of BNAH. Further applications as acid catalysts, metal ligands, and ion carriers are currently continued in this laboratory.

Acknowledgment. We are grateful to Professor T. Kunitake and N. Higashi for the use of the light-scattering apparatus. We thank Professor Y. Nakamato (Kanazawa University) for helpful discussions. Also, appreciation is expressed to S. Yamamoto (Osaka Municipal Technical Research Institute) for elemental analysis of sulfur. This research was supported in part by a grant from the Ministry of Education of Japan.

Equilibrium Constants and Rate Constants for the Transformations in Aqueous Solution of a Spirocyclic Hydroxyphosphorane

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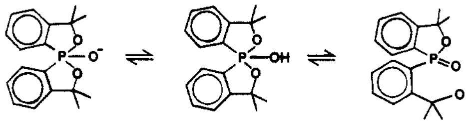
Abstract: A quantitative study is reported for the reactions in water of the hydroxyphosphorane R_vOH (Granoth and Martin, *J. Am. Chem. Soc.* **1978**, *100*, 5229; **1979**, *101*, 4618). This species equilibrates with the isomeric phosphinate $R_{iv}OH$ ($K_1 = [R_vOH]/[R_{iv}OH]$). Addition of base results in the phosphoranoxide R_vO^-, the conjugate base of R_vOH ($K_2 = [R_vO^-][H^+]/[R_vOH]$). This interconversion occurs with an apparent acidity constant $K_1K_2/(1 + K_1)$ of 1.6×10^{-11}. With estimates of K_1, pK_2 is calculated to lie in the range 9–10. Base solutions of this system are not stable; a slower transformation produces the phosphinate anion RO_2^-, the hydrolysis product of $R_{iv}OH$. RO_2^- is converted back to $R_{iv}OH/R_vOH$ in acid solutions. The overall equilibrium ($R_vOH + R_{iv}OH$) $\rightleftarrows$ RO_2^- has an apparent acidity constant of 1.8×10^{-8}. At equilibrium the ratio of the concentrations of the two anions $[RO_2^-]$:$[R_vO^-]$ is 1.3×10^3. Kinetics of the overall equilibrium have been studied as a function of pH. An analysis is presented in terms of hydronium ion and hydroxide ion catalyzed interconversion of $R_{iv}OH$ and RO_2H, the latter the conjugate acid of RO_2^-. The equilibration of $R_{iv}OH$ and R_vOH or R_vO^- is too rapid to be studied by stopped-flow spectroscopy at all pH. Comparison to analogous carbonyl group systems suggests that pentavalent intermediates of phosphoryl transfer reactions may be kinetically less stable than tetrahedral intermediates of acyl transfer reactions.

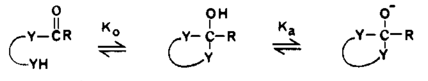
Granoth and Martin[1,2] have reported the isolation of the ion R_vO^- as its solid sodium salt. This anion, termed a phosphoranoxide ion,[1] is one of the few examples of its type and serves as a model for the pentavalent intermediate[3] of the basic hydrolysis (or alcoholysis) of phosphate esters. The conjugate acid of this ion, the hydroxyphosphorane R_vOH, was also prepared. This was found to exist in equilibrium with the isomeric phosphinate ester $R_{iv}OH$, with the position of equilibrium between the two being dependent upon temperature and solvent.[1]



(1)

R_vO^- R_vOH $R_{iv}OH$

We have recently reported[4] quantitative kinetic and equilibrium studies of two carbonyl group systems where an acyl derivative **1** and an isomeric cyclic tetrahedral intermediate **2** exist in equilibrium, and the addition of base shifts the equilibrium toward the tetrahedral form by converting it to its conjugate base **3**. The ionization which occurs at high pH has an apparent acidity constant equal to $K_0K_a/(1 + K_0)$. Only the tetrahedral anion **3** forms in base since the OH group in **2** is considerably more acidic than the YH group in **4**.



(2)

1; Y = NMe[4]
Y = O[5]

2

3

The phosphoryl system described in eq 1 is obviously closely related, since it involves an equilibrium between two neutral forms with a relatively acidic OH group in the adduct. We felt it of interest to determine if this system were amenable to quantitative analysis, and in this paper we report the results of our study.

