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Kinetic Study of the Reactions of Phenacyl Benzoates with Trialkyl Phosphites

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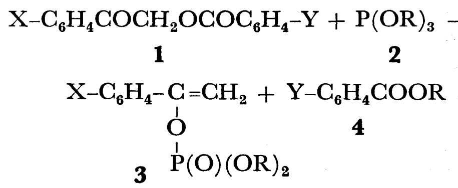
The reactions of phenacyl benzoates, $X\text{-}C_6H_4COCH_2OCOC_6H_4\text{-}Y$ (**1a**—**i**), with trialkyl phosphites (**2a**—**c**) giving dialkyl 1-arylvinyl phosphates (**3a**—**d**) in high yields were studied kinetically using the GLC technique. The overall reactions are second order, and exhibit a moderate solvent effect and catalysis upon the addition of certain organic acids. The activation energy, $E_a = 16.5$ kcal/mol, and entropy, $\Delta S^{\ne} = -38.5$ e.u., were obtained from the reaction of **1a** with **2b**, and the ρ value obtained using σ for reactions of the two series of **1a** with **2b** was $\rho_X = 3.4$ and $\rho_Y = 1.0$, respectively. The reactivity of **2** in this reaction is markedly increased in the order, Me<Et<*i*-Pr. These and other data accumulated support a mechanism for this reaction involving a rate-determining addition of phosphorus atoms in **2** to the carbonyl carbon of the phenacyl group followed by rearrangement of the phosphorus moiety to the carbonyl oxygen of the phenacyl group.

Various studies have been published on the scope and mechanism of the Perkow reaction with α-halo ketones.[1–8] It is well known that the reactions of these ketones with trialkyl phosphites (**2**) lead to ketophosphonates (the Arbuzov reaction) and/or enol phosphates (**3**) (the Perkow reaction) (Scheme 1), and that the nature of the halogen atom in the α-halo ketones and the reaction temperature have a substantial effect on the course of the reaction.

It has been found that the reactions of phenacyl benzoates (**1**) with **2** form only **3** in high yields.[9] In this paper, kinetic studies on the reactions of two series of **1** with **2**, and to discuss the mechanism of the reactions.



$$\underset{\mathbf{1}}{X\text{-}C_6H_4COCH_2OCOC_6H_4\text{-}Y} + \underset{\mathbf{2}}{P(OR)_3} \longrightarrow \underset{\mathbf{3}}{X\text{-}C_6H_4\text{-}\underset{\substack{| \\ O \\ | \\ P(O)(OR)_2}}{C}{=}CH_2} + \underset{\mathbf{4}}{Y\text{-}C_6H_4COOR}$$

1a: X=H, Y=H
1b: X=H, Y=*p*-CH$_3$
1c: X=H, Y=*p*-CH$_3$O
1d: X=H, Y=*m*-CH$_3$
1e: X=H, Y=*p*-Cl
1f: X=H, Y=*m*-Cl
1g: X=*p*-CH$_3$, Y=H
1h: X=*p*-CH$_3$O, Y=H
1i: X=*p*-Cl, Y=H
1j: X=2,4,6-(CH$_3$)$_3$, Y=H

2a: R=CH$_3$
2b: R=C$_2$H$_5$
2c: R=(CH$_3$)$_2$CH

3a: X=H, R=C$_2$H$_5$
3b: X=*p*-CH$_3$, R=C$_2$H$_5$
3c: X=*p*-CH$_3$O, R=C$_2$H$_5$
3d: X=*p*-Cl, R=C$_2$H$_5$

Scheme 1.

