bond to the carbonyl group.

On the other hand, bases retard the reaction; at lower concentrations of added triethylamine (below 0.0119 M), the plot of k vs. [Et_3N] gives a straight line, whereas at higher concentrations (above 0.0119 M) of triethylamine the plot approaches a horizontal line. The second-order rate law is not applicable at this high concentration of triethylamine, and in this case, the base-catalyzed hydrolysis of the product[25] occurs, the hydrolysis products acting as acid.

The fact that dimethylaniline has virtually no effect on k suggests that a fairly strong base is required to retard the reaction in this system. Therefore, the retarding effect of base cannot be explained as its neutralization of mineral acid which might be present in this system. This fact together with the first-order dependence of rate on 1/[Et_3N] suggests that the retardation may be due to the addition of the base to the carbonyl carbon atom to weaken its electrophilicity.



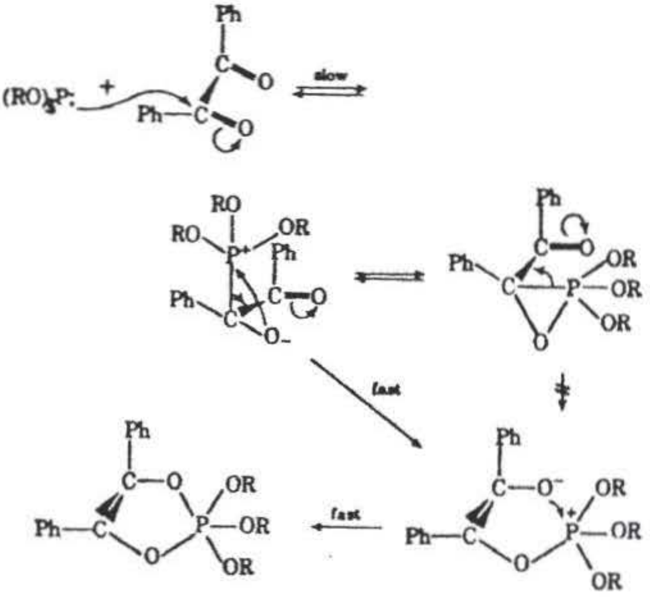
$$B: + \gt C=O \rightleftharpoons \overset{\delta+}{B}\cdots C \overset{\delta-}{=\!\!=} O \qquad (8)$$



$$(RO)_3P + \overset{\delta+}{B}\cdots C \overset{\delta-}{=\!\!=} O \rightleftharpoons (RO)_3\overset{+}{P}-C-O^- + B: \qquad (9)$$

This behavior is in contrast to the analogous Diels-Alder reaction, where both trimethylamine and trichloroacetic acid have the accelerating effect;[28] the following mechanism may operate in the present reaction, which involves a nucleophilic attack of a phosphorus atom of trialkyl phosphite on the carbonyl carbon atom of benzil (mechanism B).

The reaction of α-halo ketone with trialkyl phosphite may involve the rearrangement of phosphorus atom from carbonyl carbon to oxygen via either a concerted or a three-membered cyclic mechanism.[27] The present reaction may proceed via a concerted three-center rearrangement of the phosphorus atom initiated by nucleophilic attack of the negatively charged oxygen atom[10,29] because of the higher energy barrier for the complete fission of the C-P bond.[12,30] In analogy to the addition of nucleophile to carbonyl which is generally a reversible process,[31] the first step of the phosphorus-carbonyl addition is probably reversible.[31b, 32] The reversibility of the first step is uncertain in view of the rate law alone, but the low energy of activation implies the step to be reversible.[33] Hence, the overall mechanism is shown as follows.



2.5 Experimental Section

Materials. Benzil was prepared from benzaldehyde,[34] and recrystallized several times from CCl_4. Trialkyl phosphites were synthesized by the reaction of PCl_3 with alcohols in the presence of base,[35] and rectified several times with metallic sodium under reduced nitrogen pressure. Solvents used were purified by ordinary methods.[36]

Reaction Product Criterion. The authentic samples of 2,2,2-trialkoxy-4,5-diphenyl-1,3,2-dioxaphosphole (1)[3,6,37] was prepared by the reaction of benzil with excess phosphite in the absence of solvent under nitrogen atmosphere. The products were very hygroscopic crystals. The yield were almost quantitative. 1 (R = Me) was recrystallized from anhydrous n-hexane, mp 49-50°. Infrared spectrum (Nujol) showed peaks at 3045, 2980, 2940, 2830, 2000-1700, 1665, 1595, 1490, 1450, 1315, 1273, 1173, 1135, 1097, 1039, 951, 847, 750, 690, and 650 cm^{-1}, which were characteristic of the monosubstituted benzene ring, C=C, and P-O-C. Nmr ($CDCl_3$, internal standerd TMS) showed peaks at τ2-3 (multiplet, 10H) and 6.31 (doublet, 12H, J_{HP} = 12.6 cps). 1 (R = Et) was recrystallized from anhydrous n-hexane, mp 45-46°. The infrared spectrum (Nujol) was analogous to that of 1 (R = Me). 1 (R = i-Pr and sec-Bu) was not isolated. The uv spectra of 1 (R = Me, Et, i-Pr, and sec-Bu) in n-hexane (Figure 1) were as follows [R, λ_{max}(nm), ε]: Me, 321, 11,800; Et, 323, 11,800; i-Pr, 325, 11,200; sec-Bu, 319, 12,100.

The products of 0.2 M trimethyl phosphite with 0.2 M benzil in benzene at 25° containing an equivalent amount of acetic acid were examined by tlc (silica gel; eluent, ethyl acetate-petroleum ether 1:1), ir, uv (n-hexane), and nmr ($CDCl_3$). Besides the 1:1 adduct, small amounts of hydrolysis product of the adduct[25] and unknown product (tlc, R_f 0.40) having P=O and C=O groups were observed.

Kinetics. The reaction was started by the rapid addition of a solution of trialkyl phosphite to an equimolar solution of benzil, both of which had reached the temperature equilibrium in a thermostat. The reaction was carried out as a homogeneous system with stirring in a glass-stoppered flask. No difference in rate was observed between reactions under nitrogen and air. Aliquots were taken out at appropriate intervals of time. The reaction was stopped by diluting it with n-hexane. Products were estimated by means of ultraviolet spectrophotometry at the wavelength stated above.

In the study of the effect of acid or base catalysis addition order of three components afforded no effect on the rate constant. Initial rate constants were considered at high catalyst concentrations. No reaction of trimethyl phosphite with acetic acid or triethylamine occurs under these conditions. Interaction between benzil and acid or base was studied by uv spectrum as a slight change of molar extinction coefficient (ε) at 259 and 265 nm in n-hexane. No appreciable shift of C=O absorption (1670 and 1650 cm^{-1}) was observed.

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Chapter 3

KINETICS OF THE REACTION OF TRIMETHYL PHOSPHITE WITH SUBSTITUTED BENZILS

3 KINETICS OF THE REACTION OF TRIMETHYL PHOSPHITE WITH SUBSTITUTED BENZILS[1]

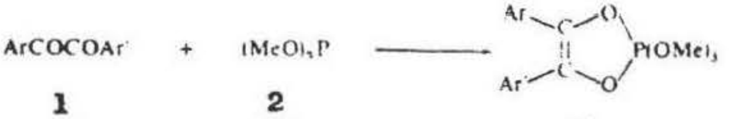
3.1 Summary

The substituent effect on the rate of the reaction of trimethyl phosphite with substituted benzils has been studied in dioxane or acetonitrile by means of uv spectrophotometry. The rates are expressed as $v = k[(MeO)_3P] \times [Ar\text{-}COCO\text{-}Ar']$. The Hammett plot in dioxane for Ar = Ar' gives a straight line with a ρ value of +2.75 (represented as ρ_X), while the plot for Ar $\neq$ Ar' and Ar = C_6H_5 gives a line bent at the origin, i.e., two ρ values of +1.86 ($\sigma > 0$, $\equiv \rho_Y$) and +1.24 ($\sigma < 0$, $\equiv \rho_Z$). In acetonitrile, the ρ_X and ρ_Y values are +2.22 ($\equiv \rho'_X$) and +1.63 ($\equiv \rho'_Y$), respectively. Hence $(\rho_X - \rho_Y)/\rho_Y = 0.48$, $\rho_Z/\rho_Y = 0.67$, and $(\rho'_X - \rho'_Y)/\rho'_Y = 0.36$. The ratio of effects of two substituents which are separated differently from the reaction site changes with the solvent polarity. This seems to be caused by the change of configuration of benzils by solvents. A mechanism which involves a nucleophilic attack of P atom on the carbonyl C atom of benzil is postulated.

3.2 Introduction

The reaction of trialkyl phosphite with α-diketone was first reported in 1958[2] and it was not decided until recentrly whether the initial attack of P atom occurs on carbonyl C or O atom of α-diketone.[2-4] In the preceding chapter, it was postulated, on the basis of substituent effect in phosphite and acid catalysis, a mechanism involving a nucleophilic attack of the P atom on the carbonyl C atom which is analogous to Litt's mechanism.[5,6]

The present chapter deals with the kinetic study on the reaction of trimethyl phosphite with substituted benzils. The rate was measured uv spectrophotometrically. The effect of substituent and solvent on the rate and the transmission of polar effect will be discussed in connection with the configuration of benzil.



1 **2** **3**

(1)

3.3 Results

The reaction of trimethyl phosphite (**2**) with substituted benzils (**1**) proceeds quantitatively at room temperature to yield 2,2,2-trimethoxy-4,5-diaryl-1,3,2-dioxaphosphole (**3**). The rate was measured by uv spectrophotometry of produced **3** or remaining benzil (**1**).

Rate Law. The rate of the reaction was measured in dioxane or acetonitrile at various temperatures. The rate law fits eq 2 with all substituted benzils used.

$$v = k[(MeO)_3P][Ar\text{-}COCO\text{-}Ar'] \qquad (2)$$

Substituent Effect of Symmetrically Disubstituted Benzils in Dioxane. The rates of the reaction of trimethyl phosphite with symmetrically disubstituted benzils (1a) were measured in dioxane at 25.0°. The second-order rate constants (k) were listed in Table I.

Table I. Rate Constants for the Reaction of Trimethyl Phosphite with Symmetrically Disubstituted Benzils in Dioxane at 25.0°

Benzil	Initial concn. (M)		10^3k (M^{-1} sec^{-1})	Relative rate (k/k_0)	log (k/k_0)	σ^a
	[1]	[2]				
Unsubstituted	0·0500	0·0500	4·83	1·00	0·000	0·000
p,p'-Dinitro-	0·00100	0·00200	432	89·4	1·951	0·778
m,m'-Dinitro-	0·00500	0·00500	297	62·0	1·792	0·710
p,p'-Dichloro-	0·0200	0·0200	19·0	3·94	0·595	0·227
p,p'-Dimethyl-	0·0500	0·100	1·68	0·349	−0·458	−0·170
p,p'-Dimethoxy-	0·0200	1·00	0·387	0·0801	−1·096	−0·268

[a] H. H. Jaffé, *Chem. Rev.* 53, 191 (1953)

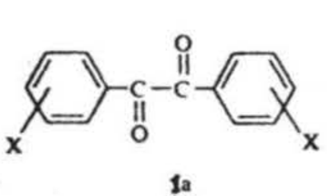
The Hammett plot with σ gives a ρ value of +2.75 ($\equiv \rho_X$) with a correlation coefficient (r) of 0.996 (Figure 1), whereas the plot with σ^+ and σ^- the correlation coefficient is smaller (r = 0.989, and 0.960, respectively).[7]

The rate measurements at 20.0°, 25.0°, and 30.0° afford data of energies of activation (E_a), entropies of activation ($\Delta S^{\ddagger}$) and frequency factors (A) as shown in Table II.

Table II. Temperature Effect and Activation Parameters for the Reaction of Trimethyl Phosphite with Symmetrically Disubstituted Benzils in Dioxane

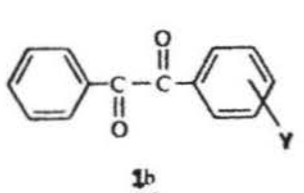
Benzil	Temperature (°)	10^3k (M^{-1} sec^{-1})	E_a* (kcal/mol)	$\Delta S^{\ddagger}$* (e.u.)	ln A* (M^{-1} sec^{-1})
Unsubstituted	20·0	3·76	9·90	−35·5	12·4
	25·0	4·83			
	30·0	6·64			
p,p'-Dinitro-	20·0	361	16·0	−41·1	10·3
	25·0	432			
	30·0	514			
m,m'-Dinitro-	20·0	224	10·3	−28·3	16·2
	25·0	299			
	30·0	390			
p,p'-Dichloro-	20·0	14·1	10·1	−34·5	13·1
	25·0	19·0			
	30·0	24·3			
p,p'-Dimethyl-	20·0	1·17	11·3	−31·5	14·5
	25·0	1·68			
	30·0	2·29			
p,p'-Dimethoxy-	20·0	0·272	13·6	−30·5	15·1
	25·0	0·387			
	30·0	0·567			

* Calculated by the least square method.



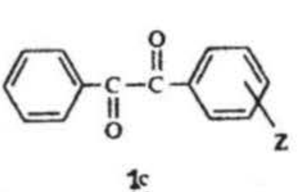
1a

X : electron-
withdrawing or
-releasing group



1b

Y : electron-
withdrawing
group



1c

Z : electron-
releasing group

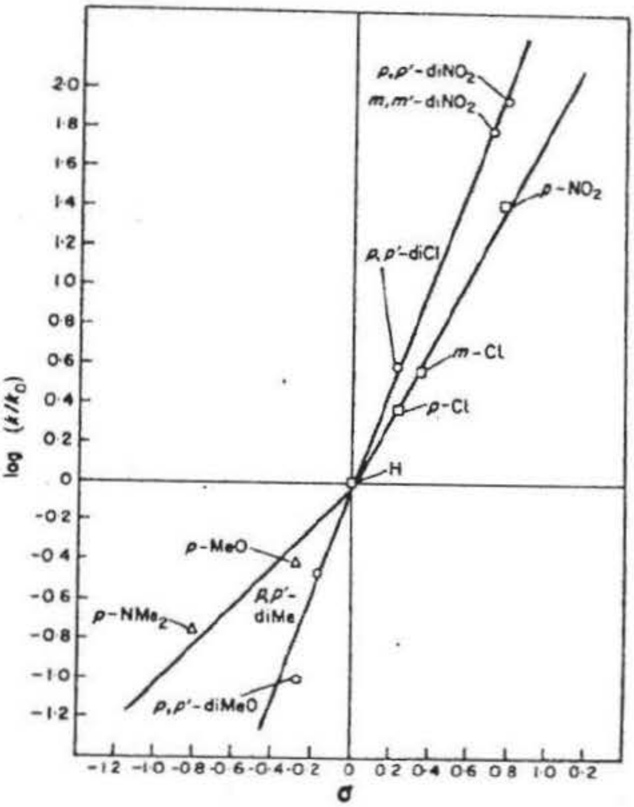


Figure 1. Hammett plot for the reaction of trimethyl phosphite with substituted benzils (**1a**-**c**) in dioxane at 25.0°.

It is of interest to note that the value of $\Delta S^{\ddagger}$ affects more than E_a on the rate of benzils with electron-withdrawing groups, whereas E_a is more important for those with electron-releasing groups.

Substituent Effect of Monosubstituted Benzils in Dioxane. The rates of trimethyl phosphite with monosubstituted benzils (1b and 1c) were measured at 25.0°. The rate constants were summarized in Table III.

The Hammett plot with σ gives a line bent at the origin. At $\sigma > 0$, the ρ value is +1.86 ($\equiv \rho_Y$) with $r = 0.996$, whereas at $\sigma < 0$, the value is +1.24 ($\equiv \rho_Z$) with $r = 0.991$ (Figure 1). The ratio of $(\rho_X - \rho_Y)$ vs. ρ_Y is 0.48, and that of ρ_Z vs. ρ_Y is 0.67. The values of E_a, $\Delta S^{\ddagger}$, and A were also listed in Table IV.

Here also the value of $\Delta S^{\ddagger}$ affects more on the rate for substituted benzils with electron-withdrawing groups, whereas E_a is more important for those with electron-releasing groups.

Effect of Solvent. The uv spectra of benzil was measured in some solvents. A slight change of the spectra was observed as shown in Table V.

The rate data in acetonitrile at 25.0° are shown in Table VI. The Hammett plot with σ gives a ρ value of +2.22 ($\equiv \rho'_X$) ($r = 0.996$) for symmetrically disubstituted benzils, and a ρ value of +1.63 ($\equiv \rho'_Y$) ($r = 0.993$) for monosubstituted benzils (Figure 2). The ratio of $(\rho'_X - \rho'_Y)$ vs. ρ'_Y is 0.36.

3.4 Discussion

In general, the mechanism for the reaction of trivalent phosphorus compounds with carbonyl compounds was obscure in that it was not decided whether the C or O atom of the carbonyl group is attacked by the P atom.[8]

Table III. Rate Constants for the Reaction of Trimethyl Phosphite with Monosubstituted Benzils (1b,c) in Dioxane

Benzil	Initial concn. (M) [1]	Initial concn. (M) [2]	10^3k (M^{-1} sec^{-1})	Relative rate (k/k_0)	log (k/k_0)	σ^a
Unsubstituted	0·0500	0·0500	4·83	1·00	0·000	0·000
p-Nitro-	0·0100	0·0100	134	27·7	1·442	0·778
m-Chloro-	0·0100	0·0300	18·1	3·75	0·575	0·373
p-Chloro-	0·0100	0·0400	11·3	2·33	0·368	0·227
p-Methoxy-	0·0100	0·250	1·82	0·377	−0·424	−0·268
p-Dimethylamino-	0·0100	1·00	0·862	0·178	−0·749	−0·600

[a] H. H. Jaffé, *Chem Rev.* 53, 191 (1953).

Table IV. Temperature Effect and Activation Parameters for the Reaction of Trimethyl Phosphite with Monosubstituted Benzils in Dioxane

Benzil	Temperature (°)	10^3k (M^{-1} sec^{-1})	E_a^a (kcal/mole)	$\Delta S^{\ddagger a}$ (e.u.)	ln A^a (M^{-1} sec^{-1})
p-Nitro-	20·0	98·3	13·4	−27·9	16·4
	25·0	134			
	30·0	177			
m-Chloro-	20·0	12·9	10·8	−32·5	14·1
	25·0	18·1			
	30·0	23·1			
p-Chloro-	20·0	8·23	11·1	−31·7	14·5
	25·0	11·3			
	30·0	15·1			
p-Methoxy-	20·0	1·40	8·73	−43·8	8·41
	25·0	1·82			
	30·0	2·25			
p-Dimethylamino-	20·0	0·630	10·4	−44·4	8·11
	25·0	0·862			
	30·0	1·12			

[a] Calculated by the least square method.

Table V. The Uv Spectra of Benzil (K-Band) in Some Solvents

Solvent	Dielectric constant	λ_{max} (mμ)	$10^{-4}\varepsilon_{max}$
n-Hexane	1·89	257	1·99
Dioxan	2·21	259	1·97
Methanol	32·6	259	2·13
Acetonitrile	37·5	260	2·16

Table VI. Rate Constants for the Reaction of Trimethyl Phosphite with Benzil in Acetonitrile at 25.0°

Benzil	10^2k (M^{-1} sec^{-1})	Relative rate (k/k_0)	log (k/k_0)	σ[a]
Unsubstituted	1·34	1·00	0·000	0·000
m,m'-Dinitro-	46·8	34·9	1·543	0·710
p,p'-Dichloro-	3·05	2·28	0·358	0·227
p-Nitro-	23·5	17·5	1·243	0·778
p-Chloro-	2·36	1·76	0·246	0·227

[a] H. H. Jaffé, *Chem. Rev.* 53, 191 (1953).