Results

Our analysis involves equilibrium and kinetic studies using UV spectroscopy in aqueous solutions. The mixture of neutrals **2** and **3** was prepared as described previously.[2] Curve A of Figure 1 shows the UV spectrum which is obtained when this is dissolved in acidic solutions. The addition to 0.1 M NaOH produces a different spectrum shown as curve B1 in Figure 1. This spectrum changes with time, and the curve B1 is in fact that obtained by extrapolation to zero time. Curve B2 describes the stable final spectrum. The effect of pH on these spectra was studied in two ways. In one set of experiments a weakly acidic solution (0.002 M HCl) was mixed in a stopped-flow spectrophotometer with various base solutions. The wavelength monitored was 275 nm, where there is a significant difference in spectra A and B1. Absorbance readings were obtained 10–50 ms after mixing and, as will become apparent after discussing kinetics, represent any absorbance change associated with the process responsible for A → B1, while the further process forming B2 has not yet begun. This experiment results in a spectroscopic titration curve (Figure 2, curve I) corresponding to an acid with an acidity constant of 1.6×10^{-11}. This constant is defined as K_{fast}(app). (The symbol "app" represents apparent.) In a second set of experiments solutions were allowed to stand for 1 month, a time sufficient for complete transformation to B2 at all pH values. The final spectra in solutions with pH less than 6 were found to be identical to curve A of Figure 1, while the spectra above pH 9.5 were identical to

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(1) Granoth, I.; Martin, J. C. *J. Am. Chem. Soc.* **1978**, *100*, 5229–5230.

(2) Granoth, I.; Martin, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 4618–4622.

(3) Westheimer, F. H. *Acc. Chem. Res.* **1968**, *1*, 70–78. Hudson, R. F.; Brown, C. *Acc. Chem. Res.* **1972**, *5*, 204–211.

(4) (a) Tee, O. S.; Trani, M.; McClelland, R. A.; Seaman, N. E. *J. Am. Chem. Soc.* **1982**, *104*, 7219–7224. (b) McClelland, R. A.; Seaman, N. E.; Cramm, D. *J. Am. Chem. Soc.* **1984**, *106*, 4511–4515.

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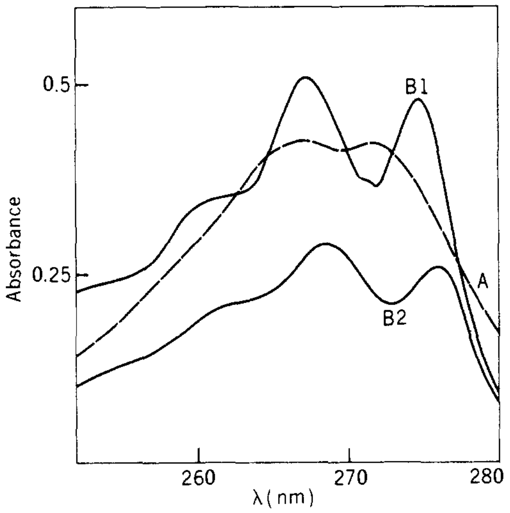


Figure 1. UV spectra of 2.4×10^{-4} M solutions: (A) pH 4; (B1) 0.1 M NaOH, after extrapolation to zero time; (B2) 0.1 M NaOH, after 1 h.

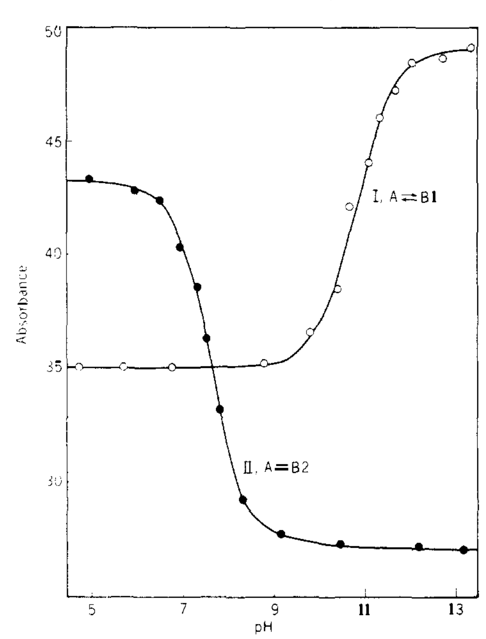


Figure 2. Absorbance readings of 2.4×10^{-4} M solutions: (I) initial (50 ms) absorbance readings, at 275 nm; (II) absorbance readings after 1 month at 267 nm.

curve B2. In the intermediate range the spectra were a mixture of curve A and curve B2. Curve II of Figure 2 plots the final absorbance at 267 nm as a function of pH. This is a second spectroscopic titration characteristic of an acid with an acidity constant defined now as $K_{\mathrm{slow}}(\mathrm{app})$ of 1.8×10^{-8}. It can be noted that at some pH values (for example, pH 9) there is very little of the initial spectral change A → B1 but a substantial amount of A → B2.

