

weighed 1.9 g. This was hydrogenated in 150 ml. of methanol with a 5% palladium chloride on carbon catalyst. The hydrogen uptake was 110 ml. (calcd. 67 ml.) in 5 hr. After the removal of the catalyst, the solution was concentrated to about 15 ml. Triphenylmethane, 0.5 g., was filtered off and the filtrate was evaporated to a dry sirup which was taken into 10 ml. of pyridine and phosphorylated with 1 ml. of diphenyl phosphorochloridate at 0° for 5 hr. The sirupy product, isolated as for the previous phosphorylation, was hydrogenated in 200 ml. of methanol with 0.8 g. of platinum oxide catalyst. The hydrogen uptake was 850 ml. (calcd. 900 ml.) in 20 hr. After the removal of the catalyst, 40 ml. of 0.345 *N* barium hydroxide was added to the alcoholic solution, and the solution was left at room temperature for 6 hr. Alcohol was removed under reduced pressure and the barium ion was precipitated by the addition of 1.9 g. of cyclohexylamine sulfate in 40 ml. of water. After the removal of the barium sulfate by centrifugation, the solution was evaporated to dryness. The residue was triturated with acetone and filtered. The solid weighed 0.7 g. Crystallization from aqueous acetone gave 0.15 g. (13% yield) of the tetrolase 4-phosphate (XVIII), m.p. 165–170° and $[\alpha]_D^{21.5}$ (water).

Anal. Calcd. for $C_{15}H_{41}O_8PN_2 \cdot 2H_2O$ (480): C, 45.0;

H, 9.44; P, 6.46; N, 5.84; CH_3O , 13.0. Found: C, 44.5; H, 9.13; P, 6.34; N, 5.59; CH_3O , 12.6.

The presence of water in the crystal was supported by the infrared spectrum, in which the intensity of the hydroxyl absorption was much stronger than that for the tetrolase 1-phosphate.

This compound was chromatographically indistinguishable from the tetrolase 1-phosphate in 2-propanol-ammonia-water (70:10:20). However, it did not consume any periodate as did the 1-phosphate. After treatment of a solution with Dowex 50(H) and hydrolysis at 40° for 4 hr., a paper chromatogram showed a single new component. The R_f value was slower than that of the ketal derivative. Treatment with 1 *N* sodium hydroxide at room temperature for 20 minutes resulted in the release of about 50% of the phosphate as inorganic phosphate. When the tetrolase 4-phosphate was heated at 100° in 1 *N* hydrochloric acid, inorganic phosphate was formed with a half-time of 15 minutes.

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The Beckmann Rearrangement. IX. A Study of Polyphosphoric Acid as a Rearrangement Medium

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The rates of rearrangement of substituted acetophenone oximes were studied in polyphosphoric acid of various phosphorus pentoxide concentrations. The rates were remarkably fast compared to those in sulfuric acid even though the H_0 of polyphosphoric acid is much less than that of sulfuric acid. Also substituents on the acetophenone oxime had little effect in changing the rate ($\rho = ca. -0.25$). A mechanism of rearrangement in polyphosphoric acid *via* an ester is proposed and discussed.

Polyphosphoric acid (PPA) is becoming a reagent of major importance in synthetic organic chemistry without truly being understood. The composition has only recently been made available,² and "very little is known about the precise mechanisms of reactions catalyzed by PPA."³ Since PPA is quite suitable as a medium for the Beckmann rearrangement and since we have had some experience with this rearrangement in sulfuric acid,⁴ we decided to study the rearrangement in PPA to compare mechanisms in the two reacting solvents and to increase knowledge about the use of PPA in general. For example, is it best for the synthesis of amides by the Beckmann rearrangement to dissolve the oxime in PPA at 100–130° and maintain for some arbitrary number of hours as is usually done?

We found early a need for a facile method of determining concentrations expressed as percentage phosphorus pentoxide in PPA,⁵ but, except

for the rather tedious titration of a hydrolyzed sample with alkali, we found none. The specific gravity was particularly insensitive to composition (see Table III) and viscosity the most sensitive (see Table IV). Yet, the latter was the most difficult to determine. The viscosities in the Experimental section extend the work of Griffith and Van Wazer² in the range most important for synthetic work. It is indeed remarkable how great the change in viscosity is in the range 81–85% P_2O_5 .

