J. Am. Chem. Soc. 1988, 110, 1890-1895

A Single Transition State in the Reaction of Aryl Diphenylphosphinate Esters with Phenolate Ions in Aqueous Solution

Nicholas Bourne, Edwin Chrystiuk, Andrew M. Davis, and Andrew Williams*

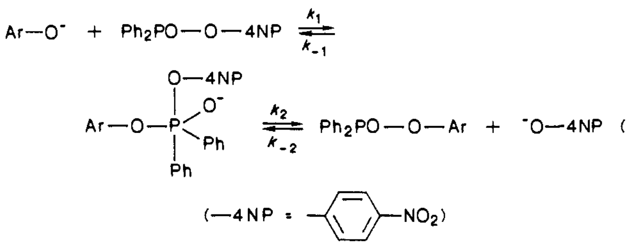
Contribution from the University Chemical Laboratories, Canterbury, England CT2 7NH.

Received August 20, 1987

Abstract: Second-order rate constants (k_{nuc}) have been measured for the nucleophilic reaction of aryl oxide ions with 4-nitrophenyl diphenylphosphinate in aqueous solvent. The Brønsted-type dependence is linear over a range of pK values greater than and less than the pK of the leaving phenol: $\log k_{nuc} = 0.46\mathrm{p}K_{ArOH} - 4.73$ ($t = 0.953$, $n = 25$). The absence of curvature is consistent with a single transition-state mechanism or a mechanism where a putative pentacoordinate intermediate lies at the base of a shallow well at a maximum on the reaction coordinate. Values of β_{lg} are measured for the reaction of constant phenolate ions with substituted phenyl diphenylphosphinate esters, and a minor extrapolation enables β_{lg} to be estimated for 4-nitrophenolate ion attack (−0.79). The values β_{nuc} and the estimated β_{lg} are for the *microscopic reverse* reactions and refer to the *same* transition state. The derived β_{eq} (1.25) is thus reliable and, combined with β_{nuc} and β_{lg}, indicates that there is charge imbalance with the diphenylphosphinoyl group (Ph_2PO) having significant positive character in the transition state.

The question of concertedness[1a] in phosphoryl group (PO_3^{2-}) transfer between nucleophiles has been addressed recently with stereochemical and electronic probes.[1b-d-3] Although there is evidence, under certain reaction conditions, that there is a metaphosphate intermediate (PO_3^-)[4,5] for phosphoryl group transfer, there is no evidence for a kinetically stable pentacoordinate intermediate for such reactions in aqueous solvent.

Stereochemical probes of mechanism give results that are consistent with a concerted mechanism for the transfer of many acyclic phosphyl[6] groups between nucleophiles.[7] Pentacoordinate phosphorus derivatives such as alkoxyphosphoranes or (aryloxy)phosphoranes are well documented,[8] and similar species have been shown to exist as intermediates in transfer reactions of phosphyl groups between strong nucleophiles.[7c,8b,9a,b] There has been some discussion of a concerted mechanism for the transfer of a phosphyl group (such as $(RO)_2PO$) in aqueous solution.[9c,d] The observation that aryl oxide ions react with 4-nitrophenyl diphenylphosphinate in water to yield the corresponding aryl ester (eq 1)[10a] provides a useful reaction to study relative timing of bond fission and formation in transfer of the phosphinoyl group. A change in rate-limiting step is predicted for the mechanism (eq 1) when $\Delta pK = pK_{ArOH} - pK_{HO\text{-}4NP} = 0$. This change would be diagnosed by a nonlinear Brønsted plot with a "break" at $\Delta pK = 0$, because the transition states for the two successive steps (k_1, k_2) would have different charges on the oxygen atom undergoing bond formation; this difference is "seen" by the polar substituents in the aryloxy group in the form of different Brønsted β_{nuc} values for the two extremes of the plot.



(1)

In order to obtain a firm diagnosis of possible charge differences on the attacking oxygen in the two putative transition states, the phenolate ion nucleophiles would be required to have ΔpK values significantly above and below zero and to suffer from no steric problems. It is also necessary to employ nucleophiles with the same structural type (i.e., in the present case *all phenolate ions*).[10b] The present study is of nucleophilic attack of phenolate ions on aryl diphenylphosphinate esters to test the stepwise mechanism. We also measure a reliable β_{eq} for transfer of the diphenylphosphinoyl group to aryl oxide acceptors in order to calibrate effective charges in the transition state with those for full bond formation or fission.

Experimental Section

Materials. Phenols were obtained commercially and, except where of AR grade, were recrystallized, sublimed, or redistilled. 1,1,1,3,3,3-Hexafluoropropan-2-ol and 2,2,2-trifluoroethanol were redistilled from commercial-grade material.

Substituted phenyl diphenylphosphinates were prepared from the acid chloride (Aldrich; 4.8 g, 0.02 mol), which was added dropwise to a stirred solution of the appropriate phenol (0.02 mol) and triethylamine (2.8 mL, 0.02 mol) in CH_2Cl_2 (40 mL). The mixture was stirred for 1 h at room temperature, the $NEt_3 \cdot HCl$ salt filtered, the solution extracted with dilute HCl and water, the CH_2Cl_2 layer dried with $MgSO_4$, and the filtered solution evaporated. A viscous oil was produced, which was induced to crystallize. The esters were recrystallized from propan-2-ol, except the 4-formyl and 4-acetyl (from Et_2O) and 2,3-dinitro and 2,5-dinitro (from toluene). Elemental analyses were carried out by A. J. Fassam with a Carlo Erba elemental analyzer, Model 1106; melting points, determined with a Kofler Thermospan instrument, are in agreement with literature values where available and are reported in Table II and the supplementary table together with the analyses. Silica gel TLC (5% MeOH/95% C_6H_6) was employed to check the purity of the esters, and the infrared (Perkin-Elmer 297 instrument) and NMR (JEOL JNM-PS 100-MHz instrument) spectra are consistent with the proposed structures.