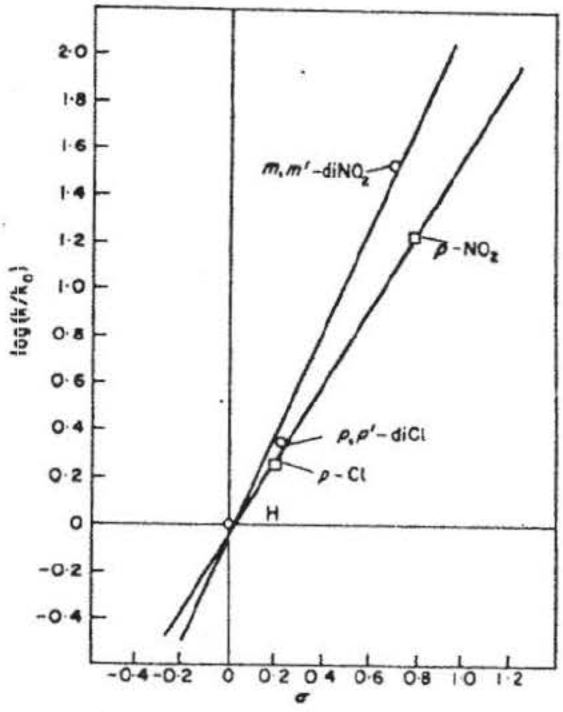


Figure 2. Hammett plot for the reaction of trimethyl phosphite with substituted benzils in acetonitrile at 25.0°.

In the preceding chapter for the studies on the kinetics of the reaction of benzil with trialkyl phosphite, it was suggested that the mechanism involves a rate-determining nucleophilic attack of the P atom on a C atom of carbonyl.[5]

In the study of the present chapter, a positive ρ value was observed for the reaction of substituted benzils, which supported the mechanism involving the nucleophilic attack of phosphite. The ρ value for benzils with electron-withdrawing group (1b) ($\equiv \rho_Y$) is +1.86. This value coresponds to the polar effect of substituent located in a benzene ring nearer from the reaction site (carbonyl C), since an electon-withdrawing group facilitates the nucleophilic attack of a P atom on the position nearer to the group. In general, the ρ value may depend on the distance between the attacked site and substituent on aromatic ring. In most cases, the absolute value of ρ may be more than unity for the reaction which has the site at α-position to the aromatic ring, while the value may be less than unity for the reaction in which the substituent and the site are separated farther, although the ρ value cannot be a measure of the α-carbon attack.[9] The ρ value observed in this reaction is a rather large positive value and it would suggest that the mechanism involves a rate-determining nucleophilic attack of a P atom on carbonyl C atom of benzil. The ρ value of the reaction of trimethyl phosphite with 1a ($\equiv \rho_X$) is +2.75, and that of the reaction with 1c ($\equiv \rho_Z$) is +1.24.

The Hammett plot for monosubstituted benzils (1b and 1c) gives a line bent at the origin. This phenomenon implies that the attacked site (CO) is convertible depending on the substituent, i.e., the P atom tends to attack on the more electrophilic carbonyl C atom among two CO groups.

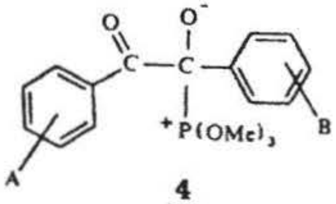
The net sensitivity to the transmitted effect of farther substituent X or Z at attacked CO may be expressed as $(\rho_X - \rho_Y)$ or ρ_Z. If these values are divided by ρ_Y, the division indicates the extent of the sensitivity to the substituent X or Z relative to that of nearer substituent Y. The observed ratio of $(\rho_X - \rho_Y)$ vs. ρ_Y is 0.48, and that of

ρ_Z vs. ρ_Y is 0.67, which represent the decreases of relative sensirivity of polar effect by insertion of CO group between substituent and attacked CO group. It has been reported that the ρ value should decrease by insertion of any group between aryl group and attacked site,[9b,10] e.g., the insertion of CH_2 group reduces it by a factor of 0.410 and even the insertion of conjugated -CH=CH- decreases it by a factor of 0.508 (observed) or 0.683 (calculated).[9b]

The crystal structure of benzil is known to be classified into two types by means of X-ray diffraction, uv spectra, and dipole moment.[11-13] In one configuration the planes of two CO twists ca. 90° each other around its CO-CO bond,[11,12] and in the other the twist angle is smaller (68°24' or so).[13] If the twist angle is ca. 90°, the resonance of both benzoyl group is inhibited, so that the effect of a substituent located farther from the reaction site should be smaller (0.410). The ratio of $(\rho_X - \rho_Y)$ vs. ρ_Y obtained in this reaction is close to that observed for the group -CH=CH- (0.508) in the dissociation of acids and the hydrolysis of esters, and the ratio of ρ_Z vs. ρ_Y is nearly equal to that calculated by the molecular orbital method for -CH=CH- (0.683).[9b] This fact suggests that the CO-CO group of benzil is probably conjugated each other to some extent and the smaller twist angle of ca. 70° is a more favourable one than ca. 90° in view of the possibility of resonance.

In the reaction of trimethyl phosphite with symmetrically disubstituted benzils, the correlation coefficient (r) of the Hammett plot is 0.996 with σ, but 0.989 with σ^+

and 0.960 with σ^-. This indicates that σ is more adequate than σ^+ and σ^- for this nucleophilic attack, and that the delocalization of positive charge on P atom or negative charge on carbonyl O atom due to resonance interaction with electron-releasing substituents or electron-withdrawing substituents contributes little to the stabilization of its transition state.



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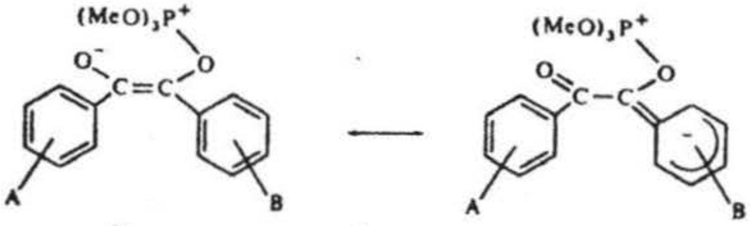


5a **5b**

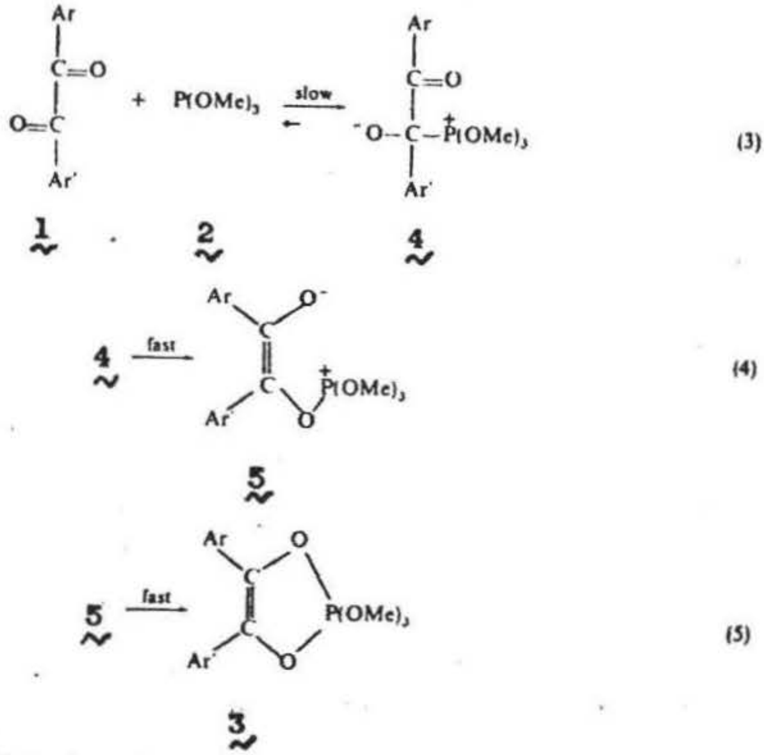
Assuming that the intermediate is **5**, in which B is a more powerful electron-withdrawing group than A, some canonical structures such as **5a**, **5b** etc. may be written, then the r value with σ^- would be larger than that with σ, but this is not the case. On the other hand, assuming the intermediate **4**, canonical structures such as **5b** is impossible because of the insulation of charges from benzene system, so that the r value with σ should be larger than that with σ^+ or σ^- as is observed. Hence, the intermediate is probably **4**, but not **5**.

The small activation energy (E_a) and large negative activation entropy ($\Delta S^{\ddagger}$) are to be noted.[5] $\Delta S^{\ddagger}$ depends on the nature of substituents and it ranges between -27.8 and -35.5 eu. For the monosubstituted benzil, $\Delta S^{\ddagger}$ is influenced strongly by such a substituent as located at a position closer to the reaction site. This fact implies that the induced negative charge in the activation complex is localized on one CO group, but little delocalized to the other CO. The hybrid orbital of attacked C atom may be converted from sp^2 to sp^3, hence the delocalization of charge to the farther benzoyl group is inhibited, i.e., the substituent effect of farther benzoyl group on $\Delta S^{\ddagger}$ is small. The increase of negative value of $\Delta S^{\ddagger}$ with decreasing electrone-withdrawing power for symmetrically disubstituted benzils may be explained similarly.

For the reaction of trimethyl phosphite with benzils substituted by the electron-releasing group, E_a is more important than $\Delta S^{\ddagger}$ which differs little with the change of substituent, i.e., $\Delta S^{\ddagger} \simeq -44$ eu for monosubstituted benzils and $\Delta S^{\ddagger} = -31 - -32$ eu for symmetrically disubstituted benzils. For mono- or disubstituted benzils, the E_a value increases with increasing electron-releasing power of group. In contrast with the little effect of farther substituent on $\Delta S^{\ddagger}$, the E_a value increases with increasing electron-releasing power of the substituents on both rings. But E_a value tends to vary irregularly with increasing electron-withdrawing power of the substituent.

These results suggest a mechanism as shown in Scheme I.

Scheme I. The Mechanism of the Reaction of Trimethyl Phosphite with Benzil[a]



[a] Ar' has an electron-withdrawing substituent more powerful than Ar.

Here, the first step is a rate-determining nucleophilic attack of a P atom on a carbonyl C atom of benzil. The reverse step of eq 3 is very slow. The steps 4 and 5 are too fast to affect the rate constant.

The uv spectra of benzil vary with solvent polarity (Table V). The value of λ_{max} increases with increasing polarity of solvent. Probably, the configuration of benzil changes with the polarity of solvent, the twist angle around CO-CO changes and sometimes it may occur that the coplanarity of phenyl and carbonyl groups is recovered,[14] which means an increase of twist angle around CO-CO.[11b]

The observed ρ values in acetonitrile are +2.22 ($\equiv \rho'_X$) for symmetrically disubstituted benzils and +1.63 ($\equiv \rho'_Y$) for monosubstituted benzils ($\sigma > 0$). The ratio of ($\rho'_X - \rho'_Y$) vs. ρ'_Y is 0.36. This indicates that the twist angle around CO-CO bond increases in acetonitrile, which is supported by the uv spectra as mentioned above, but this is inconsistent with the result of Chaudhuri et al., who reported that the molecular structure changes little by changing the phase of the molecule from solid to liquid.[13c]

The reaction of trimethyl phosphite with m,m'-dinitrobenzil in acetonitrile is somewhat different. The amount of product $\underset{\sim}{3}$ (A = B = m-NO_2) reached rapidly to a maximum value, and then gradually decreased, although the consumption of starting material, m,m'-dinitrobenzil, was continuing. The further reaction of $\underset{\sim}{3}$ is still under study.

3.5 Experimental Section

<u>Materials</u>. Benzil[15] was prepared from benzaldehyde,[16] and recrystallized from CCl_4 to give overall yield of 77%, mp 95.5 - 96° (lit.[15] mp 95°). (Found: C, 79.75; H, 4.98. $C_{14}H_{10}O_2$ requires: C, 79.98; H, 4.80%). m,m'-Dinitrobenzil was prepared by nitration of benzil with HNO_3 (d = 1.5) at 0°. Recrystallization from acetone, separation with liquid chromatography, silica gel from Mallinckrodt Chemical Works

was used as a packing, (eluent: benzene) and then recrystallization from CCl_4 gave overall yield of 35%, mp 128-129° (lit.[17] mp 132°). (Found: C, 58.61; H, 2.69; N, 9.34. $C_{14}H_8N_2O_6$ requires: C, 56.01; H, 2.69; N, 9.33%). p,p'-Dichlorobenzil was prepared by the benzoin condensation of p-chlorobenzaldehyde followed by oxidation with HNO_3. The crude material was recrystallized from CCl_4 in a overall yield of 27%, mp 195-196° (lit.[18] mp 195-196°). (Found: C, 60.87; H, 2.69. $C_{14}H_8Cl_2O_2$ requires: C,60.24; H, 2.89%). p,p'-Dimethylbenzil was prepared by the benzoin condensation of p-methylbenzaldehyde followed by HNO_3 oxidation. The product, after being extracted with ether from 10% Na_2CO_3, recrystallized from EtOH, giving overall yield of 20%, mp 103° (lit.[19] mp 104-105°). (Found: C, 79.76; H, 5.54. $C_{16}H_{14}O_2$ requires: C, 80.64; H, 5.92%). p,p'-Dimethoxybenzil was prepared from p-methoxybenzaldehyde similarly as p,p'-dimethylbenzil; overall yield 25%, mp 133° (lit.[20] mp 133°). (Found: C, 71.25; H, 5.16. $C_{16}H_{14}O_4$ requires: C, 71.10; H, 5.22%). p-Nitrobenzil was prepared by nitration of benzoin with mixed acid at 0°, followed by HNO_3 oxidation. Recrystallization from CCl_4, purification by liquid chromatography (eluent; light petroleum:EtOAc = 7:3), and then recrystallization from CCl_4 gave overall yield of 22%, mp 142° (lit.[21] mp 142°). (Found: C, 67.12; H, 3.54; N, 5.55. $C_{14}H_9NO_4$ requires: C, 65.88; H, 3.55; N, 5.49%). m-Chlorobenzil was prepared by the Grignard reaction of m-chlorobenzyl magnesium bromide followed by oxidation with selenium dioxide in Ac_2O. After being extracted with ether, the product was purified by liquid chromatography (eluent;

light petroleum:benzene = 4:1) and recrystallized from MeOH to give overall yield of 15%, mp 87-88° (lit.[22] mp 86°). p-Chlorobenzil was prepared similarly as m-chlorobenzil in a overall yield of 15%, mp 75° (lit.[22] 75.0°). (Found: C, 69.18; H, 3.45. $C_{14}H_9ClO_2$ requires: C, 68.72; H, 3.71%). p-Methylbenzil was prepared by the mixed benzoin condensation of benzaldehyde and p-methylbenzaldehyde followed by air oxidation in the presence of pyridine-cupric sulphate complex. The purification by liquid chromatography and repeated recrystallization from ligroin gave overall yield of 10%, mp 59° (lit.[23] 61-62°). (Found: C, 75.91; H, 4.57. $C_{15}H_{12}O_3$ requires: C, 74.99; H, 5.03%). p-Dimethylaminobenzil was prepared by the reaction of benzoin with p-dimethylaminobenzaldehyde[24] followed by oxidation with Fehling's soln. Recrystallization from 60% aqueous EtOH gave overall yield of 60%, mp 116-116.5° (lit.[25] 116-117°). p,p'-Dinitrobenzil was prepared through 4,5-diphenylglyoxalone by the method of Chattaway et al.[26] Recrystallization from AcOH gave overall yield of 8% (based on benzalhehyde), mp 213° (lit.[26] 213°). Trimethyl phosphite was purified by repeated distillation with metallic Na under N_2, bp 56°/101 mm (lit.[27] 111-112°). 2,2,2-Trimethoxy-4,5-diaryl-1,3,2-dioxaphospholes ($\underset{\sim}{3}$) were prepared by the reaction of substituted benzils with excess trimethyl phosphite under N_2 at 25.0° for 3-20 hr. The reaction proceeded quantitatively and there was no influence of the initial amount of trimethyl phosphite and longer reaction time on the yield. The further reaction of $\underset{\sim}{3}$ was not observed in this system. The identification and estimation of $\underset{\sim}{3}$ was done by uv spectroscopy without isolating it.

The uv spectra were measured in n-hexane and listed in Table VII together with those of substituted benzils. Solvents used were purified by ordinary methods.[28]

Kinetic Procedure. The kinetic experiments for the reaction of trimethyl phosphite with substituted benzils were carried out in dioxane or acetonitrile. The rate was followed by measuring the produced 3 or remaining 1 by means of uv spectrophotometry. The kinetics for the reaction with m,m'-dinitrobenzil in acetonitrile was limited to the initial stage because of the further reaction of product. The other kinetic procedure was the same as the preceding chapter.

Table VII. The Uv Data of Benzils (1a-c) and 1,3,2-Dioxaphospholes (3) in n-Hexane

Substituent on		1a-c		3	
Ar	Ar'	λ_{max}(mμ)	$10^{-4}\varepsilon_{max}$	λ_{max}(mμ)	$10^{-4}\varepsilon_{max}$
H	H	257	1·99	319	1·14
p-NO_2	p-NO_2	272	3·19	349	1·33
m-NO_2	m-NO_2	240	2·12	325	1·12
p-Cl	p-Cl	272	2·06	322	1·44
p-CH_3	p-CH_3	265	2·25	316	1·36
p-CH_3O	p-CH_3O	287	2·44	312	1·52
H	p-NO_2	269	2·40	382	1·16
H	m-Cl	258	2·05	322	1·12
H	p-Cl	269	2·04	322	1·20
p-CH_3O	H	286	1·54	316	1·20
p-$N(CH_3)_2$	H	341	2·09	330	1·63

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Chapter 4

KINETICS OF THE REACTION OF SOME TRIALKYL PHOSPHITES WITH BENZIL

4 KINETICS OF THE REACTION OF SOME TRIALKYL PHOSPHITES WITH BENZIL[1]

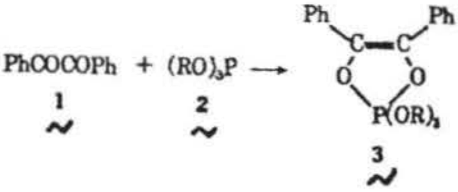
4.1 Summary

The effect of substituents on the reaction rates of trialkyl phosphites [$(RO)_3P$] with benzil has been studied. The rate constant, k, in the rate equation, $v = k[(RO)_3P] \times [PhCOCOPh]$, increases with the change of R in the order of methyl, ethyl, and isopropyl, while a little change of k is observed with R of n-propyl, n-buthyl, n-amyl, n-octyl, and sec-butyl, and the k value decreases by substitution of 2-methoxyethyl for methyl. The relative rates fit the Taft equation, $\log (k/k_o) = -3.28\ \sigma^* + 0.40\ E_s + 0.03$. Both polar and steric effects affect the rate with R of C_nH_{2n+1} ($n \geqq 3$), while polar effect alone is dominant with R of methyl and ethyl. The correlation between the ^{31}P nmr chemical shift relative to $(CH_3O)_3P$, $\Delta\delta^{31}P$, and the relative reaction rate or Taft's σ^* value is discussed. These facts present an additional support for the mechanism involving a nucleophilic attack of the phosphorus atom on the carbonyl carbon.