The high viscosity of PPA gave rise to two difficulties in the kinetic work in which the rate of rearrangement of acetophenone oximes was followed by spectroscopic determination of the rearranged ketone concentration: (1) The PPA could not be delivered accurately on a volume basis so that a weight basis was used. (2) The solution of oxime in PPA was very sluggish. Special means of solution was devised. Still a third difficulty arose because of the use of PPA: the rearrangement product, the acetanilide, could not be hydrolyzed by simple dilution and heating of an aliquot. Dilute sulfuric acid had to be added to bring about hydrolysis. The procedure described in the Experimental section overcame these difficulties and yielded the information in Tables I and II. All these rates fitted pseudo first-order rate equations.

The most noteworthy feature of Table II is that the rearrangement of all acetophenone oximes in PPA is some 12–35 times as rapid as in sulfuric acid

(1) Abstracted in major part from Ph.D. Thesis, Vanderbilt University, of R.M.S., University Microfilm, *Dissertation Abstracts*, **20**, (4), 1196 (1959), Ann Arbor, Mich.

(2) For summary see J. R. Van Wazer, "Phosphorus and Its Compounds," Vol. I, Interscience Publishers, Inc., New York, N. Y., 1958, pp. 747 and 770.

(3) F. D. Popp and W. E. McEwen, *Chem. Revs.*, **58**, 321 (1958).

(4) Beckmann Rearrangement. VIII, P. J. McNulty and D. E. Pearson, *J. Am. Chem. Soc.*, **81**, 612 (1959).

(5) In spite of the sensitivity of viscosity to composition, we believe the refractive index will provide the best compromise for a correlation of a physical property with percentage phosphorus pentoxide; see following paper.

TABLE I
RATES OF REARRANGEMENT OF ACETOPHENONE OXIME IN
POLYPHOSPHORIC ACID ($k_1 \times 10^3$ IN RECIPROCAL MINUTES)

T, °C.	P ₂ O ₅ in PPA			
	81.5%	82.5%	83.5%	84.4%
40.01	6.56 ^a	7.83	8.78	8.87
49.67	16.6 ^b	19.9 ^b	23.5 ^c	25.1 ^b
59.85		55.3 ^b		
E*, kcal. ^d	-19.4	-20.6	-20.5	-21.7
ΔS*, e.u. at 40°	-16.9	-12.9	-12.6	-8.6

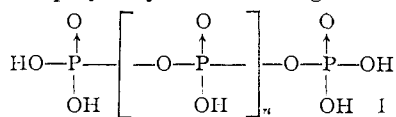
^a Standard deviation = 0.01 reciprocal minute except in b and c. ^b Standard deviation = 0.04. ^c Standard deviation = 0.03. ^d Calculated as in ref. 4.

TABLE II
COMPARISON OF RATES OF REARRANGEMENT OF SUBSTITUTED ACETOPHENONE OXIMES IN POLYPHOSPHORIC ACID AND IN SULFURIC ACID

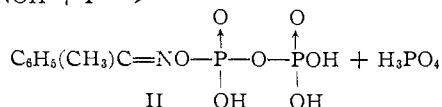
Acetophenone	PPA ^a		H ₂ SO ₄ ^b	
	$k \times 10^3$	$t_{1/2}$ ^d	$k \times 10^3$	$t_{1/2}$
Unsubstituted	7.8	89	0.38 ^f	1820
3-Bromo-	5.6	124	.16 ^e	4330
4-Chloro-	6.8	102	.33 ^e	2100
4-Methyl-	8.5	82	.69 ^f	1000

^a 82.5% P₂O₅ at 40.01°; $H_0 = -4.9$.⁶ ^b 95.8% H₂SO₄ at 41.3°; $H_0 = -8.9$. ^c k is pseudo first-order rate constant in reciprocal minutes. ^d Half-life in minutes. ^e Unpublished data. ^f Estimated.

even though the acidity function for PPA ($H_0 = -4.9$) is much less than that for sulfuric acid ($H_0 = -8.9$). The second feature is that all the rates of rearrangement of the substituted acetophenone oximes are nearly the same. A plot of $\log k/k_0$ vs. σ showed a rough linear relationship with the small slope of $-0.25 (\pm 0.05)$ compared to -1.9 for the same relationship in sulfuric acid. These features suggest that the mechanism of rearrangement in PPA is completely different from that in sulfuric acid. In sulfuric acid we have proposed that the oxime is protonated rapidly, and then water is removed from the cation in the rate-determining step by sulfuric acid.⁴ Now we propose a different mechanism for the rearrangement in PPA—a mechanism which for the present seems the most logical to explain the two experimental features shown in this paper and to correlate with other data on rearrangement of esters of oximes.^{7a} This mechanism has been suggested previously,^{7b} but no experimental evidence was offered to support the suggestion. The PPA is of course mainly a mixture of polyanhydrides of the general formula²