Inorganic salts and buffer materials were of AR grade; water was doubly distilled from glass, and dioxane (AR grade) was purged of peroxides by its passage through an alumina column. Deuterium oxide (>99.8% D) was from Aldrich.

---

(1) (a) The definition of concerted employed here is given in: Chrystiuk, E.; Williams, A. *J. Am. Chem. Soc.* **1987**, *109*, 3040. (b) Lowe, G. *Acc. Chem. Res.* **1983**, *16*, 244. (c) Buchwald, S. L.; Friedman, J. M.; Knowles, J. R. *J. Am. Chem. Soc.* **1984**, *106*, 4911. (d) Cullis, P. M.; Iagrossi, A. *Ibid.* **1986**, *108*, 7870.

(2) Skoog, M. T.; Jencks, W. P. *J. Am. Chem. Soc.* **1984**, *106*, 7597.

(3) Bourne, N.; Williams, A. *J. Am. Chem. Soc.* **1984**, *106*, 7591.

(4) Freeman, S.; Friedman, J. M.; Knowles, J. R. *J. Am. Chem. Soc.* **1987**, *109*, 3166.

(5) Cullis, P. M.; Nicholls, D. *J. Chem. Soc., Chem. Commun.* **1987**, 783.

(6) The term phosphyl group has been defined by: Hudson, R. F.; Woodcock, R. C. *Justus Liebigs Ann. Chem.* **1978**, 176.

(7) (a) Hudson, R. F.; Green, M. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 11. (b) Hudson, R. F. *Structure and Mechanism in Organophosphorus Chemistry*; Academic: New York, 1965. (c) McEwen, W. E., Berlin, K. D., Eds. *Organophosphorus Stereochemistry*; Dowden, Hutchinson and Ross: Strondsberg, PA, 1975; Vols. 1 and 2. (d) Hall, C. R.; Inch, T. D. *Tetrahedron* **1980**, *36*, 2059.

(8) (a) Walker, B. J. *Organophosphorus Chemistry*; Penguin: London, 1972. (b) Sigal, I.; Westheimer, F. H. *J. Am. Chem. Soc.* **1979**, *101*, 752. (c) Trippett, S. *Pure Appl. Chem.* **1974**, *40*, 595. (d) Kirby, A. J.; Warren, S. G. *The Organic Chemistry of Phosphorus*; Elsevier: Amsterdam, 1967. (e) Wadsworth, W. S. *J. Org. Chem.* **1987**, *52*, 1748.

(9) (a) Westheimer, F. H. *Acc. Chem. Res.* **1968**, *1*, 70. (b) Cook, R. D.; Diebert, C. E.; Schwarz, W.; Turley, P. C.; Haake, P. *J. Am. Chem. Soc.* **1973**, *95*, 8088. (c) Rowell, R.; Gorenstein, D. G. *Ibid.* **1981**, *103*, 5894. (d) Lazarus, R. A.; Benkovic, P. A.; Benkovic, S. J. *J. Chem. Soc., Perkin Trans. 2* **1980**, 377. Lazarus, R. A.; Benkovic, S. J. *J. Am. Chem. Soc.* **1979**, *101*, 4300.

(10) (a) Woodcock, R. C. Ph.D. Thesis, University of Kent, 1971. (b) Bordwell, F. G.; Hughes, D. L. *J. Org. Chem.* **1982**, *47*, 3224.

0002-7863/88/1510-1890$01.50/0

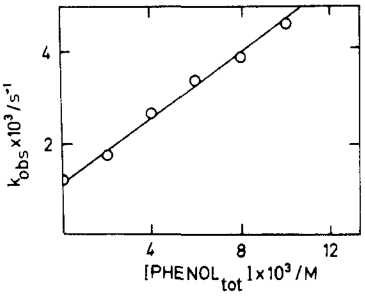


Figure 1. Reaction of phenolate ion with 2-nitro-4-chlorophenyl diphenylphosphinate in aqueous solution at pH 8.96. Conditions are as given in Table II; Tris buffer; fraction of phenol present as its base is 0.997. The line has a slope calculated from k_{nuc} given in Table II.

Methods. A typical kinetic experiment involved adding an aliquot (25–50 μL) of a stock solution of aryl ester in dioxane to an aqueous solution (2.5 mL) of aryl oxide ion in buffer in a silica cell. The solution of aryl ester was added on the flattened tip of a glass rod, and mixing was effected by rapid vertical strokes. The reaction was followed spectrophotometrically; initially the UV spectrum was scanned repetitively with a Unicam SP 800 or Perkin-Elmer Lambda 5 instrument to obtain the best single wavelength at which to monitor absorbance–time scans. The wavelengths employed are recorded in Tables I and II. Pseudo-first-order rate constants (k_{obsd}) were obtained from plots of $A_\infty - A_t$ versus time on semilogarithmic graph paper. The initial concentration of phenolate ion in the buffer was always at least 50 times the concentration of the ester (ca. 10^{-5} M) to ensure perfect first-order kinetics. The pH of the buffer solution was measured after each kinetic run with a Radiometer PHM 62 pH meter equipped with a Russell CMAWL CL5 combination electrode calibrated with EIL standard buffers to ±0.02 pH unit.

The solutions of aryl oxide ions were prepared by adding dilute KOH solution to a solution of the phenol in buffer and KCl to produce a stock solution (0.01–0.02 M) at 0.1 M ionic strength and 0.025 M buffer concentration at pH 7–11. The pH was chosen so that the phenol would be mostly completely ionized. The solutions of alcoholate ions were prepared at 0.1 M concentration, and acetate ion was at 1 M (in the latter case the ionic strength was kept at 1 M). The buffer components used throughout were as follows: pH 7–7.5, KH_2PO_4; pH 7.5–9.5, tris(hydroxymethyl)aminomethane (Tris); pH 9.5–11, $KHCO_3$. Varying concentrations of phenol with identical pH, ionic strength, and buffer composition were obtained by diluting the stock solution as prepared above with buffer solution made up in the same way but without the addition of phenol.

