

## The Reactions of Phosphorus Esters with Phenylmagnesium Bromide

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The reactions of a variety of different phosphorus esters with phenylmagnesium bromide were investigated in tetrahydrofuran. For a structurally similar series of substituted phosphonates the order of reactivity was found to be  $p\text{-ClPhP(=O)(OEt)}_2 > \text{PhP(=O)(OEt)}_2 > p\text{-CH}_3\text{PhP(=O)(OEt)}_2 > \text{EtP(=O)(OEt)}_2$ . These results support the theory that electron-withdrawing substituents increase the susceptibility of the phosphorus atom to nucleophilic attack. Since the ground state energies of these esters appear to be similar, it seems reasonable that electrophilic substituents stabilize the transition state. On the other hand, in structurally dissimilar phosphorus esters, the order of reactivity was observed to be  $\text{Ph}_2\text{P(=O)OEt} > \text{PhP(=O)(OEt)}_2 > (\text{EtO})_3\text{P(=O)-OEt} > \text{EtP(=O)(OEt)}_2 > (\text{EtO})_3\text{P(=O)}$ . Infrared spectral evidence indicates that the P=O bond strengths and thus P-O  $p\pi d\pi$  overlap in the ground states increase in the reverse orders. Thus, less energy is required to overcome the P=O character in going from the ground state to the transition state of ethyl diphenylphosphinate than of triethyl phosphate. The fact that the order of magnitude of increased reactivity is less in the aliphatic series than in the aromatic series is readily understandable in terms of the different inductive effects on the stability of the transition states. These results are totally consistent with what is known about the effect of substituents on the stability of pentavalent organophosphorus compounds and the basicity of phosphoryl compounds.

The reactions of phosphorus esters and halides with nucleophilic reagents have been used extensively to synthesize organophosphorus compounds.<sup>1</sup> In contrast, the mechanism of these reactions does not appear to be well understood. For example, nucleophilic displacements on phosphorus in phosphorus esters have been visualized as being facilitated by electron-withdrawing substituents.<sup>2</sup> Whether or not these substituents stabilize the transition state or affect the ground-state energies does not appear to have been established. This problem was first recognized when diethyl phosphonate was found to be much more reactive with regard to methyl and ethyl Grignard reagents than was diethyl phenylphosphonate.<sup>3</sup> Furthermore, the recent finding that either magnesium chloride or bromide retards the reaction of diethyl phenylphosphonate with phenylmagnesium bromide does not clarify the situation.<sup>4</sup> Conceivably, either the magnesium halide-diethyl phenylphosphonate complexes are not formed appreciably in diethyl ether or tetrahydrofuran (THF) in the presence of phenylmagnesium bromide, or, for some other reason, the primary proposal described above fails to explain the relative reactivities of the phosphonate and its complex. In an attempt to answer these questions, the reactions of several similar and different phosphoryl esters with phenylmagnesium bromide were examined in THF at 68°. This system is highly suitable for study for several reasons.<sup>5</sup>

### Results

All reactions of the phosphorus esters with phenylmagnesium bromide were carried out under identical

conditions because of the difficulties anticipated in determining the rate constants.<sup>2d</sup> The analytical procedure described earlier was used to determine the percentages of the starting ester, the intermediate esters, and the products.<sup>4</sup>

Figure 1 illustrates the effect of electron-withdrawing substituents *vs.* electron-donating substituents on the rate of disappearance of the diethyl phosphonate in its reaction with phenylmagnesium bromide. The infrared spectra of these diethyl phosphonates showed phosphoryl absorptions at nearly the same wavelength indicating that the P=O bond strengths and P=O  $p\pi d\pi$  overlap are nearly the same in all four cases.<sup>6</sup> The remaining analytical data for these diethyl phosphonates are presented in Figures 2-5.

