JOC*Article*

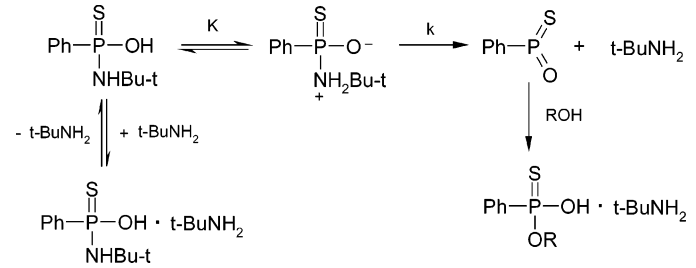
The Intermediacy of Metathiophosphonate PhPSO in the Reaction of *N-tert*-Butyl-*P*-phenylphosphonamidothioic Acid with Alcohols

Tomasz Nonas and Stefan Jankowski*

Institute of Organic Chemistry, Technical University of Lodz, Zeromskiego 116, 90-924 Lodz, Poland

jankowsk@p.lodz.pl

Received September 14, 2004



Kinetic studies of the reaction of *N-tert*-butyl-*P*-phenylphosphonamidothioic acid (**1**) with alcohols were carried out in CH_2Cl_2 by means of ^{31}P NMR spectrometry. The reaction is of the first order with respect to thio acid **1**. The first-order rate constant at 30 °C increases with increasing methanol concentration below 0.25 M, but otherwise the rate constants are either independent of alcohol concentration (MeOH above 0.25 M, BuOH) or decrease with increasing alcohol concentration (*i*-PrOH, *t*-BuOH). The effect of alcohols on the order of the reaction and parameters of activation, as well as results of competition experiments, lead us to the conclusion that reaction of **1** with alcohols occurs by an elimination−addition mechanism involving the association of the thio acid **1** and the alcohol and then formation in the rate-determining step of an encounter complex **2″** involving metathiophosphonate **4**, amine, and alcohol. Metathiophosphonate **4** reacts preferentially with the alcohol as the encounter complex (primary alcohols) or after diffusion apart as a "free" intermediate (hindered alcohols).

1. Introduction

Stereochemical studies have played a very important part in clarifying the mechanism of nucleophilic substitution at four-coordinate phosphoryl and thiophosphoryl centers. Inversion of configuration has been observed for the usual bimolecular $S_N2(P)$ pathway and nonstereospecificity for reactions that proceed by an elimination−addition mechanism involving a planar three-coordinate P(V) intermediate.[1,2] Tertiary alcohols are resistant to bimolecular phosphorylation and the phosphorylation of *t*-BuOH has been considered a test for the involvement of a reactive, sterically accessible monomeric metaphosphate intermediate.[3] The formation of racemic product in reactions of chiral (^{16}O, ^{17}O, ^{18}O-labeled) precursors with *t*-BuOH is then readily explicable as a consequence of equal attack on the two faces of the planar metaphosphate.[4] In principle nonstereospecificity could also be observed if deprotonation of the immediate precursor of the product ($RO^+H-PO_3^{2-}$) is slow enough to allow alcohol exchange, i.e., displacement of the initial alcohol molecule by another molecule of alcohol.[5]

N-tert-Butyl-*P*-phenylphosphonamidothioic acid (**1**) has been used in stereochemical studies to probe the possible involvement of the metathiophosphonate PhPSO in the reaction with alcohols.[6] Enantiopure **1** was found to react completely nonstereospecifically with *t*-BuOH in CH_2Cl_2 (0.2 M) and largely nonstereospecifically with the more nucleophilic (less hindered) *i*-PrOH, but with MeOH the product was formed with one enantiomer in large excess. With *i*-PrOH and MeOH the reactions became more stereospecific at higher concentrations and nonstereospe-

* Corresponding author. Phone: +48-42-631-3152. Fax: +48-42-636-5530.

(1) Westheimer, F. H. *Chem. Rev.* **1981**, *81*, 313.
(2) Hengge, A. C. Transfer of the Phosphoryl Group. In *Comprehensive Biological Catalysis*: *A Mechanistic Reference*; Sinnot, M., Ed.; Academic Press: San Diego, CA, 1998; Vol. 1, p 517.
(3) Ramirez, F.; Marecek, J. F.; Yemul, S. S. *J. Am. Chem. Soc.* **1982**, *104*, 1345.
(4) Friedman, J.; Freeman, S.; Knowles, J. R. *J. Am. Chem. Soc.* **1988**, *110*, 1268.
(5) Herschlag, D.; Jencks, W. P. *J. Am. Chem. Soc.* **1986**, *108*, 7938.
(6) Harger, M. J. P.; Pater, C. *Chem. Commun.* **1999**, 931.

