termining the molecular weights. Within the apparatus two small cups, one filled with solvent and the other with solution, are exposed to the vapor of the solvent. A steady state temperature difference results since the vapor condenses on the surface of the solution and the temperature of that cup rises. This temperature rise counteracts the lowering of the vapor pressure by the solute, and, therefore, it depends on the colligative properties of the solution. The difference between the temperatures of the cups is measured by two thermistors, which have high negative temperature coefficients of resistance; the thermistors used were Western Electric type 14A. A null method was used in the measurements. The bridge was first balanced with the two thermistors dipping into the solvent, and then with one thermistor still in the solvent the other was placed in the solution. The instrument could be balanced to about ±10 ohms. A detailed description of the design and operation of the apparatus is to be submitted to *Anal. Chem.*

The apparatus was calibrated using benzil as the solute in ether and in tetrahydrofuran. The former has been shown to form ideal solutions.[16] The calibrations were checked with azobenzene. It was found that the results could be expressed as $\Delta R = kN$, where ΔR is the resistance change when one thermistor is in solvent and the other is in solution, N is the mole fraction, and k is a constant which is found experimentally in the calibration and which varies with solvent. For the apparatus used, k is 23,500 for ether and 25,000 for THF. The molecular weight of the solute can be determined by using the value of N determined experimentally and the equation

$$W = w(1 - N)/Nm$$

where W is the gram molecular weight of the solute, w is the weight of the solute used and m is the number of moles of solvent used. At concentrations above $N = 2.5 \times 10^{-2}$ the calibrations were not satisfactory, and no unknown solutions were studied at these relatively high concentrations. The data are in Table II.

(16) E. Beckmann, *Z. physik. Chem.*, **63**, 197 (1908).

LOS ANGELES, CAL.

[CONTRIBUTION FROM THE MALLINCKRODT LABORATORIES OF HARVARD UNIVERSITY]

The Solvolysis of Tetrabenzylpyrophosphate

BY GERALD O. DUDEK[1] AND F. H. WESTHEIMER

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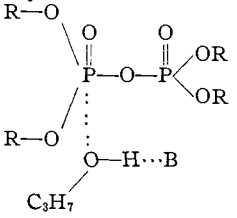
Tetrabenzylpyrophosphate reacts with 1-propanol in the presence of certain sterically hindered tertiary amines with carbon–oxygen cleavage, to yield (mostly) benzyl propyl ether and salts of tribenzylpyrophosphate. On the other hand, 2,6-lutidine and *sym*-collidine catalyze the solvolysis of tetrabenzylpyrophosphate with phosphorus–oxygen cleavage to yield dibenzyl propyl phosphate and salts of dibenzyl phosphoric acid. The solvolysis is also catalyzed by various cations, including those of lithium, magnesium and calcium. The catalysis by lutidine and collidine is only about a third as great in C_3H_7OD as it is in C_3H_7OH; presumably therefore the transfer of a hydrogen atom from the alcohol to the nitrogen base is part of the rate controlling step in P–O cleavage. These facts suggest that the activated complex for P–O cleavage is



in which R is $C_6H_5CH_2$ and B is collidine or lutidine.

The solvolysis of tetra-substituted pyrophosphates proceeds readily at moderate temperatures. A study of the reaction therefore can elucidate the mechanism of cleavage of the pyrophosphate bond[2] and supplement the findings concerned with the reactions of other phosphate esters.[3] The present investigation was undertaken with tetrabenzylpyrophosphate, since this compound is easily purified, and (in comparison to the tetraalkyl pyrophosphates of low molecular weight) is of low toxicity. However, the chemistry is complicated by the fact that the benzyl groups are easily removed by C–O cleavage. In the present work, the solvolyses were carried out in 1-propanol as solvent; both reactions 1 and 2 were observed. The experimental results allow reasonable mechanisms to be presented for these processes.

