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OXIDATION OF ORGANOPHOSPHORUS COMPOUNDS—III

KINETIC ISOTOPE EFFECTS IN THE OXIDATION OF SOME DIARYLPHOSPHINE OXIDES BY PEROXYBENZOIC ACID

R. CURCI and F. DI FURIA

Instituto di Chimica Organica dell'Università, Centro di Meccanismi di Reazioni Organiche del C.N.R.,
35100 Padova, Italy

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Abstract—Kinetic deuterium isotope effects for the oxidation of diphenylphosphine oxide and of two substituted diphenylphosphine oxides by peroxybenzoic acid were determined by measuring reaction rates in acidic and alkaline dioxan-H_2O and dioxan-D_2O solutions. Reactants were shown to exchange readily their acidic protons with deuterium in dioxan-D_2O. Kinetic isotope effects data are interpreted on the basis of a two-step oxidation mechanism involving preliminary formation of a reactive peroxide intermediate and subsequent decomposition to give the observed reaction products.

IN RECENT papers we have reported the results of studies concerning the oxidation of diarylphosphine oxides $Ar_2P(:O)H$ to the corresponding phosphinic acids $Ar_2P(:O)OH$ by organic peroxyacids RCO_3H in acidic and alkaline media.[1,2]

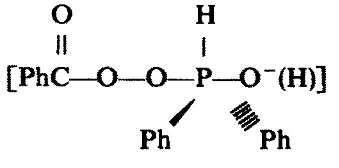
For the oxidation of diphenylphosphine oxide by peroxybenzoic acid (PBA), the profile of the curve $\log k_2(\text{obs})$ *versus* apparent pH (or H_- function) indicated the following general rate law is followed:

$$-(d[PBA]/dt) = (k_2'[PhCO_3H] + k_2''[PhCO_3^-] + k_3[PhCO_3^-][OH^-])[Ph_2PHO] \quad (1)$$

Kinetic experiments carried out in solutions of relatively high OH^- concentrations ($pH_{app} > 12$) revealed that the observed second-order rate constant is linearly dependent upon OH^- concentration, according to the equation:[1]

$$k_2(\text{obs}) = k_2'' + k_3[OH^-] \quad (2)$$

On the basis of kinetic evidence a mechanism involving preliminary nucleophilic attack on the organophosphorus substrate by the peroxidic species was proposed; this would lead to formation of a reactive pentacoordinate phosphorus intermediate, probably having a structure close to **1**, which then breaks down to yield the observed reaction products.



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Aiming to gain insight into the balance of the proposed stepwise mechanism as well as into details of the internal redox process leading from 1 to products, we undertook an investigation upon deuterium isotope effects on reactions rates.

RESULTS

In good agreement with that previously observed in MeOD solutions,[3,4] the diarylphosphine oxides employed in this study were found to exchange rapidly the hydrogen bonded to phosphorus with deuterium in dioxan-D_2O solutions. In a typical experiment, a diphenylphosphine oxide sample was quickly recovered by extraction in $CHCl_3$ shortly after dissolution in dioxan—33·2 M D_2O. Upon removal of solvent *in vacuo*, in the NMR spectrum of the recovered sample (in $CDCl_3$) the distinct doublet at τ 1·90 ppm (J_{HP} = 480 Hz) due to hydrogen bonded to phosphorus[3,4] was completely missing. Furthermore, its IR spectrum (KBr pellet) was the same as that of $Ph_2P(:O)H$, except that the P—H stretching band at 2310 cm^{-1} was replaced by a P—D band near to 1680 cm^{-1}.[4,5] The NMR spectra of $Ph_2P(:O)H$ samples dissolved in dioxan(d_8) containing from 50% down to 5% (by volume) D_2O also showed complete disappearance of the P—H resonance doublet signals before the spectra could be taken (less than three min).

As expected, samples of peroxybenzoic acid quickly recovered from dioxan-D_2O solutions had also completely exchanged the acidic proton with deuterium, as evidenced by disappearance of the broad proton signal[6] near τ −1·60 ppm in the NMR spectra (benzene-d_6).

Stoichiometry, rate law, log k_2(obs) *versus* apparent pH (or *versus* H_-) profiles, as well as other kinetic details for the oxidation reaction being studied have already been given.[1,2] In the kinetic runs carried out both in acidic and alkaline dioxan-D_2O solutions since—as said above—both reactants quickly exchange their acidic proton with deuterium and given their relatively low concentrations (from 0·007 to 0·015 M) in the reacting solutions, no previous deuterium exchange was performed on the protium-containing samples used.