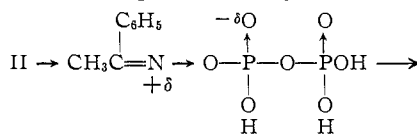
The first reaction between the oxime and any one of the anhydrides (using $n = 1$) is ester formation



(6) A. I. Gel'fshstein, G. G. Shcheglova and M. I. Temkin, *Doklady Akad. Nauk*, **107**, 108 (1956); the H_0 for 82.5% P₂O₅ ($H_0 = -4.9$) is unquestionably wrong. We estimate the value to be about -6.2 ; see following paper.

(7) (a) A. H. Blatt, *Chem. Revs.*, **12**, 215 (1933); (b) E. C. Horning and V. I. Stromberg, *J. Am. Chem. Soc.*, **74**, 2680 (1952).

The present evidence does not rule out this step as being rate-determining.⁸ The next step is either rate-determining or extremely fast



acetanilide (or ester of acetanilide) + pyrophosphate anion
Either one of the steps (I \rightarrow II or II to products) being rate-determining would rationalize the two facts established in this paper. First, the log of the rearrangement rate is not correlative with H_0 either because ester formation (I \rightarrow II) is not dependent on this function or because polyphosphate anion formation leading to rearrangement in the second step is more dependent on its own resonance stabilization for dissociation than on protonation.¹⁰ Second, the polyphosphate anion dissociates so readily (e.g., the bond-breaking step is so advanced) that substituent effects are very small (Table II). Or, if the ester formation step is rate-controlling, it would be expected to be insensitive to substituent effects.

As to the practical aspects of using PPA as a rearrangement medium, the data suggest that conditions so far recommended for synthesis are too strenuous. In most cases rearrangement of oximes will occur overnight at near room temperature. The data in Table I also suggest that PPA of high phosphorus pentoxide concentration (over 84%) is not much more effective as a rearrangement agent than that of lower concentration. The leveling off of rates in the high concentration range is probably a direct consequence of the remarkable increase in viscosity which diminishes collision frequencies¹¹ more than enough to compensate for the greater number of anhydride linkages (or more active linkages).¹² The viscosity seems to play such an important role in controlling the rates of rearrange-

(8) Both ester formation⁸ and oxime rearrangement rates are accelerated by electron-donating groups. The slope of the Hammett line, however, is too small to tell the difference between electromeric effects for the Beckmann rearrangement and presumably non-electromeric effects for ester formation.

(9) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, p. 300.

(10) We make the assumption that H_0 controls the rate of the Beckmann rearrangement in sulfuric acid in major part and should control the rate in the same manner in PPA if the mechanisms were the same. In other words, the rates of rearrangement would be the same in the two reaction solvents if H_0 were the same. And the rates are actually faster in PPA, the reaction solvent of lower H_0 . It is doubtful that the dielectric constant of PPA could be so much greater than that of sulfuric acid to account for the very considerable differences in rates in the two solvents. It is certain that the greater viscosity of PPA would tend to decrease the rate in the solvent. Thus, only a mechanism not depending on H_0 would rationalize the facts holding for the rearrangement in PPA.

Furthermore, the log rate of rearrangement vs. H_0 in various concentrations of PPA alone is not linear (see Table I—the rates level off in the higher P₂O₅ concentrations while H_0 increases regularly). This argument is not a good one, however, because increasing viscosity may distort an otherwise linear effect.

(11) E. A. Moelwyn-Hughes, "Kinetics of Reactions in Solution," Oxford at the Clarendon Press, 1933, p. 20.

(12) Other than (or in addition to) retardation by increased viscosity, the only explanation for the leveling off of rates in PPA could be that a non-reactive species (toward the oxime) is accumulating in the PPA as the phosphorus pentoxide concentration is increased. This species could be cyclic in nature. No species of this nature has been detected so far.

ment in PPA that we make no attempt at this point to interpret the activation energies or entropies of activation given in Table I.

Experimental

Polyposphoric Acid (PPA).—All procedures involving the preparation and dispensation of PPA were carried out in an efficient dry-box. Phosphorus pentoxide (Baker and Adamson, one-fourth pound bottle) was added to a tared 250-ml., glass-stoppered erlenmeyer flask. From the weight of phosphorus pentoxide, the weight of orthophosphoric acid (Merck, 83.83% H_3PO_4 , 60.73% P_2O_5) necessary to obtain the desired strength PPA was calculated and added slowly to the anhydride. After the addition, the mixture was allowed to remain at approximately 165° on a hot-plate for from 1 to 4 days depending on the ease of blending. The PPA made in this manner had a straw color.¹³ The more viscous samples had to be warmed to transfer. All transfers were done on a weight rather than volume basis.