Experimental

Materials. 1-Propanol.—Eastman Kodak White label propanol was dried over sodium hydroxide, distilled, dried with calcium hydride and then fractionated through a 100 cm. column packed with glass helices; it boiled at 97.16–97.20° at 760 mm. A Karl Fischer titration indicated less than 1 part of water in 2000. One batch was dried by azeotropic distillation; no differences in results were noted.

Ethanol.—Commercial Solvents Corporation absolute alcohol was used without purification.

2,6-Lutidine was purified by distillation from the BF_3-etherate.[4] A vapor phase chromatogram showed only a single peak.

2,4,6-Collidine was similarly[4] purified and fractionated through a 24 cm. column packed with glass helices; it boiled at 90° at 57 mm.

Tribenzylamine.—Eastman tribenzylamine, after recrystallization from alcohol, melted at 93.2–94.4°.[5] No NH bond was observed in its infrared spectrum.

2,6,N,N-Tetramethylaniline was prepared by methylating 2,6-dimethylaniline.[6] It was distilled through a 24 cm. column packed with glass helices, and boiled at 90.8° (23 mm.).

Triethylamine was purified by distillation from acetic anhydride and finally from solid potassium hydroxide through a 100 cm. column packed with glass helices. It boiled at 89.8–90.0°.

Cyclohexylamine was purified by distillation from potassium hydroxide through a 100 cm. column packed with glass helices. It boiled at 134.5–135.0°.

Triethanolamine (Eastman) was used without purification. 2,4-Dinitrophenol, 2,4,6-tribromophenol, *p*-nitro-

(1) Predoctoral Fellow, National Institutes of Health, 1957–1958.

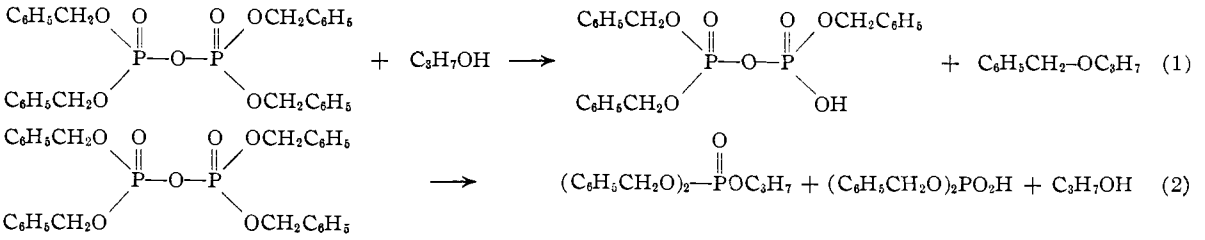
(2) A preliminary report of some of this work was presented by F. H. Westheimer, *Special Publ. Chem. Soc.*, No. 8, 1 (1957).

(3) For a review of phosphate ester chemistry, see *ibid.*, No. 8, 17 ff. (1957).

(4) H. C. Brown, S. Johnson and H. Podall, THIS JOURNAL, **76**, 5556 (1954).

(5) H. Limpricht, *Ann.*, **144**, 305 (1867).

(6) H. C. Brown and M. Grayson, THIS JOURNAL, **75**, 20 (1953).



phenol and *m*-nitrophenol were Eastman products, recrystallized at least four times from two different solvents or solvent pairs.

Pyridine was precipitated from its hydrochloride with perchloric acid.[7] The perchlorate salt was decomposed with 50% sodium hydroxide; the pyridine was dried with potassium hydroxide and then with calcium hydride and fractionated. It boiled at 115.0°.

Propanol-OD.—Anhydrous, purified propanol was equilibrated with equivalent amounts of D_2O at least 6 times. The heavy water was removed each time with freshly dried potassium carbonate and was recovered; it then was used for the initial equilibrations of later batches of solvent. The resulting product was fractionated through a 26 cm. column of glass helices. The final alcohol was analyzed by examining the hydroxyl region of its infrared spectrum. For calibration, 0.5% of C_3H_7OH was added to a sample; the comparison showed that the original alcohol contained about 0.4% of ordinary hydroxyl groups (OH). The material boiled at 97.7° at atmospheric pressure.

