## Anchimeric Assistance in Solvolysis of Haloalkylphosphines

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Summary: Kinetic data are presented which reveal haloalkylphosphines undergo anchimerically-assisted cyclization with the ring-size preference 5 > 6 > 3 > 4. Also, phenylthio and diphenylphosphino groups are shown to have similar intramolecular nucleophilicities.

Although anchimerically-assisted displacement reactions involving the nitrogen, oxygen, and sulfur atoms in ring closure rate studies are well characterized,<sup>1</sup> evidence for assistance by neighboring groups containing the larger nuclei in groups V and VI is largely qualitative. Studies of neighboring selenium<sup>2</sup> revealed a pattern similar to that observed for sulfur<sup>1</sup> and the halogens:<sup>3</sup> heavier nuclei in a family show a higher intramolecular nucleophilicity than smaller ones. Trivalent phosphorus is a powerfully nucleophilic atom<sup>4</sup> whose intramolecular nucleophilicity has been largely ignored. It is especially interesting to characterize the properties of the phosphorus neighboring group since the intermolecular nucleophilicity of group VI atoms differs from group V atoms. For example, the respective decreasing orders of reactivity toward CH<sub>3</sub>I in methanol are: Et<sub>2</sub>Se > Et<sub>2</sub>S > Et<sub>2</sub>O but Et<sub>3</sub>P > Et<sub>3</sub>As > Et<sub>3</sub>N.<sup>4</sup> For substrates with phosphorus neighboring groups, only accounts which show product evidence strongly supporting neighboring group participation have appeared.<sup>5</sup> In the present letter we consider the question of ring size on the effectiveness of anchimeric assistance by a neighboring proups.

We have prepared a series of haloalkyldiphenylphosphines<sup>6</sup> and determined their pseudo firstorder solvolysis rates in aqueous trifluoroethanol (TFE) and in some cases aqueous ethanol (EtOH), Table 1. The question of whether or not these systems are reacting by an anchimerically-assisted process ( $\underline{k}_{a}$ ) or by solvent-assisted displacement ( $\underline{k}_{s}$ ) can be addressed in a number of ways.<sup>1</sup> The rates of <u>n</u>-butyl chloride in 60% aq. EtOH were available from a previous study;<sup>7</sup> therefore, we can compare the reactivity of this model system with 4-chlorobutyl diphenylphosphine. Selecting an intermediate temperature for the rate comparisons, we determine the following rate ratio:

at 80 °C  $\frac{\underline{k}(Ph_2PCH_2CH_2CH_2CH_2CI)}{\underline{k}(CH_3CH_2CH_2CH_2CI)} = \frac{4.56 \times 10^{-3} \text{ sec}^{-1}}{1.82 \times 10^{-6} \text{ sec}^{-1}} = 2507$ 

Also, the chlorobutylphosphine quantitatively yields the cyclic phosphonium salt. Clearly, anchimeric assistance by phosphorus is indicated in this case. Assuming that all of the substrates react by a cyclization mechanism, eq. 1, comparing the rates in 97% aq. TFE of the series of phosphines at a

$$\begin{array}{ccc} \operatorname{Ph}_{2}\operatorname{P}(\operatorname{CH}_{2})_{n-1}\operatorname{CI} & \longrightarrow & \operatorname{Ph}_{2}\operatorname{P}^{+}(\operatorname{CH}_{2})_{n-1} & (\text{eq. 1}) \\ 1 & 2 & 2 \end{array}$$

common temperature gives the relative cyclization rate order. The observed order is the same as that of

1, n = 3 4 5 6  
$$\underline{k}_{rel}$$
 (25 °C) 15 1.0 1785 105

analogous nitrogen substrates but differs from the order for sulfur substrates, where three-membered ring formation is best (3 > 5 > 6 > 4).<sup>1</sup> It is well known that the nitrogen and sulfur derivatives may suffer ion pair return upon cyclization.<sup>1</sup> It is not clear that this would occur for the phosphorus analogues. For example, the four- to six-membered rings containing the phosphonium groups are more stable than analogous sulfur or nitrogen salts and those which have been studied undergo hydrolysis by attack at phosphorus.<sup>8</sup> However, few properties of phosphiranium ions are known.