Identities of the products of the reaction of phenolate ions with the 4-nitrophenyl ester were determined by extraction of the product buffer (without acidification) with CH_2Cl_2, evaporation, and TLC analysis with aluminum-backed silica gel plates (5% MeOH/95% C_6H_6). HPLC analysis was also carried out with a Zorbax reversed-phase column: 50:50 MeOH/0.3% tetrabutylammonium phosphate at pH 7; wavelength, 267 nm; flow rate, 2 mL/min at 1430 psi. The latter method was only used for reaction of parent phenol with the 4-nitrophenyl ester, and the retention times of the putative products PhOH, Ph_2PO_2H, and Ph_2POOPh are 1.85, 1.54, and 10.12 min, respectively.

Measurements of p*K* were made with a Radiometer pH titration set comprising REC 61 servograph, REA titratigraph, PHM 62 pH meter, TTT 60 titrator, and ABU 11 autoburette.

A BBC microcomputer was used to make statistical calculations.

Results

Release of aryl oxide anions from the phosphinate esters in buffers obeys excellent pseudo-first-order rate laws up to about 90% of the total release. TLC analysis of the products of the reaction for 4-formyl-, 4-cyano-, 4-acetyl-, and parent phenolate anion on the 4-nitrophenyl ester indicates that the reaction involves complete nucleophilic attack; analysis of the above phenolate anion reaction by HPLC confirms the TLC result. The pseudo-first-order rate constants are linear in nucleophile concentration (eq 2, Figure 1); the value of $k_{intercept}$ is the background rate constant

$$k_{obsd} = k_{intercept} + k_{nuc}[\text{nucleophile}] \qquad (2)$$

due to buffer component and lyate species and is constant at a constant pH. The slope of the rate constant versus total phenol concentration for reaction of the 4-nitrophenyl ester in phenol buffers is proportional to the fraction of phenolate ion present in solution (Figure 2), confirming eq 2. The values of k_{nuc} for other phenolate ions and nucleophiles are determined at a constant pH assuming that the rate law (eq 2) holds for all cases, and the data are recorded in Table I.

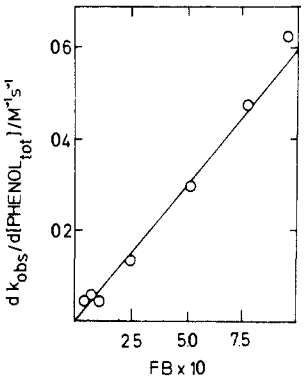


Figure 2. Dependence of $dk_{obsd}/d[\text{phenol}_{total}]$ on the fraction of phenol present as phenolate ion (FB) for decomposition of 4-nitrophenyl diphenylphosphinate in phenol-containing buffers. Conditions as in Table I with Tris and carbonate buffers; line calculated from k_{nuc} given in Table I.

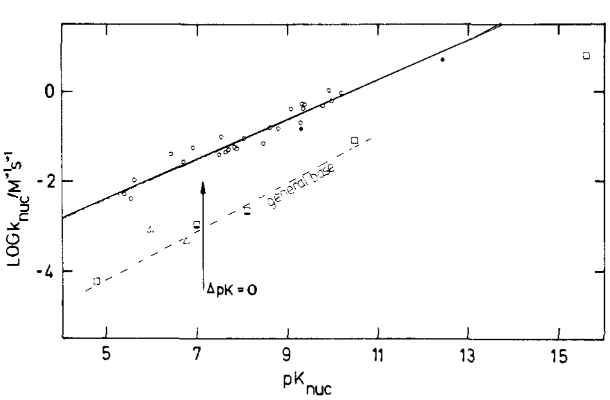


Figure 3. Brønsted dependence of k_{nuc} for attack of aryl oxide ions on 4-nitrophenyl diphenylphosphinate. Conditions are given in Table I. The identities of the phenolate species (○) and alcoholate ions (●) are coded in Table I. Upper limits (△) are denoted for two hindered phenolate ions. General-base catalytic terms (□) identified in Table I are included. The line for the nucleophilic attack of phenolate ions is calculated from eq 3; the dashed line for general-base catalysis has a slope of 0.5.

A Brønsted plot for the data of Table I is illustrated in Figure 3, and k_{nuc} for phenolate ions obeys a linear equation (3) over a Δp*K* range (omitting 2,6-disubstituted species) significantly greater than and less than zero.

$$\log k_{nuc} = (0.46 \pm 0.03)pK_{nuc} - 4.73 \pm 0.25 \quad (r = 0.953,\ n = 25) \quad (3)$$

Values of k_{nuc} for attack of phenolate ion, 4-acetylphenolate ion, and 4-formylphenolate ion on substituted phenyl diphenylphosphinates and the conditions of the experiments are given in Table II. The Brønsted dependencies are illustrated in Figure 4, and linear eq 4–6 are obeyed for phenolate, 4-acetylphenolate,

$$\log k_{PhO} = (-0.66 \pm 0.06)pK_{lg} + 4.72 \pm 0.37 \quad (r = 0.968,\ n = 11) \quad (4)$$

$$\log k_{4AcPhO} = (-0.72 \pm 0.11)pK_{lg} + 4.50 \pm 0.63 \quad (r = 0.940,\ n = 8) \quad (5)$$

$$\log k_{4CHOPhO} = (-0.77 \pm 0.12)pK_{lg} + 4.58 \pm 0.70 \quad (r = 0.940,\ n = 8) \quad (6)$$

and 4-formylphenolate ions, respectively. The value of β_{lg} from eq 4–6 depends on the phenolate nucleophile involved; over the range of pK_{nuc} employed, values of β_{lg} are linearly dependent on pK_{nuc} (eq 7). Equation 7 may be used to calculate the value of

$$\beta_{lg} = (0.072 \pm 0.008)pK_{nuc} - 1.31 \pm 0.07 \qquad (7)$$

β_{lg} for attack of the 4-nitrophenolate anion on aryl diphenyl-

Table I. Reaction of Nucleophiles with 4-Nitrophenyl Diphenylphosphinate[a]