Results

The reaction of **1** with **2**, which quantitatively yields enol phosphates (**3**), was studied kinetically in solution using the GLC technique (see Experimental). The reactions obey good second-order kinetics, and are first order with respect to both **1** and **2**, as shown by linear plots of log $(a-x)/(b-x)$ *vs.* time. The relative constancy of k_2 for the reaction of **1a** with **2b** for differing ratios of reactants is shown in Table 1. The rate law is expressed as

$$v = k_2[\text{triethyl phosphite}][\text{phenacyl benzoate}]. \quad (1)$$

TABLE 1. REACTION OF **1a** WITH **2b** AT 140 °C IN TETRALIN

[**1a**], M	[**2b**], M	[**2b**]/[**1a**]	$10^4 k_2$, $M^{-1} s^{-1}$
0.40	0.40	1.0	1.13
0.20	0.80	4.0	1.16
0.50	0.30	0.6	1.19

TABLE 2. REACTION OF PHENACYL BENZOATES (**1a**—**i**) WITH **2b** AT 140 °C IN TETRALIN[a)]

Compound	$10^4 k_2$, $M^{-1} s^{-1}$
1a	1.16
1b	0.77
1c	0.72
1d	1.23
1e	2.22
1f	3.40
1g	0.28
1h	0.11
1i	5.14

a) 0.2 M/l of **1**, 0.8 M/l of **2b**.

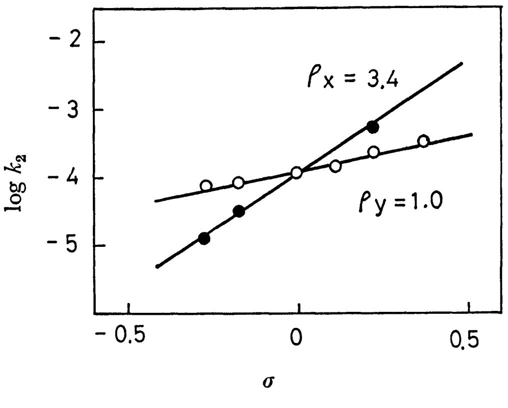


Fig. 1. Hammett plots of rates on the reaction of phenacyl benzoates ($X\text{-}C_6H_4COCH_2OCOC_6H_4\text{-}Y$) with triethyl phosphite in tetralin at 140 °C.

The rates of the reactions of phenacyl benzoates (**1a**—**i**) with **2b** at 140 °C are give in Table 2. The kinetic data gave a straight lines for Hammett plots with $\rho_X = +3.4$ and $\rho_Y = +1.0$ using the σ values shown in Fig. 1.

The rate constants ($M^{-1} s^{-1}$) of the reaction of **1a** with **2b** in tetralin at various temperatures were 3.10×10^{-5} at 110 °C, 4.64×10^{-5} at 120 °C, 1.16×10^{-4} at 140 °C, and 1.90×10^{-4} at 150 °C. The plots of log k_2 *vs.* $1/T$ produced a straight line, from which the energy, 16.5 kcal/mol, and the entropy of activation, −38.5 e.u., were obtained.

Table 3. Solvent effect on the rate of the reaction of **1a** with **2b** at 140° C[a)]

Solvent	Dielectric constant, ε	$10^4 k_2$, $M^{-1} s^{-1}$
Tetralin	2.77	1.16
Phenetole	4.22	1.85
Acetophenone	17.39	3.13

a) 0.2 M/l of **1a**, 0.8 M/l of **2b**.

Table 4. Effect of propionic acid and *m*-chlorobenzoic acid on the reaction of **1a** with **2b**[a)]

Added acid	Concn, M/l	$10^4 k_2$, $M^{-1} s^{-1}$
None	—	1.13
C_2H_5COOH	0.014	1.35
C_2H_5COOH	0.020	1.41
C_2H_5COOH	0.030	1.55
m-ClC_6H_4COOH	0.014	1.44

a) 0.4 M/l of **1a**, 0.4 M/l of **2b** in tetralin at 140 °C.