Worthy of note is the fact that the *p*-chlorophenyl-diphenylphosphine oxide underwent substitution with phenylmagnesium bromide to form triphenylphosphine oxide. Following addition of another equivalent of phenylmagnesium bromide to the reaction mixture, the formation of triphenylphosphine oxide was nearly complete after 24 hr at 68°. Similar displacements of benzene from triphenylphosphine oxide by alkyl lithium compounds have been observed previously.<sup>7</sup>

The results of a similar comparative study of triethyl phosphate, diethyl phenylphosphonate, and ethyl diphenylphosphinate are illustrated in Figures 6 and 7. The infrared spectra of these phosphorus esters and triphenylphosphine oxide showed a steady progression of the phosphoryl absorption from 1272  $\text{cm}^{-1}$  to 1252  $\text{cm}^{-1}$  to 1236  $\text{cm}^{-1}$  to 1200  $\text{cm}^{-1}$  with increasing substitution of phenyl groups for ethoxy groups. Similarly the phosphoryl absorptions varied for the series triethyl phosphate (1272  $\text{cm}^{-1}$ ), diethyl ethylphosphonate (1253  $\text{cm}^{-1}$ ). Figure 8 illustrates the order of reactivity observed for the aliphatic series of phosphorus esters with phenylmagnesium bromide.

*O,O*-Diethyl phenylthiophosphonate did not react with phenylmagnesium bromide in THF at 68° over a period of 6 hr.

(1) K. D. Berlin, T. H. Austin, M. Peterson, and M. Nagabhushanam, "Topics in Phosphorus Chemistry," Vol. 1, Wiley-Interscience, New York, N. Y., 1964, p 17.

(2) (a) K. D. Berlin and G. B. Butler, *Chem. Rev.*, **60**, 243 (1960); (b) K. D. Berlin, T. H. Austin, and K. L. Stone, *J. Amer. Chem. Soc.*, **86**, 1787 (1964); (c) K. D. Berlin and M. E. Peterson, *J. Org. Chem.*, **32**, 125 (1967); (d) K. D. Berlin and R. U. Pagilagan, *ibid.*, **32**, 129 (1967).

(3) H. R. Hays, *ibid.*, **33**, 3690 (1968).

(4) H. R. Hays, *ibid.*, **33**, 4201 (1968).

(5) Tetrahydrofuran was selected as the solvent because of its higher boiling point and because many of these reactions are heterogeneous in diethyl ether (see ref 2c and 2d). Phenylmagnesium bromide was selected as the Grignard reagent because the reaction products are readily separated and analyzed by gc. The ethyl esters were selected over the methyl esters since the former gave <1% C-alkylation (see ref 2d).

(6) *p*-ClPhP(=O)(OEt)<sub>2</sub>, 1256  $\text{cm}^{-1}$ ; PhP(=O)(OEt)<sub>2</sub>, 1255  $\text{cm}^{-1}$ ; *p*-CH<sub>3</sub>PhP(=O)(OEt)<sub>2</sub>, 1253  $\text{cm}^{-1}$ ; EtP(=O)(OEt)<sub>2</sub>, 1253  $\text{cm}^{-1}$ . Recorded with a Perkin-Elmer 21 (see ref 9).

(7) D. Seyferth, D. E. Welch, and J. K. Heeren, *J. Amer. Chem. Soc.*, **86**, 1100 (1964).

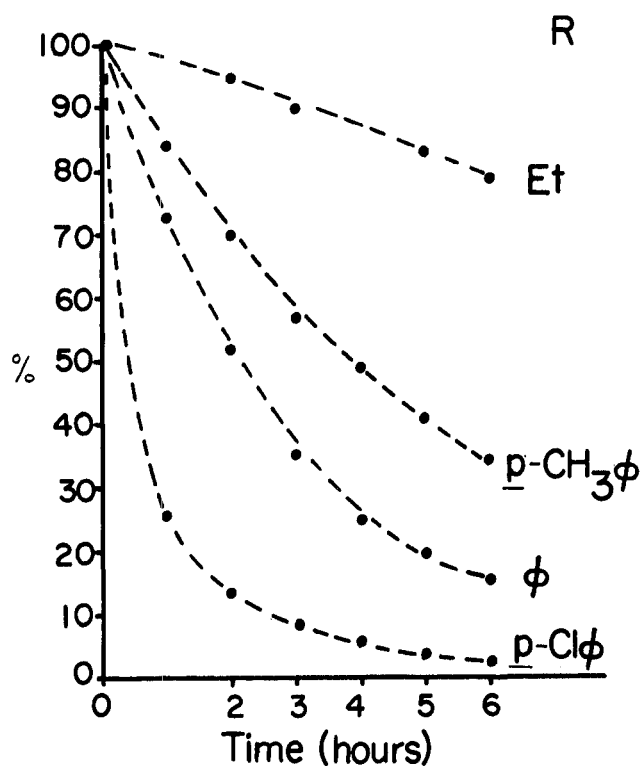


Figure 1.—The per cent of  $\text{RP}(=\text{O})(\text{OEt})_2$  vs. time in the reaction of  $\text{RP}(=\text{O})(\text{OEt})_2$  with  $2\text{PhMgBr}$  in THF at  $68^\circ$ .