4.2 Introduction

In the preceding chapters,[2-4] kinetics of the reaction of trialkyl phosphite with benzil and substituted benzils favored a mechanism involving a nucleophilic attack of a phosphorus atom of phosphite on a carbonyl carbon atom of benzil, which is similar to a mechanism proposed by Litt for aliphatic α-diketones.[5]

The present chapter deals with the kinetic study on the reaction of a number of trialkyl phosphites (2) with benzil (1) forming substituted 1,3,2-dioxaphospholes (3) (eq 1) to clarify the effect of substituents at phosphorus atom. The rate was measured by means of uv spectrophotometry.[6-8]



(1)

4.3 Results

The reaction of a number of trialkyl phosphites (2) with benzil (1) proceeds quantitatively at room temperature to yield 2,2,2-trialkoxy-4,5-diphenyl-1,3,2-dioxaphospholes (3). The rate was measured by means of ultraviolet spectrophotometry of the product 3.

<u>Rate Law</u>. The rate was measured in dioxane at 20.0, 25.0, 30.0, and 35.0°. The rate law is expressed as eq 2

up to high conversion for all phosphites used as has been observed with trimethyl phosphite.[2-4]

$$v = k\ [(RO)_3P][PhCOCOPh] \qquad (2)$$

Effect of Substituents at Phosphorus Atom. The rate in dioxane at 25.0° is summarized in Table I. The rate increases with an increase of the electron-releasing power of substituents of alkyl groups of the phosphites. Both polar and steric effects in the Taft equation are important, since the correlation between the logarithm of the relative rate constant and Taft's σ^* or E_a alone is not so good.

The rate measurements at various temperatures afford energies of activation (E_a), entropies of activation ($\Delta S^\ddagger$), and frequency factors (A) as shown in Table II. As obvious from the table, both E_a and $\Delta S^\ddagger$ are low.

^{31}P Nmr Chemical Shift. The ^{31}P nmr chemical shift relative to $(CH_3O)_3P$, $\Delta\delta^{31}P$, was measured by a JNM-C60-HL high-resolution spectrometer at 24 MHz neat at room temperature. The values of $\Delta\delta^{31}P$ are listed in Table III. A plot of $\Delta\delta^{31}P$ vs. σ^* for R of CH_3, C_2H_5, n-C_3H_7, n-C_4H_9, and sec-C_4H_9 gave a correlation coefficient (r) of -0.925 except for R of sec-C_4H_9. (sec-$C_4H_9O)_3P$ has a little different value.

A plot of $\Delta\delta^{31}P$ vs. log (k/k_0) for all phosphites, except R of sec-C_4H_9 and $CH_3OCH_2CH_2$, seems to show a good correlation coefficient (r = 0.969). The substituents of sec-C_4H_9 and $CH_3OCH_2CH_2$ seem to give a somewhat different effect on $\Delta\delta^{31}P$.

Table I. Second-Order Rate Constants for the Reaction of Trialkyl Phosphites (**2**) with Benzil (**1**) in Dioxane at 25.0°

$(RO)_3P$, R =	Concentration, (M)		10^3 k, $(M^{-1}sec^{-1})$	Relative rate (k/k_o)	log (k/k_o)	σ^* [a]
	[**1**]	[**2**]				
CH_3	0.05	0.05	4.83	1.00	0.000	0.000
C_2H_5	0.05	0.05	10.8	2.34	0.369	-0.100
$i\text{-}C_3H_7$	0.02	0.1	13.5	2.80	0.447	-0.200
$sec\text{-}C_4H_9$	0.02	0.1	9.19	1.90	0.279	-0.210
$n\text{-}C_3H_7$	0.05	0.05	8.37	1.73	0.238	-0.115
$n\text{-}C_4H_9$	0.05	0.05	9.64	2.00	0.301	-0.130
$n\text{-}C_5H_{11}$	0.05	0.05	10.4	2.15	0.332	
$n\text{-}C_8H_{17}$	0.1	0.1	10.1	2.09	0.320	
$CH_3OCH_2CH_2$	0.01	0.1	2.94	0.609	-0.216	

[a] R. W. Taft, Jr., *J. Amer. Chem. Soc.*, **75**, 4231 (1953).

Table II. Temperature Effect and Activation Parameters for the Reaction of Trialkyl Phosphites with Benzil in Dioxane[a]

$(RO)_3P$, R =	10^3 k, $(M^{-1}sec^{-1})$				E_a, (kcal/mol)	$\Delta S^{\ddagger}$, [b] (eu)	ln A, $(M^{-1}sec^{-1})$
	20.0°	25.0°	30.0°	35.0°			
CH_3	3.76	4.83	6.64		9.90	-35.5	12.4
C_2H_5	8.08	10.8	12.8		8.32	-41.1	9.78
i-C_3H_7	10.3	13.5	16.8		9.12	-38.4	11.1
sec-C_4H_9	7.29	9.19	11.1		7.85	-43.6	8.53
n-C_3H_7	6.10	8.37	11.4		11.2	-32.9	13.9
n-C_4H_9	7.64	9.64	13.8		10.9	-32.9	13.9
n-C_5H_{11}	7.68	10.4	13.1		9.78	-36.9	11.9
n-C_8H_{17}		10.1	12.9	16.6	9.92	-36.5	12.1
$CH_3OCH_2CH_2$	2.18	2.94	3.82		10.4	-37.3	11.7

[a] Calculated by the least-squares method.

[b] $\Delta S^{\ddagger}$ was calculated at 25.0°.

Table III. ^{31}P Nmr Chemical Shifts from $(CH_3O)_3P$

$(RO)_3P$, R =	$\Delta\delta\ ^{31}P$,[a] ppm
CH_3	0.00
C_2H_5	+1.21
i-C_3H_7	+1.16
sec-C_4H_9	+0.16
n-C_3H_7	+1.01
n-C_4H_9	+0.98
n-C_5H_{11}	+1.08
n-C_8H_{17}	+1.06
$CH_3OCH_2CH_2$	+0.75[b]

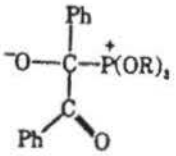
[a] The + sign indicates the higher field shift.

[b] In ca. 50% CCl_4 solution.

4.4 Discussion

The mechanism of the reaction of trialkyl phosphites with benzil may involve a nucleophilic attack of a phosphorus atom of phosphite either on a carbonyl carbon atom or an oxygen atom of benzil;[2-4,9] thus, the corresponding intermediate may be **4** or **5**, respectively. A probable mechanism involving path A or B may be written as Scheme I.

In view of the data of acid catalysis,[2] it seems that acid accelerates the reaction, while base retards it. The substituent effect in benzil gave a good Hammett's correlation with σ but not with σ^- or σ^+, and it afforded a large positive ρ value.[3] Moreover, the substituent effect in aliphatic α-diketones revealed that the steric substituent constant, E_s, controls the rate.[4] These results suggest that a more probable intermediate may be **4** and that the reaction involves a nucleophilic attack of the phosphorus atom of phosphite on a carbonyl carbon atom of the α-diketone in the rate-determining step.



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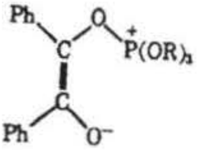

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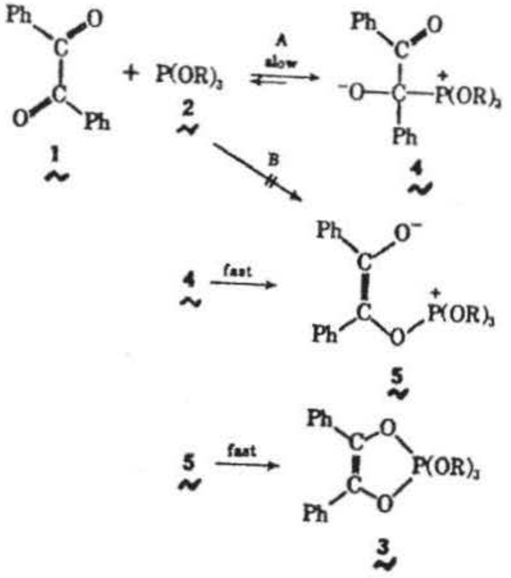
With the change of an alkyl group R of the phosphite from CH_3 to a more electron-releasing group, e.g., C_2H_5 and i-C_3H_7, a modest increase of the rate was observed, while with the change to an electron-withdrawing group such as $CH_3OCH_2CH_2$ the rate decreased (Table I).

As will be discussed later, the substituent effect in phosphites implies that a nucleophilic attack of phosphorus atom is involved in the rate-determining step, since an electron-releasing group on phosphite accelerates the reaction. Both rearrangement of **4** to **5** and the cyclization of **5** to **3** involve an electrophilic attack of a phosphorus atom, since the phosphorus atom has a positive charge. Hence, the observed substituent effect in phosphite suggests that these steps cannot be rate-determining.

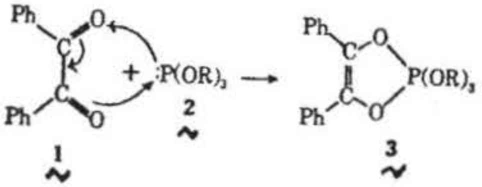
Scheme I. Mechanism for the Reaction of Trialkyl Phosphites with Benzil



Therefore, path A in Scheme I may be more probable than path B. The concerted one-step cycloaddition of α-diketone with phosphite (Scheme II) may be excluded, since, the first step must involve an attack of phosphite on an oxygen atom of carbonyl, which is inadequate as stated above.

The observed small value of E_a and the large negative value of $\Delta S^{\ddagger}$ are characteristic of this sort of reaction,[2-4] e.g., the condensation of carbonyl compounds with amines.[10] In general, a large negative value of $\Delta S^{\ddagger}$ is observed in the reaction in which the total number of species decreases or a strongly polarized and/or crowded transition states are involved.[11] Hence, it is supported that the first step is rate determining. The values of E_a and $\Delta S^{\ddagger}$ for $(n\text{-}C_nH_{2n+1}O)_3P$ ($n \geqq 3$) are nearly constant, but the alkyl substituents such as C_2H_5, $i\text{-}C_3H_7$, and $sec\text{-}C_4H_9$ decrease the E_a value.

Scheme II. Concerted Mechanism Involving a One-Step Cycloaddition Reaction of Trialkyl Phosphites with Benzil



A plot of log (k/k_o) vs. σ^* (Figure 1) gives a very poor correlation coefficient (r) of -0.806; this implies that not only a polar effect but also a steric effect of phosphite is a controlling factor in the rate-determining step. The negative value of r also supports the rate-determining nucleophilic attack of phosphite.

A plot of log (k/k_o) vs. E_s (Figure 2) may be classified into three groups with the change of substituents, i.e., (1) CH_3 and C_2H_5, (2) $i\text{-}C_3H_7$, $n\text{-}C_3H_7$, $n\text{-}C_4H_9$, $n\text{-}C_5H_{11}$, and $n\text{-}C_8H_{17}$, and (3) $sec\text{-}C_4H_9$. For group 2 the plot gives a negative correlation coefficient, which indicates the accelation of reaction by releasing the steric hindrance of phosphites by going to the transition state.[12] This may not be the case, since the negative Taft's ρ^* value and the large negative $\Delta S^\ddagger$ value were observed in this reaction and positive Hammett's ρ value was observed in the substituent effect of benzil.[3]

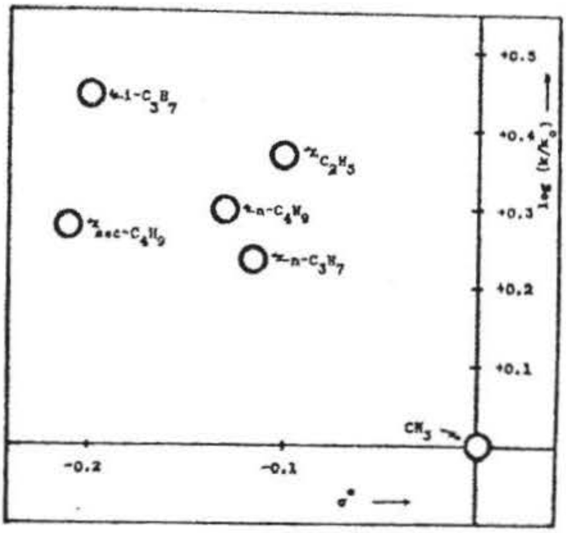


Figure 1. Plot of log (k/k_o) vs. Taft's σ^* for the reaction of $(RO)_3P$ with PhCOCOPh in dioxane at 25.0°.

Figure 1 shows that the steric effect operates little upon C_2H_5 but much upon sec-C_4H_9. A line passing through the points for CH_3 and C_2H_5 (= l_o, with slope of -3.69) was drawn and the deviation from the line [= Δ log (k/k_o)] was calculated with various alkyl groups. The plot of Δ log (k/k_o) vs. E_s gave a straight line whose slope was +0.46 ($r = 0.977$). When the slope of l_o was changed little, the correlation between Δ log (k/k_o) and E_s becomes worse

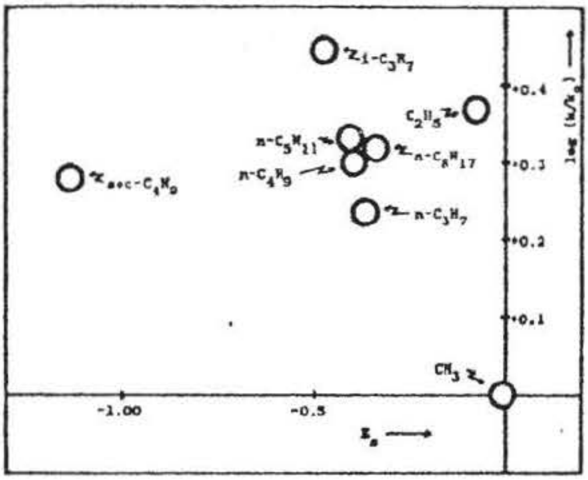


Figure 2. Plot of log (k/k_o) vs. Taft's E_s for the reaction of $(RO)_3P$ with PhCOCOPh in dioxane at 25.0°.

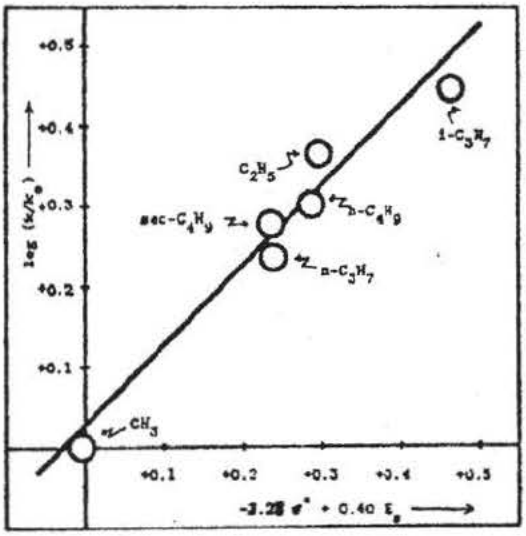


Figure 3. Plot of log (k/k_o) vs. $(-3.28\sigma^* + 0.40E_s)$ for the reaction of $(RO)_3P$ with PhCOCOPh in dioxane at 25.0°.

($r < 0.977$). A plot of $\log (k/k_o)$ vs. $(-3.69\ \sigma^* + 0.46\ E_s)$ gave a straigh line with a slope of +0.888 ($r = 0.981$). In other words, the Taft equation may be applied, which is expressed in a form of eq 3 for this reaction (Figure 3).

$$\log (k/k_o) = -3.28\ \sigma^* + 0.40\ E_s + 0.03 \qquad (3)$$

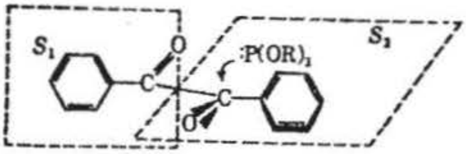
As apparent from the coefficients of the equation the polar effect is more important. In view of the reported value of E_s for n-C_5H_{11} (-0.40) and n-C_8H_{17} (-0.33),[13] a probable σ^* value for n-C_5H_{11} and n-C_8H_{17} may be -0.140.

Assuming the activated complex **4** (path A), in which a carbonyl carbon atom of benzil was attacked by a nucleophilic phosphorus atom of phosphite, the reaction site of benzil (carbonyl carbon) is shielded by two benzene rings, a carbonyl group, and an oxygen atom. Then a phosphorus atom carrying bulky alkyl groups is prevented from an attack of the carbonyl carbon atom. Figures 1-3 imply that for $(C_nH_{2n+1}O)_3P$, the steric factor of $(C_nH_{2n+1}O)_3P$ is less important when n is 1 and 2, but it is more important when $n \geqq 3$.

On the contrary, if the intermediate were **5** (path B) the steric factor would be less important, since the attacked carbonyl oxygen is out of the plane of the benzil molecule.

These data also show that the phosphorus atom attacks on the carbonyl carbon atom in the rate-determining step (path A).

The lower side of the carbonyl carbon atom on the S_2 plane is hindered by the benzene ring on S_1 plane, and vice versa.[14] The phosphorus atom may chiefly attack on the carbonyl carbon atom from one side, probably from an upper side of the S_2 plane.



The ^{31}P nmr chemical shifts relative to $(CH_3O)_3P$ ($\equiv \Delta\delta^{31}P$, ppm) were measured at room temperature. The shift may reflect the shielding efficiency of substituents on the phosphorus atom. The studies on $\delta^{31}P$ have been reported for many phosphorus compounds.[15-19] The linear correlation between $\delta^{31}P$ and the additive group contribution ($\Sigma\sigma^P$) has been known with secondary and tertiary phosphines, phosphorus halides, phosphonium salts, etc.[16,17] The Taft equation is applicable to the $\delta^{31}P$ values of some alkyl or aryl phosphorus difluorides[18] but not to those for phosphine and some of other phosphorus compounds,[16a,e,19] since many factors, besides the inductive effect, may influence $\delta^{31}P$.[15b,20]

The plot of log (k/k_o) vs. $\Delta\delta^{31}P$ gives a correlation coefficient of 0.969 except for sec-C_4H_9 and $CH_3OCH_2CH_2$. The good correlation with $\Delta\delta^{31}P$ seems to mean the control of rate by the electronic state of the phosphorus atom, while the poor correlation with E_s ($r = -0.254$) seems to mean that the steric effect on $\Delta\delta^{31}P$ is unimportant.

Assuming the virtually constant bond angle of ca. 100° for O-P-O of the phosphite,[20a,21] the substituent effect may be parallel to the polar effect. The observed poor correlation in σ^* with sec-C_4H_9 and $CH_3OCH_2CH_2$ may reflect the deviation of the O-P-O angle and the other factors influencing $\Delta\delta\,^{31}P$, e.g., the effect of oxygen atom.

4.5 Experimental Section

Materials. Trialkyl phosphites were prepared by the reaction of phosphorus trichloride with corresponding alcohols in the presence of base below 15° [22] and purified by repeated distillations with metallic sodium under reduced pressure with nitrogen atomosphere. The characteristics of prepared trialkyl phosphites were listed in Table IV. Benzil was prepared as mentioned in the preceding chapters.

2,2,2-Trialkoxy-4,5-diphenyl-1,3,2-dioxaphospholes (3) were prepared by the reaction of benzil with excess trialkyl phosphite without solvent or in anhydrous dioxane under nitrogen atmosphere at 25.0° for 3-12 hr. The structure of 3 (R = Me) was confirmed by ir, nmr, and uv spectra.[2] The uv spectra of 3 were measured in anhydrous n-hexane and listed in Table V.