The transformation producing spectrum B2 follows pseudo-first-order kinetics. Rate constants as a function of pH are given in Figure 3. It can be noted that above pH 12 these rate constants refer to the spectral change B1 to B2 while below pH 10 they refer to A to B2. The initial spectra between these limits are a mixture of A and B1. Rate constants were also obtained by preparing a 0.002 M NaOH solution, waiting a sufficient time (30 min) so that the transformation to B2 is complete, and acidifying to a pH value less than 7. Spectrum A is regenerated in this experiment in a pseudo-first-order process. These rate constants are also shown in Figure 3. It can be noted that the rate–pH profiles obtained in the two kinetic experiments produce together one continuous curve. This is to be expected since as will be shown they refer to the same equilibrium being approached in the two different directions.

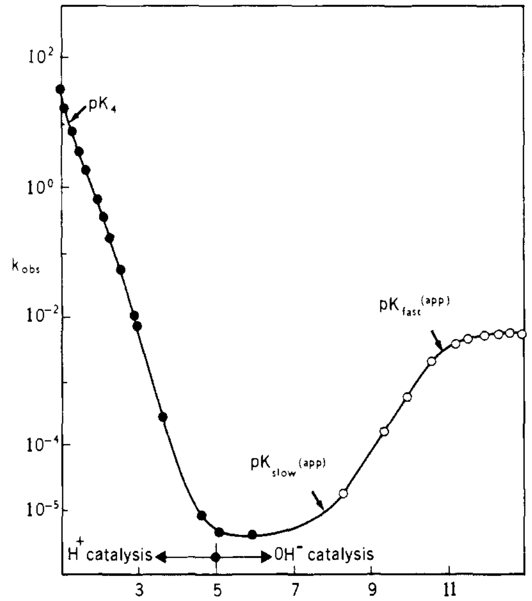
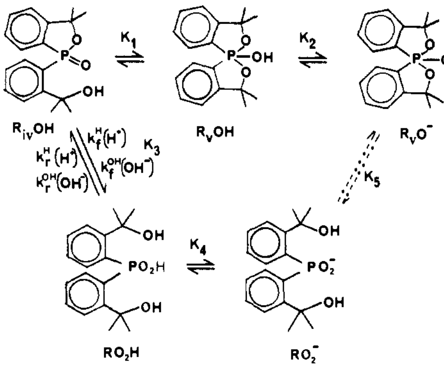


Figure 3. First-order rate constants at 25 °C, ionic strength 0.1: (○) starting with neutral substrate and adding to base; (●) by preparing a base solution (0.002 M NaOH), waiting 1 h and acidifying. The points are experimental; the curve is calculated on the basis of eq 11.

The spectral change associated with the fast acid:base equilibrium (A ⇄ B1) is extremely fast and it proved not possible to perform kinetic studies. In the set of experiments resulting in curve I of Figure 2, a weakly acidic solution was made basic on a stopped-flow instrument. The absorbance changes which occur were observed to be complete within the 3 ms dead-time of the apparatus. In a second set of experiments a solution in 0.01 M NaOH was reacidified to pH 3, 4, and 6 within 20–30 s of its preparation. In this way there is little conversion in the base solution of B1 to B2. The reacidification results in spectrum A and again the transformation is complete within the stopped-flow dead-time. These two sets of experiments provide a lower limit of 200 s^{-1} for the first-order rate constant for A ⇄ B1 at all pH.

Discussion

Equation 3 summarizes species, equilibrium constants, and rate constants required to explain the experimental data. Three neutral compounds appear, the hydroxyphosphorane R_vOH, the isomeric ring-opened phosphinate $R_{iv}OH$, and the hydrolysis product of this ester, the phosphinic acid RO_2H. Two anionic species are also needed, R_vO^-, the conjugate base of the hydroxyphosphorane, and RO_2^-, the conjugate base of the phosphinic acid. The proton transfer equilibria (K_2 and K_4) are rapid and, as will be discussed, so is the isomerization of $R_{iv}OH$ and R_vOH. Thus the three species at the top of eq 3 will be treated as being in a rapid equilibrium with one another. This is obviously also true for the two species at the bottom of eq 3. The kinetics which have been observed refer to interconversion between these two sets. This transformation presumably occurs by way of $R_{iv}OH$ and RO_2H and is a simple ester hydrolysis and its reverse.[5] As with most ester



(3)

hydrolyses this interconversion will be shown to occur with both acid and base catalysis, and the following relationship can be noted

$$K_3 = \frac{[\mathrm{RO_2H}]}{[\mathrm{R_{iv}OH}]} = \frac{k_f^{\mathrm{H}}}{k_r^{\mathrm{H}}} = \frac{k_f^{\mathrm{OH}}}{k_r^{\mathrm{OH}}} \qquad (4)$$