Deuterium isotope effects in acidic media were evaluated by measuring the rate constants for the oxidation of diphenylphosphine oxide, bis(*p*-chlorophenyl)phosphine oxide and bis-*p*-tolylphosphine oxide by PBA in dioxan-11·1 M D_2O and dioxan-11·1 M H_2O (Table I); no buffers or base were added to the reaction solution. It was ascertained that the increase in medium acidity from the beginning to the end of each reaction, due to production of benzoic and phosphinic acids, corresponds to 0·3–0·5 apparent pH (or pD) units under the given conditions. This acidity change is unimportant since, as evident from inspection of Fig. 1 in our previous work,[2] kinetic runs were performed at a medium acidity where the rate constant is virtually unaffected by moderate pH changes. According to the rate law seen above (eq. 1), when the medium is sufficiently acidic so that peroxybenzoic acid is present almost completely in its unionized form, it is $k_2(\text{obs}) \simeq k'_2$. This allows one to obtain the ratios $[(k'_2)^{H}_{H_2O}/(k'_2)^{D}_{D_2O}]$ given on Table II.

The deuterium isotope effects in alkaline media were determined by running kinetic experiments in dioxan-33·2 M D_2O by varying OD^- concentrations, always in excess over the reactants initial concentrations (Table I). Equation 2 may now be generalized as follows, with L = H or D:

$$k_2(\text{obs}) = (k''_2)^{L}_{L_2O} + (k_3)^{L}_{OL} \cdot [OL^-] \qquad (3)$$

TABLE I. OXIDATION RATES OF SOME DIARYLPHOSPHINE OXIDES BY PEROXYBENZOIC ACID, AT 25°[a]

Compound	Solvent		Rate Constants[b]	
$(p\text{-Cl}\cdot C_6H_4)_2PHO$	Dioxan—11·1 M H_2O		$10^2k'_2 = 10^2k_2$(obs) =	164·0 ± 1·3
$(p\text{-Cl}\cdot C_6H_4)_2PDO$	Dioxan—11·1 M D_2O			49·5 ± 1·3
$(p\text{-Me}\cdot C_6H_4)_2PHO$	Dioxan—11·1 M H_2O			7·30 ± 0·20
$(p\text{-Me}\cdot C_6H_4)_2PDO$	Dioxan—11·1 M D_2O			3·65 ± 0·20
$(C_6H_5)_2PHO$	Dioxan—11·1 M H_2O			20·30 ± 0·30
$(C_6H_5)_2PDO$	Dioxan—11·1 M D_2O			8·60 ± 0·30
$(C_6H_5)_2PHO$	Dioxan—33·2 M H_2O	(from 0·030 to 0·390 M OH^-)[c]	$10^2k''_2$ =	10·40 ± 0·8
			k_3 =	2·23 ± 0·04
$(C_6H_5)_2PDO$	Dioxan—33·2 M D_2O	(0·040 M OD^-)	10^2k_2(obs) =	45·80
		(0·070 M OD^-)		61·50
		(0·097 M OD^-)		87·30
		(0·132 M OD^-)		126·00
		(0·164 M OD^-)		152·00
		(0·340 M OD^-)		310·00
			$10^2k''_2$ =	3·9 ± 2·1
			k_3 =	8·99 ± 0·13

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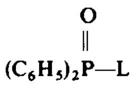
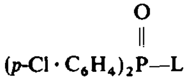
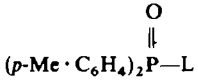
[a] Reactant concentrations were kept in the range 0·005 to 0·01 M in the majority of runs; (0·02–0·04) × 10^{-2} M EDTA disodium salt was also present

[b] k_2(obs), k'_2 and k''_2 values are in $M^{-1}sec^{-1}$; k_3 is in $M^{-2}sec^{-1}$; the numerical values are given along with their estimated probable errors

[c] Complete rate data have been reported in our previous work (reference 1)

TABLE II. SUMMARY OF DEUTERIUM ISOTOPE EFFECTS OBSERVED IN THE OXIDATION OF SOME SECONDARY DIARYLPHOSPHINE OXIDES BY PEROXYBENZOIC ACID[a]