Tetra-*n*-butylammonium perchlorate was prepared from the corresponding bromide and perchloric acid.[8] The compound, recrystallized three times from ethanol–ligroin, melted at 217.4–218.2°.

Lithium Perchlorate.—Lithium carbonate (reagent grade) was decomposed with reagent grade perchloric acid. The trihydrate, which crystallized from the concentrated solution, was dried in a vacuum oven at 75° for 24 hr., to produce the monohydrate.[9] This was then dried to the anhydrous salt at 100° and 10^{-5} mm. as needed.

Benzyl propyl ether[10] was prepared by refluxing benzyl chloride with excess sodium propoxide in propanol solution for 24 hr. The reaction mixture was decomposed with water, the ether extracted with cyclohexane and the solution washed and dried. It was then fractionated; the ether boiled at 97° (24 mm.). A small amount was distilled from sodium prior to determining its infrared spectrum.

Dibenzyl Propyl Phosphate.—Diazopropane[11] was passed into an ethereal solution of dibenzyl hydrogen phosphate. The resulting solution was concentrated, washed twice with a bicarbonate solution, once with water, and ester was then distilled in high vacuum; it boiled at 120° at 10^{-5} mm. The same compound was also synthesized by the procedure used earlier by Todd and his collaborators.[12] This method consists of allowing dibenzyl phosphorochloridate to react with propanol in the presence of lutidine. After purification and molecular distillation (100° at 10^{-5} mm.) the material showed the same infrared and nuclear magnetic resonance spectra as that prepared by the diazopropane procedure. The material was also identical with that prepared (*vide infra*) from tetrabenzylpyrophosphate.

Anal. Calcd. for $C_{17}H_{21}PO_4$: P, 9.67; sapon. equiv., 320. Found: P, 9.75; sapon. equiv., 324 and 318.

Although Todd and his collaborators[12] indicated that they had prepared this compound and although they identified it by converting it to the calcium salt of benzyl propyl phosphate, they published no analyses for the material. Samples prepared in this research were sent to four different microanalytical laboratories, and the results from the same batch of material were poor and badly scattered; the carbon analyses reported (on the same material) ranged from 60.0 to 65.2% and the hydrogen from 6.3 to 7.7% (theory, C, 63.72, H, 6.61%). Many phosphorus compounds have proved hard to analyze; the widely scattered carbon–hydrogen analyses on the material suggest that the analytical difficulties are great. The compound, presumably, is nevertheless correctly identified. The evidence consists of three independent syntheses (Todd's method, the diazopropane synthesis and the synthesis from tetrabenzylpyrophosphate), Todd's degradation, phosphorus analysis, saponification equivalent and nuclear magnetic resonance spectrum.

N.M.R. Spectrum.—The n.m.r. spectrum of dibenzyl propyl phosphate (Fig. 1) corresponds accurately to that predicted for the compound. The peak at a corresponds to aromatic hydrogen atoms. The split peak at b corresponds to the benzyl methylene group, split by the adjacent P^{31}. The three peaks of the propyl group are, respectively, the methylene group at c, split by an adjacent methylene group and by the P^{31}, the methylene group, at d split by the adjacent methylene and methyl groups and the final peak at e, for the methyl group, split into three by the adjacent methylene group. The somewhat sloppy shape of the methyl triplet is typical of many spectra of propyl derivatives.[13] The general cleanliness of the spectrum, as well as the proper splittings, confirms the structure.

The n.m.r. spectrum was obtained for a 40% solution of the ester in carbon tetrachloride. A Varian Associates model V4300 nuclear magnetic resonance spectrometer, equipped with superstabilizer, was used for the measurements at 40.01 megacycles on spinning samples.

Dibenzyl hydrogen phosphate[14] was purified by dissolving it in bicarbonate solution and precipitating with acid. After several recrystallizations from chloroform–ligroin, it melted at 80.8–81.4°.