10.1021/jo0483769 CCC: $30.25
Published on Web 12/17/2004

cific at lower concentrations. Those obervations can be rationalized in terms of two competing pathways: stereospecifc $S_N2(P)$ and nonstereospecific elimination−addition (EA), the former bimolecular process being favored relative to the latter by more nucleophilic (less hindered) alcohols and higher concentrations of alcohols.[6−10] There is, however a third possibility: a preassociative pathway.[11] If the metathiophosphonate intermediate is not sufficiently long-lived to allow diffusion away from the leaving group (*t*-$BuNH_2$) it will merely recombine with the leaving group unless the nucleophile (ROH) is already in place. The preassociation process can be stepwise or concerted with a loose S_N2-like transition state, and proceed with inversion of configuration at phosphorus.

Nitrogen and hydrogen kinetic isotope effects for the reaction of **1** with alcohols are slightly sensitive to steric hindrance of alcohol, as expected for an elimination−addition process. This conclusion was supported by results of semiempirical calculations on the PM3 level. However, for the reaction with methanol the addition−elimination mechanism cannot be excluded.[12]

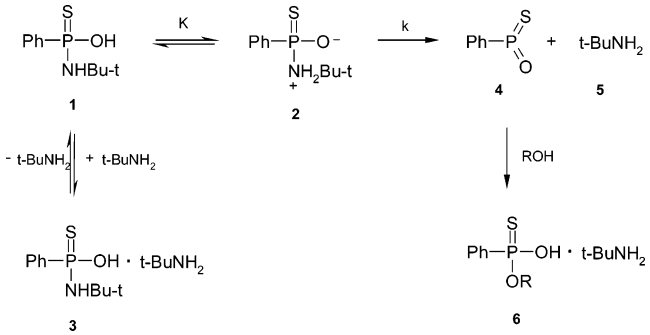
We have now undertaken kinetic studies intended to establish more definitively the mechanism(s) by which **1** reacts with alcohols, in particular to establish whether there is any reason to invoke a new pathway, in addition to stereospecific $S_N2(P)$ and completely nonstereospecific EA. If there is, we would hope to be able to ascertain its stereochemistry.

2. Results and Discussion

In alcohol-free conditions the fragmentation of **1** leads to a complex mixture of several products. The ^{31}P NMR spectrum recorded after completion of the reaction contains 13 signals of similar intensities (δ_P 67.3, 66.5, 66.1, 64.5, 63.5, 63.0, 62.0, 61.6, 61.5, 61.1, 59.7, 56.2, 54.3). Decomposition of **1** follows the first-order kinetics with rate constant of $(8.08 \pm 0.38) \times 10^{-4}$ s^{-1} in dichloromethane at 32 °C. In the presence of alcohols only the formation of esters **6**[6,13−15] was observed, except that with *tert*-butyl alcohol traces of pyrothiophosphonate were detected in the ^{31}P NMR spectra, as reported previously (Scheme 1).[6]

In the course of reaction the ^{31}P NMR chemical shifts of the substrate **1** (and the product **6)** were changing because of the interaction of the liberated amine with the acidic substrate (and product). The acid **1** and its amine salt **3** were observed in the ^{31}P NMR spectrum as one signal due to fast chemical exchange. The position of the ^{31}P NMR signal is a measure of this equilibrium. The molar fraction of the acidic form **1** of the

SCHEME 1



substrate was determined by eq 1:

$$x_{acid} = \frac{\delta - \delta_{salt}}{\delta_{acid} - \delta_{salt}} \qquad (1)$$

where δ is the observed chemical shift of the substrate, δ_{acid} the chemical shift of pure acid **1**, and δ_{salt} the chemical shift of the *tert*-butylammonium salt **3**. For calculation of the first-order rate constants the observed substrate concentration was corrected by multiplication by x_{acid}. The reaction of **1** with alcohols followed first-order kinetics for at least 2−3 half-lives. In all cases the rate constants were found to be independent of the thio acid **1** concentration. For the reaction with methanol the rate constant is not affected by the alcohol concentration above 0.25 M and the average rate constant is then equal to $(7.83 \pm 0.23) \times 10^{-4}$ s^{-1} at 30 °C (Figure 1).