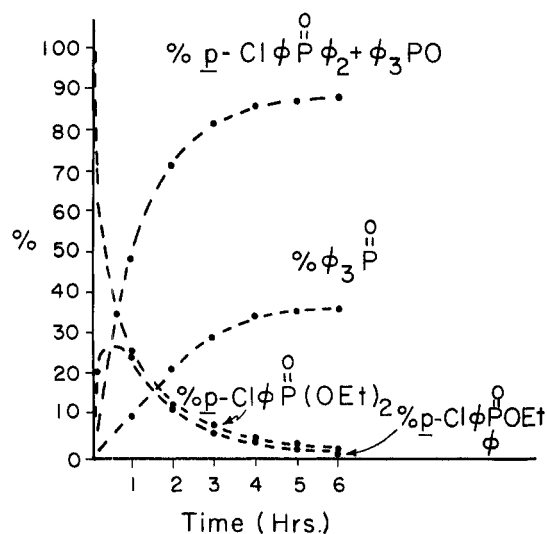
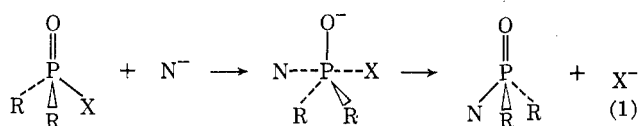


Figure 2.—The reaction of  $p\text{-Cl}\phi\text{P}(=\text{O})(\text{OEt})_2$  with  $2\text{PhMgBr}$  in THF at  $68^\circ$ .

### Discussion

The reaction of phosphoryl compounds with nucleophiles has been pictured as proceeding *via* a pentacovalent trigonal bipyramidal transition state.<sup>8</sup> Using



this model the results of this investigation can be explained in the following manner in terms of the different

(8) R. F. Hudson, "Structure and Mechanism in Organophosphorus Chemistry," Academic Press, New York, N. Y., 1965, pp 53-57.

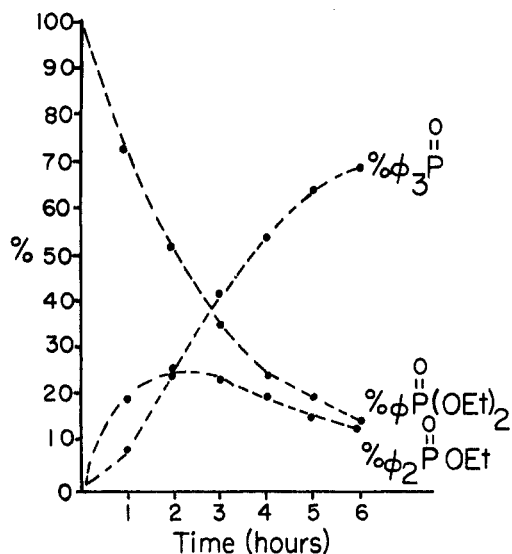


Figure 3.—The reaction of  $\text{PhP}(=\text{O})(\text{OEt})_2$  with  $2\text{PhMgBr}$  in THF at  $68^\circ$ .