Tetrabenzylpyrophosphate was prepared according to Khorana and Todd.[15]

After three recrystallizations from CCl_4-ligroin, it melted at 62.6–63.4°.

Products. Products Obtained with Low Lutidine Concentration.—A solution of 2.16 g. of tetrabenzylpyrophosphate and 0.50 g. of lutidine in 150 cc. of propanol was heated at 50° for 3 hr. Another 0.5 g. of lutidine was added and the solution maintained at 50° for another 30 hr. The solvent was removed under vacuum, with the addition of ethoxyethanol to ensure complete removal of the propanol. The residue was dissolved in benzene, and extracted once with cold dilute sulfuric acid (to remove the lutidine) and then four times with saturated sodium bicarbonate solution.

The bicarbonate extracts were acidified and extracted with chloroform. The chloroform extract yielded 0.288 g. of dibenzyl hydrogen phosphate, which was identified by "mixed melting point" and by its infrared spectrum.

The benzene solution was dried and the solvent removed. The residue, which weighed 1.87 g., consisted of a white, semi-solid material, which presumably contained the sodium salt of tribenzylpyrophosphate. This residue was extracted with ether, and benzyl propyl phosphate was recovered (see below) from this extract. The residue which remained weighed 1.36 g. It melted at 192°; the value reported[16] for the sodium salt of tribenzylpyrophosphate is 216°. The optical density of a sample of the salt, dissolved in water, was 681 and 262 mμ. The ultraviolet spectra of other phosphate esters give a value of 213 per benzyl group, or a theoretical value of 639 for the triester; the value for the sodium salt is then 7% high. The addition of acidic silver nitrate

(7) F. Arndt and P. Nachtwey, *Ber.*, **59**, 448 (1926).
(8) E. J. Bair and C. A. Kraus, THIS JOURNAL, **73**, 2459 (1951).
(9) J. P. Simmons and C. D. L. Ropp, *ibid.*, **50**, 1650 (1928).
(10) J. B. Senderens, *Compt. rend.*, **178**, 1412 (1924).
(11) D. W. Adamson and J. Kenner, *J. Chem. Soc.*, 1551 (1937).
(12) J. Lecocq and A. R. Todd, *ibid.*, 2381 (1954); R. J. W. Cremlyn, G. W. Kenner, J. Mather and A. R. Todd, *ibid.*, 528 (1958).
(13) N. F. Chamberlain, "A Catalogue of the Nuclear Magnetic Resonance Spectra of Hydrogen in Hydrocarbons and their Derivatives," Spectrum No. 152.
(14) F. R. Atherton, H. T. Openshaw and A. R. Todd, *J. Chem. Soc.*, 382 (1945); F. R. Atherton, H. T. Howard and A. R. Todd, *ibid.*, 1106 (1948).
(15) H. G. Khorana and A. R. Todd, *ibid.*, 2257 (1953).
(16) L. Zervas and I. Dilaris, *Ber.*, **89**, 925 (1956).

solution to an aqueous solution of the sodium salt precipitated the silver salt.

Anal. Calcd. for $C_{21}H_{21}P_2O_7Ag$: Ag, 19.44. Found: Ag, 19.57. An aqueous solution of the sodium salt was made 2 *N* in sulfuric acid and the solution extracted with carbon tetrachloride. This solution of the free acid was dried with sodium sulfate and its infrared spectrum determined. This infrared spectrum was identical with that of the free acid similarly prepared from a sample of sodium tribenzylpyrophosphate which had been prepared by Zervas' method.[16]

For the identification of the propyl benzyl ether, 20 g. of tetrabenzylpyrophosphate was solvolyzed for 37 hr. at 50° with 25 g. of tribenzylamine in 8000 cc. of propanol. The propanol and other volatile materials were collected by vacuum distillation. Fractionation of this propanol gave a residue which was then distilled from sodium. Its infrared spectrum was identical with that of an authentic sample of benzyl propyl ether.