We must of course question whether the slowest reacting system above, 1 (n = 4), reacts with anchimeric assistance. Eliel and coworkers have recently addressed this question for analogous oxygen and sulfur<sup>9</sup> neighboring groups finding that four-membered ring formation is limiting in cases where alkyl branches are present. However, they did not find evidence of anchimeric assistance in the solvolysis of either RSCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OTs or the analogous oxygen system. Grob and Jenny<sup>10</sup> found that 3-chloropropyldimethylamine undergoes complete cyclization in 80% aq. EtOH and assigned this process as a  $k_{\Delta}$ -type. In the course of another study,<sup>11</sup> we have obtained evidence suggesting that the phosphorus substrate, 1 (n = 4), reacts by a  $k_{\Delta}$  mechanism. Our evidence comes from the finding that added thiourea retards the rate of these reactions. Studies with several model systems have shown that the rates of  $k_{\Delta}$  substrates are accelerated by thiourea while the rates of  $k_{\Delta}$  substrates are slightly retarded.<sup>12</sup> Although we did not isolate four-membered ring phosphonium salts in this study, substituted

Although we did not isolate four-membered ring phosphonium salts in this study, substituted analogs have been previously isolated and studied.<sup>13</sup> The three-membered rings are, however, elusive intermediates perhaps because of their high reactivity. They have been postulated as intermediates in the dimerization of (2-substituted ethyl) diphenylphosphines, where they are thought to undergo attack at C,<sup>5a</sup> and in the base-catalyzed reaction of (PhCHBr)<sub>2</sub>P<sup>+</sup>Ph<sub>2</sub>, where attack at P is thought to occur.<sup>14</sup> Our kinetic results, run with dilute solutions, tend to support formation of three-membered ring intermediates rather than a direct bimolecular route to the cyclic dimeric diphosphonium salts. Isotopic labeling experiments, which we hope will confirm this, are in progress.

Finally, to compare the phosphorus neighboring group with literature rates<sup>2</sup> of its periodic table neighbors, the rate of 1 (n = 2) was run in 80% aq. EtOH (w/w). At 25 <sup>o</sup>C we find the following

Substrate	Solvent 97% TFE	Temp. ( <sup>O</sup> C) 45.5	10 <sup>4</sup> <u>k</u> (sec <sup>-1</sup> ) 0.131 <u>+</u> 0.008	$\Delta$ H <sup>‡</sup> (kcal/mol) $\Delta$ S <sup>‡</sup> (eu)	
Ph <sub>2</sub> P(CH <sub>2</sub> ) <sub>2</sub> CI				17.3	-26.9
		73.7	1.21 <u>+</u> 0.15		
		101.1	8.85 <u>+</u> 0.17		
	80% EtOH	73.5	0.259 <u>+</u> 0.021	16.8	-31.4
		99.7	1.54 <u>+</u> 0.09		
Ph <sub>2</sub> P(CH <sub>2</sub> ) <sub>3</sub> CI	97% TFE	73.5	0.279 <u>+</u> 0.001	22.4	-15.2
		88.3	1.28 <u>+</u> 0.02		
		102.3	3.22 <u>+</u> 0.05		
Ph <sub>2</sub> P(CH <sub>2</sub> ) <sub>4</sub> CI	97% TFE	25.0	2.09 <u>+</u> 0.07	18.3	-13.9
		35.2	6.23 <u>+</u> 0.08		
		45.6	16.5 <u>+</u> 0.2		
	80% EtOH	24.8	0.300 <u>+</u> 0.017	8.89 <sup>b</sup>	-49.3 <sup>b</sup>
		38.5	0.625 <u>+</u> 0.015		
	60% EtOH	35.4	1.42 <u>+</u> 0.10	16.4	-23.2
		44.4	2.86 <u>+</u> 0.03		
		58.2	9.30 <u>+</u> 0.02		
Ph <sub>2</sub> P(CH <sub>2</sub> ) <sub>5</sub> CI	97% TFE	45.8	0.953 <u>+</u> 0.004	17.9	-20.9
		60.7	3.56 <u>+</u> 0.03		
		75.0	11.1 <u>+</u> 0.1		

 Table 1. Rates and Activation Parameters for Solvolysis of Chloroalkyl Diphenylphosphines in

 Aqueous Alcohols.<sup>a</sup>

<sup>a</sup>Aqueous TFEs are wt/wt. Aqueous EtOHs are vol/vol. Each sample was normally run in triplicate. Samples contained <u>ca.</u>  $10^{-3}$  M each in substrate and 2,6-lutidine (acid scavenger) in 10 mL of solvent. Rates were determined conductimetrically. <sup>b</sup>Because of the narrow temperature range and slow reactions, these activation parameters may not be reliable.

relative rate ratio:

## $PhSeCH_2CH_2CI: PhSCH_2CH_2CI: Ph_2PCH_2CH_2CI = 1350: 15.6: 1$

For the purpose of comparison, if we assume that ion pair return is a constant and that the second phenyl has no effect on the reactivity of the  $Ph_2P$  group, selenium is the better internal nucleophile with sulfur being an order of magnitude better than phosphorus. However, since Eliel and Knox<sup>8</sup> found no evidence for RS-4 in the solvolysis of RSCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OTs yet we did determine that ArP-4 participation

occurs in analogous systems, it seems that these two neighboring groups are closely matched with other factors being important in which is the better. The reversal in order is not surprising since for RS-n participation the order is different from the phosphorus order being 3 > 5 > 6 > 4.<sup>1</sup>

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