The hydrolysis product of 3 (R = Me) showed new peaks in ir and uv spectra: ir 3350 (OH, broad) and 1230 cm^{-1} (P=0, broad); uv λ_{max} 285 nm but not 313 nm (in dioxane). Solvents were purified and dried before use.

Kinetic Procedure. The kinetic experiments for the reaction of trialkyl phosphite with benzil were carried out in anhydrous dioxane. The rate measurements were done by means of the procedure as mentioned in the preceding chapters. An isosbestic point was observed during the reaction of 1 (R = Me) at 287 nm in dioxane .

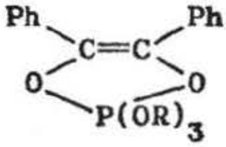
The ^{31}P nmr chemical shifts were measured by a JNM-

Table IV. Characteristics of Trialkyl Phosphites Prepared by the Reaction of Phosphorus Trichloride with Corresponding Alcohols

$(RO)_3P$, R =	Base	Yield, (%)	Bp, °C (mm)	n^D (deg)
C_2H_5	Diethylaniline	60	54 (17)	1.4104 (25)
i-C_3H_7		70	57 (9)	1.4049 (25)
sec-C_4H_9		70	77-78 (3.5-4)	1.4294 (25)
$CH_3OCH_2CH_2$		80	99 (1.5)	1.4365 (25)
n-C_3H_7	Pyridine	73	89 (10)	1.4239 (24)
n-C_4H_9		65	100-101 (4)	1.4307 (25)
n-C_5H_{11}		64	94-99 (1-1.5)	1.4369 (25)
n-C_8H_{17}		67	189-195 (1)	1.4468 (25)

C60-HL model of Japan Electron Optics Laboratory Co., Ltd., at 24 MHz with proton decoupling at room pemperature. The data were shown in Table III.[20a,23-25]

Table V. Uv Spectra of Dioxaphospholes (3) in n-Hexane

 R =	λ_{max}, nm	$\varepsilon_{max} \times 10^{-4}$
CH_3	319	1.14
C_2H_5	323	1.18
i-C_3H_7	322	1.12
sec-C_4H_9	319	1.23
n-C_3H_7	321	1.28
n-C_4H_9	321	1.21
n-C_5H_{11}	321	1.19
n-C_8H_{17}	322	1.19
$CH_3OCH_2CH_2$	316	1.15

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Chapter 5

KINETICS OF THE REACTION OF TRIMETHYL PHOSPHITE WITH ALIPHATIC α-DIKETONES

5 KINETICS OF THE REACTION OF TRIMETHYL PHOSPHITE WITH ALIPHATIC α-DIKETONES[1]

5.1 Summary

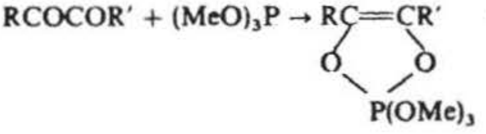
The substituent effect on the rate of reaction of trimethyl phosphite with aliphatic α-diketones has been studied in anhydrous dioxane by uv spectrophotometry. The rate constant (k) in the rate equation, $v = k[(MeO)_3P][RCOCOR']$, decreases with change of R and R' in the order methyl, ethyl, n-propyl, n-butyl, iso-propyl, iso-butyl, and sec-butyl. Practically no reaction was observed with t-BuCOCOBu-t at room temperature. The reaction of $(MeO)_3P$ with RCOCOR fits the Taft equation, $\log (k/k_0) = +1.08\ E_s + 0.012$, which shows the predominance of steric effect, while the reaction of $(MeO)_3P$ with MeCOCOR' fits the equation, $\log (k/k_0) = +1.17\ \sigma^* + 0.001$, which shows the superiority of polar effect. These results are discussed in terms of the previous mechanism involving a nucleophilic attack of phosphorus on a carbonyl carbon of an α-diketone, and may exclude an one-electron transfer mechanism.

5.2 Introduction

The reaction of trialkyl phosphites with α-diketones has been known,[2-5] but few studies on the mechanism have been reported.[6,7] In the preceding chapters, it was postulated for the reaction of trialkyl phosphite with benzil that a mechanism involving a nucleophilic attack of phosphorus atom on a carbonyl carbon atom in view of the acid-base catalysis,[8a] and substituent effects of benzils[8b] and phosphites.[8c]

Another mechanism which involves radical ions via one-electron transfer is considered in view of the reactions of aromatic amines and chloranil[9] and the easiness of reduction of quinones.

The present chapter deals with the kinetic study on the reaction of phosphite (2) with aliphatic α-diketones (1) (eq 1) to obtain further support to the mechanism of the nucleophilic attack of the phosphorus atom on carbonyl carbon.



(1)

1 2 3

The rate was measured by uv spectrophotometry. The substituent effect will be discussed in connection with the Taft's E_s and σ^* constants and the attacked site.

5.3 Results

The reaction of trimethyl phosphite (2) with aliphatic α-diketones (1) (except for R = R' = t-Bu) proceeds quantitatively at room temperature to yield 2,2,2-trimethoxy-4,5-dialkyl-1,3,2-dioxaphospholes (3).

Rate Law. The reaction was conducted in anhydrous dioxane at 30.0°, 35.0°, and 40.0°, and the rate was measured by means of uv spectrophotometry of the $n\pi^*$ transition of the carbonyl group of the disappearing α-diketones (Table VII). The rate law is expressed as eq 2 up to high conversion (over 80%).

$$v = k[(MeO)_3P][RCOCOR'] \qquad (2)$$

Substituent Effect of Symmetrical Aliphatic α-Diketones. The rate for the reaction of excess trimethyl phosphite with symmetrical aliphatic α-diketones were measured in dry dioxane at 35.0°. The second-order rate constants (k) are listed in Table I.

Table I. Second-Order Rate Constants, k, for the Reaction of Trimethyl Phosphite with Symmetrical Aliphatic α-Diketones in Dioxane at 35.0°

RCOCOR R	Initial concn. (M) [**1**]	 [**2**]	$10^4 k$ ($M^{-1} sec^{-1}$)	Relative rate (k/k_0)	$\log (k/k_0)$	E_s in Taft eq.
Me	0·3	0·5	8·52	1·000	0·000	0·00
Et	0·3	0·6	6·86	0·805	−0·094	−0·07
n-Pr	0·3	0·8	4·27	0·501	−0·300	−0·36
iso-Pr	0·3	0·8	1·88	0·221	−0·656	−0·47
n-Bu	0·3	0·8	4·07	0·353	−0·452	−0·39
iso-Bu	0·3	0·9	0·990	0·116	−0·936	−0·93
sec-Bu	0·3	1·1	0·449	0·0527	−1·29	−1·13
t-Bu	0·5	1·3	too slow to be measured			
Ph	0·05	0·1	82·5	9·68		

The plot of log (k/k_0) vs. Taft's steric substituent constants, E_s, gives a straight line, whose reaction constant, δ, is +1.08 (correlation coefficient, r, is 0.985) as shown in eq 3 (Figure 1). Taft's polar term, $\rho^*\sigma^*$, has substantially no effect on the rate.

$$\log (k/k_o) = +1.08\ E_s + 0.012 \qquad (3)$$

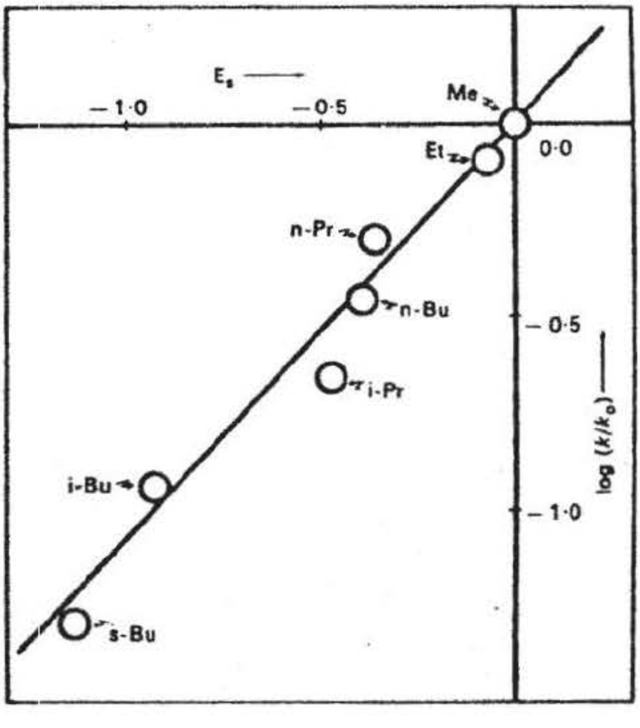


Figure 2. Taft plot for the reaction of trimethyl phosphite with symmetrical aliphatic α-diketones in dioxane at 35.0°.

The rates at 30.0°, 35.0°, and 40.0° afford energies of activation (E_a), entropies of activation ($\Delta S^{\ddagger}$) and frequency factors (A) as shown in Table II. It seems that alkyl groups on α-diketones diminish both E_a and $\Delta S^{\ddagger}$ values.

Table II. Temperature Effect and the Activation Parameters for the Reaction of Trimethyl Phosphite with Symmetrical Aliphatic α-Diketones in Dioxane

RCOCOR R	Temp.	$10^4 k$ ($M^{-1} sec^{-1}$)	E_a (kcal/mol)	$\Delta S^{\ddagger a}$ (e.u.)	$\ln A^a$ ($M^{-1} sec^{-1}$)
Me	30·0	6·19	13·3	−28·6	14·7
	35·0	8·52			
	40·0	12·0			
Et	30·0	4·74	13·4	−29·4	14·8
	35·0	6·86			
	40·0	9·57			
n-Pr	30·0	3·01	13·2	−30·6	13·7
	35·0	4·27			
	40·0	5·96			
iso-Pr	30·0	1·41	10·5	−40·4	8·72
	35·0	1·88			
	40·0	2·45			
n-Bu	30·0	3·01	11·0	−37·7	10·1
	35·0	4·07			
	40·0	5·33			
iso-Bu	30·0	0·718	12·1	−36·5	10·7
	35·0	0·990			
	40·0	1·36			
sec-Bu	30·0	0·334	12·1	−38·4	9·76
	35·0	0·449			
	40·0	0·628			
Ph	30·0	66·4	10·1	−34·8	11·6
	35·0	82·5			
	40·0	113			

[a] Calculated by the least square method. The values at 35·0 were used

The rate of benzil (1, R = R' = Ph) is ca. ten times as fast as that of butane-2,3-dione (1, R = R' = Me). Virtually no reaction of trimethyl phosphite with 2,2,5,5-tetramethylhexane-3,4-dione (1, R = R' = t-Bu) was observed at room temperature within two weeks.

Substituent Effect of Unsymmetrical Aliphatic α-Diketones. The observed second-order rate constants for the reaction of trimethyl phosphite with unsymmetrical aliphatic α-diketones in dioxane at 30.0° are listed in Table III.

The plot of log (k/k_o) vs. Taft's σ^* affords a straight line, which gives ρ^* of +1.17 (r = 0.925). The Taft equation can be written as eq 4 (Figure 2).

$$\log (k/k_o) = +1.17\ \sigma^* + 0.001 \qquad (4)$$

The values of E_a, $\Delta S^\ddagger$ and A are listed in Table IV. The correlation coefficient for log (k/k_o) vs. σ^* seems to decrease with rising tempetature. Also an alkyl group tends to decrease both E_a and $\Delta S^\ddagger$ values.

Effect of Hydrogen Chloride. Addition of a small amount of dry HCl to the reaction results in a sharp increase of rate constant as shown in Table V. Acid catalysis has been observed in the reaction of trimethyl phosphite with benzil.[8a]

5.4 Discussion

In the reaction of trialkyl phosphites with benzil, addition of acids accelerated the reaction, while bases retarded it,[8a] which may be due to the change of electrophilicyty of carbonyl by the interaction with acids or bases. The substituent effect in benzil gave Hammett's ρ value of +1.86. The correlation with σ was better than that with σ^- or σ^+.[8b] This suggests that the resonance of negative or positive charge with substituent is forbidden in the transition state. The substituent effect in phosphite fits the Taft equation, $\log (k/k_o) = -3.28\ \sigma^* + 0.40\ E_s + 0.03$.[8c] These facts suggest a mechanism involves a rate-determining nucleophilic attack of phosphorus atom on a carbonyl carbon

Table III. Second-Order Rate Constants for the Reaction of Trimethyl Phosphite with Unsymmetrical Aliphatic α-Diketones in Dioxane at 30.0°

MeCOCOR′ R′	Initial concn. (M) [1]	[2]	$10^4 k$ ($M^{-1} sec^{-1}$)	Relative rate (k/k_0)	log (k/k_0)	σ^* in Taft eq.
Me	0·3	0·5	6·19	1·000	0·000	0·000
Et	0·3	0·7	5·18	0·837	−0·0776	−0·100
iso-Pr	0·3	0·7	3·70	0·598	−0·224	−0·200
iso-Bu	0·3	0·5	3·91	0·632	−0·199	−0·125
PhCOCOPh	0·05	0·1	66·4	10·7	+1·03	+0·600

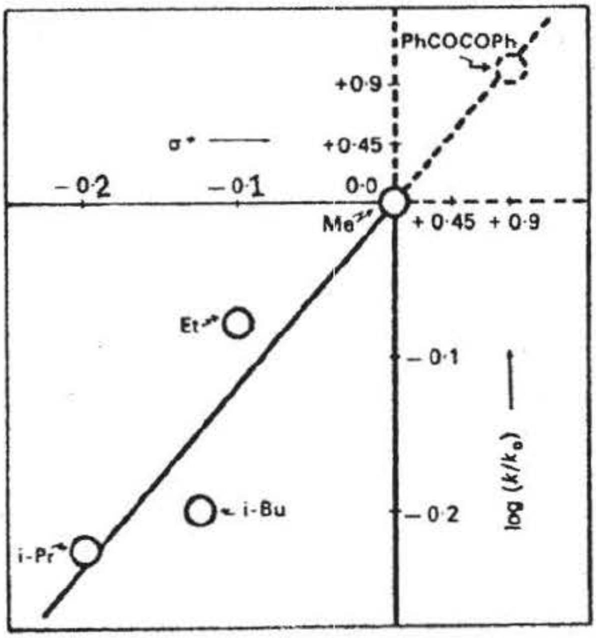


Figure 2. Taft plot for the reaction of trimethyl phosphite with unsymmetrical aliphatic α-diketones in dioxane at 30.0°.

Table IV. Temperature Effect and Activation Parameters for the Reaction of Trimethyl Phosphite with Unsymmetrical Aliphatic α-Diketones in Dioxane

MeCOCOR' R'	Temp.	$10^4 k$ ($M^{-1} sec^{-1}$)	E_a (kcal/mol)	$\Delta S^{\ddagger}$[a] (e.u.)	ln A[a] ($M^{-1} sec^{-1}$)
Et	30·0	5·18	13·0	−30·0	14·0
	35·0	7·02			
	40·0	10·2			
iso-Pr	30·0	3·70	13·1	−30·2	13·9
	35·0	5·28			
	40·0	7·36			
iso-Bu	30·0	3·91	11·0	−36·7	10·6
	35·0	5·26			
	40·0	7·01			

[a] Calculated by the least square method. The values at 35·0° were used.

Table V. Effect of a Small Amount of HCl on the Second-Order Rate Constants in Dioxane

MeCOCOR' R'	Initial concn. (M) **[1]**	Initial concn. (M) **[2]**	Temp.	$10^3 k$ ($M^{-1} sec^{-1}$)
Et	0·3	0·6	30·0	1·22
			35·0	1·77
			40·0	2·44
iso-Pr	0·3	0·6	30·0	0·711
			35·0	0·965
			40·0	1·31
iso-Bu	0·3	0·6	30·0	0·412
			35·0	0·558
			40·0	0·773

atom of benzil.

The substituent effect in trialkyl phosphite implies that the steric factor will be dominant in the substituent effect in aliphatic α-diketones, since even the substituent being situated in β-position of the phosphorus partially participated in the reaction rate. Table I and Figure 1 show that the rate is decreased with increasing bulkiness of alkyl groups, i.e., the E_s value controls the rate for symmetrical aliphatic α-diketones. The positive δ value implies that the steric hindrance is operating in the rate-determining step. Two bulky t-Bu groups in t-BuCOCOBu-t inhibit the reaction.

The E_s value is known to control the rate of the acid-catalyzed alcoholysis of β-naphtyl carboxylate[10] and ethylation of 2-alkyl pyridine,[11] whose mechanism are known to involve an attack on the next site of an alkyl group.

On the other hand, Table III and Figure 2 show that the rate decreases with an increase of electron-releasing power of alkyl group, i.e., the σ^* value contrals the rate for unsymmetrical aliphatic α-diketones. Since the alkyl group nearer to the primarily attacked carbonyl group retards the reaction by steric hindrance, the attack may occur on the farther carbonyl group from R' of MeCOCOR', i.e., carbonyl of acetyl group. Thus the steric effect does not influence the farther carbonyl group. The positive ρ^* value indicates a nucleophilic attack on carbonyl. With an increase of reaction temperature the correlation coefficient r decreases (temperature, r; 30.0°, 0.925; 35.0°, 0.898; 40.0°, 0.850). This means that the selectivity of carbonyl group attacked by phosphorus atom decreases with an increase of temperature, since an alkyl group which lies nearer to the carbonyl initially attacked exerts a steric effect, whereas a farther one influences a polar effect alone. The temperature dependent stereoselectivity was also reported for the asymmetric synthesis.[12]

The reaction of benzil is ca. ten times as fast as that of biacetyl. The neighbouring phenyl and carbonyl groups in benzil are known to be almost coplanar, while two carbonyl groups twist ca. 70° from each other.[8b,13] In contrast, two carbonyls in aliphatic α-diketones such as glyoxal, biacetyl and dipivaloyl have a coplanar and trans configuration.[14] If a benzoyl group of benzil is coplanar and a phosphorus atom attacks vertically into the plane, there is no steric effect of phenyl group. Since the transmitted polar effect of phenyl group via a carbonyl group is reduced by a factor of ca. 0.5,[8b, 15] the total σ^* value in benzil may be +0.9, i.e., $\sigma^*_{Ph} + 0.5\,\sigma^*_{Ph} = +0.6 + 0.3 = +0.9$. The ρ^* value in Figure 2 is +1.17, then the expected logarithm of relative rate for benzil to biacetyl, $\log(k/k_o) = \rho^*(\sigma^*_{Ph} + 0.5\,\sigma^*_{Ph})$, may be 1.05, i.e., $0.9 \times 1.17 = 1.05$, which is close to the observed value of $\log(k/k_o) = +1.03$. The increase of rate for benzil may be explained by Taft's σ^* value (Figure 2).

Tables II and III show the small energies and entropies of activation. These values are characteristic for this reaction. The variation of E_a and $\Delta S^{\ddagger}$ is somewhat irregular. The more powerful electron-releasing group decreases the values of E_a and $\Delta S^{\ddagger}$. Since they stabilize the intermediate (**4** in Scheme I) by slightly neutralising the formed positive charge on phosphorus, and bring about a highly oriented and charge-separated intermediate.

HCl accelerates the reaction. This may be explained by increased electrophilicity of carbonyl carbon by interaction of acid.[8a]

If one-electron transfer from phosphorus to carbonyl is involved in the rate-determining step, the polar effect would be a dominant factor and the steric effect would be unimportant. The close approach of reactants is unnecessary for the one-electron transfer and hence there is little steric effect. It was reported that an electron transfer occurred at 7 Å, and that no ortho effect was observed for reduction potential of phenanthrenequinones.[17] Therefore, the one-electron transfer mechanism may be excluded.