Four repetitions of this analysis gave about the same results. The amount of dibenzylphosphoric acid corresponds to about a 25% yield of P–O cleavage; the yield of tribenzylpyrophosphate accounts for the residual material as carbon–oxygen cleavage.

The ether solution, mentioned above, was evaporated to yield 0.52 g. of an oil, identified by its infrared spectrum as impure propyl dibenzylphosphate.

Products Obtained in the Presence of Tribenzylamine.—A solution of 2.16 g. of tetrabenzylpyrophosphate (0.004 mole) and 2.43 g. of tribenzylamine in 125 cc. of propanol was heated for 30 hr. at 50°. After removal of solvent and neutralization with bicarbonate solution, the tribenzylamine was filtered and washed.

The combined washings and mother liquor were acidified (*p*H 3) with perchloric acid and barium tribenzylpyrophosphate was precipitated by the addition of a saturated aqueous solution of barium nitrate. The solid (1.20 g.) was filtered, well washed and dried.

The filtrate was acidified to *p*H 1 and extracted with chloroform. The chloroform extract yielded an oil which crystallized on standing. It weighed 0.242 g. (0.00087 mole) and was identified as dibenzylphosphoric acid by infrared spectrum and melting point.

Products Obtained in the Presence of a High Concentration of Lutidine.—A solution of 2.16 g. of tetrabenzylpyrophosphate and 5.7 g. of lutidine in 100 cc. of propanol was heated to 50° for 20 hr.

The propanol was removed and water added. The solution was extracted with a small amount of ether to remove the excess lutidine. The barium tribenzylpyrophosphate, precipitated as before, weighed 0.808 g.

The filtrate was acidified and extracted with chloroform. The chloroform yielded 0.558 g. (0.00200 mole) of dibenzylphosphoric acid.

Products from the Mg^{++} Catalyzed Reaction.—A solution of 2.16 g. of tetrabenzylpyrophosphate, 1.5 g. of lutidine and 1.9 g. of anhydrous magnesium perchlorate in 125 cc. of propanol was allowed to stand at room temperature for an hour. The products (obtained by the methods described above) were 1.18 g. of dibenzyl phosphoric acid and 1.24 g. of triester. On molecular distillation, 0.92 g. of pure triester was recovered, with infrared spectrum identical with that of a sample of the synthetic material.

Products from the Reaction with Propoxide.—A solution of 7.5 mmoles of sodium propoxide and 2.15 g. (4 mmoles) of tetrabenzylpyrophosphate in 40 cc. of propanol was allowed to stand at room temperature for 90 minutes. The resulting solution was brought to *p*H 5 with a small amount of concentrated sulfuric acid and the propanol removed by vacuum distillation with the aid of toluene as a "chaser." Analysis gave 1.02 g. of dibenzyl hydrogen phosphate and 1.05 g. of dibenzyl propyl phosphate.

Kinetic Procedures. General Method.—A weighed quantity of tetrabenzylpyrophosphate was added to a thermostated solution of an amine (*e.g.*, 2,6,N,N-tetramethylaniline) plus salt in propanol; the compound dissolved completely (with shaking) in about half a minute. Aliquots (usually 4 cc.) were removed at definite intervals with a syringe and dissolved in 10 cc. of water. The solution was then titrated rapidly, using a Beckman model G *p*H meter to determine the end-point. The equivalence point was found to be a "*p*H" reading (in this mixed solvent) of 9.25 for lutidine, 9.50 for collidine and 7.00 for tribenzylamine and

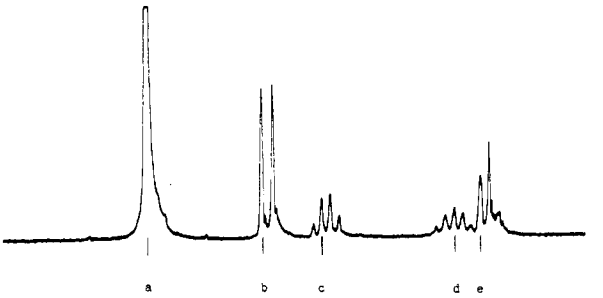


Fig. 1.—Nuclear magnetic resonance spectrum of dibenzyl propyl phosphate.

