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CONCERNING INVESTIGATIONS INTO MECHANISMS OF SECONDARY PHOSPHINE OXIDE REACTIONS

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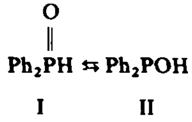
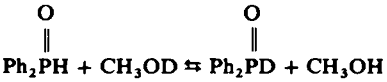
Abstract—The deuterium exchange reaction between diphenylphosphine oxide (DPPO) and methanol-d_1 has been investigated. The reaction was found to be first-order in DPPO. Diphenylphosphinic acid (DPPA) and DCl catalyzed the exchange reaction; a first-order dependence of reaction rate on each was observed. Detectable amounts of DPPA contaminate samples of DPPO prepared by previously reported techniques. The acid impurity complicates mechanistic interpretations, and the need for careful purification prior to kinetic studies on DPPO reactions is demonstrated.

We have been examining the mechanistic aspects of the reactions of secondary diarylphosphine oxides (I) in an attempt to clarify the role of the phosphinous acid form (II) as a reaction intermediate (Eq 1). Substantial kinetic evidence had been presented to demonstrate the analogous phosphite intermediate in the deuterium exchange and oxidation reactions of secondary phosphonates.[2–8] The situation is less clear for the secondary phosphine oxides.[9–10]



$$\underset{\text{I}}{\mathrm{Ph_2\overset{\overset{O}{\|}}{P}H}} \rightleftarrows \underset{\text{II}}{\mathrm{Ph_2POH}} \qquad (1)$$

We examined the exchange reaction of DPPO with methanol-d_1 (Eq 2) at −8°; NMR spectroscopy was used as the analytical method (Experimental). The data have been treated by the integrated plot method; the reaction was found to be first-order with respect to phosphine oxide concentration in all kinetic runs. When DPPA and DCl were separately added as catalysts, first-order dependences on these substances were observed. A rate law can be formulated (Eq 3), where k_w is the acid-independent first-order rate constant and where k_2 and k_3 are the second-order rate constants for catalysis by DPPA and DCl, respectively. The mechanism(s) which can be postulated



$$\mathrm{Ph_2\overset{\overset{O}{\|}}{P}H + CH_3OD \rightleftarrows Ph_2\overset{\overset{O}{\|}}{P}D + CH_3OH} \qquad (2)$$

$$\text{Rate} = k_1(\text{obs})[\mathrm{Ph_2\overset{\overset{O}{\|}}{P}H}] = [\mathrm{Ph_2\overset{\overset{O}{\|}}{P}H}]\{k_w + k_2[\mathrm{Ph_2\overset{\overset{O}{\|}}{P}OH}] + k_3[\mathrm{DCl}]\} \qquad (3)$$

for the H/D exchange reaction are substantially similar to those already given for secondary phosphonates and for secondary phosphine oxides.[2–6, 10]

In the course of our investigation* of the uncatalyzed and catalyzed exchanges, it was found that DPPA present as residual impurity in DPPO samples prepared via previously-reported synthetic methods[9, 11] catalyzed the deuterium exchange reaction. Evidence for such catalysis was:

a. The apparent first-order rate constant k_1 for the exchange reaction of DPPO increased with initial DPPO concentration. Some data are presented in the first four entries of Table 1. This is explicable on the basis of an impurity in DPPO that catalyzes the reaction.

b. When small amounts of sodium methoxide were added to reaction solutions, the DPPO exchange rate decreased with increasing methoxide concentration up to a point beyond which further addition of methoxide caused the rate to be too fast to measure. Data are given in the last five entries in Table 1. A reasonable explanation for this observation is that neutralization of a catalytically-active acid impurity in the DPPO samples obtains at low concentrations of base. After neutralization of acid is complete methoxide ion itself acts as a powerful catalyst.