	nucleophile	pK_{nuc}	10^2k_{nuc}[b]	pH[c]	10^2[nuc],[d] M	10^3k_{obsd},[e] s^{-1}	n[f]
			Phenolate				
1	2,3,4,5,6-F_5	5.40	0.52	8.01	0.2–1.0	0.05–0.095	12
2	2,3,5,6-F_4	5.53	0.36	8.06	0.2–1.0	0.065–0.090	14
3	2,3,4,5-Cl_4	5.64	1.0	8.05	0.1–1.0	0.06–0.17	11
4	2,4,6-Cl_3	5.99	0.085[g]	7.95	0.2–1.0	0.04–0.05	9
5	2,3,5-Cl_3	6.43	4.0	8.00	0.1–0.7	0.05–0.29	6
6	2,4,5-Cl_3	6.72	2.8	8.01	0.1–1.0	0.06–0.3	8
7	2,6-Cl_2	6.78	0.045[g]	7.96	0.4–2.0	0.054–0.063	6
8	2,3,4-Cl_3	6.92	5.9	7.96	0.1–0.4	0.08–0.27	5
9	2,5-Cl_2	7.51	3.6	8.04	0.5–2.0	0.04–0.54	5
10	3,4,5-Cl_3	7.55	10	10.04	0.3–1.3	3.2–4.5	10
11	4-CHO	7.66	4.1[h]	10.06	0.4–2.0	3.2–3.8	9
				8.22	0.25–1.0		
12	2,3-Cl_2	7.71	4.5	8.05	0.2–1.0	0.05–0.55	6
13	2,4-Cl_2	7.85	5.8	7.93	0.1–0.6	0.03–0.27	6
14	4-CN	7.95	5.2	10.12	0.2–0.8	1.5–2.2	6
15	4-$COCH_3$	8.05	8.9[h]	10.05	0.4–2.0	3.2–4.3	9
				8.60	0.35–0.75		
16	2-Cl	8.48	6.4	10.09	0.4–2.0	2.9–4.1	7
17	3,4-Cl_2	8.62	15	10.00	0.2–2.0	3.3–6.6	10
18	2-F	8.82	15	10.12	0.4–2.0	3.5–6.0	6
19	3-Cl	9.08	43	10.05	0.3–1.0	3.6–7.5	4
20	4-CO_2^-	9.31	20	10.07	0.4–2.0	2.5–5.9	6
21	4-Br	9.34	52	10.01	0.4–2.0	3.7–12.2	6
22	3-F	9.36	42	10.05	0.4–2.0	3.5–10.5	6
23	4-Cl	9.38	50	10.09	0.4–2.0	3.2–11.6	6
24	3-CO_2H	9.78	47	10.05	0.4–2.0	3.1–9.1	6
25	4-F	9.92	110	10.03	0.5–2.0	3.5–15.5	4
26	parent	9.99	59	8.36–11.36[i]	0.6–2.0	3.2–13.3	28
27	4-OCH_3	10.20	96	10.18	0.4–2.0	3.8–13	6
			Other Nucleophiles[j]				
28	$CH_3CO_2^-$[k]	4.76	5.3×10^{-3}	7.9	0.3–1.0	3.4–8.7[l]	5
29	$CH_3CO_2^-$[k] (D_2O)	4.76	2.0×10^{-3}	8.37[m]	0.1–1.0	3.5–5.0[l]	8
30	1,1,1,3,3,3-F_6C_2CHOH	9.3	14	10.10	0.02–0.1	3.5–17.4	6
31	2,2,2-F_3CCH_2OH	12.43	540	10.02	0.02–0.1	3–5.2	7
32	imidazole	7.05	0.10[n]	ref 11a			
33	Tris	8.10	0.22	8.00	2.5–10.0	0.06–0.14	4
34	hydroxide		730[n]	ref 11a			
35	triethylamine	10.65	8.4	10.90	5.0–25	38–50	4

[a] Conditions: 25 °C; ionic strength maintained at 0.1 M with KCl; [buffer] = 0.025 M; kinetics followed at 400 nm. [b] Units: $M^{-1}\ s^{-1}$; experimental error no greater than ±5%. [c] pH averaged over all the runs. [d] Maximum and minimum concentrations of total nucleophile employed. [e] Range of rate constants observed. [f] Number of data points not including duplicates. [g] Upper limit. [h] Average of values obtained at two different pH's. [i] Determined at several fractions of base (FB) of phenol (see Figure 2). [j] The value of k_{nuc} in these cases refers to either nucleophilic attack or general-base catalysis. [k] Ionic strength 1.0 M. [l] Value = 10^5k_{obsd}, s^{-1}. [m] pD determined from apparent pH (pH_a) and pD = pH_a + 0.4: D'Rozario, A. P.; Greig, D. J.; Hudson, R. F.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1981**, 590. [n] Ionic strength 0.1 M.

phosphinates (−0.79) by a very small extrapolation. The value of $\beta_{eq} = \beta_{nuc} - \beta_{lg}$ for transfer of diphenylphosphinoyl between 4-nitrophenolate anion and aryl oxide anion acceptors is thus 1.25.

Inspection of space-filling models indicates that nucleophilic attack at phosphorus in diphenylphosphinates has relatively high steric requirements; previous work[11a,b] has indicated that the steric requirement is sufficient to force imidazole to act as a general base rather than as a nucleophile in its reaction with diphenylphosphinate aryl esters. Product analysis indicates that the reaction of the phenolate ions with the esters is nucleophilic, and this is confirmed by the fact that the rate constants are very much larger than those from bona fide general-base mechanisms

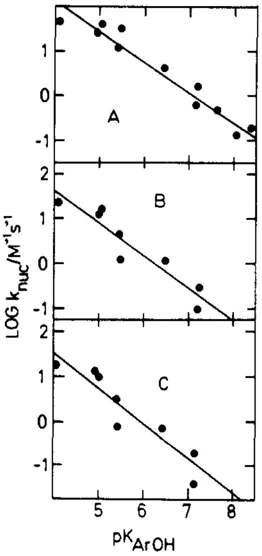


Figure 4. Dependence of k_{nuc} on the leaving group pK for attack of phenolate (A), 4-acetylphenolate (B), and 4-formylphenolate (C) ions on aryl diphenylphosphinates. Conditions and data are from Table II, and lines are calculated from eq 4–6, respectively.