If a carbonyl oxygen atom of α-diketone is attacked by a phosphorus atom, the steric effect would be negligible. Eq 3 rules out this mechanism.

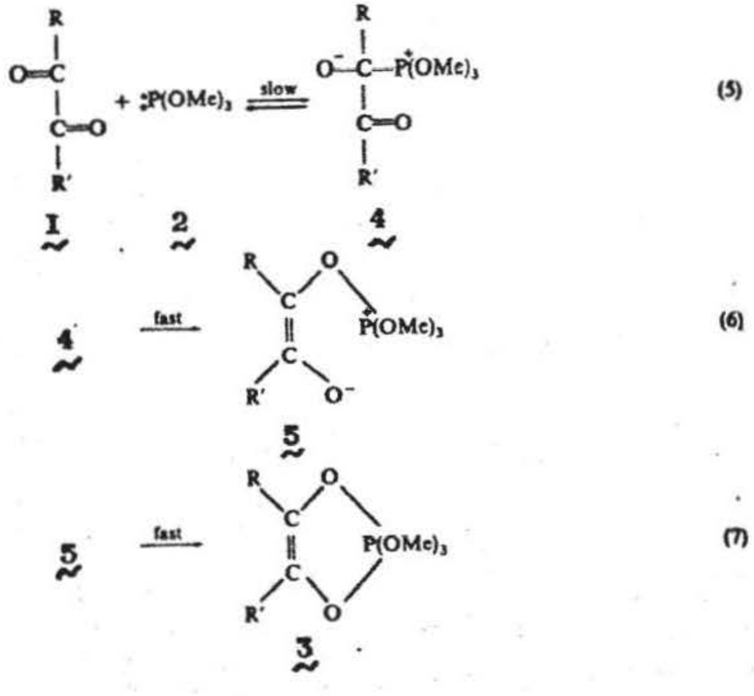
The control of rate by E_s value indicates the attack of phosphorus atom on the carbonyl carbon in the rate-determining step. It is reported by other workers that the E_s value controls the rate for the reaction of tervalent phosphorus compounds with Ac_2O, and that the mechanism involves a nucleophilic attack of phosphorus on the carbonyl carbon atom.[18,19]

For unsymmetrical aliphatic α-diketones, MeCOCR', the σ^* value of R' controls the rate. The phosphorus atom should attack selectively the less crowded carbonyl carbon, i.e., acetyl carbon. The bulky alkyl group, R', seems to have steric influence on the farther carbonyl group, hence the polar effect transmitted by one carbonyl group controls the reaction rate.

The reaction of substituted benzils with trimethyl phosphite has large ρ values (i.e., +2.75 for symmetrically disubstituted benzils and +1.86 for monosubstituted benzils) and the control of rate by E_s for symmetrical aliphatic α-diketones suggest that the reverse of the first addition step is less important.

In conclusion, the mechanism of the reaction of trialkyl phosphite with α-diketones may be written as Scheme I.

Scheme I. The Mechanism of the Reaction of Trimethyl Phosphite with Aliphatic α-Diketones



Here, eq 5 is a rate-determining nucleophilic attack of phosphite, and eqs 6 and 7 are fast. R is a less bulky alkyl group than R'.

5.5 Experimental Section

Materials. Benzil was prepared as mentioned before.[8a]

Hexane-3,4-dione was prepared by H_2SO_4-catalyzed ethyl esterification of propionic acid (71%), followed by acyloin reductive condensation of ethyl propionate to give hexane-4-ol-3-one (49%),[20] and then oxidation of the acyloin with $Cu(OAc)_2 \cdot H_2O$ in AcOH aq.[21] The crude material was washed with 5% $NaHCO_3$ aq, dried and distilled repeatedly to yield pure hexane-3,4-dione, bp 58°/51 mm, overall yield 16%.

2,2,5,5,-Tetramethylhexane-3,4-dione was prepared by CrO_3 oxidation of 2,2,5,5-tetramethyl-4-ol-3-one prepared by the similar procedure,[14a] bp 65-66°/20 mm, overall yield 70%.

Butane-2,3-dione (commercial G. R. grade) was purified by distillation, bp 87-88°. The other symmetrical aliphatic α-diketones were prepared by the procedure similar to hexane-3,4-dione and listed in Table VI.

Pentane-2,3-dione was prepared by oximation of pentane-2-one with MeONO and HCl to give pentane-3-oxime-2-one,[22] followed by steam distillation with 10% H_2SO_4.[23] The crude material was purified by the procedure similar to hexane-3,4-dione, bp 65-65.5°/137 mm, overall yield 40%. The other unsymmetrical aliphatic α-diketones were prepared similarly. The purity of aliphatic α-diketones was checked by glc using

Apiezon grease L 3% on celite 545.

Trimethyl phosphite was purified by repeated distillation with metallic Na under N_2, bp 52°/86 mm (lit.[24] bp 111-112°).

2,2,2-Trimethoxy-4,5-dialkyl-1,3,2-dioxaphospholes (3) were prepared by the reaction of aliphatic α-diketones with excess trimethyl phosphite under N_2 at room temperature. These reactions were complete within 3-24 hr. Virtually no reaction of 2,2,5,5-tetramethylhexane-3,4-dione with trimethyl phosphite was observed at room temperature within 2 weeks (the decrease of uv absorption at 373 nm was ca. 2% after 2 weeks' reaction).

Solvents used were dried and purified before use.

Uv Spectra. The uv spectra of aliphatic α-diketones and 3 were measured in anhydrous n-hexane. Aliphatic α-diketones had absorption in visible region (λ_{max}, 370-440 nm), while 3 did not in the above region (Table VII).

Kinetic Procedure. The kinetic experiments for the reaction of trimethyl phosphite with aliphatic α-diketones were carried out in dioxane. The rate was followed by measuring the remaining α-diketone by means of uv spectrophotometry (Table VII) at appropriate time intervals. The effect of HCl-addition was measured by introducing a small amount of dry HCl into the dioxane solution of aliphatic α-diketone. The other kinetic procedure was the same as the proceding chapters.[8]

Table VI. Overall Yields and Boiling Points of Aliphatic α-Diketones Produced from Carboxylic Acids[a] or Aliphatic Ketones[b]

RCOCOR′		Overall yield (%)	b.p. [°(mm)]
R	R′		
Me	Me	—	87–88
Et	Et	16[a]	58 (51)
n-Pr	n-Pr	47[a]	72–73 (25)
iso-Pr	iso-Pr	39[a]	63–64 (34)
n-Bu	n-Bu	41[a]	100–101 (21)
iso-Bu	iso-Bu	57[a]	85–86 (21)
sec-Bu	sec-Bu	69[a]	81–82 (21)
t-Bu	t-Bu	70[a]	65–66 (20)
Me	Et	40[b]	65–65·5 (137)
Me	iso-Pr	26[b]	62–63 (111)
Me	iso-Bu	49[b]	79–81 (110)

Table VII. Uv Spectra of Aliphatic α-Diketones ($n\pi^*$ Transition of Carbonyl Groups) in n-Hexane

RCOCOR′		λ_{max} used for kinetic study (nm)	ε_{max} used for kinetic study
R	R′		
Me	Me	421	22·2
Et	Et	435	13·7
n-Pr	n-Pr	435	19·4
iso-Pr	iso-Pr	436	22·6
n-Bu	n-Bu	435	19·2
iso-Bu	iso-Bu	439	22·1
sec-Bu	sec-Bu	442	30·7
t-Bu	t-Bu	373	13·8
Me	Et	419	15·6
Me	iso-Pr	429	21·2
Me	iso-Bu	432	17·8

[a] The number of peaks in visible region was small for symmetrical aliphatic α-diketones, whereas it was many for unsymmetrical α-diketones. The highest peak was used for kinetics

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Chapter 6

KINETICS OF THE REACTION OF TRIMETHYL PHOSPHITE WITH CYCLIC α-DIKETONES

6 KINETICS OF THE REACTION OF TRIMETHYL PHOSPHITE WITH CYCLIC α-DIKETONES[1]

6.1 Summary

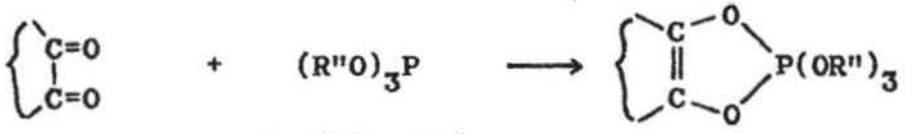
The kinetics of the reaction of trimethyl phosphite (1) with alicyclic α-diketones, 9,10-phenanthrenequinones (5a-e), and acenaphthenequinone (6) to form cyclic adduct has been studied in anhydrous dioxane. The rates are expressed as $v = k[(MeO)_3P][\alpha\text{-diketone}]$. The rate constant (k) decreases with an increase in size of ring of alicyclic α-diketones in the order: $5\ (2) \gg 6\ (3) > 10\ (4)$, while $6 > 5a$ with the condensed ring system. This suggests that the reaction proceeds with releasing strain by changing a carbonyl C atom of 2 from sp^2 to sp^3, and that a β-ketophosphonium intermediate, i.e., an attack of carbonyl C atom by P atom, is involved. The Hammett equation for 5a-e gives ρ value of +1.5 for the reaction.

6.2 Introduction

The reaction of phosphites or phosphines with cyclic α-diketones, e.g., cyclohexane-1,2-dione (3)[2] and 9,10-phenanthrenequinone (5a)[3] is known.

The preceding chapters reported that the reaction of phosphites with α-diketones may involve a rate-determining nucleophilic attack of phosphorus atom on the carbonyl carbon atom in view of the acid catalysis[4] and substituent effect of α-diketones[5,6] and phosphites.[7]

In the reaction of cyclic compounds, the reaction is accelerated with an increase of ring strain in reactants, if the strain is released by the progress of reaction.[8] In the Arbuzov reaction, the cyclic five-membered ring shows reduced reactivity.[9] The reaction of phosphite of a rigid structure, e.g., 2,8,9-trioxa-1-phospha-adamantane with biacetyl is slow.[10] These ring size effect suggests that the formation of a phosphonium intermediate is rate-determining in these reactions.



(1)

1 $(R'' = Me)$

2	Cyclopentane-1,2-dione
3	Cyclohexane-1,2-dione
4	Cyclodecane-1,2-dione
5a	9,10-Phenanthrenequinone
6	Acenaphthenequinone

The present chapter deals with the kinetic study on the reaction of trimethyl phosphite with cyclic α-diketones to see the effect of ring strain on the nucleophilic attack of phosphorus atom on the carbonyl carbon atom. The substituent effect of **5a** will be discussed in connection with the mechanism.

6.3 Results

The reaction of trimethyl phosphite (1) with cyclic α-diketones to yield 1:1 adducts proceeded at room temperature. The reaction in anhydrous dioxane was followed by uv spectrophotometry of disappearing α-diketones or resulting products. The obtained rate law is expressed as equation 2 up to high conversion.

$$v = k[(MeO)_3P][\alpha\text{-diketone}] \qquad (2)$$

The Reaction with Alicyclic Diketones. The reaction of trimethyl phosphite (1) with alicyclic α-diketones was followed by measuring the disappearing absorption of α-diketones in a visible region (see Experimental Section). The observed second-order dependence of rate and rate constants (k) at various temperature are listed in Tables I and II, respectively. The value of k for 2 was much higher than that for 3 or 4.

A slow keto-enol equilibrium with 2 and 3 is known.[11] The approximate enol content (%) for these two ketones in dioxane were measured by bromination and nmr spectra (see Experimental Section) and is shown in Table III together with the second-order rate constants (k') corrected by taking the content of keto tautomer into account (see Discussion).

The Reaction with Aromatic Diketones. The reaction of 1 with 9,10-phenanthrenequinones (5a-e) and acenaphthenequinone (6) were followed spectrophotometrically by measuring the appearing absorption of 1:1 adducts and disappearing absorption of α-diketone (see Experimental Section). The second-order dependence of rate and rate constants (k) for 5a and 6 are listed in Tables IV and V, respectively. The consumption rate of starting material agrees with the formation rate of product for 5a, indicating that the consumption of 5a is rate-determining, but not for 6 at lower

Table I. The Observed Second-Order Dependence of Rate for the Reaction of **1** with Alicyclic α-Diketones in Dioxane at 35°

α-Diketone	Initial concentration, (M)		Oberved rate constant
	[**1**]	[Diketone]	10^4 k, (M^{-1} sec^{-1})
2	0.0954	0.0441	11
	0.225	0.0441	12
	0.450	0.0139	9
3	0.533	0.628	2.5
	0.585	0.196	2.3
	0.763	0.246	2.8
4	0.745	0.258	2.41
	0.321	0.208	2.35

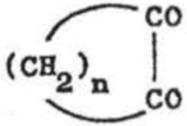
Table II. The Observed Second-Order Rate Constants in Dioxane at Various Temperatures

α-Diketone	Initial concn. (M)		10^4 k ($M^{-1}sec^{-1}$)			E_a	$\Delta S^{\ddagger}$ [a]	ln A
	[1]	[Diketone]	30.0°	35.0°	40.0°	(kcal/mol)	(eu)	($M^{-1}sec^{-1}$)
4	0.745	0.258	1.67	2.41	3.30	13.1	-32.0	13.0
n-BuCOCOBu-n[b]	0.803	0.302	3.01	4.07	5.33	11.0	-37.7	10.1

[a] Values at 35.0°.

[b] Reference 6.

Table III. Relative Second-Order Rate for the Reaction of Trimethyl Phosphite (1) with Alicyclic α-Diketones in Dioxane at 35.0°

 n	Initial concn. (M)		Oberved rate const. 10^4 k ($M^{-1}sec^{-1}$)	Approximate enol content of diketone (%) in dioxane		Rate const. with keto alone 10^4 k' ($M^{-1}sec^{-1}$)	Relative rate
	[1]	[Diketone]		25°	35°		
3 (2)	0.0954	0.0441	11	94-97^{a,c}	84-96^{a,c} 96^{b,c}	69-275	23-91
4 (3)	0.533	0.628	2.5	2^{a,d}	15-17^{a,d} 16^{b,e}	3.0	1
8 (4)	0.745	0.258	2.41			2.41	0.8
^{n}BuCOCOBu^n ^{f}	0.803	0.302	4.07			4.07	1.4

[a] Estimated by bromination method.[11a]

[b] Based on nmr spectra.

[c] Concentration of 0.881 M.

[d] Concentration of 1.26 M.

[e] Concentration of ca. 9.1 wt/wt %.

[f] Reference 6.

Table IV. The Observed Second-Order Dependence of Rate for the Reaction of 1 with Phenanthrenequinone (5a) and Acenaphthequinone (6) in Dioxane

α-Diketone	Temperature (°C)	Initial concentration, (M)		10^3 k
		[1]	[Diketone]	($M^{-1}sec^{-1}$)
5a	22	0.734	0.000870	2.40
		0.248	0.000870	2.53
6	33	0.329	0.0170	19.9
		0.165	0.0170	19.6
		0.329	0.00850	19.3

Table V. The Second-Order Rate Constants for the Reaction of Trimethyl Phosphite (1) with Phenanthrenequinone (5a) and Acenaphthenequinone (6) in Dioxane

α-Diketone	Initial concn. (M)		10^3 k ($M^{-1}sec^{-1}$)			E_a	$\Delta S^{\ddagger}$ [b] (eu)	ln A
	[1]	[Diketone]	20.0°	25.0°	30.0°	(kcal/mol)		($M^{-1}sec^{-1}$)
5a	0.210	0.0115	2.10	2.96	4.12	6.29	-30.2	15.3
6 [a]	0.0230	0.0108	7.84	10.8	14.8	5.94	-29.9	15.4

[a] The kinetics was done by measuring the uv spectra of the product.

[b] The values at 25.0°.

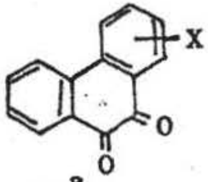
temperature (ca. 20°). But at higher temperature (ca. 30°) both rates agreed within experimental error and showed the second-order rate dependence (Table IV)

The substituent effect of **5** on k was measured at 21.5° and is shown in Table VI. The Hammett plot with ordinary σ gives a straight line, which is in contrast to that for monosubstituted benzil.[5] The ρ value was calculated by the least square method to be +1.5 (σ) with a correlation coefficient (r) of 0.99.[12] This indicates a nucleophilic attack of phosphorus atom on carbonyl group of α-diketone. The reduction potentials of these diketones[13] correlate with the logarithm of relative rates. (Figure 1 shows the plot).

6.4 Discussion

The probable reaction mechanism of trialkyl phosphite with α-diketone may involve a rate-determining attack of a phosphorus atom of phosphite either on a carbonyl carbon atom or an oxygen atom of α-diketone. As reported previously, addition of acids accelerated the reaction of trimethyl phosphite with benzil.[4] The substituent effect in benzil gave a Hammett's correlation with σ better than with σ^- or with σ^+, and it afforded a large positive ρ value for symmetrically disubstituted benzils, while that for monosubstituted benzils gave two different positive values (one is for electron-attractive groups and the other is for electron-releasing groups).[5] The substituent effect in phosphites fits Taft's equation: $\log (k/k_o) = -3.28\sigma^* + 0.40 E_s$.[7] Furthermore, Taft's steric substituent constant (E_s) alone controlls the

Table VI. The Substituent Effect on the Rate of the Reaction of Trimethyl Phosphite (1) with Phenanthrenequinones (5a-e) in Dioxane at 21.5° ± 0.5°

 X[a]		Initial concn. (M)		10^3 k	Logarithm of relative rate	Hammett's σ value[b]	Reduction potential[c]
		[1]	[5]	($M^{-1}sec^{-1}$)			E_o (mV)
H	(5a)	0.248	0.000870	2.4	0.00	0.00	458
2-NO_2	(5b)	0.248	0.000818	25	1.01	0.71	540
3-Br	(5c)	0.248	0.000477	3.5	0.17	0.23	499
2-NH_2	(5d)	0.248	0.000583	1.5	-0.21	-0.16	443
3-OMe	(5e)	0.497	0.000819	0.71	-0.53	-0.27	419

[a] 2- And 3-positions correspond to m- and p-positions, respectively.

[b] Reference 12.

[c] Reference 13.