TABLE 1. EXCHANGE REACTION OF DIPHENYLPHOSPHINE OXIDE (DPPO) WITH METHANOL-d$_1$ AND WITH METHANOL-d$_1$ IN THE PRESENCE OF METHOXIDE ION[a]

[DPPO], M	$[CH_3O^-] \times 10^3$, M	$k_1 \times 10^2$ (min^{-1})
0·320	0	2·1
0·461	0	2·5
0·462	0	2·6
0·598	0	2·9
0·414	1·9	1·0
0·522	4·7	0·69
0·612	7·5	0·13
0·635	19	too fast to measure
0·553	75	too fast to measure

[a] $T = -8°$

TABLE 2. CATALYSIS BY DIPHENYLPHOSPHINIC ACID OF THE EXCHANGE REACTION OF DIPHENYLPHOSPHINE OXIDE IN METHANOL-d$_1$[a]

[DPPO], M	Added [DPPA] $\times 10^3$, M	$k_1 \times 10^2$ (min^{-1})
0·461	0	2·6
0·414	0·76	3·6
0·424	1·51	4·5
0·408	3·02	5·1
0·499	3·95	5·9

[a] $T = -8°$

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* We carried out a large number of exchange experiments. Only those which bear directly on the present article are reported here. The results of other experiments are fully consistent with the data given here.

c. A standard solution of DPPA was prepared and titrated with sodium hydroxide. A pK_a of 2·7 in 95% H_2O–5% EtOH at 25° was observed [lit.[12] pK_a 2·32 (water) and 4·24 (80% EtOH)]. DPPO samples were then titrated in water with sodium hydroxide and a titration curve similar to that for DPPA was obtained; $6{\cdot}8 \times 10^{-3}$ mmole of acid was found per 0·5 mmole of DPPO.

d. When DPPA was added to DPPO in methanol-d_1, the exchange reaction was catalyzed by the DPPA. Data are given in Table 2. A plot of k_1 against added DPPA was linear and a catalytic constant of $7{\cdot}4 \pm 1{\cdot}5$ M^{-1} min^{-1} was calculated from the slope. The error limits are derived from a least squares analysis and partially take into account the nonidentical initial concentration of DPPO in each kinetic experiment. From this value of k_2 for DPPA catalysis, a value of $3{\cdot}7 \pm 1{\cdot}4 \times 10^{-3}$ mmole of acid per 0·5 mmole of DPPO was calculated, if it is assumed that the observed rate was due only to the DPPA catalyzed reaction. If one considers the difference in techniques between the titration and kinetic procedures and the amounts involved, the values for the amount of acid present in the same DPPO samples obtained by the two methods are in reasonable agreement.

e. To see if catalysis occurs with other acids, catalysis of the exchange reaction in the presence of DCl was studied and some data are given in Table 3. A plot of k_1 against DCl concentration was linear and a catalytic constant, k_3, of 78 M^{-1} min^{-1} was obtained.*

TABLE 3. CATALYSIS BY DCl OF THE EXCHANGE REACTION OF DIPHENYLPHOSPHINE OXIDE IN METHANOL-d_1[a]

[DPPO], M	[DCl] × 10^3, M	$k_1 \times 10^2$ (min^{-1})
0·461	0	2·6
0·556	0·45	5·8
0·388	1·25	13
0·513	1·88	17

[a] $T = -8°$

It can, therefore, be said that samples of DPPO prepared and purified via previously reported routes,[9, 11] are likely to be contaminated with small quantities (about 0·5%) of DPPA.† Other substituted diarylphosphine oxides examined by us also appear to be contaminated with the corresponding diarylphosphinic acids, though likely to a lesser extent than with DPPO.

A better method for removal of DPPA impurity was explored. The purest samples of DPPO that we obtained came from the collection of DPPO on a cold finger of a vacuum sublimator as described in the experimental section. Such samples had a melting point of 56–57°, which is the highest reported value for DPPO.[9, 11] The exchange rate constant at −8° was approximately 4×10^{-4} min^{-1}. This can be taken as an upper limit for the acid independent exchange rate constant in methanol-d_1.

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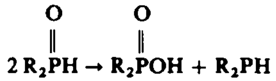
* Since this constant is approximately tenfold greater than the catalytic constant for DPPA, the fact that the initial concentrations of DPPO were not the same should have little effect on the DCl value.