---

(11) (a) Williams, A.; Naylor, R. A. *J. Chem. Soc. B* **1971**, 1967. (b) Haake, P.; Diebert, C. E.; Marmor, R. S. *Tetrahedron Lett.* **1968**, 5247. (c) Microscopic medium or solvent effects have been discussed by: Bruice, T. C.; Benkovic, S. J. *Bioorganic Mechanisms*, Part 1; Benjamin: New York, 1966; p 153. Crystiuk, E.; Williams, A. *J. Am. Chem. Soc.* **1987**, *109*, 3040. (d) Equation 8 may be derived assuming rate constants k_1, k_2, and k_{-1} obey the Brønsted equations

$$\log k_1 = \beta_1 \Delta pK + C_1$$

$$\log k_2 = \beta_2 \Delta pK + C_2$$

$$\log k_{-1} = \beta_{-1} \Delta pK + C_2$$

The common C_2 for k_2 and k_{-1} enables k_{-1} to equal k_2 at $\Delta pK = 0$; ΔpK is defined in the introduction. The equations are combined according to the rate law $k_{nuc} = k_1k_2/(k_{-1} + k_2)$ to give

$$k_{nuc} = 10^{C_1}10^{\beta_1 \Delta pK}/(1 + 10^{(\beta_{-1}-\beta_2)\Delta pK})$$

The value k_0 is given by $^1/_2 10^{C_1}10^{\beta_1 \Delta pK}$ and this equals $^1/_2 k_1$.

Table II. Reaction of Phenolate Anions with Aryl Diphenylphosphinates[a]

	aryl subst (leaving phenol)	pK_{lg}	k_{nuc}[b]	pH[c]	10^2[nuc],[d] M	10^3k_{obsd},[e] s^{-1}	n[f]	λ,[g] nm	mp,[h] °C
				Parent Phenolate Ion Nucleophile					
1	2,4-$(NO_2)_2$	4.09	45	7.09	2.0–12.0	11–17	12	400	118-122
2	2,3-$(NO_2)_2$	4.96	26	8.01	0.2–1.0	1.7–3.9	5	420	132–135
3	2,5-$(NO_2)_2$	5.04	40	7.97	0.4–1.0	2.7–6.4	4	400	149-151
4	3,4-$(NO_2)_2$	5.42	12	8.01	0.6–1.4	0.6–2.2	4	400	85-87
5	2-Cl-4-NO_2	5.45	33	7.94	0.7–2.0	1.9–7.7	5	400	116–118
6	2-NO_2-4-Cl	6.46	4.3	8.96	0.2–1.0	1.2–4.6	6	420	120-123
7	4-NO_2	7.16	0.59	(see Table I)					155–156
8	2-NO_2	7.21	1.6	10.08	0.2-0.8	6.6–13.5	5	400	101–102
9	4-CHO	7.66	0.48	10.05	0.1–1.0	3–5.5	13	330	95-96
10	4-CH_3CO	8.05	0.13	10.06	0.3–1.0	1.3–2.0	4	325	114-115
11	3-NO_2	8.38	0.19	10.13	0.2–1.0	2.0–3.0	6	400	124-125
				4-Acetylphenolate Ion Nucleophile					
1	2,4-$(NO_2)_2$	4.09	24	8.60	0.25–1.0	73–240	4	400	
2	2,3-$(NO_2)_2$	4.96	13	8.92	0.1–0.5	26–82	7	420	
3	2,5-$(NO_2)_2$	5.04	16	9.77	0.1–0.5	7.0–70	6	400	
4	3,4-$(NO_2)_2$	5.42	4.4	8.60	0.25–1.0	8.0–34	4	400	
5	2-Cl-4-NO_2	5.45	1.3	8.60	0.25–1.0	2.7–10	4	400	
6	2-NO_2-4-Cl	6.46	1.2	8.60	0.25–1.0	2.6–9.8	4	400	
7	4-NO_2	7.16	0.089	(from Table I)					
8	2-NO_2	7.21	0.3	8.60	0.25-1.0	0.59-2.5	4	400	
				4-Formylphenolate Ion Nucleophile					
1	2,4-$(NO_2)_2$	4.09	17	8.22	0.25–1.0	33–200	4	400	
2	2,3-$(NO_2)_2$	4.96	13	9.82	0.1–0.5	2.9–85	6	400	
3	2,5-$(NO_2)_2$	5.04	9.6	8.92	0.1–0.5	7.0–64	6	400	
4	3,4-$(NO_2)_2$	5.42	2.9	8.22	0.25–1.0	5.6–22	4	400	
5	2-Cl-4-NO_2	5.45	0.76	8.22	0.25–1.0	1.8–6.5	4	400	
6	2-NO_2-4-Cl	6.46	0.74	8.22	0.25–1.0	1.8–6.1	4	400	
7	4-NO_2	7.16	0.041	(from Table I)					
8	2-NO_2	7.21	0.19	8.22	0.25–1.0	0.36–1.5	4	400	

[a] Conditions: 25 °C; ionic strength maintained at 0.1 M with KCl; [buffer] = 0.025 M, see the Experimental Section for identity of buffer. [b] Units: M^{-1} s^{-1}; experimental error no greater than ±5%. [c] pH averaged over all the runs. [d] Maximum and minimum concentrations of total phenol. [e] Range of rate constants observed. [f] Number of data points not including duplicates. [g] Wavelength for kinetics. [h] Melting points of the aryl diphenylphosphinate esters.

(imidazole and acetate ion attack). Phenolate anions with ortho chloro and fluoro substituents show little difference in reactivity compared with phenolate ions with vacant ortho positions with similar pK. Increasing steric bulk (by 2,6-disubstitution) leads to a marked reduction in reactivity; this is consistent with nucleophilic reaction for the more reactive phenolate anions and, for the former anions, with a substantial proportion of the reaction flux being taken by a general-base mechanism.