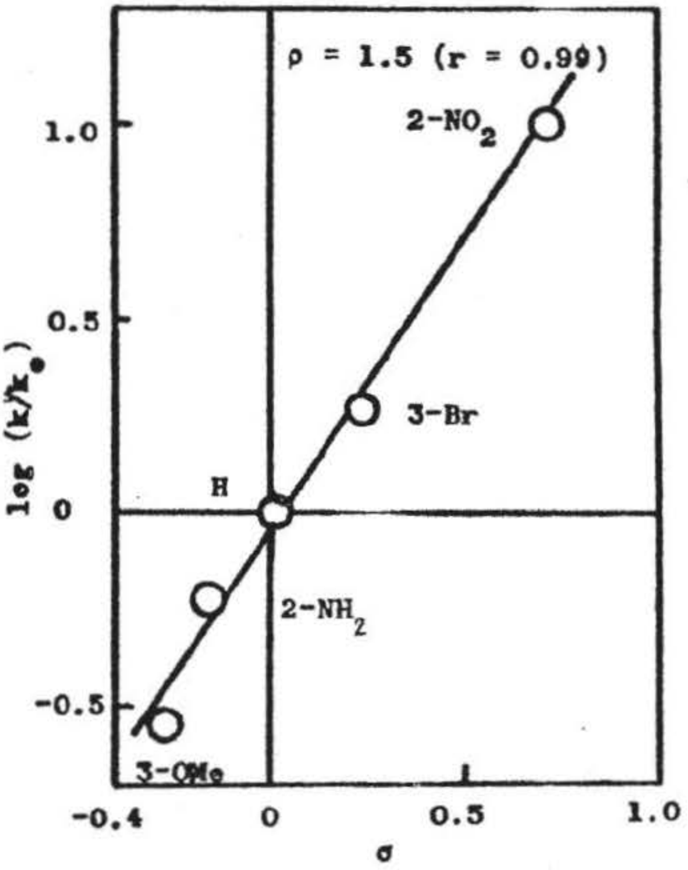
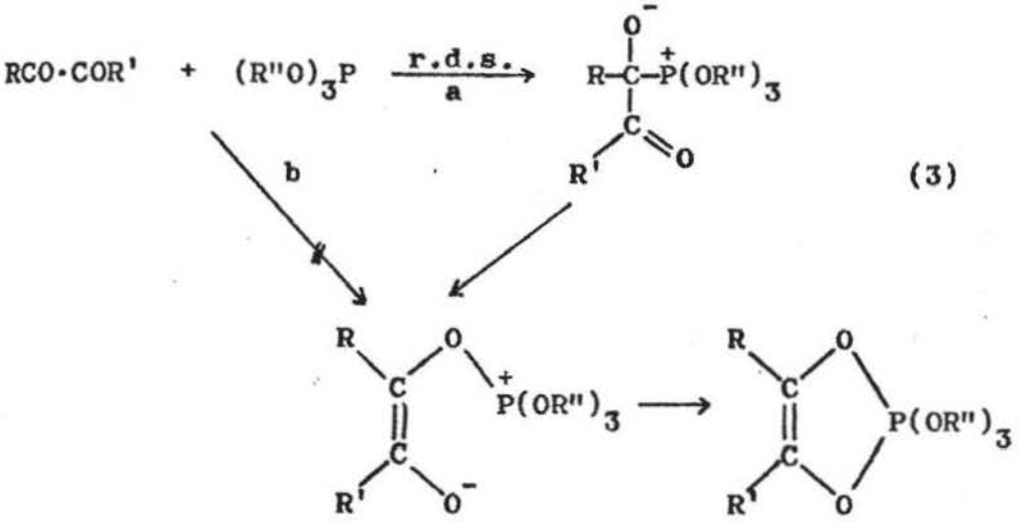


Figure 1. The Hammett's plot for the reaction of trimethyl phosphite (1) with substituted 9,10-phenanthrenequinones (5a-e) in dioxane at 21.5°.

rate of the reaction of trimethyl phosphite with aliphatic α-diketones.[6] These evidences suggest that the reaction may involve a rate-determining nucleophilic attack of phosphorus atom on the carbonyl carbon atom (path a), but not on carbonyl oxygen atom (path b).



(3)

Here, R and R' may be either alkyl or aryl group, and R" is alkyl group. The hybridization of carbonyl carbon atom changes from sp^2 to sp^3 at the rate-determining step, thus the effect of ring strain of alicyclic α-diketones is expected.

The kinetic study on the reaction of biacetyl with cyclic phosphites[10] shows that the phosphorus atom has the sp^3 hybridization in the transition state, because cyclic phosphite with rigid structure retards the rate, but this result cannot distinguish whether the attack of phosphorus atom occurs on a carbonyl carbon or oxygen atom.

The keto-enol equilibulia for **2** and **3** are slow,[11] hence it may be assumed that the concentration of enol tautomer is constant during the kinetic study.

7 8

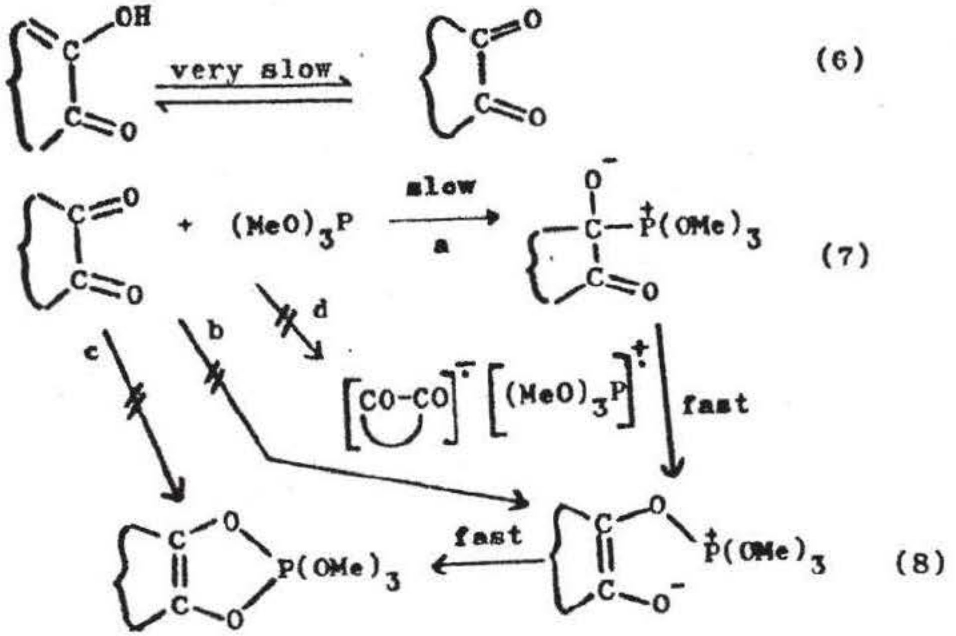
(4)

Therefore, the rate is expressed as:

$$v = k'[1][7] \tag{5}$$

The observed k' value are shown in Table III. Cyclopentane-1,2-dione (2) reacts 20-90 times as fast as cyclohexane-1,2-dione (3). The observed rate enhancement for 2 is attributable to the ring strain effect, but not to the acid catalysis of the enol tautomer, because the concentration of 2 and 3 differs by a factor of 14 (Table III). The diimide reduction of cyclopentene is 16 time as fast as that of cyclohexene.[14] The analogus effect of ring size suggests that both the reaction have an analogous transition state, i.e., a sp^3 hybridized carbon atom. The change from sp^2 to sp^3 releases the strain for 2 but not so much for 3, because the angle of 109°28' (sp^3) is more desirable for a pentagon than a hexagon. This higher reactivity of cyclopentanedione is also observed with 5a and 6, i.e., the order of the reactivity for 1 is 6 > 5a. These facts suggest a nucleophilic attack of the phosphorus atom on the carbonyl carbon atom (path a), but not on the carbonyl oxygen atom (paths b and c), since there is no change of hybridization on the carbon atom in paths b and c (Scheme I). The one-electron transfer mechanism (path d) is also eliminated.[6]

On the basis of the concept of "hard" and "soft" acids and bases,[15] $(RO)_3P$ and >CO are a soft base and hard acid,



Scheme I. The probable reaction mechanism of cyclic α-diketones with trimethyl phosphite (1). (9,10-Phenanthrenequinone (5a) and acenaphthenequinone (6) do not require keto-enole equilibrium.)

respectively.[16] Since the bonding between soft base and hard acid is weak, the rearrangement of phosphorus atom from carbon to oxygen atom should easily occur (eq 8).

The Hammett equation is applicable with phenanthrenequinone (5a-e). The obtained positive ρ value coincides with the proposed mechanism above. The order of reactivity of 5a-e agrees with the easiness of reduction, which is estimated by the reduction potential[13] as a measure of the electrophilicity of carbonyl group.

The Hammett plot gave a line bent at the origin with benzils,[5] but not with 5a-e. The configuration of two carbonyls of 9,10-phenanthrenequinone is reported to be complete cis, but that of benzil is skew on the basis of the dipole moment.[17] Therefore, the substituent effect transmitted through the carbonyl group may be more effective with 5 than benzil by more effective conjugation, and hence give rises to the difference between two plots, i.e., monosubstituted benzil gave a bent line in the Hammett plot, while 5 gives a straight line.

The twist angle (θ) of two carbonyl groups in alicyclic α-diketone increases with increasing size of ring ($0 \lesssim \theta \lesssim 180°$),[18] i.e., the values of θ is reported to be 0-10°, 0-60°, 90-110°, 100-140°, and 100-180° for five-, six-, seven-, eight-, and eighteen-membered cyclic α-diketones, respectively, and 90-180° for open chain aliphatic α-diketones. In view of the kinetic data for cyclic and acyclic aliphatic α-diketones with $(MeO)_3P$, the relative rate for 3, 4, and n-BuCOCOBu-n is almost the same. Therefore, the steric effect[6] seems to have much more influence than the twist angle effect. This may also eliminate the synchronous attack of phosphite on carbonyl oxygen atoms.

Provided that no ring strain is concerned during the reaction, aromatic α-diketones such as benzil, 5a and 6 are much reactive toward 1 than aliphatic α-diketones. This may be explicable by Taft's σ^* value, i.e., the polar substituent constant for aromatic groups, has a positive value (electron-attracting), while that for alkyl groups has a negative value (electron-releasing), thus the electrophilicity of aromatic α-diketones becomes to be larger than that of aliphatic ones.

The reaction with 6 is curious, i.e., at lower temperature (below 20°) the consumption of diketone is much faster than the appearance of 1:1 adduct on the basis of spectral change at least. This strange phenomenon at lower temperature is still under study.

6.5 Experimental

Materials. Cyclopentane-1,2-dione (2) was prepared by decarboxylation of adipic acid[19] followed by bromination and treatment with FeCl$_3$,[20] bp 60-62°/4 mm (lit.[20] bp 78-86°/8 mm), mp 54-55° (lit.[20] mp 55-56°), overall yield 4%. Cyclohexane-1,2-dione (3) was prepared by oxidation of cyclohexanone with SeO$_2$,[21] bp 81-82°/19 mm (lit.[21] bp 75-79°/16 mm), mp 38° (lit.[11] mp 38°), yield 45% (based on SeO$_2$). Cyclodecane-1,2-dione (4) was prepared by intramolecular acyloin reductive condensation of diethyl sebacate[22] followed by oxidation of sebacoin with CrO$_3$,[23] bp 81-84°/4 mm (lit.[23] bp 104-105°/10 mm), overall yield 9%. 9,10-Phenanthrenequinone (5a) was prepared by CrO_3 oxidation of phenanthrene,[24] mp 210° (lit.[24] mp 208.5-210°), yield 51%. 2-Nitro-9,10-phenanthrenequinone (5b) was prepared by nitration of 5a with excess 63% nitric acid,[25] mp 261-262° (lit.[25] mp 264.8-265.3°), yield 23% (recrystallization from chlorobenzene). 3-Bromo-9,10-phenanthrenequinone (5c) was prepared by photobromination of 5a in the presence of BPO (5a:Br_2 = 1:1.2),[26] mp 254-255° (recrystallization from acetic acid) (lit.[26] mp 264-266°), yield 86%. 2-Amino-9,10-phenanthrenequinone (5d) was prepared by reduction of 5b with Sn-HCl,[27] mp 190-195° (decompd.) [lit.[27] mp 213° (decompd.)], yield 60%. 3-Methoxy-9,10-phenanthrenequinone (5e) was prepared by the reaction of sodium methoxide with 5c in methanol, mp 200-205° (lit.[28] mp 209-209.5°), yield 30%. Acenaphthenequinone (6) was prepared by $Na_2Cr_2O_7$ oxidation of acenaphthene,[29] and purified by sublimation and then by recrystallization from *o*-dichlorobenzene, mp 261° (lit.[29] mp 259-260°), yield 52%. Trimethyl phosphite (1) was purified by distillation with metallic Na under N_2, bp 58°/116 mm (lit.[30] 111-112°). Trimethyl phosphite (1)-5a (1:1) adduct was prepared by the reaction of 5a with excess 1 at room tempertture under N_2 without solvent or in dioxane for ca. 10 hr. The other 1-cyclic α-diketone (1:1) adducts were prepared by the same method. Solvents were dried and purified by the ordinary methods before use.

Ultarviolet Spectra. Ultraviolet spectra of α-diketones and 1-cyclic α-diketone (1:1) adducts were measured in dioxane or in n-hexane by Hitachi double beam 124 type uv spectrophotometer and/or Hitachi EPU-2A type photo-electric spectrophotometer. The data used for kinetic studies were as follows: compound, λ_{max}, $\log\varepsilon$, solvent; 2, 247nm, 3.55, dioxane; 2, 400 nm, 1.48, dioxane (shoulder); 3, 264 nm, 3.64, dioxane; 3, 400 nm, -0.46, dioxane(shoulder); 4, 392 nm, 1.00, dioxane; 5a, 245 nm, 4.41, n-hexane; 5a, 250 nm, 4.45, n-hexane; 5a, 313 nm, 3.42, n-hexane; 5a, 393 nm, 2.98, dioxane; 5b, 378 nm, 3.52, dioxane; 5c, 381 nm, 3.04, dioxane; 5d, 390 nm, 3.11, dioxane; 5e, 380 nm, 3.09, dioxane; 6, 298 nm, 3.83, n-hexane; 6, 311 nm, 3.86, n-hexane; 6, 336 nm, 3.77, n-hexane; 6, 473 nm, 1.24, dioxane; 1-5a 1:1 adduct, 306 nm, 4.04, n-hexane; 1-5a 1:1 adduct, 319 nm, 4.09, n-hexane; 1-6 1:1 adduct, 317 nm, 3.77, n-hexane; 1-6 1:1 adduct, 337 nm, 3.73, n-hexane. All adducts had no λ_{max} in a visible region.

Products. The structure of the products was confirmed by means of uv and ir spectra.

Kinetic Procedure. The kinetic experiments for the reaction of 1 with 2-6 were carried out in a glass-stoppered flask or in a uv cell. The rate in dioxane was followed by estimating the remainlng α-diketone or appearing product by means of uv spectrophotometry at appropriate intervals of time. A solution which had reached the keto-enole equilibrium was used with 2 and 3 alone. The other kinetic procedure was the same as reported in the preceding chapters.[4]

Kinetic Analysis. Assuming the constancy of enol content during the kinetic experiments, and assuming the completion of reaction at the time when the change of ultraviolet or visible absorption becomes unappreciable, the second-order rate constant (k) was obtained as shown in Tables I and IV. The k value for 2 and 3 were corrected by the keto content to give rate constant with keto alone (k') in Table III. For the other α-diketones the k value were used for discussion.

Enol Content of 2 and 3. The enol content (%) of 2 and 3 in dioxane was measured by means of Br_2 titration of enol[11b] and/or nmr spectra at 25° and 35° after attainment of the equilibrium (after more than one day). The nmr spectra was as follows: compound, δ ppm from dioxane; 2, 3.06 (singlet, enol OH), 2.84 (triplet, vinyl proton adjacent to OH), and near -1.2 (multiplet, the other protons); 3, 3.54 (singlet, enol OH), 2.43 (triplet, vinyl proton adjacent to OH), and -0.75 - -2.35 (multiplet, the other protons).

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Chapter 7

CONCLUSION

7 CONCLUSION

7.1 The Reaction Mechanism

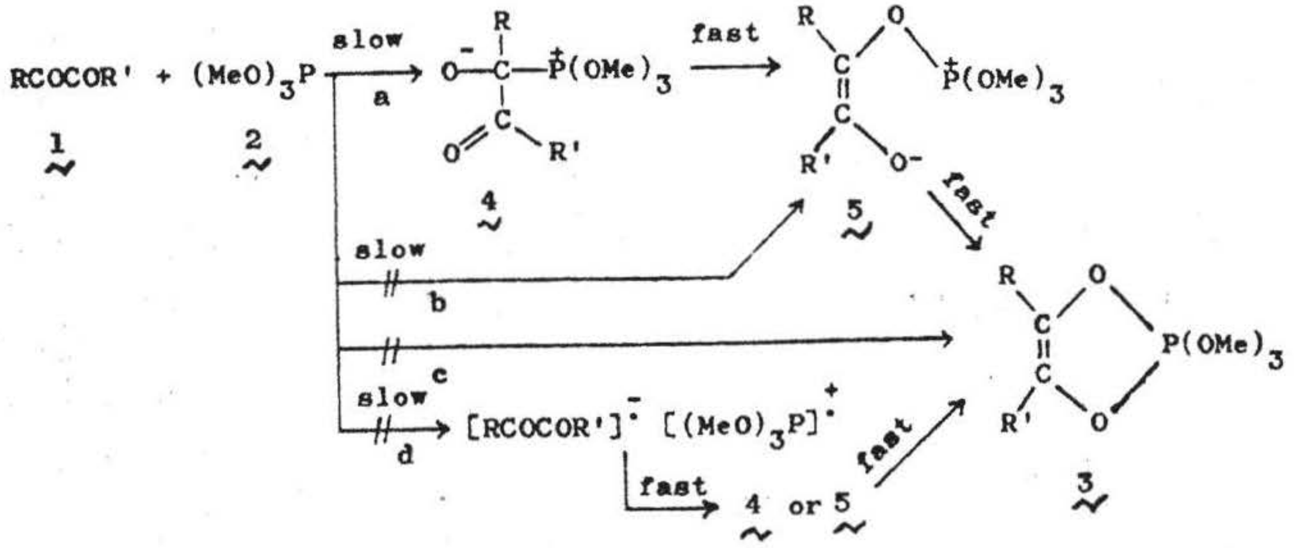
The reaction of trialkyl phosphites with α-diketones may proceed via path a in Scheme I, on the basis of the kinetic data described in Chapters 2-6.

The first addition step of phosphorus atom on carbonyl carbon atom is rate-determining. The steps 4 to 5 and 5 to 3 may be fast. The reverse reaction, or 4 to 1 + 2, will virtually unimportant if at all, since the successive step is faster than the reverse one.

The rearrangement of phosphorus atom from carbon to oxygen atom (4 to 5) is reasonably proposed in Perkow reaction under similar reaction condition to this one.[1]

The reasonable energy profile may be drawn as Figure 1. The reaction of phosphite with α-diketone is exothermic. The transition state will be close to the structure of 4, since the energy profile may be written as up-hill pattern. 4 is rather unstable because of the bonding between "soft" base of phosphorus atom and "hard" acid of carbonyl carbon atom,[2] therefore the next energy barrier to be passed will be low.

Scheme I. The Probable Reaction Mechanism of Trialkyl Phosphites with α-Diketones



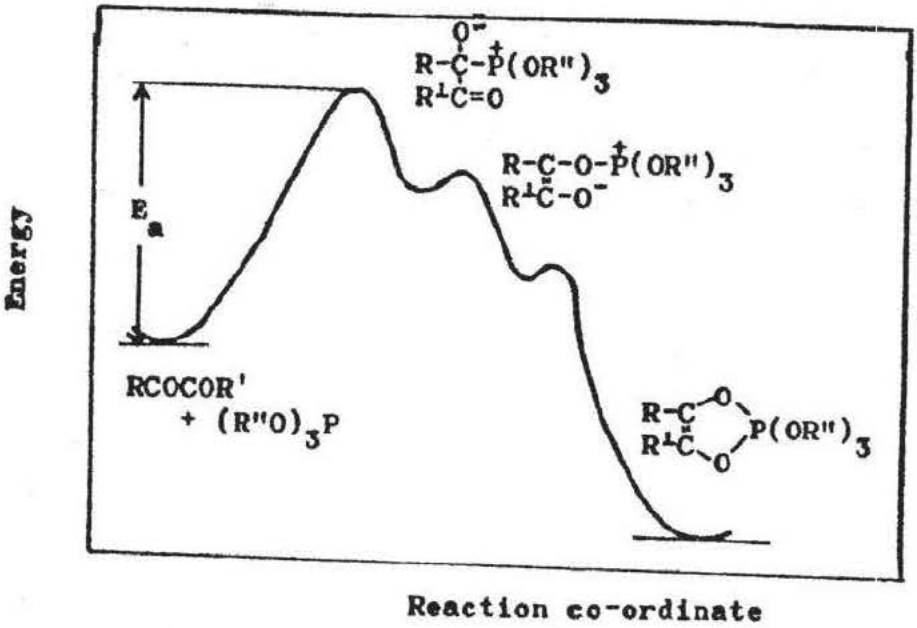


Figure 1. The probable energy profile for the reaction of trialkyl phosphites with α-diketones.