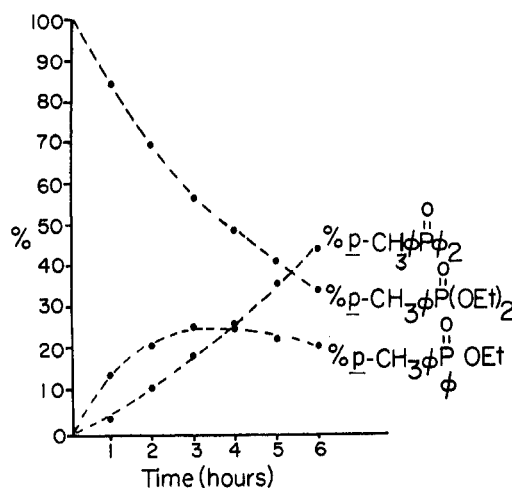


Figure 4.—The reaction of  $p\text{-CH}_3\phi\text{P}(=\text{O})(\text{OEt})_2$  with  $2\text{PhMgBr}$  in THF at  $68^\circ$ .

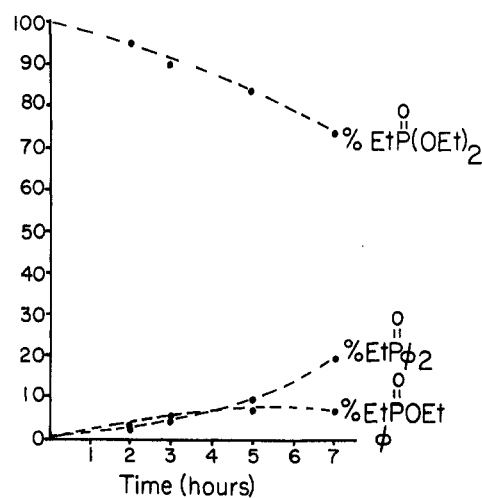


Figure 5.—The reaction of  $\text{EtP}(=\text{O})(\text{OEt})_2$  with  $2\text{PhMgBr}$  in THF at  $68^\circ$ .

effects of substituents on the ground states and the transition states.

The increase in rate of reaction of the four differently substituted diethyl phosphonates with phenylmagne-

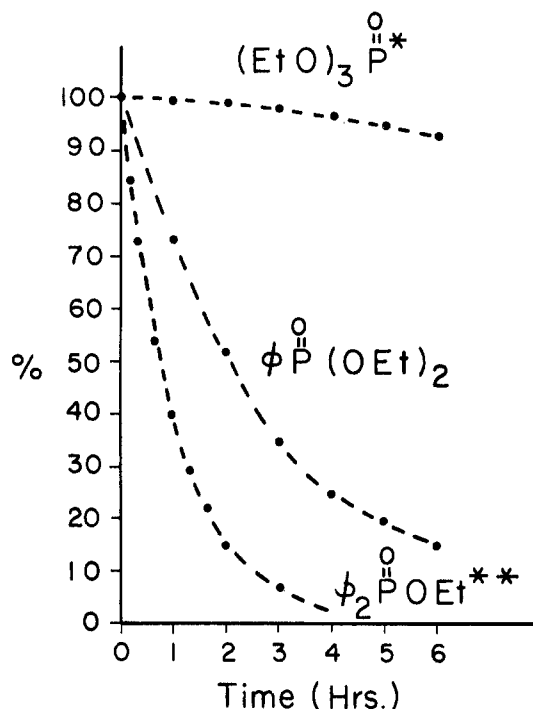


Figure 6.—The per cent of phosphorus ester *vs.* time in the reaction of ester with 2PhMgBr in THF at 68°: \*, statistically corrected; \*\*, only 1PhMgBr was used.

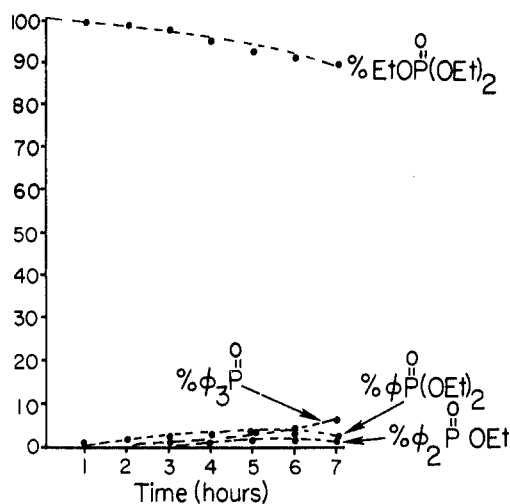


Figure 7.—The reaction of  $\text{EtOP(OEt)}_2$  with 2PhMgBr in THF at 68°.