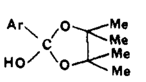
The first equilibrium to be considered is that involving the three neutral species. We will start by ignoring RO_2H since the analysis will show that at equilibrium it is unimportant. Granoth and Martin[1] were able to obtain equilibrium constant values for the equilibrium involving $R_{iv}OH$ and R_vOH at lower temperatures in CD_3OD. These compounds have significantly different ^{31}P chemical shifts, and at lower temperature (less than 0 °C) their interconversion is sufficiently slow that separate signals are observed. With use of their data,[6] extrapolation to 25 °C with a plot of log K_1 vs. $1/T$ gives a value of 0.05 for K_1. Since the solvent in our system is H_2O[7] and since this extrapolation is quite lengthy, we use a range of 0.01–0.20 in our calculations and admit that the true value may even be outside this. This analysis suggests that whatever the value of K_1 the phosphorane R_vOH is likely a minor component of the equilibrium. For most of the constants to be derived this means that the exact value of K_1 is not crucial.

The UV spectrum observed in acids (curve A of Figure 1) represents the equilibrium mixture of $R_{iv}OH$ and R_vOH and the initial spectrum (curve B1) in base can be assigned to R_vO^- (the OH group in $R_{iv}OH$ is unlikely to be sufficiently acidic to account for ionization at pH 11). The spectroscopic titration curve (curve I of Figure 2) thus represents the equilibration of three species. The acidity constant calculated from the curve is therefore not a true acidity constant, but it is related to the acidity constant K_2 by the relationship

$$K_{\mathrm{fast}}(\mathrm{app}) = \left(\frac{K_1}{1 + K_1}\right)K_2 \qquad (5)$$

Substitution of the measured value of $K_{\mathrm{fast}}(\mathrm{app})$ and the estimated K_1 gives pK_2 in the range 9–10.[8] (pK_2 = 10.0 for K_1 = 0.2, pK_2 = 8.8 for K_1 = 0.01.)

This calculation, along with that of Granoth and Martin,[2,8] shows that the hydroxy group in hydroxyphosphoranes is relatively acidic, in particular when compared to simple alcohols. A substantial portion of this increase in acidity can be attributed to the inductive effect of the additional oxygen atoms. Rather than using simple alcohols a more suitable comparison is with hemiorthoester type tetrahedral intermediates ($HOCR'(OR)_2$) which also have two acidifying oxygen atoms. These are predicted to be more acidic than simple alcohol analogues by a factor of 4–5 pK units (or 2–2.5 pK units per oxygen).[9] We have obtained a pK_a value of 10.4 for the pinacol derivative **4a** with Ar = *p*-nitrophenyl and, using the Hammett σp equation, estimated a pK_a value of 11.2 for **4b** with Ar = phenyl.[5] This latter compound is a reasonable carbon analogue of the hydroxyphosphorane R_vOH (although an exact comparison is obviously not possible because of the different valencies of the central atoms). Comparison of the number for **4b** (pK_a = 11.2) with that estimated for R_vOH (p$K_a \approx$ 9–10) suggests that there may be an additional acidifying effect in the hydroxyphosphorane, perhaps of the order of 1–2 pK_a units. This is not unexpected since the phosphorus is probably more electronegative than carbon.[10]



4a, Ar = 4-$NO_2C_6H_4$
4b, Ar = C_6H_5

The slow spectral change which results in the second titration curve and the acidity constant pK_{slow}(app) represents the overall equilibration of the system. The assumption that RO_2H is unimportant ($K_3 \ll 1$) produces the following equations.

$$K_{\mathrm{slow}}(\mathrm{app}) = \frac{K_1K_2 + K_3K_4}{1 + K_1} \qquad (6)$$

$$K_{\mathrm{slow}}(\mathrm{app}) - K_{\mathrm{fast}}(\mathrm{app}) = \frac{K_3K_4}{1 + K_1} \qquad (7)$$

$$\frac{K_{\mathrm{slow}}(\mathrm{app}) - K_{\mathrm{fast}}(\mathrm{app})}{K_{\mathrm{fast}}(\mathrm{app})} = \frac{K_3K_4}{K_1K_2} = K_5 \qquad (8)$$

The constant K_5 produced in eq 8 is the pH-independent equilibrium constant relating the two anions $[RO_2^-]/[R_vO^-]$. The value obtained from the two observed acidity constants is 1.3×10^3, showing that at equilibrium in water the phosphinate anion predominates over the phosphoranoxide ion (an observation qualitatively made by Granoth and Martin[2]).