Specific Gravities of PPA.—The specific gravities, based on the weight of water at 25°, were determined in 25-ml., Hubbard specific gravity bottles. The glass ground, capillary stopper had to be resealed occasionally to prevent the expanding PPA from lifting the stopper. The figures in Table III are averages of four determinations for each concentration and temperature.

TABLE III

SPECIFIC GRAVITIES OF POLYPHOSPHORIC ACIDS

T, °C.	81.5%	P ₂ O ₅ in PPA		
		82.5%	83.5%	84.4%
54.93	2.021	2.039	...	2.068
49.72	2.029	2.044	2.057	...
44.68	2.030	2.048	2.060	2.071
39.94	2.033			
35.00	2.045			
24.94	2.048			

Viscosities of PPA.—Viscosities were determined by means of a model HV-303 Hoesppler precision rolling ball viscosimeter.¹⁴ The ball constants were re-evaluated using the known viscosity of a 60% sucrose solution as a standard. The PPA and ball were introduced into the tube while warm to prevent the trapping of air bubbles, and equilibration allowed to take place over a period of 6–8 hours. Ten to fifteen measurements were taken of each sample at each temperature, and the results are shown in Table IV. The enthalpy and entropy of viscosity changes are discussed elsewhere.¹

(13) The straw color could be removed by heating PPA with a few drops of hydrogen peroxide. The procedure for decoloration, however, was not used in obtaining the results of this paper.

(14) T. E. McGoury and H. Mark in A. Weissberger, "Technique of Organic Chemistry, Vol. I, Physical Methods," Interscience Publishers, Inc., New York, N. Y., 1949, Part 1, p. 336.

TABLE IV

VISCOSITIES (IN CENTIPOISES) OF POLYPHOSPHORIC ACIDS

T, °C.	81.5%	P ₂ O ₅ in PPA		
		82.5%	83.5%	84.4%
54.62	2340	3780	6640	16,800
49.47	3000	4880	9230	19,700
44.42	4170	6890	13,500	27,600
39.32	6000			
34.37	8740			
24.92	21,700			

Determination of Rates of Rearrangement of Oximes in PPA.—About 25–30 mg. of freshly sublimed oxime (nearly twice the amount necessary to give 100% optical density in the aliquots) was added to about 60 g. (accurately weighed) of PPA contained in a 60-ml. test-tube fitted with a female 34/35 standard tapered joint. The male joint was drawn to include an 8 mm. tube, 2 inches long. The tube was fitted with a length of rubber tubing so that a 5-mm. glass rod fitted snugly and served as a stirring device. Immediately after the introduction of the oxime on to the surface of the PPA, the test-tube was plunged into a very hot oil-bath until the oxime was observed to melt. As soon as the oxime was melted, the tube was cooled in water while the contents were stirred vigorously with the glass rod. When the temperature of the solution had returned to near the operating temperature and the oxime had all dissolved, the tube was stoppered with the male joint containing the glass rod and immersed in a constant temperature bath. The length of time from melting the oxime to immersing the tube was approximately 1 minute. Dry air was passed over the surface of the PPA while the tube was open. About 1.5-g. aliquots (weighed accurately) were removed at appropriate intervals by means of a pipet and added to 20 ml. of water mixed with 1.8 ml. of concentrated sulfuric acid contained in a French square type 2-ounce bottle having Teflon liner. The weight of the aliquot was obtained by weighing the French square bottle containing the dilute sulfuric acid before and after the addition of the aliquot. When all the samples had been collected, the bottles were submerged to the level of the liquid in an oil-bath at 65°. Care was taken to ensure that the bottles were tightly stoppered. Usually ten samples were taken—a blank, eight samples covering two half-lives, and a sample 24 hr. later to test for complete rearrangement. After 24 hr. of hydrolysis, the bottles were removed, allowed to cool to room temperature, and opened to receive 24.0 ml. of isoöctane (Phillips Spectro-grade). The bottles were again securely capped, shaken well, and allowed to stand from 2 to 24 hours. The samples then were analyzed by measuring the absorbancy of the isoöctane layer relative to the isoöctane layer of the blank sample at the wave length of maximum absorption of the ketone. Calculations were made as reported previously.⁴ The results are shown in Tables I and II.

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