The steric requirements for nucleophilic substitution probably give rise to microscopic medium effects,[11c] causing the observed scatter in the Brønsted plots. Deviations for reactions of a constant nucleophile with esters with varying leaving groups are regular and proportional to those for a different constant nucleophile on the same set of esters. Supplementary Figure 1 illustrates the linear relationship between deviations for the 4-acetylphenolate and 4-formylphenolate anion nucleophiles reacting with a series of esters. The deviations, which are *not* due to experimental error, place a limit on the accuracy with which we can determine curvature.

The mechanism of eq 1 gives rise to a theoretical eq 8,[11d] where $\Delta\beta = \beta_2 - \beta_{-1}$ and the values β_1, β_2, and β_{-1} refer to the Brønsted equations governing k_1, k_2, and k_{-1}, respectively. Curvature in

$$k_{nuc}/k_0 = 10^{\beta_1 \Delta pK}/(1 + 10^{-\Delta\beta\Delta pK}) \qquad (8)$$

the plot of log k_{nuc} versus pK_{ArOH} for the data of the unhindered phenolate anions in Table I (Figure 3) is effectively measured by $\Delta\beta$; when $\Delta\beta = 0$ eq 8 becomes linear. The data are fit to eq 8 by a grid-search program, which scans sets of given values of $\Delta\beta$, β_1, and k_0 to obtain the set giving the least sum of squares of the deviations from the calculated values (log k_{nuc}^{calcd} – log k_{nuc}^{obsd}). The data set giving the best fit in a grid of given values of β_1 (0.4–0.8 in units of 0.1), $\Delta\beta$ (0–0.3 in units of 0.1), and log k_0 (0.4–1.0 in units of 0.1) is $\beta_1 = 0.4$, $\Delta\beta = +0.1$, and log $k_0 = 0.9$. The difference between the sum of squares of the deviations between the best and the next best set of given parameters ($\beta_1 = 0.5$, $\Delta\beta = 0$, and log $k_0 = 0.8$ is *only 3% of the total sum.* When $\Delta\beta$ is fixed at 0.2, the set of k_0 and β_1 best fitting the data has a sum of squares of deviations substantially greater than those for the two best fits above; we conservatively place an upper limit of 0.2 on the uncertainty in $\Delta\beta$. The data for reaction of phenolate anions with 4-nitrophenyl diphenylphosphinate exhibit no evidence for curvature outside the proposed limit in $\Delta\beta$.

General-base catalysis of the hydrolysis of 4-nitrophenyl diphenylphosphinate is observed with acetate ion buffers as evidenced by the solvent deuterium oxide isotope effect of 2.7 (Table I); it is reasonable to assume that Tris and triethylamine behave similarly, as they are both hindered species (see earlier).[11a] The Brønsted line (Figure 3) does not include the hydroxide value. The upper limits on reaction of the two 2,6-disubstituted phenolate anions come within the range predicted from the general-base Brønsted line (Figure 3).

The alcoholate anions have rate constants that fit the phenolate regression line reasonably well, but they are not included in the correlation as they have a different structure.[10a] For a similar reason the rate constant for the acetate ion is not included; this rate constant in any case refers to a general-base reaction and not a nucleophilic one.

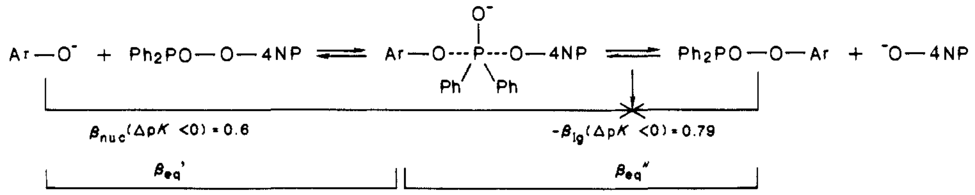
Discussion

Effective Charge for Diphenylphosphinoyl Transfer to Phenolate Anions. The quantity β_{eq} for the overall transfer of the diphenylphosphinoyl group from a donor to aryl oxide anion acceptor may be determined from β_{lg} and β_{nuc} provided the reactions yielding these values are strictly the microscopic reverse of each other. This requirement and that the same rate-limiting step is being observed are met in the present case. The value of 1.25 for β_{eq} indicates that the diphenylphosphinoyl group is more electron withdrawing than is hydrogen but less than is the neutral phosphoryl species ($(HO)_2PO$), which has $\beta_{eq} = 1.83$.[12a] We have

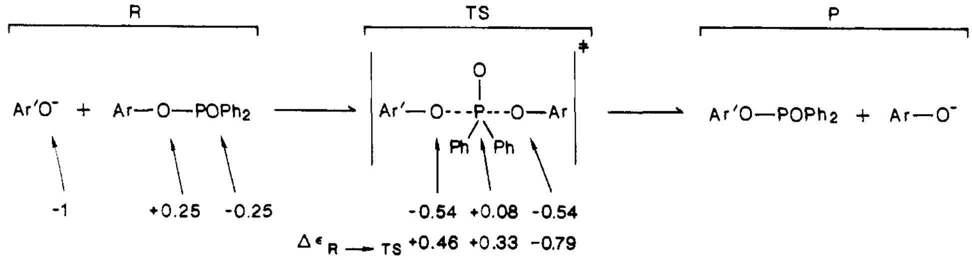
---

[12] (a) Bourne, N.; Williams, A. *J. Org. Chem.* **1984**, *49*, 1200. (b) Basaif, S., University of Kent, 1987; unpublished work.