The kinetics which are observed at pH >9.5 represent the conversion of the mixture of $R_{iv}OH$, R_vOH, and R_vO^- essentially completely to RO_2^-. If the assumptions are made that the first three species are rapidly equilibrating and that RO_2^- forms from the reaction of hydroxide ion with $R_{iv}OH$, the following rate expression is derived.

$$k_{\mathrm{obsd}}(\mathrm{pH} > 9) = \frac{\left(\dfrac{k_f^{\mathrm{OH}}K_w}{1 + K_1}\right)}{[\mathrm{H^+}] + \left(\dfrac{K_1K_2}{1 + K_1}\right)} \qquad (9)$$

This equation has the form $k_{\mathrm{obsd}} = a\,K_w/([\mathrm{H^+}] + b)$ where $a = k_f^{\mathrm{OH}}/1 + K_1$ and $b = K_1K_2/(1 + K_1) = K_{\mathrm{fast}}(\mathrm{app})$. This provides an excellent fit[11] to the experimental data with the constants a = 3.6 $M^{-1}\ s^{-1}$ and $-\log b$ = 10.9, the latter in good agreement with the spectroscopic value of pK_{fast}(app). The shape of the rate–pH profile at high pH can be explained in the following way. At pH values significantly less than pK_1(app) the equilibrium involving $R_{iv}OH$, R_vOH, and R_vO^- favors the two neutrals, and the rate of formation of RO_2^- follows hydroxide ion because of its involvement in the rate-determining step. As the pH is increased, however, the initial equilibrium shifts toward R_vO^-. This results in a levelling of the observed rate constants because there is now a counterbalancing effect, increasing hydroxide ion concentration decreasing the concentration of the reactive species $R_{iv}OH$.

The kinetic behavior which is observed in acid solutions represents conversion back to the two neutrals, $R_{iv}OH$ and R_vOH. The rate–pH profile below pH 4.5 shows two regions of behavior, one from pH 4.5 to about pH 1.5 where the observed rate constant shows a second-order dependency on the hydronium ion concentration and a second at lower pH where the dependency approaches

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(5) (a) A referee has suggested that the interconversion could proceed via hexacoordinated species formed from R_vOH, in acid-catalyzed and base-catalyzed mechanisms which are kinetically indistinguishable from those involving $R_{iv}OH$. The hexacoordinated route cannot be rigorously excluded on the basis of available data. One can note, however, recent evidence that hexacoordinated intermediates are not involved in the hydrolysis of methyl ethylene phosphate.[5b] (b) Kluger, R.; Thatcher, G. R. J. *J. Org. Chem.*, in press.

(6) $K_1 = 1/2.5$ at −50 °C. $K_1 = 1/3.3$ at −30 °C, and $K_1 = 1/8.5$ at −10 °C. We ignore the value of ≈1/50 at 5 °C since this is not very precise (and it falls well off the log K_1 vs. $1/T$ correlation).

(7) The solubility of the neutral solid in H_2O is less than 10^{-3} M, precluding the recording of ^{31}P NMR spectra.

(8) Granoth and Martin[2] provided a pK estimate of 10–11 based upon ^1H NMR chemical shifts obtained with the sodium salt of R_vO^- and nitromethane in $CDCl_3$. This value is in fact also an apparent acidity constant since this experiment would also have formed a mixture of R_vOH and $R_{iv}OH$.

(9) Hine, J.; Koser, G. F. *J. Org. Chem.* **1971**, *36*, 1348–1351. Fox, J. P.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *58*, 1281–1294. Guthrie, J. P. *J. Am. Chem. Soc.* **1978**, *100*, 5892–5904. Guthrie, J. P.; Cullimore, P. A. *Can. J. Chem.* **1980**, *58*, 1281–1294.

(10) (a) Tetrahedral P has an electronegativity of 2.79, while tetrahedral C is 2.48.[10b] (Unfortunately no value is listed for pyramidal P.) (b) Ensley, J.; Hall, D. "The Chemistry of Phosphorus"; Harper and Row: London, 1976; p 74.

(11) A plot of $1/k_{\mathrm{obsd}}$ vs. $[\mathrm{H^+}]$ is linear with a slope of $1/a$ and an intercept of b/a.

Table I. Rate and Equilibrium Constants (25 °C, $\mu = 0.1$)

constant	value[a]		method of calculation
pK_{fast}(app)	10.8		spectra, see Figure 2
	10.9		kinetics at pH >9
pK_{slow}(app)	7.7		spectra, see Figure 2
a, $M^{-1}\ s^{-1}$	3.6		kinetics at pH >9
pK_4	1.2		kinetics at pH <5
k_r^H, $M^{-1}\ s^{-1}$	4.9×10^2		kinetics at pH <5
$K_5 = K_3K_4/K_1K_2$	1.3×10^3		$[K_{slow}(app) - K_{fast}(app)]/K_{fast}(app)$
k_r^{OH}, $M^{-1}\ s^{-1}$	1.1×10^7		k_f^{OH}/K_3
K_1	0.2	0.01	estimates
pK_2	10.0	8.8	$(1 + K_1)K_{fast}(app)/K_1$
K_3	3.8×10^7	3.2×10^7	$(K_{slow}(app) - K_{fast}(app))(1 + K_1)/K_4$
k_f^{OH}, $M^{-1}\ s^{-1}$	4.3	3.6	$a(1 + K_1)$
k_f^H, $M^{-1}\ s^{-1}$	1.9×10^{-4}	1.6×10^{-4}	k_r^H/K_3