The solvent effect on the reaction of **1a** with **2b** at 140 °C is shown in Table 3. The rate constants increase with increasing solvent dielectric constant. When organic acids are added to the reaction mixture, the rate constants at 140 °C increase for the incipient step of the reaction (up to a conversion of about 30%) as shown in Table 4. The plots of k_2 *vs.* [propionic acid] show a straight line with a slope of $+1.40 \times 10^{-3}$ as expressed by

$$k_2 = 1.13 \times 10^{-4} + 1.40 \times 10^{-3}\,[\text{propionic acid}]. \quad (2)$$

The effect of the alkyl groups of **2** in the reactions with **1a** in tetralin was also studied, and the results are shown in Table 5. The reaction rates decrease in the order, *i*-Pr>Et>Me, corresponding to the nucleophilicity order of the phosphites.

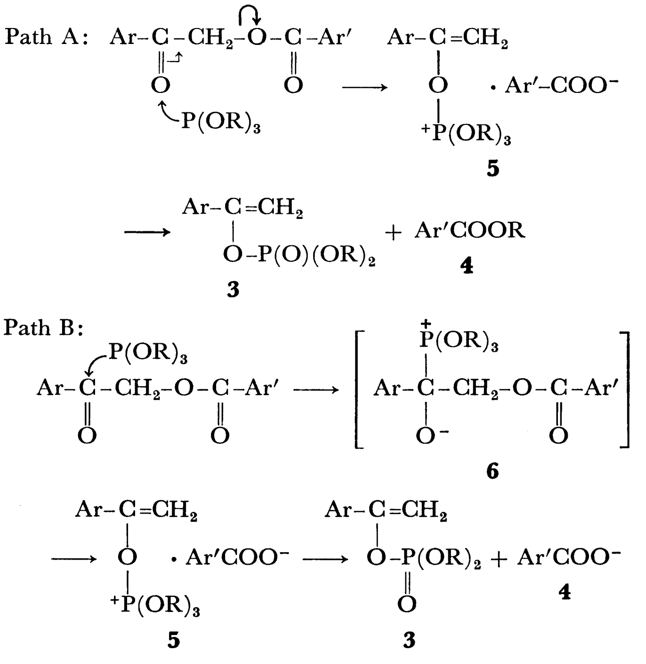
Table 5. Effect of alkyl groups on the reaction of **2a**—**c** with **1a**[a)]

Compound	σ^*	$10^4 k_2$, $M^{-1} s^{-1}$
2a	0	0.10 (110 °C)
2b	−0.10	0.26 (110 °C)
2b	−0.10	1.16 (140 °C)
2c	−0.19	3.34 (140 °C)

a) 0.2 M/l of **1**, 0.8 M/l of **2** in tetralin.

Discussion

Although various mechanisms have been proposed for the Perkow reaction, the most likely for the reaction of **1** with **2** include pathway A: the addition of **2** to the carbonyl oxygen of the phenacyl group gives directly an enol phosphonium salt (**5**), and pathway B: the addition of phosphite to the carbonyl carbon of the phenacyl groups followed by rearrangement of the phosphorus moiety to oxygen giving **5** (Scheme 2).



Scheme 2.

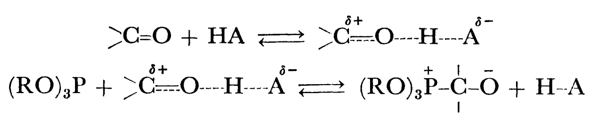
Pathway A, formally an S_N2' type reaction, involves the loss of a benzoate anion in the rate-determining step. From the ρ value obtained and the solvent effect, the rate along this pathway, which was proposed by Miller,[10)] Trippett,[11)] and Ramirez *et al.*[12)] may be considerable. However, this pathway appears to be unacceptable in our experiments from a consideration of the role of the acid catalysis. Therefore, pathway A is excluded.

On the other hand, pathway B, involving a rate-determining addition of phosphite to the carbonyl carbon of the phenacyl group followed by fast rearrangement and Arbuzov cleavage, is supported by the following facts.

A) The ρ values, $\rho_X = +3.4$ and $\rho_Y = 1.0$, obtained from the reaction with $X\text{-}C_6H_4COCH_2OCOC_6H_4\text{-}Y$ show that the reaction rate is determined by the nucleophilic addition of phosphite to the carbonyl carbon of the phenacyl group. The reaction of 2,4,6-trimethylphenacyl benzoate (**1j**) with **2b** with no solvent did not occur at 140 °C for 10 h because of steric hindrance due to the mesityl group.