At lower concentrations of methanol (0.05−0.25 M), the rate constant increases with increasing alcohol concentration. The average rate constant for reaction with BuOH is equal to $(3.20 \pm 0.20) \times 10^{-4}$ s^{-1} at 30 °C over the whole concentration range of 0.05−0.75 M. In the case of the sterically hindered alcohols *i*-PrOH and *t*-BuOH, the reaction is not much slower but the rate constants do decrease slightly with increasing alcohol concentration. At lower concentrations of methanol (0.05−0.25 M) (Figure 1) the observed first-order constant was found to increase with increasing the alcohol concentration. This can be explained by the possibility that reaction with methanol follows two different pathways simultaneously, the first-order EA process and the second-order AE mechanism, according to eq 2:

$$-\frac{dc_P}{dt} = {}^1k c_P + {}^2k c_P[ROH] = {}^1k_{exp} c_P \qquad (2)$$

From the linear plot of $^1k_{exp}$ against methanol concentration both rate constants were estimated: $^1k = 4.1 \times 10^{-4}$ s^{-1} and $^2k = 1.4 \times 10^{-3}$mol L^{-1} s^{-1}. However, this concept does not explain the steady first-order constants above 0.25 M of methanol.

The lack of a strong steric effect of the alcohol is consistent with little if any involvement of a sterically sensitive bimolecular $S_N2(P)$ reaction with bulky alcohols. In the reaction of **1** with methanol and other alcohols first-order plots were observed at all concentrations of alcohol. In the EA mechanism the rate constant k of the rate-limiting amine departure step (Scheme 1) should not

(7) Quin, L. D.; Jankowski, S. *J. Org. Chem.* **1994**, *59*, 4402.
(8) Quin, L. D.; Hermann, P.; Jankowski, S. *J. Org. Chem.* **1996**, *61*, 3944.
(9) Jankowski, S.; Quin, L. D.; Paneth, P.; O'Leary, M. H. *J. Am. Chem. Soc*. **1994**, *116*, 11675. Jankowski, S.; Quin, L. D.; Paneth, P.; O'Leary, M. H. *J. Organomet. Chem.* **1997**, *529*, 23.
(10) Harger, M. J. P. *Chem. Commun.* **2004**, 1952.
(11) Jencks, W. P. *Acc. Chem. Res*. **1980**, *13*, 161. Jencks, W. P. *Chem. Soc. Rev*. **1981**, 345.
(12) Jankowski, S.; Mazur, A.; Nonas, T.; Vokal, B. *J. Organomet. Chem.* **2004**, in press.
(13) Harger, M. J. P. *J. Chem. Soc.*, *Perkin Trans. 2*. **1978**, 326.
(14) Evdakov, V. P.; Alipova, E. I. *J. Gen. Chem. USSR* (*Engl. Trans.*) **1967**, *37*, 2573.
(15) Mikołajczyk, M. *Pol. J. Chem.* **1979**, *53*, 317.