[a] Values above the dotted line are independent of the assigned value of K_1. Values below depend on K_1.

first order. This behavior implies a mechanism where the neutral phosphinic acid RO_2H is undergoing H^+-catalyzed ring closure, and a second-order H^+ dependency arises because of ionization to RO_2^-. Such a mechanism requires the following rate expression:

$$k_{obsd}(pH < 5) = \frac{k_r^H[H^+]^2}{[H^+] + K_4} \qquad (10)$$

This can be fit[12] to the experimental data to give $k_r^H = 4.9 \times 10^2$ $M^{-1}\ s^{-1}$ and $pK_4 = 1.2$. The latter is not unreasonable for the dissociation constant of a phosphinic acid. Diphenylphosphinic acid, for example, has a pK_a value of 1.7.[13]

With a value of K_4 determined from this kinetic analysis, it is now possible with eq 7 to determine K_3; a value of 3.8×10^{-7} is obtained for $K_1 = 0.2$ and a value of 3.2×10^{-7} for $K_1 = 0.01$. This calculation reveals that there is very little neutral phosphinic acid in equilibrium with the cyclic phosphinate ester $R_{iv}OH$, as assumed in previous analyses. Despite the thermodynamic instability of this neutral form, however, the anionic phosphinate is the thermodynamically favored species at high pH because of the greater inherent stability of a phosphinate ion $R_2PO_2^-$ as compared to a phosphoranoxide ion R_4PO^-.

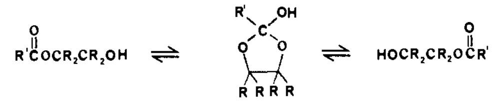
The determination of a value for K_3 now permits the calculation of values of k_r^{OH} and k_f^H by use of eq 4 and the appropriate rate constants for the opposite direction k_f^{OH} and k_r^H which have also been measured in the two kinetic analyses. This means now that all of the rate and equilibrium constants of eq 3 have been determined or estimated. A summary and the method of calculation are given in Table I. It can be noted that there are three classes of constants, a group whose value is independent of the actual value of K_1, a group whose value depends on $(1 + K_1)$, and a third group whose value is directly dependent on K_1. The last group contains only K_2 and of course K_1 itself. Since K_1 is significantly less than unity the uncertainty in the exact value of this constant transforms into a much smaller error in the values of the constants of the middle group. Thus, of all the constants, it is only K_1 and K_2 that carry a large uncertainty.

In terms of the complete rate–pH profile, the observed rate constant must be expressed as the sum of rate constants for reactions in the forward direction (formation of RO_2H) and reverse direction (formation of $R_{iv}OH$), and with assumptions of rapid equilibration of the acid:base pair $RO_2H{:}RO_2^-$ and the group $R_{iv}OH$, R_vOH, and R_vO^-, eq 11 is produced.

$$k_{obsd} = (k_f^H[H^+]^2 + k_f^{OH}K_w) \times \left(\frac{1}{(1 + K_1)[H^+] + K_1K_2} + \frac{1}{K_3[H^+] + K_3K_4}\right) \qquad (11)$$

The curve drawn in Figure 3 is based on this equation and the constants of Table I. An excellent fit to the experimental data is obtained. This is not surprising for the regions above pH 9.5 and below pH 4.5, since in these regions eq 11 reduces to eq 9 and eq 10 respectively, the equations used in the original analysis. The intermediate region, however, was not used and a satisfactory fit is obtained here. Perhaps the most interesting region is that between pH 5 and 7 where the rate constants are approximately independent of pH. In this pH region the overall equilibrium favors $R_{iv}OH/R_vOH$ since the pH is less than pK_{slow}(app). Moreover, since pH is greater than pK_4 then $[RO_2^-]$ is greater than $[RO_2H]$, so that the rate constant k_{obsd} region represents the conversion of RO_2^- to $R_{iv}OH/R_vOH$. Above pH 4.5, however, the reaction involves hydroxide ion catalyzed cyclization of RO_2H;[14] thus pH-independent kinetics result because of the two opposing effects of changing hydroxide ion concentration. Increasing hydroxide ion concentration increases the rate of cyclization of RO_2H but decreases the concentration of this species relative to RO_2^-. It can be noted that the concentration of RO_2H is in fact very small at these acidities but cyclization still occurs because of the very large value for the rate constant k_r^{OH}.