	$\left[\dfrac{(k'_2)^H_{H_2O}}{(k'_2)^D_{D_2O}}\right]$	$\left[\dfrac{(k''_2)^H_{H_2O}}{(k''_2)^D_{D_2O}}\right]$	$\left[\dfrac{(k_3)^H_{OH^-}}{(k_3)^D_{OD^-}}\right]$
 $(C_6H_5)_2\overset{\overset{O}{\|}}{P}—L$	2·36 ± 0·09[b]	2·7 ± 1·5[c]	0·248 ± 0·005[c]
 $(p\text{-Cl}\cdot C_6H_4)_2\overset{\overset{O}{\|}}{P}—L$	3·31 ± 0·05[b]	—	—
 $(p\text{-Me}\cdot C_6H_4)_2\overset{\overset{O}{\|}}{P}—L$	2·00 ± 0·12[b]	—	—

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[a] Ratios values are shown along their estimated probable error

[b] Dioxan 11·1 M L_2O solutions

[c] Dioxan 33·2 M L_2O solutions

On this basis, by plotting k_2(obs) values *versus* $[OD^-]$ a straight line (corr. coeff. 0·99) was obtained and $(k''_2)^D_{D_2O}$ and $(k_3)^D_{OD^-}$ values could be evaluated (Fig. 1). Through the values of the corresponding quantities obtained in dioxan-33·2 M H_2O alkaline solutions, also reported in Table I, the ratios shown in Table II could be calculated.

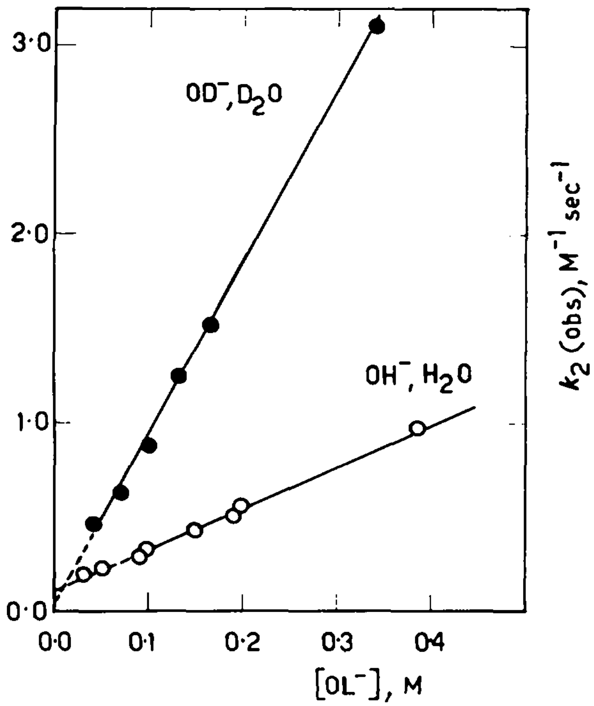
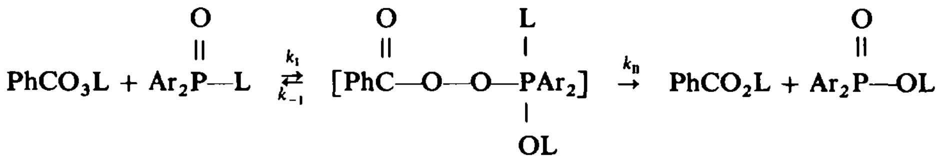


FIG 1. Linear relationship observed among the observed second-order rate constant values and base concentrations at relatively high alkalinity levels

DISCUSSION

For the purpose of discussing the kinetic isotope effects observed in acidic media, the following reaction scheme may be considered



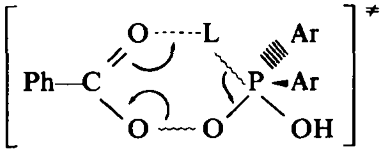
$$\mathrm{PhCO_3L} + \mathrm{Ar_2}\overset{\overset{\displaystyle O}{\|}}{\mathrm{P}}\mathrm{—L} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \Big[\mathrm{Ph}\overset{\overset{\displaystyle O}{\|}}{\mathrm{C}}\mathrm{—O—O—}\underset{\underset{\displaystyle OL}{|}}{\overset{\overset{\displaystyle L}{|}}{\mathrm{P}}}\mathrm{Ar_2}\Big] \xrightarrow{k_{II}} \mathrm{PhCO_2L} + \mathrm{Ar_2}\overset{\overset{\displaystyle O}{\|}}{\mathrm{P}}\mathrm{—OL} \qquad (4)$$

2

in which it is L = H or D. Accordingly, if a steady-state concentration of intermediate **2** is attained, it is $k_2(\mathrm{obs}) = k'_2 = k_1k_{II}/(k_{-1} + k_{II})$.