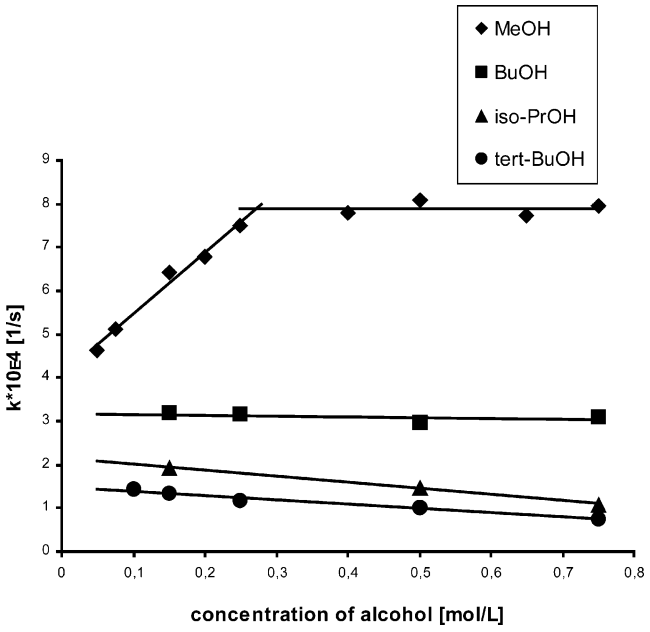
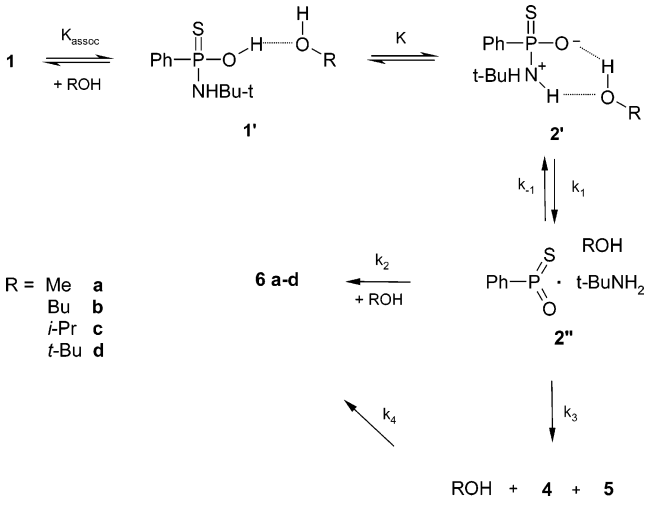


FIGURE 1. Kinetics of the reaction of **1** with alcohols in dichloromethane at 30 °C.

SCHEME 2



depend on the alcohol structure but the alcohol may influence the proton transfer in the preequilibrium step, altering the equilibrium constant K. Thus, the changes of the experimental rate constants k_{exp} reflect the changes of the equilibrium constant K. A possible modification of the mechanism presented as Scheme 1 is the association of the acid **1** and the alcohol. It consists of the association process, equilibrium between hydrogen-bonded neutral form **1′** and dipolar species **2′**, and formation of the metathiophosphonate **4** within the encounter complex **2″** or as a "free" intermediate (Scheme 2). A cyclic six-membered intermediate (comparable with **2′**) was first proposed over 45 years ago for hydrolysis of phosphonamidates.[16] Recently a computational study of the hydrolysis of the methyl phosphate anion evidenced the dissociative mechanism also including a six-centered water-assisted transition state.[17,18]

If the equilibrium constant K is much less than unity ($K \ll 1$)[7,19] the concentration of the dipolar species **2′** is given by eq 3:

$$[\mathbf{2'}] = \frac{K_{assoc} \times K[\mathrm{ROH}]c_P}{1 + K_{assoc}[\mathrm{ROH}]} \quad (3)$$

where c_P is the corrected substrate concentration (observed concentration multiplied by x_{acid}).

The steady-state approximation for the complex **2″** and the metathiophosphonate **4** concentration gives the equation for the rate of reaction (eq 4):

$$-\frac{dc_P}{dt} = \frac{d[\mathbf{6}]}{dt} = \frac{k_1(k_2[\mathrm{ROH}] + k_3) \times K_{assoc} \times K[\mathrm{ROH}]c_P}{(k_{-1} + k_2[\mathrm{ROH}] + k_3)(1 + K_{assoc}[ROH])} \quad (4)$$

When $K_{assoc}[\mathrm{ROH}] \ll 1$, the second-order kinetics should be observed. If the association complex is stable enough and $K_{assoc}[\mathrm{ROH}] \gg 1$, the first-order kinetics describe the reaction (eq 5):

$$-\frac{dc_P}{dt} = \frac{d[\mathbf{6}]}{dt} = \frac{k_1(k_2[\mathrm{ROH}] + k_3)}{(k_{-1} + k_2[\mathrm{ROH}] + k_3)} \times K \times c_P = k_{exp}c_P \quad (5)$$

If the formation of **2″** is the rate-determining step and the encounter complex **2″** transforms to product faster than it reverts to zwitterion **2′** ($k_2[\mathrm{ROH}] + k_3 \gg k_{-1}$), $k_{exp} = k_1 \times K$. It must be emphasized here that although the association constant (K_{assoc}) is not present in the rate equation, the association with the alcohol should affect the concentration of dipolar species **2′**. This assumption was deduced from the observation that the experimental rate constants increase with increase of alcohol hydrogen-bond donation, measured by the Kamlet−Taft parameter α: MeOH, 0.93; BuOH, 0.79; *i*-PrOH, 0.76; and *t*-BuOH, 0.68.[20]