7.2 The Reaction Controlling Factors

The reaction of phosphite with α-diketone is entirely controlled by the bulky substituents in diketone (Chapter 5). The ring strain in the small ring α-diketone accelerates the reaction (Chapter 6). The bulky substituents in phosphite affords a little steric hindrance (Chapter 4). Essentially no effect of twist angle of CO-CO plain was observed (Chapter 6).

The more powerful the nucleophilicity of phosphite and the electrophilicity of carbonyl group of α-diketone became, the faster the reaction rate was observed. The more powerful the polarity and the acidity of solvent became, the faster the reaction became. These factors are listed in Table I.

Table I. The Rate Controlling Factors

Steric factor:	
	Bulkiness of substituents in α-diketone and phosphite
	Ring strain of α-diketone
	(Twist angle of CO-CO is minor factor)
Electronic factor:	
	Nucleophilicity of phosphite
	Electrophilicity of carbonyl group
Solvent:	
	Polarity of solvent
	Acidity of solvent (general acid catalysis)

7.3 Direct Detection of the Intermediate 4

All atempts to detect the intermediate 4 were in vain.[3] But there remains some possibility of detection of

4, when the first addition step could be much faster and the next step could be much slower than the reactions mentioned in Chapters 2-6 by changing these substrates used.

Finally, the author regrets that the more extensive studies on the reaction mechanism of trivalent phosphorus compounds with carbonyl compounds could not be performed during this period. He wishes that these reactions will be researched comprehensively.

7.4 References

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Appendix

KINETICS OF THE AUTOXIDATION OF SOME TRIVALENT PHOSPHORUS COMPOUNDS

Appendix

A KINETICS OF THE AUTOXIDATION OF DIALKYL PHENYLPHOSPHONITES[1]

A.1 Summary

The kinetics of autoxidation of dialkyl phenylphosphonites was studied in o-dichlorobenzene using 2,2'-azobisisobutyronitrile (AIBN) as a radical initiator. The reaction has a long chain length, its rate law being expressed as $-d[O_2]/dt = k[\text{AIBN}][\text{PhP(OR)}_2]$. A mechanism is postulated which involves R'O·, $R'O_2$·, and R'· as chain carriers and the unimolecular deactivation of $R'O_2$· as the termination. The substituent in the alkyl groups of ester affects little on the rate.

A.2 Introduction

It has been known that trivalent phosphorus compounds are autoxidized to pentavalent ones, which have a stable P=O bond.[2] The autoxidation of trialkylphosphine gives mainly corresponding phosphine oxide and phosphinate, while a small amount of phosphonate and phosphate.[3] A dadical mechanism involving R'·, R'O·, and $R'O_2$· has been postulated on the basis of the observed necessity of a radical initiator, the inhibition by a radical inhibitor, and the presence of inductive period.[3,4] The autoxidation of trialkyl phosphite is known to give corresponding phosphate.[5] The rate law for phosphine and phosphite were reported as eqs 1 and 2, respectively.[6]

$$-d[O_2]/dt = k[AIBN][R_3P]/p_{O_2} \qquad (1)$$

$$-d[O_2]/dt = k[AIBN][(RO)_3P] \qquad (2)$$

Here, p_{O_2} is the partial pressure of oxygen.

The autoxidation of phosphonite and phosphinite is little known.[7] The present appendix deals with the kinetic study on the autoxidation of dialkyl phenylphosphonites in *o*-dichlorobenzene using a radical initiator. The probable reaction mechanism will be discussed.

A.3 Results

Autoxidation of Dimethyl Phenylphosphonite (**1**). The autoxidation of dimethyl phenylphosphonite (**1**) at 60-80° with AIBN gave quantitatively dimethyl phenylphosphonate. The observed stoichiometry is shown in Table I, and expressed as eq 3. No reaction of **1** with AIBN or *o*-dichlorobenzene was observed.

$$PhP(OR)_2 \quad + \quad \frac{1}{2}\,O_2 \quad \xrightarrow{AIBN} \quad PhP(O)(OR)_2 \qquad (3)$$

(**1**) R = Me
(**2**) R = Et
(**3**) R = i-Pr

Effect of Initial Concentration of **1**. The autoxidation of dimethyl phenylphosphonite (**1**) in *o*-dichlorobenzene with AIBN was followed by measuring the consumption of O_2 in the apparatus previously reported.[8] The effect of concentration of **1** at a constant partial pressure of O_2 (p_{O_2}) and at a constant concentration of AIBN is shown in Table II. The pseudo-first-order rate constant holds constancy up to 70-85% conversion.

Effect of Concentration of AIBN. The effect of the concentration of AIBN at a constant partial pressure of O_2 and a constant concentration of **1** was shown in Table III. No reaction was observed without the radical initiator.

Effect of Partial Pressure of O_2. The effect of p_{O_2} on the rate was measured at constant concentration of **1** and AIBN. The zero-order dependance on p_{O_2} was observed as shown in Table IV.

Rate Law. Tables II-IV show that the rate law of autoxidation of dimethyl phenylphosphonite (**1**) in *o*-dichlorobenzene is expressed as

$$v = -d[O_2]/dt = k[PhP(OMe)_2][AIBN] \qquad (4)$$

and the value of k was calculated to be 0.105 (M^{-1} sec^{-1}).

Effect of Substituent in Dialkyl Phenylphosphonites. The effect of substituent R of $PhP(OR)_2$ on the autoxidation rate was estimated in *o*-dichlorobenzene at 60.0°. The rate law for $PhP(OR)_2$ [R = Et (**2**) and R = i-Pr (**3**)] was the same as that of $PhP(OMe)_2$. The second-order rate constants (k) for R at 60.0° were Me, 0.105; Et, 0.110; and i-Pr, 0.112 (M^{-1} sec^{-1}).

The Taft plot for $PhP(OR)_2$ gives a ρ^* value of -0.058 (correlation coefficient, r, -0.95).

A.4 Discussion

The autoxidation of trialkylphosphine and trialkyl

Table I. The Stoichiometry in Autoxidation of Dimethyl Phenylphosphonite in o-Dichlorobenzene at 60.0° [a]

$PhP(OMe)_2$ (10^{-4} mol)	O_2 absorption (10^{-4} mol)	Molar ratio of $O/PhP(OMe)_2$
5.55	2.68	0.97
6.61	3.24	0.98

[a] 5×10^{-6} Mol of AIBN was used.

Table II. Effect of Concentration of Dimethyl Phenylphosphonite on the Autoxidation Rate in o-Dichlorobenzene at 60.0°

Partial pressure of O_2, (mmHg)	$[PhP(OMe)_2]_o$ [a] (10^{-2}M)	$[AIBN]_o$ [a] (10^{-3} M)	10^4 k (sec^{-1})
200	1.31	5.39	5.00
200	3.92	5.39	4.02
200	6.54	5.39	4.84
		Av.	4.62

[a] $[\ ]_o$ means initial concentration.

Table III. Effect of Concentration of AIBN on the Rate of Autoxidation of $PhP(OMe)_2$ in o-Dichlorobenzene at 60.0°

Partial pressure of O_2, (mmHg)	$[PhP(OMe)_2]_o$ [a] (10^{-2} M)	$[AIBN]_o$ [a] (10^{-3} M)	$10^4 k_a$ (sec^{-1})
200	5.94	9.25	10.4
200	5.94	4.62	4.50
200	5.94	2.31	3.22
200	5.94	0	0

[a] $[\ ]_o$ means initial concentration.

Table IV. Effect of Pattial Pressure of O_2 on the Rate of Autoxidation of $PhP(OMe)_2$ in o-Dichlorobenzene at 60.0°

Partial pressure of O_2, (mmHg)	$[PhP(OMe)_2]_o$ [a] (10^{-2} M)	$[AIBN]_o$ [a] (10^{-3} M)	$10^4 k_a$ (sec^{-1})
420	5.55	4.42	6.17
200	5.55	4.42	6.17
100	5.55	4.42	6.15
		Av.	6.16

[a] $[\ ]_o$ means initial concentration.

phosphite was reported to involve a radical mechanism.[3,4] The autoxidation of dialkyl phenylphosphonite was also found to involve a radical mechanism, since no autoxidation occurs without AIBN, which was confirmed by means of glc analysis of the reaction product.

The zero-order dependance on p_{O_2} was observed over a range of 25-420 mm Hg of p_{O_2}. The same phenomenon has been observed in the autoxidation of tributyl phosphite.[6] This suggests a mechanistic similarity of the autoxidation of phosphonite to that of phosphite.

The first-order dependance on AIBN concentration suggests that the autoxidation may involve a unimolecular termination.[9] The autoxidation product of dialkyl phenylphosphonites was the corresponding phosphonates. These results suggest the following mechanism.

$$\mathrm{AIBN} \xrightarrow{k_i} 2\mathrm{R'}\cdot + \mathrm{N_2} \qquad (5)$$

$$\mathrm{R'}\cdot + \mathrm{O_2} \xrightarrow{k_1} \mathrm{R'O_2}\cdot \qquad (6)$$

$$\mathrm{R'O_2}\cdot + \mathrm{PhP(OR)_2} \xrightarrow{k_2} \mathrm{PhP(O)(OR)_2} + \mathrm{R'O}\cdot \qquad (7)$$

$$\mathrm{R'O}\cdot + \mathrm{PhP(OR)_2} \xrightarrow{k_3} \mathrm{PhP(O)(OR)_2} + \mathrm{R'}\cdot \qquad (8)$$

$$\mathrm{R'O_2}\cdot \xrightarrow{k_t} \text{inactive product} \qquad (9a)$$

$$\mathrm{R'O}\cdot \xrightarrow{k'_t} \text{inactive product} \qquad (9b)$$

Here, R is Me, Et, and i-Pr, and R' is $\mathrm{Me_2CCN}$. Even if O_2 may be producd from steps 9a and 9b the amount of formed O_2 is negligible when the radical chain length is long enough. Thus the rate of absorption of O_2 is expressed as

$$v = -d[\mathrm{O_2}]/dt = k_1[\mathrm{R'}\cdot][\mathrm{O_2}] \qquad (10)$$

If the termination occurs via step 9a alone, the application of steady state method assuming approximate constant concentrations of $R'O_2\cdot$, $R'O\cdot$, and $R'\cdot$ as probable carriers leads to eqs 11, 12, and 13, respectively, since $k'_t[R'O\cdot] \sim 0$.

$$k_1[R'\cdot][O_2] = k_2[R'O_2\cdot][PhP(OR)_2] + k_t[R'O_2\cdot] \qquad (11)$$

$$k_2[R'O_2\cdot][PhP(OR)_2] = k_3[R'O\cdot][PhP(OR)_2] \qquad (12)$$

$$2k_i[AIBN] + k_3[R'O\cdot][PhP(OR)_2] = k_1[R'\cdot][O_2] \qquad (13)$$

Combination of eqs 11 and 13 gives

$$\begin{aligned}2k_i[AIBN] &+ k_3[R'O\cdot][PhP(OR)_2] \\ &= k_2[R'O_2\cdot][PhP(OR)_2] + [R'O_2\cdot]\end{aligned} \qquad (14)$$

On the other hand, eq 12 leads to

$$k_2[R'O_2\cdot] = k_3[R'O\cdot] \qquad (15)$$

Eqs 14 and 15 give

$$[R'O\cdot] = \frac{2k_ik_2}{k_3k_t}[AIBN] \qquad (16)$$

Eqs 13 and 16 give

$$[R'\cdot] = \frac{2k_i[AIBN] + (2k_ik_2/k_t)[AIBN][PhP(OR)_2]}{k_1[O_2]} \qquad (17)$$

Introduction of eq 17 into eq 10 gives

$$v = 2k_i[AIBN] + \frac{2k_ik_2}{k_t}[AIBN][PhP(OR)_2] \qquad (18)$$

Since $k_t \ll k_2$,

$$v = k[AIBN][PhP(OR)_2] \qquad (19)$$

Here, $k = 2k_ik_2/k_t$

If the termination is effected by step 9b alone, the application of steady state approximation with $R'O_2\cdot$, $R'O\cdot$, and $R'\cdot$ as carriers gives eqs 20, 21, and 22, respectively.

$$k_1[R'\cdot][O_2] = k_2[R'O_2\cdot][PhP(OR)_2] \qquad (20)$$

$$k_2[R'O_2\cdot][PhP(OR)_2] = k_3[R'O\cdot][PhP(OR)_2] + k'_t[R'O\cdot] \qquad (21)$$

$$2k_i[AIBN] + k_3[R'O\cdot][PhP(OR)_2] = k_1[R'\cdot][O_2] \qquad (22)$$

The analogous derivation above gives

$$v = 2k_i[AIBN] + \frac{2k_ik_3}{k'_t}[AIBN][PhP(OR)_2] \qquad (23)$$

Since $k'_t \ll k_3$,

$$v = k'[AIBN][PhP(OR)_2] \qquad (24)$$

Here, $k' = \dfrac{2k_ik_3}{k'_t}$

The other termination mechanisms (e.g., $R'\cdot \longrightarrow$ inactive product or simultaneous reactions of 9a and 9b) lead rate equations conflicted with the observed rate law. In general, $R'O\cdot$ seems to be more reactive than $R'O_2\cdot$ with dialkyl phenylphosphonites. Therefore, the unimolecular termination of $R'O_2\cdot$ is more probable than that of $R'O\cdot$.

The substituents in dialkyl phenylphosphonites affect little on the rate, i.e., ρ^* value of -0.058. This fact suggests that the stability of P=O bond[10] affects the autoxidation rate much more than that of the radical intermediate.

The radical chain length (C. L.) was calculated to be 200-2000 by means of eq 25, using values of a = 0.6 and $k_i = 3.2\times10^{-6}\ \mathrm{sec}^{-1}$.[6]

$$\begin{aligned} \text{C. L.} &= (k_2[R'O_2\cdot] + k_3[R'O\cdot])[PhP(OR)_2]_o/2ak_i[AIBN]_o \\ &= k_a[PhP(OR)_2]_o/2ak_i[AIBN] \qquad (25) \end{aligned}$$

Here, a is the efficiency of initiation and k_i is the decomposition rate of radical initiator (AIBN), and k_a is apparent first-order rate constant.[6]

A.5 Experimental Section

Materials. Phenylphosphonous dichloride was prepared by the Friedel-Crafts reaction of benzene with PCl_3,[11] bp 101-104°/17 mm (lit.[11] bp 68-70°/1 mm), yield 68%. Dimethyl phenylphosphonite was prepared by the esterification of phenylphosphonous dichloride,[12] bp 101-102°/23 mm (lit.[12] bp 98°/ 17 mm), yield 30%. Diethyl and diisopropyl phenylphosphonite were also prepared by the similar procedure, bp and yield were 78-79°/8 mm (lit.[13] bp 110-111°/10-13 mm), 27% and 82-85°/8 mm (lit.[14] bp 121-122°/10 mm), 11%, respectively. Dimethyl phenylphosphonate was prepared by the Ullmann reaction of trimethyl phosphite with iodobenzene,[15] bp 122-125°/7 mm (lit.[15] bp 115°/0.9 mm), yield 35%. Diisopropyl phenylphosphonate was prepared by the esterification of phenylphosphonic dichloride, bp 116-117°/3 mm (lit.[15] bp 94°/0.1 mm), yield 33%. All phosphonates were identified by ir (a Perkin-Elmer Model 337 spectrophotometer) and nmr (a JNM-C-60HL spectrometer). Commercial solvents, AIBN, O_2 and N_2 were purified by ordinary methods and used.

Product Analysis. The autoxidation product of dialkyl phenylphosphonite was confirmed to be the corresponding phosphonate alone by means of glc (a Yanagimoto GCG 550F gas chromatograph with a flame ion detector) with 3% Apiezone Grease L on Cellite 545 using programming attachment.

Kinetic Procedure. The autoxidation apparatus has been reported previously.[8] A typical kinetic run was as follows: O_2 gas at 200 mm Hg and N_2 gas at 350 mm Hg were mixed in the apparatus and introduced into the reaction vessel at 60.0° containing 6.54×10^{-2} M dimethyl phenylphosphonite in o-dichlorobenzene (10 ml), then 5.39×10^{-3} M AIBN in o-dichlorobenzene (1 ml) was run into it from buret. The reaction was started with vigorous stirring. The partial pressure difference between the reaction mixture and the reference solution was measured at appropriate intervals of time. The observed pseudo-first-order rate constant (k_a) was calculated by

$$\log (a-2x) = -\frac{2}{2.303} k_a t + \log a \qquad (26)$$

Here, a and (a-2x) are the concentration of substrate at the atart and at time t, respectively.

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B KINETICS OF THE AUTOXIDATION OF TRIMETHYL PHOSPHITE, METHYL DIPHENYLPHOSPHINITE, AND TRIPHENYLPHOSPHINE[1]

B.1 Summary

Autoxidation of trimethyl phosphite (**1**), methyl diphenylphosphinite (**2**), and triphenylphosphine (**3**) has been studied kinetically in o-dichlorobenzene at 60.0° using 2, 2'-azobisisobutyronitrile (AIBN) as a radical initiator. The autoxidation proceeded after a short induction period to give predominantly the corresponding pentacovalent phosphorus compounds. The rates are always independent of oxygen pressure and the rate law for **1** and **2** is $v = -d[O_2]/dt = k'_2[\text{AIBN}][\text{substrate}]$, which was analogous to that for dimethyl phenylphosphonite. On the other hand, the rate law for **3** was $-d[O_2]/dt = k'_1[\text{AIBN}](1 + k'_2[\text{substrate}])$. The autoxidation may have a radical mechanism involving chain carriers $R\cdot$, $RO\cdot$, and $RO_2\cdot$. The different kinetic behaviour of **3** is atributable to the stability of a radical carrier, $Ph_3\dot{P}O_2R$, and resulting lower reactivity of $RO_2\cdot$ with Ph_3P. The rate constants decrease in the order: **2** > **1** > **3**. The application of Taft equation, $\log(k/k_0) = \rho^* \sum\sigma^*$, to these compounds, **1**, **2**, and $PhP(OMe)_2$, gives a ρ^* value of -0.380, which implies a mechanism involving a nucleophilic attack of phosphorus atom.

B.2 Introduction

It is known that trivalent phosphorus compounds such as trialkylphosphine and trialkyl phosphite are autoxidized photochemically or in the presence of a radical initiator.[2,3] The main products were pentacovalent phosphorus compounds.

$$P(OEt)_3 \xrightarrow[\text{peroxide}]{O_2} P(O)(OEt)_3 \qquad (1)$$

$$PBu_3 \xrightarrow[\text{radical source}]{O_2} \underbrace{P(O)Bu_3 + P(O)(OBu)Bu_2}_{\text{major products}} +$$

$$\underbrace{P(O)(OBu)_2Bu + P(O)(OBu)_3}_{\text{minor products}} \qquad (2)$$

A few workers have reported the kinetic studies on their autoxidation, where the rate laws were $v = k[AIBN][Bu_3P]/p_{O_2}$ and $v = k[AIBN][(RO)_3P]$.[4] The autoxidation of phosphinites and phosphonites has been scarcely known.[5,6] The previous kinetic study on the autoxidation of dialkyl phenylphosphonites revealed the rate law of $v = k[AIBN][PhP(OR)_2]$, and relatively long chain process involving alkyl, alkoxy, and alkylperoxy radicals as mentioned in the appendix A.[7] The rate of autoxidation was reported to be in the order of $(BuO)_3P < Bu_3P$, but little systematic study has been known, and no convincing explanation of the order was presented.