The failure, even with use of stopped-flow spectroscopy, to observe the kinetic behavior associated with the K_a(fast) process implies that the equilibration of $R_{iv}OH$ and R_vOH/R_vO^- occurs with a first-order rate constant greater than $2 \times 10^2\ s^{-1}$ at all pH values. This conclusion is consistent with the observation[1] of a coalesced ^{31}P NMR signal for the $R_{iv}OH{:}R_vOH$ equilibrium mixture in neutral methanol at 25 °C. The hydroxyphosphorane R_vOH is the pentavalent intermediate of a phosphoryl transfer reaction which can be viewed as a degenerate intramolecular reaction in which the phosphoryl group moves from one oxygen in $R_{iv}OH$ to the other. It is of interest to compare this reaction with analogous ones involving acyl group transfer. One example which provides a fairly close model is the degenerate acyl transfer of glycol monoesters, which proceed by way of cyclic tetrahedral intermediates or hemiorthoesters.



(12)

A number of recent studies[15,16] have shown that by starting with appropriate precursors hemiorthoester intermediates can be observed as transient species and rate constants for their breakdown to the acyl product can be directly measured. This breakdown is both acid-catalyzed and base-catalyzed and thus a statement regarding the kinetic stability must be qualified according to the pH. Maximum lifetimes are usually found at weakly acidic pH where half-lives at 25 °C of the order of 1 s have generally been observed. For example, 2-hydroxy-2-phenyl-1,3-dioxolane (R′ = Ph, R = H in eq 12) and its 4,4,5,5-tetramethyl derivative (R′ = Ph, R = Me) have maximum half-lives of 0.4 and 9.6 s, respectively.[16] Interestingly these hemiorthoesters are quite thermodynamically unstable,[17] equilibrium constants for their ring-opening to the glycol monobenzoate being 4×10^8 and 3×10^4, respectively. Thus the hydroxyphosphorane of the present study is more thermodynamically favored with respect to its breakdown products, and yet kinetically it is much more labile. The nature of the catalysis responsible is obviously unknown since rate contants could not be measured at any pH. The conclusion which arises from this limited comparison however, is that the pentavalent intermediates of phosphoryl transfer reactions are kinetically less

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(12) A plot of $[H^+]/k_{obsd}$ vs. $1/[H^+]$ is linear with a slope of K_4/k_r^H and an intercept of $1/k_r^H$.

(13) Mastryukova, T. A.; Malenteva, T. A.; Shipov, A. E.; Kabachnik, M. I. *J. Gen. Chem. USSR* **1959**, *29*, 2145.

(14) (a) The reaction involving hydroxide assumes importance in acidic media since $k^{OH} \gg k^H$. This same feature is found in the analogous reaction of the carbonyl group, namely the reversible cyclization of hydroxy acids to lactones.[14b,c] (b) Fife, T. H.; Benjamin, B. M. *J. Am. Chem. Soc.* **1973**, *95*, 2059–2064. (c) McClelland, R. A.; Alibhai, M. *Can. J. Chem.* **1981**, *59*, 1169–1176.

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(17) Although hemiorthoesters are known which are thermodynamically stable, some special stabilizing feature is required.[15]

stable than the tetrahedral intermediates of acyl transfer reactions or, in other words, activation barriers for the breakdown of pentavalent intermediates are lower.

Experimental Section

Materials. The solid compound having either structure $R_{iv}OH$ or R_vOH was prepared as described by Granoth and Martin.[2] Reagents for the preparation of acid, base, or buffer solutions were analytical grade and were used directly as received. The ionic strength of all solutions was maintained constant at 0.1 M by the addition of sodium chloride. All experiments were carried out at 25.0 ± 0.1 °C. Conventional spectroscopic experiments were carried out with a Cary 2390 spectrophotometer interfaced with an Apple IIe microcomputer. A Durrum-Gibson spectrophotometer interfaced with a Tektronic 4051 microcomputer was employed for stopped-flow experiments.

Spectroscopic Acidity Constants. Curve I of Figure 2 was obtained by preparing a 4.8×10^{-4} M solution of $R_{iv}OH/R_vOH$ in 0.002 M HCl and placing this in one syringe of the stopped-flow apparatus. This was mixed with various sodium hydroxide or buffer solutions to give the desired final pH, and a wavelength of 275 nm was monitored. Absorbance readings are constant from 10 to 50 ms and were used to construct curve I.