The parameters of activation are in accord with the proposed mechanism. The free energy of activation is almost independent of the alcohol structure and concentration (Table 1). For the primary alcohols (MeOH and BuOH) the calculated enthalpies of activation are the same and the entropy of activation is only slightly more negative for BuOH. For the bulky alcohols (*i*-PrOH and *t*-BuOH) the enthalpies of activation are significantly higher and the entropies of activation are less negative, compared with the unhindered alcohols. This is probably due to stronger interaction of unhindered alcohols with zwitterion **2**. Primary alcohols are more intimately involved in reaction (more negative entropies of activation) and provide more assistance (smaller enthalpies of activation).

To answer the question of the role of alcohol solvation we have performed competition experiments with both

(16) Chanley, J. D.; Frageson, E. *J. Am. Chem. Soc.* **1958**, *80*, 2686.
(17) Hu, C.-H.; Brinck, T. *J. Phys. Chem. A* **1999**, *103*, 5379.
(18) Bianciott, M.; Berthelat, J.-C.; Vigroux, A. *J. Am. Chem. Soc.* **2002**, *124*, 7573.
(19) Benkovic, S. J.; Sampson, E. J. *J. Am. Chem. Soc.* **1967**, *89*, 4714. Benkovic, S. J.; Sampson, E. J. *J. Am. Chem. Soc.* **1971**, *93*, 4009.
(20) Kamlet, M. J.; Abboud, J. L. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem.* **1983**, *48*, 2877.

TABLE 1. Activation Parameters of the Reaction of 1 with Alcohols ROH in Dichloromethane

R	alcohol concn, M	ln *A*, s^{-1}	E_a, kJ/mol	$\Delta H^{\ddagger}_{303}$, kJ/mol	$\Delta S^{\ddagger}_{303}$, J/(mol K)	$\Delta G^{\ddagger}_{303}$, kJ/mol
Me	0.15	22.0 ± 3.6	73.8 ± 3.4	71.3	−70.6	92.6
	0.50	21.93 ± 0.99	73.4 ± 2.5	70.9	−71.0	92.4
Bu	0.15	21.67 ± 0.43	74.9 ± 1.1	72.4	−73.1	94.6
	0.50	21.4 ± 1.5	74.1 ± 3.9	71.6	−75.8	94.6
Pr^i	0.15	23.6 ± 1.2	81.1 ± 3.1	78.6	−56.9	95.8
	0.50	23.4 ± 1.2	81.4 ± 3.2	78.9	−56.9	96.1
Bu^t	0.15	25.6 ± 1.2	86.8 ± 3.2	84.3	−40.6	96.6
	0.50	25.2 ± 1.0	86.7 ± 2.7	84.4	−43.5	97.5

TABLE 2. Kinetics of the Competitive Reaction of 1 with MeOH and *t*-BuOH in Dichloromethane at 32 °C

concn, M			
1	MeOH	*t*-BuOH	10^4k, s^{-1}
0.05	0.75	-	9.60 ± 0.18
0.05	0.95	0.05	6.84 ± 0.28
0.05	0.90	0.10	5.76 ± 0.16
0.05	0.70	0.30	5.82 ± 0.20
0.05	0.50	0.50	5.46 ± 0.15
0.05	0.30	0.70	2.692 ± 0.074
0.05	0.10	0.90	1.113 ± 0.049
0.05	0.025	0.975	0.541 ± 0.016

TABLE 3. The Calculated Ratios k_{MeOH}/k_{t-BuOH} for Competitive Reaction of 1 with MeOH and *t*-BuOH

initial concn, M		product ratio	
MeOH	*t*-BuOH	**6a/6d**	k_{MeOH}/k_{t-BuOH}[a]
0.10	0.90	76/24	36
0.15	0.85	76/24	37
0.20	0.80	83/17	41
0.25	0.75	92/8	37

[a] For details of calculations see the Experimental Section.

MeOH and *t*-BuOH present in the solution in different ratios (Table 2).