Inspection of data summarized on Table II reveals that for all three diarylphosphine oxides considered $[(k'_2)^{H}_{H_2O}/(k'_2)^{D}_{D_2O}]$ ratios greater than unit are found. This seems to indicate that, within the scheme above, decomposition of the intermediate **2** involving the breaking of the P—L bond should be slower than its formation; in fact, even though it can be estimated[7] that the acid strength of $PhCO_3H$ in H_2O can be as much as 2–3 times greater than $PhCO_3D$ in D_2O, this factor should not play an important role since kinetic data have shown that the reaction being studied is not significantly affected by acid catalysis.[2]

On the basis of the stretching frequencies of the P—H and P—D bonds a primary isotope effect (k^H/k^D) $\simeq$ 4·8 can be estimated.[8,9] The lower ratios actually observed (Table II) might, of course, be attributed to a different timing of the P—L *versus* the O—O bond breaking in the t.s. leading from **2** to products, and/or to a cyclic structure (such as **3**) of the same t.s.:[10]



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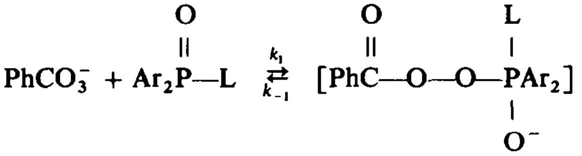
Cyclic transition states are rather common in peroxide reaction mechanisms.[11]

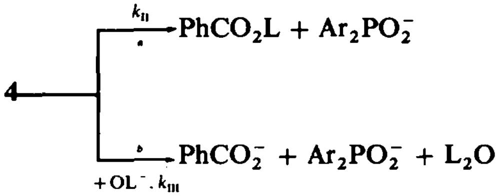
As far as the Swain criterion[12] for distinguishing proton from hydride abstraction may be applied to our system, the observed increase in the ratio expressing the overall kinetic isotope effect on passing from *para*-methyl to the *para*-chloro substituted compound seems to point out a fair proton character of the hydrogen removal from phosphorus in the t.s. This agrees with kinetic data previously reported.[1,2]

The oxidation process occurring in alkaline media might be outlined as follows:



$$\mathrm{PhCO_3^-} + \mathrm{Ar_2}\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\mathrm{P}}\mathrm{—L} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} [\mathrm{Ph}\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}\mathrm{—O—O—}\underset{\underset{\displaystyle \mathrm{O^-}}{|}}{\overset{\overset{\displaystyle \mathrm{L}}{|}}{\mathrm{P}}}\mathrm{Ar_2}] \qquad (5)$$

4



(6)

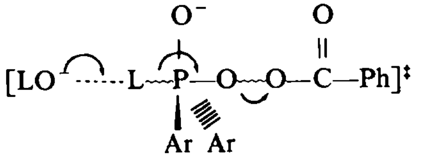
Assuming again a steady-state concentration of intermediate **4**, the overall-rate constant k_2(obs) would be defined through equation 7:

$$k_2(\mathrm{obs}) = (k_I k_{II} + k_I k_{III}[\mathrm{OL^-}])/(k_{-I} + k_{II} + k_{III}[\mathrm{OL^-}]) \qquad (7)$$

As already pointed out,[1] the finding that at high alkalinity levels the observed second-order rate constant is linearly dependent on $\mathrm{OL^-}$ concentration (equation 3) is in itself a clear indication that, under the given conditions, decomposition of the reactive intermediate **4** dominates the kinetics; in fact, in equation 7 it should be $k_{-I} \gg (k_{II} + k_{III}[\mathrm{OL^-}])$.

Provided the obtained k_2'' values (Table I) can be taken as to represent the OL^- concentration independent process which takes place in alkaline media (equations 5 and 6, path *a*), the ratio $[(k_2'')^{H}_{H_2O}/(k_2'')^{D}_{D_2O}] = 2{\cdot}7$ also seems to indicate that cleavage of P—L bond occurs in a slow step. However, considering that the value of this ratio is affected by a relatively high probable error (see Table I), on this point no detailed discussion is allowed.