B) When the solvent is changed from tetralin (ε= 2.77) to acetophenone (ε=17.39), the rate increases by a factor of 2.7 (Table 3). The reaction *via* a charge-separated complex (**6**) should be facilitated by an increase in the polarity of the solvent.[13)]

C) When organic acids are added to the mixture of **1a** and **2b**, the rate constant increases in the incipient step of the reaction as shown in Table 4. As the reaction proceeds, however, the accelerating effect gradually decreases. This phenomenon is due to the fact that a reaction of **2** with an acid occurs. In the presence of the acid, **1** may form weak hydrogen bonds



$$\gt C{=}O + HA \rightleftharpoons \gt \overset{\delta+}{C}{\equiv}O{---}H{---}\overset{\delta-}{A}$$

$$(RO)_3P + \gt \overset{\delta+}{C}{\equiv}O{---}H{---}\overset{\delta-}{A} \rightleftharpoons (RO)_3\overset{+}{P}{-}\overset{|}{\underset{|}{C}}{-}\overset{-}{O} + H{-}A$$

Scheme 3.

between the phenacyl group and the acid added, and the resulting bonds activate the carbonyl group for the nucleophilic attack by **2**. The reaction is believed to progress as shown in Scheme 3.

m-Chlorobenzoic acid is a more effective catalyst in this reaction (Table 4), because it is more acidic and, thus, more effective in forming a hydrogen bond with the carbonyl group. The acid catalysis and solvent effect, which have been observed for the reaction of α-halo ketones[4,5,8,13,14] and benzil[15] with trivalent phosphorus compounds, are similar to those obtained in this work. According to this mechanism, the second step, a rearrangement of the phosphorus moiety to oxygen, is not rate-determining in terms of the acid effect. The last step, Arbuzov cleavage of the alkyl group by the benzoate anion, which has been shown to be rapid and not rate-determining in the reaction of phosphite with ethyl iodide,[16] should not be accelerated in a polar solvent.

D) In view of the σ^* of Taft,[17] the nucleophilicity of the phosphites is considered to be in the order $(MeO)_3P<(EtO)_3P<(i\text{-}PrO)_3P$. The observed reactivity for the reaction of **1** with **2** is in agreement with the nucleophilicity of trialkyl phosphite.

E) For the reaction of aryl-substituted α-haloisobutyrophenones with **2b**, in which the rate-determining step is carbonyl addition, $E_a=12.8$—13.3 kcal/mol and $\Delta S^{\neq}=-41$—-42 e.u.[4] These data are quite similar to those presented here. Also, the reaction of benzil with **2** has been postulated to proceed *via* a similar mechanism.[15] The large negative entropy of activation obtained should be consistent with a dipolar transition state **6**.[18,19]

F) This reaction leads exclusively to enol phosphate in very high yields.[9] Since the facility of the elimination of a leaving group in an S_N2 reaction is generally in the order $I>Br>Cl>OCOCH_3$,[20] the elimination of a benzoate anion should be more difficult than that of a halide anion. Consequently, it is believed that this reaction proceeds along pathway B shown in Scheme 2.

Experimental

Materials. Phenacyl benzoates (**1a**—**i**) were prepared from corresponding phenacyl bromides and sodium benzoates.[9] **1j** was prepared by the method described above. Mp 87.5—88.3 °C. NMR (CD_3Cl): δ 2.20 (s, 9H, $(CH_3)_3$), 5.02 (s, 2H, CH_2), 6.60—8.10 (m, 7H, aromatic-H). MS: *m/e* 283 (M^+). Trialkyl phosphites (**2a**—**c**) were prepared from a reaction of phosphorus trichloride with alcohols in the presence of a base and were distilled from metallic sodium.[21] All of the solvents used were purified by the usual method.[22]

Instruments. NMR spectra were recorded on a Hitachi Model R-24 (60 Mc) spectrometer using TMS as an internal standard. Mass spectra were recorded on a Hitachi Model RM-50GC gas chromatograph-mass spectrometer. GLC measurements were carried out on a Shimadzu Model GC-4BPT instrument equipped with a 0.5×2 m silicone SE-30 (5 wt%) on Chromosorb G (60—80 mesh) column at 200 °C, using H_2 as the carrier gas (90 ml/min). Melting points were determining on a Yanaco MP apparatus and uncorrected.