The presence of *t*-BuOH in place of MeOH causes retardation of the reaction, although the product of reaction with *t*-BuOH was observed in ^{31}P NMR spectra only when the fraction of *t*-BuOH in the alcohol mixture was 0.75 and higher (Table 3). The decrease of the rate of reaction without formation of **6d** must originate from the decrease of the concentration of reactive form **2′** in the presence of *t*-BuOH. Detection of both products **6a** and **6d** at high enough concentrations of *t*-BuOH allowed the estimation of the ratio k_{MeOH}/k_{t-BuOH} for the reaction of metathiophosphonate **4** with MeOH and *t*-BuOH (Table 3). This ratio was found to be unexpectedly high and equal to about 40.

Previous competition experiments with metathiophosphate EtO−POS in reaction with ethanol and *tert*-butyl alcohol gave the ratio k_{EtOH}/k_{t-BuOH} equal to 2.1.[21] Reaction of methanol and *tert*-butyl alcohol with $PhPO_2$, generated thermally from phenyl-2,3-oxaphosphabicyclo-[2.2.2]octene, yields the ratio $k_{MeOH}/k_{t-BuOH} = 1.8$.[22] Generated from phosphate or phosphonate, anion PO_3^- reacts in dichloromethane solution faster with methanol than with *t*-BuOH by the factor of 3−7.[23] Thus, influences

(21) Jankowski, S.; Quin, L. D. *J. Am. Chem. Soc.* **1991**, *113*, 7011.
(22) Jankowski, S.; Cieplucha, A. Work in progress.
(23) Ramirez, F.; Marecek, J. F.; Yemul, S. S. *Tetrahedron Lett.* **1982**, *23*, 1515.

TABLE 4. The Enantiomeric Excess (ee) of 6 Formed in the Reaction of Enantiopure 1 (0.05 M) with Alcohols in Dichloromethane at 30 °C

alcohol concn, M			ee, %		
MeOH	BuOH	*t*-BuOH	**6a**	**6b**	**6d**
1.0			88		
	1.0			81	
0.5			81		
	0.5			72	
0.7		0.3	85		—[a]
0.5		0.5	82		—[a]
0.3		0.7	83		13
0.1		0.9	82		6
		1.0			6
		0.7			3
	0.3	0.7		76	9

[a] Not detectable by ^{31}P NMR.

other than steric factors should be considered to explain this very high value of the calculated rate constant ratio (k_{MeOH}/k_{t-BuOH}) in reaction of **4** with alcohols. If the metathiophosphonate **4** had a finite existence under the experimental conditions and the alcohols could compete equally, the ratio k_{MeOH}/k_{t-BuOH} would be expected to be much lower than observed. However, if the MeOH and *t*-BuOH concentrations are different in the solvation sphere relative to the bulk solution and MeOH wins the competition, the calculated values of the ratio k_{MeOH}/k_{t-BuOH} will not properly reflect the reactivity of the metathiophosphonate toward the two alcohols. Besides the preferential solvation the high proportion of MeOH product **6a** may originate from the direct displacement of amine moiety by methanol (less likely for *tert*-butyl alcohol) in stereospecific reaction (k_2) with an encounter complex **2″.**

We have examined the enantiomeric excess of products **6** in the reaction of enantiopure acid **1** with MeOH, BuOH, and *t*-BuOH (Table 4). The reactions were carried out under the same conditions as the kinetic experiments and the results are complementary to those reported previously.[6] The reaction with BuOH (not previously examined) is less stereospecific than that with methanol, but more stereospecificic than that with *tert*-butyl alcohol (Table 4).

The addition of *t*-BuOH practically does not affect the enantiomeric excess of esters **6a** and **6b**. With the ROH−*t*-BuOH mixture in a 3:7 ratio, ee of *tert*-butyl ester **6d** was found to be 13% in the presence of methanol and 9% in the presence of butanol, while the reaction with *t*-BuOH without any other alcohol present was almost completely nonstereospecific (ee 3%) as in the previous report.[6] If observed differences are significant, it may suggest that not only another molecule of methanol but

even *t*-BuOH can react (k_2) with an ancounter complex **2″** formed by methanol.