Finally, the oxidation process occurring in strongly alkaline media (equations 5 and 6, path *b*) needs to be discussed. Here the t.s. for the step leading from H to products was thought[1] to be as follows:



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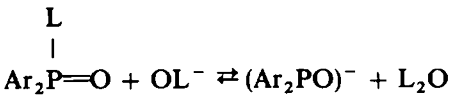
This would bear some resemblance with the t.s. that is usually pictured for some polar fragmentation reactions of peroxide molecules which are promoted by the attack of a base on an hydrogen atom bonded to a carbon atom in the α position to an O—O bond.[11, 13]

Considering **5**, it would be possible to anticipate that a primary isotope effect $(k^H/k^D) \simeq 4{\cdot}8$ (see above) should arise from P—L bond breaking together with a "secondary" isotope effect due to the greater base strength of OD^- (in D_2O) when compared to OH^- (in H_2O).[14, 15] The latter can be evaluated to be $(k_{OH^-}/k_{OD^-}) \simeq 0{\cdot}5$ on the basis of K_B value[15] for the equilibrium $2OD^- + H_2O \rightleftarrows 2OH^- + D_2O$. Normally, for a proton transfer to the base of about 50% in the t.s., one would anticipate the above-mentioned primary and secondary isotope effects to overlap somewhat yielding an overall rate constants ratio close to 2·5–3·0.

The markedly less than unit value (0·25) found for the ratio $[(k_3)^{H}_{OH^-}/(k_3)^{D}_{OD^-}]$ might therefore be interpreted as that either the proton transfer from phosphorus of **4** to the base is achieved in a fast preequilibrium step prior to a slow cleavage of the peroxidic bond or, within t.s. **5**, the said proton transfer to OH^- is well more advanced than O—O bond breaking.[15, *] This is not surprising since the exchange experiments have shown the relatively high kinetic "mobility" of hydrogen bonded to phosphorus in *sec*-phosphine oxide molecules.

It can hardly be over emphasized, however, that some alternative reaction paths for our reaction in strongly alkaline media can also be envisaged. For example, in these conditions the possibility exist that the oxidation by $PhCO_3^-$ involves the preliminary equilibrium:



$$Ar_2\overset{\displaystyle L}{\overset{|}{P}}{=}O + OL^- \rightleftarrows (Ar_2PO)^- + L_2O$$

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[*] Whereas it could be argued that the observed ratio value is about one half of the limit ($\simeq 0{\cdot}5$) set forth for a secondary isotope effect (k_{OH^-}/k_{OD^-}) for elimination reactions in water,[15] it should also be reminded that in our case any quantitative prediction of such ratio is precluded since a number of important factors—as *e.g.*, K_B value in the mixed solvent employed—are not known.

even though—as already discussed[1]—at present time we have reasons to believe this rather unlikely.

In spite of the well recognized utility of deuterium isotope effects as a tool in the elucidation of reaction mechanisms, applications in the field of peroxide reactions have been rare. Their determination might prove useful in gaining more insight into many multi-step oxidation processes involving hydroperoxides.

EXPERIMENTAL

Materials and solvents. Diphenylphosphine oxide, bis-*p*-tolylphosphine oxide, bis(*p*-chlorophenyl)-phosphine oxide and peroxybenzoic acid samples used in this work have been described.[2] Dioxan (C. Erba. high purity) was further purified according to the method given by Fieser.[16] b.p. 101–101·6°. Protium oxide was laboratory distilled water which had been redistilled over $KMnO_4$. Deuterium oxide (Merck. ≥99·5% deuterium label) purity was checked by NMR. KOH standard solns were made by dissolving AnalaR grade KOH (Merck) into freshly deaerated distilled water. KOD solns were prepared by decomposing K amalgam in D_2O; the amalgam was previously prepared by electrolysis of a KCl (Merck. A.R.) saturated soln with a Hg cathode and Pt anode, with constant stirring of the Hg layer, in an apparatus similar to that reported by Vogel.[17] Dioxan-H_2O and dioxan-D_2O mixed solvents were made by weighing the proper amount of H_2O or D_2O into volumetric flasks, then bringing up to volume with dioxane in a thermostatic bath at 25·0°. Due care was exercised in manipulating D_2O containing solns.

Kinetics. Known volumes of standard solns of each reagent in the mixed solvent were added—at zero time—to a reaction flask containing standard solns of KOH (or KOD) in dioxan-H_2O (or dioxan-D_2O). Small amounts of EDTA disodium salt (C. Erba, A.R.) were also present in each reacting soln; this is to sequester trace amounts of heavy metal ions, which—if present—could induce a rapid decomposition of the peroxyacid.[18] Aliquots were withdrawn at time intervals and the peroxybenzoic acid concentration determined according to the iodometric technique reported.[2] Rate constant values (Table I) are usually average values from two or more independent runs.

Spectra. IR spectra were taken on Perkin-Elmer 337 or 621 instruments; NMR spectra were recorded by using a Perkin-Elmer R 12 or a Varian A 60-A spectrometer.

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