Scheme I. Map of β Values for Changes in the ArO–P Bonding



Scheme II. Charge Distribution along the Reaction Coordinate (Change in Charge Denoted by $\Delta\epsilon$)



recently shown that β_{eq} for transfer of the diethylphosphoryl group to aryl oxide ion acceptors ((EtO)$_2$PO)[12b] is similar to that of the parent neutral phosphoryl group. The difference between phosphinoyl and phosphoryl groups is possibly because of the extra P–O dipoles in the latter. The lower electron-attracting power of the diphenylphosphinoyl group is consistent with its participation as a migratory species in carbonium ion rearrangements.[13]

A Single Transition State. The absence of any observable curvature in the Brønsted-type plot of aryl oxide ion reactivity against pK_{ArOH} for attack on the 4-nitrophenyl ester (Figure 3) is consistent with a mechanism involving a single transition state or a shallow well at an energy maximum in the reaction coordinate. The upper limit to the diagnosis of an observable change in slope corresponds to a value of $\Delta\beta$ <0.2 unit. Thus, the transition states corresponding to decay of such an intermediate would lie less than 0.2 unit apart (with respect to a coordinate spanning 1.25 units) on the reaction map and have very similar charge structures.

There seems to be little room on the energy surface (within the 0.2-unit limits) for such an intermediate if it is to have a significant barrier for its collapse, because its structure would be less than 0.1 unit of charge distant from one of its transition states. Skoog and Jencks[2] and Dietze and Jencks[14] have discussed this situation for other systems where there is little perceived bond order difference between intermediate and the transition states for its breakdown; they show that it is difficult to account for the stability of such an intermediate.

The question could be raised as to whether any experimental technique such as the present one, oxygen exchange, or inversion of stereochemistry can distinguish between a concerted mechanism having a single transition state and a mechanism where there is a very reactive intermediate. Such an intermediate would decompose to reactants or forward to products faster than it could racemize or exchange and thus give results consistent with a concerted mechanism. The values of β_{-1} and β_2 would be lower than the experimentally observable limit on $\Delta\beta$ in the present case. We recognize this possibility and suggest that the energy surface corresponding to such an intermediate does not possess an energy well sufficiently well defined for it to differ considerably from a somewhat flattened area on a maximum. In our view there is little to be gained by discussing this matter further as there is, to our knowledge, no experimental method capable of distinguishing between such close alternatives. At present the data indicate that the transition states for the decomposition of the putative pentacoordinate intermediate are so close in structure as to be indistinguishable. The same arguments would be applicable to reactions shown to be concerted in earlier work using the present methods as well as the exchange and stereochemical techniques.

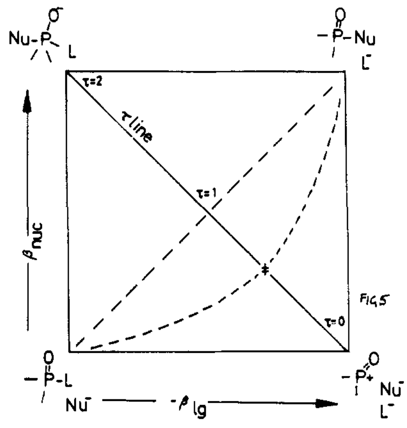


Figure 5. Reaction map (schematic three-dimensional potential energy diagram) for transfer of the diphenylphosphinoyl group between aryl oxide leaving groups and nucleophiles. The horizontal and vertical scales are calibrated in terms of β_{nuc} and $-\beta_{lg}$, which have ranges from 0 to 1.24; the transition state lies at $\beta_{nuc}, -\beta_{lg}$ = 0.45, 0.79.

Step k_2 would be rate limiting at ΔpK <0, assuming the existence of a discrete intermediate; in this region of pK the value of β_{nuc} should be $\beta_1 - \beta_{-1} + \beta_2$. Perusal of the Brøsted dependence (Figure 3) indicates that β_{nuc} is no greater than 0.6 in this region of ΔpK. Thus, β_{eq}' for formation of the putative pentacoordinate intermediate is less than 0.6, since β_{nuc} refers to change in charge from ground state to transition state of k_2 and must be greater than the change in charge (β_{eq}') seen for the intermediate (see Scheme I). The value of β_{-2} (β_{lg}) would be –0.79 thus, β_{eq}'' for formation of products from the pentacoordinate intermediate is greater than 0.79. These arguments are illustrated in Scheme I.

Since β_{eq}' (<0.6) corresponds to a full bond formation (eq 1) whereas β_{eq}'' (>0.79) measures only a hybridization change from phosphorus to oxygen from intermediate to product, these inequalities are not compatible with the stepwise model but can be explained by a mechanism of the form proposed above.

Charge Distribution in the Transition State. As the reaction under investigation is symmetrical we can determine the effective charges on entering and leaving oxygen atoms in the transition state by use of β_{nuc} and β_{eq} (Scheme II). Since the effective charges on entering and leaving atoms are obtained by standardization against the same ionization and possess the same calibration reaction,[15] it is permissible to compare these values. The observed imbalance in change in charge ($\Delta\epsilon$) of –0.33 between the oxygens (see Scheme II) is presumably made up by +0.33

---

(13) (a) Cann, P. F.; Howells, D.; Warren, S. G. *J. Chem. Soc., Perkin Trans. 2* **1972**, 304. (b) Howells, D.; Warren, S. G. *Ibid.* **1973**, 1472, 1645.

(14) Dietze, P. E.; Jencks, W. P. *J. Am. Chem. Soc.* **1986**, *108*, 4549.

(15) (a) Williams, A. *Acc. Chem. Res.* **1984**, *17*, 425. (b) Thea, S.; Williams, A. *Chem. Soc. Rev.* **1986**, *15*, 125.

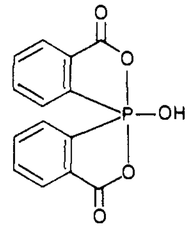
unit from the diphenylphosphinoyl group. The transition-state structure, as perceived from the effective charge distribution, may be placed on a reaction map (Figure 5) where the horizontal and vertical axes refer to effective charge on leaving and entering groups, respectively. The charge distribution indicates considerable Ph_2PO^+ character, and the geometry of the transition state would be trigonal-bipyramidal with elongated axial distances to entering and leaving oxygens. Since the reaction is symmetrical, the transition state will lie on a diagonal (the τ diagonal of Kreevoy),[16] and the tightness parameter (τ)[16a] is 0.74. The mechanism is essentially uncoupled concerted with an open or loose transition state. Lazarus, Benkovic, and Benkovic[9d] came to a similar conclusion for the intramolecular attack of amine on a phosphodiester. Application of a more recent value of β_{eq}[12a] does not alter their conclusions significantly.