The conclusion from the present work on reaction of **1** with alcohols is that stereochemical and kinetic results are in agreement if the elimination−addition mechanism with alcohol assistance is invoked. The reactive form of thio acid **1** is the zwitterion **2′** associated with an alcohol molecule that converts to an encounter complex **2″** in the rate-determining step. From this complex metathiophosphonate **4** can be liberated as a "free" intermediate in the presence of sterically hindered alcohols or can react with primary alcohols within the complex.

3. Experimental Section

3.1. General. ^{31}P NMR spectra were recorded at 101.20 MHz with 85% H_3PO_4 as external standard. Downfield shifts are positive.

3.2. Synthesis of *N*-*tert*-Butyl-*P*-phenylphosphonamidothioic Acid (1). Both racemic and enantiopure acid **1** were obtained by a previously published procedure.[6,13] The acid was generated from its *tert*-butylammonium salt immediately before use. The measurement of the ^{31}P NMR chemical shift was carried out in $CDCl_3$ solution at −30 °C to avoid decomposition (δ_P 66.4). The chemical shift of the *tert*-butylammonium salt of **1** was 50.7 ppm.[6]

3.3. Solvents for Kinetic Measurements. In all cases a mixture of CH_2Cl_2/CD_2Cl_2 (5:1) was used as solvent. The mixture was dried by fractional distillation over P_2O_5. The alcohols used in the reactions were dried by distillation over magnesium (methyl alcohol) or over calcium hydride (isopropyl, butyl, and *tert*-butyl alcohols).

3.4. Kinetic Measurements. Reactions were carried out in NMR tubes, either in the spectrometer or in a water bath, at constant (within ±0.1 °C) temperature. The temperature of a sample in the spectrometer was calibrated based on a glycol NMR thermometer.[24] A sealed 1-mm glass capillary containing a 0.05 M solution of triphenylphosphine oxide in CH_2Cl_2/CD_2Cl_2 (9:1) was coaxially placed in the 5-mm NMR tube containing 0.7 mL of the solution containing **1** and the alcohol, and was used as a standard. The NMR tube was sealed under argon. The rate of disappearance of substrate was determined by diminution of its ^{31}P NMR signal compared to the standard, when only ^{31}P NMR signals for the substrate, product, and standard were detected. The actual substrate concentration was taken as the product of starting material signal integration (a result of acid−*tert*-butylammonium salt equilibrium) and the molar fraction of substrate in the acidic form in the acid−salt mixture. The ^{31}P NMR spectra were recorded at 67.6-s intervals (usually 30−50) for kinetics conducted in the spectrometer. In water-bath experiments the spectra were measured at various time intervals (no less than 10 spectra) after removal and cooling of the tube.

Calculations of the rate constants and Arrhenius parameters were carried out by the least-squares method. All data are given with standard deviations. The enthalpy and entropy of activation were calculated for 30 °C according to Eyring theory.

The ratio of reaction rate constants for methyl and *tert*-butyl alcohols with metathiophosphonate **4** was determined by ^{31}P NMR, for reactions 46−56% complete, based on the following equation:

$$\frac{k_{\mathrm{MeOH}}}{k_{t-\mathrm{BuOH}}} = \frac{I_{\mathrm{MeOH}}}{I_{t-\mathrm{BuOH}}} \times \frac{C_{t-\mathrm{BuOH}}}{C_{\mathrm{MeOH}}}$$

where $k_{\mathrm{MeOH}}/k_{t-\mathrm{BuOH}}$ is the ratio of reaction rate constants for methyl and *tert*-butyl alcohols; I_{MeOH} and $I_{t-\mathrm{BuOH}}$ are integrations of product signals with methyl and *tert*-butyl alcohols; and C_{MeOH} and $C_{t-\mathrm{BuOH}}$ are mean concentrations of alcohols during the reaction.

Acknowledgment. We are indebted to Dr. Martin J. P. Harger for numerous helpful discussions during manuscript preparation. This work was supported by grant 4T09A 117 24 from the State Committee for Scientific Research (KBN, Poland).

Supporting Information Available: Full list of rate constants for the reaction of *N*-*tert*-butyl-*P*-phenylphosphonamidothioic acid (**1**) with alcohols (MeOH, BuOH, *i*-PrOH, *t*-BuOH) in dichloromethane. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0483769

(24) Ralford, D. S.; Fisk, C. L.; Becker, E. D. *Anal. Chem.* **1979**, *51*, 2050.