† The catalysis of the exchange reaction in methanol-d_1 is probably by DPPA but our data are insufficient to distinguish catalysis by the deuteronium ion produced by DPPA ionization, followed by proton exchange with the solvent.

The presence of small amounts of DPPA (a reaction byproduct in the synthesis of DPPO) is certainly connected with the difficulties encountered in purifying this compound by the usual techniques. For example, recrystallizations of DPPO samples from solvents often result in an increase of DPPA impurity with increasing solvent temperature, probably due to disproportionation[13–15] to phosphine and phosphinic acid (Eq 4) or air oxidation. In view of the fact that in general prototropic equilibria



$$2\,R_2\overset{\overset{O}{\|}}{P}H \rightarrow R_2\overset{\overset{O}{\|}}{P}OH + R_2PH \qquad (4)$$

and specifically phosphonate–phosphite tautomerizations,[2–8] are subject to acid catalysis which is important in reaction mechanisms, we feel that any detailed investigation into the reactions of secondary phosphine oxides must take into consideration the fact that compounds prepared and purified by previously reported techniques will likely have enough phosphinic acid present to complicate mechanistic data just as it has complicated the present investigation.

EXPERIMENTAL

Diphenylphosphine oxide was prepared according to the method of Hunt and Saunders[11] as modified by Grayson *et al.*,[9] m.p. 52–55° (reported 53–56°).[11] Further purification was obtained by placing $\sim$0·5 g of DPPO in the base of a micro vacuum sublimator. The base was immersed in a water bath, *ca* 80°, and DPPO was collected on the cold finger at 2 mm for 2–3 hr. The DPPO sample contained a characteristic odour of phosphine and the residue in the base of the sublimator was acidic. At high temp, DPPO appears to disproportionate to DPPA and diphenylphosphine, and the latter is collected on the cold finger with the DPPO. After collection DPPO samples were kept at room temp under constant evacuation (at 2 mm) for 2–3 days. Such samples melted at 56–57°.

Diphenylphosphinic acid (K & K Laboratories) was recrystallized from spectrograde MeOH (m.p. 197–198 1/2°). DCl solns in MeOD were prepared by adding D_2O (Stohler—99% D label) dropwise, stirring constantly, to dichlorodimethyl silane (Aldrich);[16] the evolved DCl gas was bubbled in MeOD, after passing through a trap containing Drierite. Sodium methoxide was prepared by the reaction of sodium and methanol-d_1 and its concentration determined by titration with standard HCl. Methanol-d_1 (Stohler Isotope—99% D label) was used without further purification. All other compounds were of reagent grade.

Kinetics. DPPO samples were weighed in a dry box into a 1-ml volumetric flask. This flask and a second flask containing MeOD (1% TMS) were precooled to −10°. The MeOD contained the appropriate amounts of DCl, NaOMe, or DPPA. MeOD was added to the flask containing the DPPO sample, the soln vigorously shaken, and a timer activated. About 0·5 ml of reaction soln was rapidly transferred to an NMR tube precooled to −8° in the variable temp probe of a Varian A-60A spectrometer. Temp calibrations of the NMR probe were made using a Varian MeOH sample. The exchange reaction was monitored by following the disappearance of the low field half of the phosphorus-hydrogen (P-H) doublet at about 12·1 ppm relative to TMS. Peak intensity was assumed to be proportional to concentration,[2, 4, 6, 17] and TMS was used as an internal standard to compensate for changes in the rf field stability between measurements. Each time the P-H peak was scanned, the TMS signal was also viewed. A plot of the $\log_{10}$ P-H peak height divided by the TMS peak height against time was linear for at least two half-lives and the negative of the slope multiplied by 2·3 was taken as the first-order rate constant k_1.

Acid and base titrations. NaOH aq was standardized against primary standard potassium acid phthalate. HCl solns were standardized by titration against the standard NaOH. The pK_a of DPPA was determined in 95% H_2O–5% EtOH by adding small amounts of base to a DPPA soln and measuring the pH as a function of added NaOH. The half-neutralization point was taken as the pK_a and was equal to 2·7. DPPO samples were titrated in the same manner as DPPA except that a 100% H_2O system was used.

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