This appendix reports the results of the kinetic study on the AIBN-initiated autoxidation of trimethyl phosphite, methyl diphenylphosphinite, and triphenylphosphine in o-dichlorobenzene, and the discussion about the effect of their structure including dimethyl phenylphosphonite.

B.3 Results

The autoxidation of trimethyl phosphite (**1**), methyl diphenylphosphinite (**2**), and triphenylphosphine (**3**) initiated by AIBN was conducted in *o*-dichlorobenzene at 60.0° at oxygen pressure of 50-550 mm Hg. The reaction products were analyzed by means of glc, tlc, and ir, and it was confirmed that **1** gave dominantly trimethyl phosphate, **2** gave methyl diphenylphosphinate, and **3** gave triphenylphosphine oxide. The rate of autoxidation were measured by manometric method,[6,7] at the total pressure of 550 mm Hg.

Stoichiometry. The observed stoichiometry is shown in Table I. As the table shows, the autoxidation of trivalent phosphorus compounds needs one gram atom equivalent of oxygen.

$$R^1R^2R^3P + \frac{1}{2}O_2 \xrightarrow[60°]{AIBN} R^1R^2R^3PO \qquad (3)$$

1; $R^1 = R^2 = R^3 = MeO$
2; $R^1 = R^2 = Ph$, $R^3 = MeO$
3; $R^1 = R^2 = R^3 = Ph$

Therefore, the observed pseudo-first-order rate constants (k_{1a}) were calculated by means of equation 4.

$$\log (a-2x) = -\frac{2}{2.303} k_{1a} t + \log a \qquad (4)$$

Here, a and a-2x are the concentrations of substrate at the start and at time t, respectively.

Autoxidation of $(MeO)_3P$. Autoxidation of $(MeO)_3P$ (**1**) was carried out in *o*-dichlorobenzene at the initial concentrations 1×10^{-2} - 1×10^{-1} M of **1** and 0 - 4×10^{-3} M of

AIBN at 60.0°. The observed pseudo-first-order rate constants are listed in Table II. As Table II shows, the rate law for **1** is expressed as equation 5. The rate is independent of oxygen pressure.

$$v = -d[O_2]/dt = k_{1a}[\mathbf{1}] = k'_2[\mathbf{1}][\mathrm{AIBN}] \qquad (5)$$

The second-order rate constant (k'_2) was calculated to be $8.34 \times 10^{-2}\ M^{-1}sec^{-1}$ (Table II).

Autoxidation of $Ph_2P(OMe)$. Autoxidation of $Ph_2P(OMe)$ (**2**) was carried out similary at the initial concentrations of $5 \times 10^{-3} - 4 \times 10^{-2}$ M of **2** and $0 - 5 \times 10^{-3}$ M of AIBN, the observed kinetic data being summerized in Table III. The zero-order dependence on oxygen pressure was also observed. The rate law is expressed as eq 6.

$$v = k_{1a}[\mathbf{2}] = k'_2[\mathbf{2}][\mathrm{AIBN}] \qquad (6)$$

The second-order rate constant (k'_2) is $3.76 \times 10^{-1}\ M^{-1}sec^{-1}$. The autoxidation of $Ph_2P(OMe)$ is faster than that of $PhP(OMe)_2$, since k'_2 for $PhP(OMe)_2$ is $1.05 \times 10^{-1}\ M^{-1}sec^{-1}$.[7]

Autoxidation of Ph_3P. Autoxidation of Ph_3P (**3**) was carried out in *o*-dichlorobenzene at 60.0° at the initial concentrations of $1 \times 10^{-2} - 8 \times 10^{-2}$ M of **3** and $0 - 1 \times 10^{-3}$ M of AIBN. The independence of rate on the partial pressure of oxygen and first-order dependence on AIBN concentration, i.e., $v = k''_1[\mathrm{AIBN}]$, was observed as shown in Table IV. The effect of the initial concentration of **3** is shown in Table V. The plot of zero-order rate constant (k_0) vs. initial concentration of **3** gave an intercept, which gave a value of 2.88×10^{-2} M sec^{-1} (Figure 1), the rate being expressed as eq 7.

$$v = k'_1[\mathrm{AIBN}](1 + k'_2[\mathbf{3}]) \qquad (7)$$

From the intercept and slope in Figure 1, the first-order

Table I. Stoichiometric Relationship for the Autoxidation of 1, 2, and 3 in *o*-Dichlorobenzene at 60°

Trivalent phosphorus compound (10^{-4} mole)		AIBN (10^{-5} mole)	Partial pressure of O_2 (mm Hg)	Consumed O_2 (10^{-4} mole)	O/P[a]
$(MeO)_3P$	6.50	1.64	400	2.64	0.93
	5.00	2.26	200	2.28	0.89
$Ph_2P(OMe)$	2.16	1.19	200	2.18	1.01
	2.16	1.19	100	2.25	0.98
	2.16	1.19	100	2.12	1.04
Ph_3P	4.78	1.24	200	2.37	0.99
	4.78	1.24	200	2.46	1.03
	4.78	1.24	400	2.29	0.96

[a] The ratio of consumed atomic oxygen to used trivalent phosphorus compound.

Table II. Autoxidation of **1** in *o*-Dichlorobenzene at 60.0°

Partial pressure of O_2, (mmHg)	Initial concentration, (M) $[\mathbf{1}]_o \times 10^2$	$[AIBN]_o \times 10^3$	$10^4 k_{1a}$ (sec^{-1})	$10^2 k'_2$ $(M^{-1} sec^{-1})$
50	10.8	2.78	2.18	7.99
100	10.8	2.78	2.02	
200	10.8	2.78	2.37	
400	10.8	2.78	2.29	
200	8.33	3.77	3.05	8.18
200	4.17	3.77	3.48	
200	2.08	3.77	2.94	
200	1.04	3.77	2.88	
200	8.33	1.89	1.73	8.81
200	8.33	0.943	0.821	8.72
200	8.33	0.471	0.451	9.58
200	8.33	0	0	—
Mean second-order rate constant				8.34

Table III. Autoxidation of $\underset{\sim}{2}$ in *o*-Dichlorobenzene at 60.0°

Partial pressure of O_2, (mmHg)	Initial concentration, (M) $[\underset{\sim}{2}]_0 \times 10^2$	$[AIBN]_0 \times 10^3$	$10^4\ k_{1a}$ (sec^{-1})	$10^2\ k'_2$ $(M^{-1}\ sec^{-1})$
100	4.12	1.98	7.48	3.94
200	4.12	1.98	7.91	
400	4.12	1.98	7.99	
550	4.12	1.98	7.77	
200	2.06	2.13	8.25	3.90
200	1.03	2.13	8.25	
200	0.515	2.13	8.47	
200	4.12	4.51	16.9	3.75
200	4.12	2.26	8.17	3.61
200	4.12	1.07	3.00	2.81
200	0.515	0	0	—
Mean second-order rate consatnt				3.76

Table IV. Autoxidation of $\underset{\sim}{3}$ in o-Dichlorobenzene at 60.0°

Partial pressure of O_2, (mmHg)	Initial concentration, (M)		$10^5 k_{1a}$ [a] (sec^{-1})	$10^3 k''_1$ [b] (sec^{-1})
	$[\underset{\sim}{3}]_o \times 10^2$	$[AIBN]_o \times 10^3$		
100	7.29	2.25	4.77	1.55
200	7.29	2.25	4.87	1.58
400	7.29	2.25	5.04	1.63
550	7.29	2.25	6.00	1.94
200	7.97	1.83	5.70	2.48
200	7.97	0.915	3.19	2.78
200	7.97	0.458	1.41	2.45
200	7.97	0	0	——

[a] Initial pseudo-first-order rate constant.

[b] The value of k''_1 was calculated by $k_{1a}[\underset{\sim}{3}]_o = k''_1[AIBN]_o$.

Table V. Rate Dependence on Initial Concentration of Substrate in Autoxidation of $\underset{\sim}{3}$ at 60.0°

Partial pressure of O_2, (mmHg)	Initial concentration, (M)		$10^5 k_{1a}$[a]	$10^7 k_o$[b]
	$[\underset{\sim}{3}]_o \times 10^2$	$[\mathrm{AIBN}]_o \times 10^3$	(sec^{-1})	$(\mathrm{M\ sec}^{-1})$
200	7.61	2.30	6.00	4.57
200	3.81	2.30	10.0	3.81
200	1.90	2.30	17.4	3.30
200	0.95	2.30	31.5	3.00

[a] Initial pseudo-first-order rate constant.

[b] The value of k_o was calculated by $k_{1a} [\underset{\sim}{3}]_o = k_o$.

Table VI. Substituent Effect in Trivalent Phosphorus Compounds on the Autoxidation Rate in o-Dichlorobenzene at 60.0°

Trivalent phosphorus compounds	$10^2 k'_2$ $(\mathrm{M}^{-1}\mathrm{sec}^{-1})$	$\log (k'_2/k'_{2o})$	$\sum\sigma^*$[b]
$P(OMe)_3$	8.34	0.000	4.38
$PhP(OMe)_2$[a]	10.5	0.100	3.52
$Ph_2P(OMe)$	37.6	0.654	2.66

[a] Reference 7.

[b] The sum of σ^* (σ^* values for Ph and OMe groups are +0.600 and +1.46, respectively).

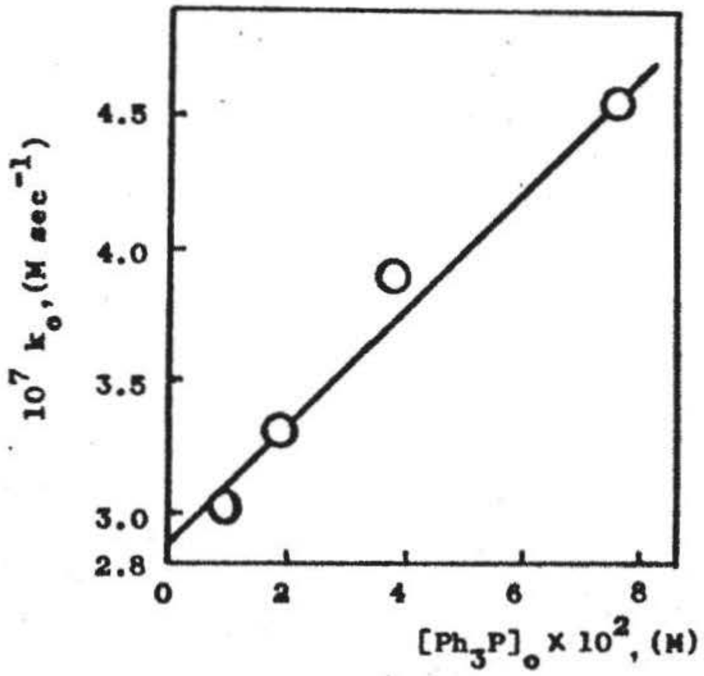

Figure 1. Plot of zero-order rate constant (k_o) vs. initial concentration of Ph_3P. The intercept is 2.88×10^{-4} M sec^{-1} and the slope is 2.22×10^{-6} sec^{-1}.

rate constant (k'_1) and the second-order rate constant (k'_2) were calculated to be 1.25×10^{-4} sec^{-1} and 1.78×10^{-2} $M^{-1} \times$ sec^{-1}, respectively.

B.4 Discussion

As shown in Tables II-IV, the autoxidation of 1-3 needs a radical initiator, which suggests the reaction may involve a radical mechanism, as known with trialkylphosphine and trialkyl phosphite.[2]

Autoxidation of 1 and 2. The observed independence of rate on oxygen pressure,[4] and first-order dependence on AIBN, as well as the formed products, the autoxidation of 1 and 2 may have a mechanism involving a unimolecular termination of $RO_2\cdot$ or less probably $RO\cdot$,[9] which is similar as that of autoxidation of dialkyl phenylphosphonite.[8]

$$\text{AIBN} \xrightarrow{k_i} 2R\cdot + N_2 \tag{8}$$

$$R\cdot + O_2 \xrightarrow{k_1} RO_2\cdot \tag{9}$$

$$RO_2\cdot + R^1R^2R^3P \xrightarrow{k_2} R^1R^2R^3PO + RO\cdot \tag{10}$$

$$RO\cdot + R^1R^2R^3P \xrightarrow{k_3} R^1R^2R^3PO + R\cdot \tag{11}$$

$$RO_2\cdot \xrightarrow{k_t} \text{inactive product} \tag{12a}$$

$$RO\cdot \xrightarrow{k'_t} \text{inactive product} \tag{12b}$$

Here, R^1, R^2, and R^3 represent phenyl or methoxy group, and $R\cdot$ is a radical species such as $Me_2\dot{C}CN$.

Even if O_2 may be produced from steps 12a and 12b, the amount of formed O_2 is negligible, if the chain length is long enough. Thus the rate of absorption of O_2 is expressed as eq 13.

$$v = -d[O_2]/dt = k_1[R\cdot][O_2] \qquad (13)$$

The application of the steady state method assuming the approximate constant concentrations of R·, RO·, and $RO_2\cdot$ leads to eq 14 as mentioned in the appendix A.[7]

$$v = 2k_i[AIBN] + \frac{2k_ik_2}{k_t}[AIBN][R^1R^2R^3P] \qquad (14)$$

When the chain is long enough, i.e., $k_t \ll k_2$, eq 14 leads to eq 15.

$$v = k[AIBN][R^1R^2R^3P] \qquad (15)$$

Where, $k = \dfrac{2k_ik_2}{k_t}$

Therefore, the autoxidation mechanism of 1 and 2 may be expressed by eqs 8-12. Since RO· is a reactive species more than $RO_2\cdot$, then eq 12a may be a predominant termination step.

Autoxidation of 3. Because of the observed rate law for 3 (eq 7), the first term in the right member of eq 14 cannot be neglected in this case. Then, eq 14 coincides with the observed rate law. This shows that eqs 8-12 are pperating in the mechanism for 3 and that k_2/k_t for 3 is smaller than that for 1 or 2 and $(k_2/k_t)[R^1R^2R^3P]$ is comparable to unity. This may be attributable to the stability of carrier radical, $R^1R^2R^3\dot{P}O_2R$ ($R^1 = R^2 = R^3$ = Ph) by resonance with phenyl groups.

Since the reactivity of RO· radical is known to be high, the rate constant k_3 may be larger than k_2.

Substituent Effect in Trivalent Phosphorus Compounds. The autoxidation rate which have a same rate law increase in the order: $P(OMe)_3 < PhP(OMe)_2 < Ph_2P(OMe)$. Application of Taft equation to their reaction rates gives eq 16 (Table

VI).

$$\log (k/k_o) = -0.380 \Sigma\sigma^* \quad (16)$$

Here, $\Sigma\sigma^*$ represents a sum of σ^* values for substituents in trivalent phosphorus compounds. The correlation coefficient (r) is -0.928. The negative ρ^* value implies that a radical attack of phosphorus atom in eqs 10 and 11 is of nucleophilic trend, i.e., $RO_2\cdot$ and $RO\cdot$ are electrophilic radicals toward the trivalent phosphorus compounds, although the trend is poor.

Taft equation was also applicable to the substituent effect in dialkyl phenylphosphonites, $PhP(OR)_2$ (R = Me, Et, and i-Pr).[7] The correlation was expressed as eq 17.

$$\log (k/k_o) = -0.058\ \sigma^* \quad (17)$$

The r value was -0.95. The observed smaller negative ρ^* value than that obtained in the present study may be attributable to the β-position of substituents for the reaction site.

It has been reported that the autoxidation rate of Bu_3P was faster than that of $(BuO)_3P$ by a factor of about 1.5.[4] This may be explained by the above substituent effect in trivalent phosphorus compounds qualitatively.

Radical Chain Length. The radical chain length (C. L.) may be calculated by means of eq 18,[6] using values of the efficiency of initiation (a) of 0.6 and the decomposition rate of radical initiator (k_i) of 3.2×10^{-6} sec^{-1}.[4]

$$C.\ L. = k_a[R^1R^2R^3P]_o/2ak_i[AIBN]_o \quad (18)$$

Here, k_a is an observed first-order rate constant. The calculated C. L. values were 500-5000, 1000-10000, and ca. 860 for **1**, **2**, and **3**, respectively; these agree with the proposed mechanism which has a long chain length.

B.5 Experimental Section

Materials. Trimethyl phosphite (1) was purified before use, bp 51°/83 mm (lit.[10] bp 111-112°). Methyl diphenylphosphinite (2) was prepared by disproportionation of $PhPCl_2$[11] followed by esterification, overall yield of 40%, bp 123-124°/3 mm (lit.[12] bp 151-152°/10 mm). Trimethyl phosphate was synthesized from $POCl_3$ and MeONa,[13] in a yield of 60%, bp 92°/21 mm (lit.[13] bp 73°/10 mm). Methyl diphenylphosphinate was prepared by the reaction of 2 with benzoyl peroxide (BPO), the crude product being used for glc analysis and ir spectra as an authentic sample. Triphenylphosphine oxide was synthesized from triphenylphosphine (3) and BPO.[14] Recrystallization from ligroin gave a yield of 91%, mp 156° (lit.[14] mp 153.5°). Commercial G.R. grade of 3 and AIBN were used. *o*-Dichlorobenzene was purified before use, bp 86-88°/41-43 mm.

Autoxidation of Trivalent Phosphorus Compounds. Autoxidation of 1, 2, and 3 was carried out with addition of ca. 0.1 mole equivalent of AIBN and at 200 mm of oxygen pressure in *o*-dichlorobenzene and/or in neat at 60.0° for 1-3 days. They consumed 0.5 mole equivalent of oxygen and dominantly gave corresponding pentacovalent phosphorus compounds, i.e., trimethyl phosphate, methyl diphenylphosphinate, and triphenylphosphine oxide, respectively. Trimethyl phosphate was identified by glc (Cromosorb W, acid washed, coated with 8% silicone SE 30; column temperature at 90°) using the authentic sample. Methyl diphenylphosphinate was identified by glc (Chromosorb W, acid washed, coated with 8% silicone SE 30; column temperature at 160°), tlc (silica gel; eluent, EtOAc:petroleum ether = 3:8), and ir spectra (1442 and 1017 cm^{-1} (P-Ph);[15,16] 1228 cm^{-1} (P=O)[17,18] in o-dichlorobenzene) comparing with the authentic sample. Triphenylphosphine oxide was identified by tlc (silica gel; eluent, EtOAc:petroleum ether = 3:7) compared with the authentic sample.

Kinetic Procedure. The apparatus for autoxidation has been reported previously.[8] A typical kinetic run was as follows: 4.12×10^{-2} M methyl diphenylphosphinite in o-dichlorobenzene (5 ml) and 1.98×10^{-3} M AIBN in o-dichlorobenzene (1 ml) were mixed in a reaction vessel of 96 ml, then gaseous O_2 at 200 mm and gaseous N_2 at 350 mm were mixed and introduced into the apparatus. The apparatus was soon thermostated at 60.0° and the autoxidation was started with vigorous magnetic stiring. The partial pressure difference between the reaction mixture and the reference solution was measured at appropriate intervals of time. The partial pressure of oxygen was corrected by at the temperature, and used for calculation. The observed pseudo-first-order rate constants (k_{1a}) were calculated by eq 4.

B.6 References

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