sium bromide is readily seen to parallel the increasingly negative inductive effect of the substituents (Figure 1). Because the four esters are structurally very similar with regard to the central phosphorus atom, these results suggest that the pentacovalent transition state is stabilized by electron-withdrawing substituents. This proposal is not only consistent with the proposal of Berlin and coworkers<sup>2</sup> but also agrees with what is known about stable pentacovalent phosphorus compounds. Thus pentacovalent phosphorus compounds with highly electronegative substituents are markedly more stable than those compounds containing less electronegative substituents.<sup>9</sup> Contingent to this interpretation is the

(9) (a) G. Wittig, "De la chimie du phosphore pentavalent, Composes Organique du Phosphore," Centre National de la Recherche Scientifique, 1966, p 145; (b) F. Ramirez, J. F. Pilot, and C. P. Smith, *Tetrahedron*, **24**, 3735 (1968).

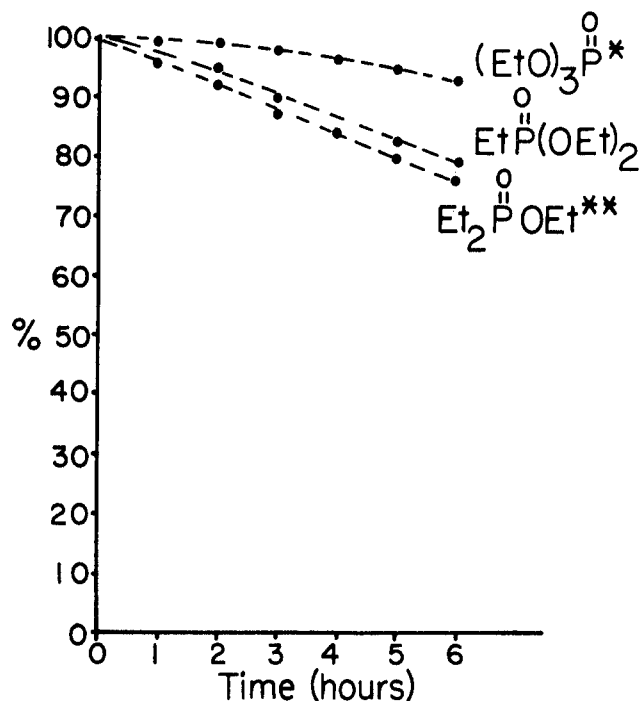


Figure 8.—The per cent of phosphorus ester *vs.* time in the reaction of ester with 2PhMgBr in THF at 68°: \*, statistically corrected; \*\*, only 1PhMgBr was used.

belief that the four phosphonate esters have similar ground-state energies. Evidence in support of this belief is the fact that all four of the phosphoryl stretching frequencies which in turn are related to the P=O bond energies and the P=O bond order (in terms of P=O  $\text{p}\pi\text{d}\pi$  overlap)<sup>10</sup> are very nearly the same ( $\pm 2 \text{ cm}^{-1}$ ) for all four of the diethyl phosphonate esters.

In more general terms, the stability of the transition state may also be influenced by factors other than the inductive effect of the substituent on phosphorus. Berlin and Pagilagan<sup>2d</sup> have shown that ethyl diphenylphosphinate and different Grignard reagents react at different rates dependent upon the size of the organic part of the Grignard reagent. That steric factors do not predominate in the preceding series is suggested from the order of reactivity and the fact that a phenyl group is larger than an ethyl group.

In contrast to the four esters described above the order of reactivity of the series of esters,  $\text{Ph}_2(\text{O}=\text{O})\text{P}(\text{OEt})_2 > \text{Ph}(\text{O}=\text{O})\text{P}(\text{OEt})_2 > (\text{EtO})_3(\text{O}=\text{O})\text{P}$ , to phenylmagnesium bromide cannot be simply explained by the reasoning described above. If inductive stabilization of the transition state by electron-withdrawing groups were the only factor to consider, the reverse order of reactivity would be expected since the transition state for  $(\text{EtO})_3\text{P}(\text{O}=\text{O})$  would be expected to have the lowest energy. This suggests that differences in ground-state energies are the predominant factors in determining the observed order of reactivity in this series. Relatively large differences in ground-state energies in this series would not be surprising in view of the quite different electronic properties of the groups attached to the phosphorus atom. This can be seen more clearly by consideration of the model system shown in eq 1, the P=O