Kinetic Measurements. The reactions were carried out in a rubber-stoppered glass tube maintained at a given temperature using a stirred thermostatically-controlled bath. The reaction rates were estimated from the relative peak areas (corrected), which were determined by means of the internal standard method using the GLC technique. Pyrene was used as the internal standard. In a typical reaction, 2 mmol of **1**, 8 mmol of **2** and 0.3 g of pyrene were placed in a 10-ml volumetric flask. Then this solution was quickly increased to 10 ml with the addition of tetralin. This solution was transferred into a tube displaced with nitrogen, and was allowed to react at 140 °C. Aliquots were taken out by syringe at appropriate time intervals and their compositions were determined immediately by the GLC technique. No reaction of **1j** with **2b** occurred for 10 h at 140 °C, and both **1j** and **2b** were recovered.

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References

1) F. W. Lichtenthaler, *Chem. Rev.*, **61**, 607 (1961).

2) R. F. Hudson, "Structure and Mechanism in Organophosphorus Chemistry," Academic Press, New York (1965), p. 153.

3) A. Arcoria and S. Fisichella, *Tetrahedron Lett.*, **1971**, 3347.

4) I. J. Borowitz, S. Firstenberg, G. B. Borowitz, and D. Schuessler, *J. Am. Chem. Soc.*, **94**, 1623 (1972).

5) P. A. Chopard, V. M. Clark, R. F. Hudson, and A. J. Kirby, *Tetrahedron*, **21**, 1961 (1965).

6) E. M. Gaydon, G. Buono, and R. Freze, *Bull. Soc. Chim. Fr.*, **1973**, 2284.

7) J. Konecny, R. Dousse, and J. Rosales, *Helv. Chim. Acta*, **55**, 3048 (1972).

8) I. J. Borowitz, M. Anschel, and S. Firstenberg, *J. Org. Chem.*, **32**, 1723 (1967).

9) S. Hashimoto and I. Furukawa, *Sulfur and Phosphorus*, in press.

10) B. Miller, *J. Am. Chem. Soc.*, **88**, 1841 (1966).

11) S. Trippett, *J. Chem. Soc.*, **1962**, 2337.

12) F. Ramirez, N. Ramanathan, and N. B. Desai, *J. Am. Chem. Soc.*, **85**, 3465 (1963).

13) R. Huisgen and P. Otto, *J. Am. Chem. Soc.*, **90**, 5342 (1970).

14) I. J. Borowitz and L. J. Grossman, *Tetrahedron Lett.*, **1962**, 471.

15) Y. Ogata and M. Yamashita, *J. Am. Chem. Soc.*, **92**, 4670 (1970).

16) G. Aksnes and D. Aksnes, *Acta Chem. Scand.*, **18**, 38 (1964).

17) R. W. Taft, Jr., *J. Am. Chem. Soc.*, **75**, 4231 (1953).

18) A. J. Speziale and D. E. Bissing, *J. Am. Chem. Soc.*, **85**, 3878 (1963).

19) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York (1960), p. 182.

20) E. R. Thornton, "Solvolysis Mechanism," Ronald Press Co., New York (1964), p. 165.

21) A. H. Ford-Moore and B. J. Perry, *Org. Synth.*, Vol. 31, 111 (1951).

22) J. A. Riddick and W. B. Bunger, "Organic Solvent," 3rd ed, John Wiley & Sons, Inc., New York (1970).