It is difficult from the present experiments to indicate the shape of the surface near the transition state, because it is impossible to estimate p_y ($d\beta_{nuc}/dpK_{nuc}$).[16b] If there were a measurable p_y, it would appear to be difficult in practice to distinguish this curvature from that arising from a change in rate-limiting step in this system.

The value of p_{xy} ($d\beta_{lg}/dpK_{nuc}$)[16b] may be determined however, and it is in the direction predicted (see eq 7): increase in the basicity of the attacking phenolate anion raises the energy of the bottom two corners in the reaction map. The transition state should move parallel to the reaction coordinate toward the bottom left corner and perpendicular to it toward the top left corner. The net movement should be in a positive direction with respect to β_{lg}, toward the left, and it agrees with β_{lg} for phenolate anion attack being more positive than that for the 4-formylphenolate reaction (see eq 4–6). The value of p_{xy} is similar to and of the same sign as that discovered by Khan and Kirby[17] for the attack of oxyanion nucleophiles on aryl phosphate esters. A similar change in β_{lg} is observed by Rowell and Gorenstein[9c] for a similar series of phosphate reactions.

Considerations of effective charge changes and the consequent equation of these with bonding changes are not sufficient to diagnose a concerted mechanism. Although there is a significant bond fission to the leaving group ($-\beta_{lg} = +0.79$ compared with an overall β_{eq} of 1.24), this could be due to very weak apical bonds in a pentacoordinate phosphorus intermediate. It is known that pentacoordinate species have apical bonds that are significantly longer than regular single bonds.[18,19] Such bonds could be considered to be composed of a doubly occupied p orbital from the central atom bonded with two singly occupied orbitals from two collinear ligands; the resultant "hypervalent" bonds are consequently weaker than regular σ bonds.[20]

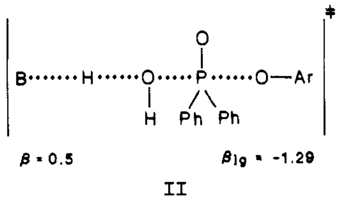
The results of this paper are consistent with the putative intermediate having an energy higher than that of the transition state (Figure 5). Segall and Granoth[21] isolated an analogue of the putative intermediate with weak nucleophilic oxygen apical ligands (I). The stability of this species is enhanced by the equatorial oxygen existing in its neutral from rather than as the anion; there is thus little driving force for decomposition. A chelate effect will also contribute to stability, which might not be seen in the acyclic species, and constraints imposed by the five-membered rings could minimize additional steric repulsions.[22] We do not therefore think that the isolation of I is inconsistent with our present conclusions.



I

Pentacoordinate intermediates have been demonstrated for strongly basic ligands in both acyclic and cyclic phosphyl systems. We propose that the single-transition-state mechanism is favored here because of the leaving ability of weakly nucleophilic ligands; we are not, however, suggesting that the mechanism is an "enforced concerted" one[23] where the reaction coordinate passes through the structure of an intermediate that has a lifetime less than that of a bond vibration. Rowell and Gorenstein[9c] indicated that a concerted mechanism would result as the nucleophile became weaker, because bond fission to the leaving group would get progressively more advanced in the transition state.

General-Base-Catalyzed Hydrolysis. The value of β_{eq} for transfer of the diphenylphosphinoyl group between aryl oxide anion acceptors and a donor leaving group may be used to determine the effective charge distribution for the general-base-catalyzed hydrolysis of aryl diphenylphosphinates previously studied.[11a] Comparison of the β_{lg} (−1.29)[11a] with β_{eq} (1.25) indicates that P–O fission is almost complete in the transition state; the discrepancy in the β values is within the uncertainty limits in measuring Brønsted exponents. The error in β_{eq} will of course be greater than that for a rate constant. The value of β (0.5) for variation of base species indicates that the charge buildup is only 0.5 that of the final charge. The imbalance of charge change must be made up by the $H_2O{\cdot}Ph_2PO$ group of atoms taking on a positive charge (II), and the charge distribution would be more consistent with a concerted process than with one involving a pentacoordinate intermediate.



II

Acknowledgment. We thank the British Science and Engineering Research Council for studentships (N.B., E.C.) and a research grant (GR/C/75529).

Supplementary Material Available: Table of physical properties and elemental analyses and graph of leaving group deviations from regression line (2 pages). Ordering information is given on any current masthead page.

---

[16] (a) Kreevoy, M. m.; Lee, I.-S. H. *Chem. Soc. Rev.* **1984**, *106*, 2550. (b) Jencks, D. A.; Jencks, W. P. *Ibid.* **1977**, *99*, 7948.

[17] Khan, S. A.; Kirby, A. J. *J. Chem. Soc. B* **1970**, 1172.

[18] Perozzi, E. F.; Martin, J. C.; Paul, I. C. *J. Am. Chem. Soc.* **1974**, *96*, 6735.

[19] (a) Ramirez, F. *Acc. Chem. Res.* **1968**, *1*, 168. (b) McDowell, R. S.; Streitwieser, A. *J. Am. Chem. Soc.* **1985**, *107*, 5849.

[20] Musher, J. I. *Adv. Chem. Ser.* **1972**, *110*, 44; *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 54.

[21] Segall, Y.; Granoth, I. *J. Am. Chem. Soc.* **1978**, *100*, 5130; **1979**, *101*, 3687.

[22] Benkovic, S. J.; Schray, K. J. In *The Enzymes*, 3rd ed.; Boyer, P. D., Ed.; Academic: New York, 1973; p 201. Gandour, R. D., Schowen, R. L., Ed. *Transition States of Biochemical Processes*; Plenum: New York, 1978; p 493.

[23] Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345.