(10) E. L. Wagner, *J. Amer. Chem. Soc.*, **85**, 161 (1963). The phosphoryl absorption frequencies of a wide variety of phosphoryl compounds were shown to correlate very well with the bond orders calculated by the LCAO-MO methods.

bond energies<sup>11</sup> and the P=O stretching frequencies of these three esters. First the model system involves going from a tetrahedral phosphoryl compound with a relatively high degree of P=O  $p\pi d\pi$  overlap in the ground state to an anionic pentacovalent transition state in which the negative charge resides largely upon the oxygen atom. In other words the  $p\pi d\pi$  overlap between the phosphorus and the phosphoryl oxygen atoms has been greatly diminished if not eliminated in the transition state. Accordingly, any increase in the  $p\pi d\pi$  overlap in the phosphoryl group in the ground state, *i.e.*, increase in the phosphoryl bond strength, should markedly increase the activation energy to reach the transition state. The fact that  $p\pi d\pi$  overlap in the phosphoryl group is greatest in  $(\text{EtO})_3(\text{O}=\text{P})$ , next in  $\text{Ph}(\text{O}=\text{P})(\text{OEt})_2$ , and least in  $\text{Ph}_2(\text{O}=\text{P})\text{OEt}$ , as evidenced by the P=O bond energies<sup>11</sup> and the P=O stretching frequencies, appears consistent with this interpretation of the observed order of reactivity  $(\text{EtO})_3(\text{O}=\text{P}) < (\text{EtO})_2(\text{O}=\text{P})\text{Ph} < \text{EtO}(\text{O}=\text{P})\text{Ph}_2$ . Inductive stabilization of the transition state by electron-withdrawing groups is important in this series as can be seen below in the comparison with the purely aliphatic esters. However, in the series of  $\text{Ph}_2(\text{O}=\text{P})\text{OEt}$ ,  $\text{Ph}(\text{O}=\text{P})(\text{OEt})_2$ , and  $(\text{EtO})_3(\text{O}=\text{P})$ , the effect of substituents on the transition state appears of lesser importance than their effect upon the ground state in determining the activation energy.<sup>12</sup>

In the aliphatic series of phosphorus esters the same relative order of reactivity toward phenylmagnesium bromide was observed, *i.e.*,  $\text{EtO}(\text{O}=\text{P})\text{PEt}_2 > (\text{EtO})_2(\text{O}=\text{P})\text{Et} > (\text{EtO})_3(\text{O}=\text{P})$ . This order can also be explained in terms of different ground-state energies as was the case for the aromatic series. However, the order of magnitude of increase in reactivity was not as great as in the aryl series. This is understandable upon consideration of the relative destabilizing effect on the transition state of the electron-donating ethyl group *vs.* the electrophilic phenyl group. This is in spite of even greater decreases in the P=O bond strengths and P=O  $p\pi d\pi$  overlap in the aliphatic series than in the aryl series as evidenced by the greater shifts of the P=O stretching frequency to longer wavelengths in going from  $(\text{EtO})_3(\text{O}=\text{P})$  to  $(\text{EtO})_2(\text{O}=\text{P})\text{Et}$  to  $\text{EtO}(\text{O}=\text{P})\text{Et}_2$ .

The fact that *O,O*-diethyl phenylthiophosphonate did not react with phenylmagnesium bromide under the same conditions as diethyl phenylphosphonate may be explained in the following manner. From a consideration of the P=S bond energy *vs.* the P=O bond energy, the ground-state energy of the thiophosphonate might be predicted to be larger than that of the phosphonate.<sup>13</sup> However, on the basis of Pauling's electronegativities of sulfur (2.5) and oxygen (3.5), oxygen

(11) See ref 8, pp 11 and 68.