Curve II of Figure 2 was obtained by mixing the stock 0.002 M HCl solution of $R_{iv}OH/R_vOH$ equally with various buffers and placing the resultant solution in a constant-temperature bath for 1 month. Full spectra were recorded on the Cary spectrophotometer. A wavelength of 267 nm was chosen for analysis.

Spectroscopic acidity constants were determined according to the formula $K_a = [H^+](A_{acid} - A)/(A - A_{base})$, where A_{acid}, A_{base}, and A are respectively the absorbance readings in acid, base, and the solution in question. Values of K_a were calculated for several solutions of intermediate pH, and the average was taken.

Kinetic Measurements. Kinetic measurements above pH 8 were carried out by addition of 2 μL of a stock acetonitrile solution of the substrate directly to a thermostated cuvette to give a solution of $2-5 \times 10^{-4}$ M. The decrease in absorbance at 267 nm was recorded as a function of time on the Cary spectrophotometer, first-order rate constants being calculated as the slope of plots of $\ln (A - A_\infty)$ vs. t.

The kinetic measurements below pH 7 were carried out by addition of the stock acetonitrile solution to 0.01 M NaOH. This solution was kept for at least 30 min to allow for completion of the transformation to B2. Measurements from pH 2.5 to 6 were carried out on the Cary by mixing the base solution with an appropriate acid or acidic buffer solution. Below pH 2.5, the stock base solution was placed in one syringe of the stopped-flow apparatus and mixed with the appropriate HCl solution. In both cases the increase in absorbance at 267 nm was recorded, and first-order rate constants were calculated as the slopes of plots of $\ln(A_\infty - A)$ vs. time.

Acknowledgment. Continued financial support of the National Sciences and Engineering Research Council of Canada is gratefully acknowledged.

Registry No. $R_{iv}OH$, 67771-45-3; R_vOH, 67759-42-6.

Stereochemistry of the $R_1(X{=})C(sp^2){-}N(sp^3)R_2R_3$ Fragment. Mapping of the Cis-Trans Isomerization Path by Rotation Around the C-N Bond from Crystallographic Structural Data

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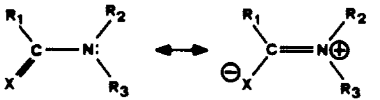
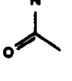
Contribution from the Centro di Strutturistica Diffrattometrica e Dipartimento di Chimica, Università di Ferrara, 44100 Ferrara, Italy. *Received July 30, 1985*

Abstract: The geometry of the $R_1(X{=})C(sp^2){-}N(sp^3)R_2R_3$ molecular fragment has been studied in 90 X-ray crystallographically determined molecules containing such a group (amides, thioamides, enamines, amidines, anilines, etc.). This tends to be planar owing to the partial double bond character of the C-N bond. In a crystal environment, however, it is often deformed from planarity, the deformation being described by the torsion angle τ around C-N ($0 \leq |\tau| \leq 90°$) and the out-of-plane bending of the amino nitrogen, χ_N, ranging from 0° for planar sp^2 to 60° for tetrahedral sp^3 nitrogen. It is shown that out-of-plane deformations are consistent with two different processes: (a) the simple out-of-plane bending of sp^2 nitrogen (a vibrational coordinate) and (b) a more complex motion combining the twisting around the C-N bond and the nitrogen bending (which, according to the structural correlation method, can be considered to map the geometrical changes of the group along the "reaction" path of cis,trans-isomerization of the group itself). An energetic model of the isomerization process, based on molecular mechanics considerations, has been proposed. Proper choice of the parameters in the force field gives rise to an energy map, $E(\tau,\chi_N)$, where the experimentally determined deformations are shown to be nicely located along the energy valley leading from the planar conformation to the rotated and pyramidalized transition state.

The $R_1(X{=})C(sp^2){-}N(sp^3)R_2R_3$ (hereafter shortly indicated as $C(sp^2){-}N(sp^3)$) molecular fragment **1** is found in a variety of organic molecules, such as amides and carbamates (O), thioamides and dithiocarbamates (S), amidines (N), enamines (D), anilines (A), and naphthylamines (B). The group displays a definite tendency to be planar, which can be accounted for by the contribution of the polar form **1a** to its fundamental state. A large number of dynamic NMR measurements have been carried out in an attempt to evaluating the barriers for rotation around the C-N bond. Typical values for *N*-dimethyl derivates are, on the average, 20.7, 18.1, 12.8, 9.0, and 5.1 kcal mol^{-1} for thioamides, amides, amidines, enamines and anilines, respectively.[1-5] This



1 **1a**



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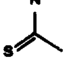

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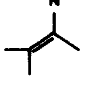

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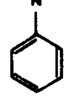

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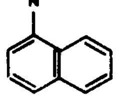

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