(12) Several points suggest that the observed order of reactivity is not due to differences in basicity or degree of complexation. First, a separate study [H. R. Hays, *J. Amer. Chem. Soc.*, **91**, 2736 (1969)] indicates ethyl diphenylphosphinate and diethyl phenylphosphonate are completely complexed with the phenylmagnesium bromide under the conditions of the present study. Secondly, the observed order of reactivity  $\text{Ph}_2(\text{O}=\text{P})\text{OEt} > \text{Et}_2(\text{O}=\text{P})\text{OEt}$  is exactly opposite of the expected basicity order  $\text{Et}_2(\text{O}=\text{P})\text{OEt} > \text{Ph}_2(\text{O}=\text{P})\text{OEt}$ . See P. Haake, R. D. Cook, and G. H. Hulse, *ibid.*, **89**, 2650 (1967), and ref 8, p 281. Finally, in the first series of four esters the observed order of reactivity is also exactly the opposite of the anticipated order of basicity.

(13) See ref 8, p 68.

should stabilize the pentacovalent transition state more than sulfur. This difference in transition energies appears sufficiently great to overcome the difference in ground-state energies.

In view of the fact that electron-withdrawing groups accelerate the reactions of diethyl phosphonates with phenylmagnesium bromide, several questions remain about the manner in which magnesium halides retard the reaction of diethyl phenylphosphonate with phenylmagnesium bromide. If complexation of the phosphonate with magnesium halides occurs as has been suggested, a rate enhancement would be expected on the basis of electronic effects. The fact that a rate decrease is observed suggests one of several alternative effects may predominate. For instance, the highly solvated complex may be hindered to reaction with the Grignard reagent which is also solvated. An alternative explanation is that the mechanism of reaction of the phosphorus ester with the Grignard reagent may require complexation before subsequent reaction. In this case the magnesium halide would compete with the phenylmagnesium bromide for the phosphorus ester. Still another possible explanation is that the phenylmagnesium bromide may be deactivated by complexation with the magnesium halide. At present it is not possible to rule out any of these explanations.

### Experimental Section

**Starting Materials.**—Triethyl phosphite and diethyl ethylphosphonate were obtained commercially. Diethyl phenylphosphonate, ethyl diphenylphosphinate, triphenylphosphine oxide, ethyl diethylphosphinate, and the phenylmagnesium bromide were prepared in an earlier study.<sup>4</sup> *O,O*-Diethyl phenylthiophosphonate was prepared in the same manner as diethyl phenylphosphonate. Diethyl *p*-tolylphosphonate and diethyl *p*-chlorophenylphosphonate were prepared in a separate study.<sup>14</sup> All of the phosphorus esters were freshly distilled and their purity confirmed by gas chromatographic analysis and by their infrared, proton, and phosphorus nmr spectra. The phenylmagnesium bromide was freshly prepared and then analyzed by the double titration method of Vlismas and Parker.<sup>15</sup> The reaction conditions, concentrations, and product analysis were the same as described earlier for the reaction of diethyl phenylphosphonate with phenylmagnesium bromide in THF at 68°. Ethyl diethylphosphinate was so water soluble that repeated extractions of the hydrolysis mixture with diethyl ether followed by drying and concentrating was found to be necessary. Reference samples of the products were prepared in all cases by standard synthesis and their retention times compared with those products of the reactions investigated in this study.

**Registry No.**—Phenylmagnesium bromide, 100-58-3; *p*-ClPhP(O)(OEt)<sub>2</sub>, 2373-43-5; PhP(O)(OEt)<sub>2</sub>, 1754-49-0; *p*-CH<sub>3</sub>PhP(O)(OEt)<sub>2</sub>, 1754-46-7; EtP(O)(OEt)<sub>2</sub>, 78-38-6; Ph<sub>2</sub>P(O)OEt, 1733-55-7; (EtO)<sub>3</sub>P(O), 78-40-0; Et<sub>2</sub>P(O)OEt, 4775-09-1; Ph<sub>3</sub>P(O), 791-28-6; *p*-ClPhPhP(O)OEt, 4559-69-7; *p*-CH<sub>3</sub>PhPhP(O)Ph<sub>2</sub>, 6840-28-4; *p*-CH<sub>3</sub>PhPhP(O)OEt, 26926-25-0; EtP(O)Ph<sub>2</sub>, 1733-57-9.

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(14) H. R. Hays, *J. Org. Chem.* submitted for publication.

(15) T. Vlismas and R. D. Parker, *J. Organometal. Chem.*, **10**, 193 (1967).