for tetramethylaniline. The infinity point was taken after six "half-lives," and with a few exceptions came within 1 or 2% of the calculated value. However, with longer times, slightly higher values for the infinity point were obtained, and some error in the absolute values of the rate constants may arise from uncertainty as to the correct final value for the titrations. When the base was tetramethylaniline, the drift in end-point was especially severe (about 10%) and a calculated value of the infinity point was used in calculation. A similar procedure was used for the autocatalytic reactions carried out without added base.

Metal-ion Promoted Reactions.—The base and the pyrophosphate were dissolved in propanol and the solution equilibrated at 0°. An aliquot of a solution of the salt (*e.g.*, calcium perchlorate) in propanol at 0° then was transferred with a syringe to the pyrophosphate solution. Samples were removed at known intervals with a syringe and dissolved in 10 cc. of water which contained about 200 mg. of potassium sulfate; the rapid precipitation of the divalent cation slowed the hydrolysis down so that the end-points were reasonably stable.

Reactions with Propanol-OD.—Essentially the same technique was employed here as for the experiments with ordinary propanol, except that the volumes were smaller (a total of 25 cc. of propanol-OD in each "run") and the volumetric flasks were closed with a rubber stopple, to diminish contamination of the solvent with moisture from the air. The bases also had to be handled with care since they are hygroscopic.

Indicator Studies.—Buffer solutions of amine and perchloric acid were prepared at various "*p*H" values in the propanol solvent. The indicators were dissolved in propanol, and the absorption spectra in the fully acid and in the fully basic form were determined; the extinction coefficients at the two absorption maxima have been recorded. The indicators then were dissolved in the buffers and the spectra measured. From these measured optical densities, the relative base strengths of the indicators as compared to collidine and lutidine were computed.

Calculation of Rate Constants.—The reactions of equations 1 and 2 both generate one mole of hydrogen ion for each mole of tetrabenzylpyrophosphate which is solvolyzed. The "uncatalyzed" reaction is a first-order process, and the rate in the presence of tetramethylaniline is independent of the concentration of amine. The calculated values of k so obtained are constant over the first 3 half-lives of the reaction. When, however, collidine or lutidine is present, the rate is linear in the amine, and base is consumed by the acid produced. The rate is then given by equation 3

$$d(H^+)/dt = k_1[p_0 - (H^+)] + k_2[p_0 - (H^+)][b_0 - (H^+)] \quad (3)$$

where p_0 is the initial concentration of pyrophosphate and b_0 is the initial concentration of the base present. Integration of equation 3 gives (4)

$$\ln \frac{p_0}{p_0 - (H^+)} + \ln \left[1 - \frac{k_2(H^+)}{k_1 + k_2 b_0}\right] = k_{obs}\, t = [k_1 - k_2 p_0 + k_2 b_0]t \quad (4)$$

In equation 4, the first term on the left is much larger than the second term for all the concentrations of pyrophosphate and base used in these investigations. As a first approximation

$$\ln \frac{p_0}{p_0 - (H^+)} = k_{obs}'\, t = (k_1 + k_2 b_0)t \quad (5)$$

Approximate values of k_1 and k_2 can be obtained by applying equation 5 to the data at several concentrations of lutidine. These approximate values of k_1 and k_2 can then be substituted into the second term of equation 4, and a second approximation obtained for k_{obs}, and hence for k_1 and k_2. The second approximation differs very little from the first.

Results

Products.—The yields of products obtained under various experimental conditions are summarized in Table I. The production of dibenzylphosphoric acid was accompanied by the formation of dibenzyl propyl phosphate, whereas the production of tribenzylpyrophosphoric acid was accompanied by the formation of benzyl propyl ether. The yields are (at least roughly) in accord with the statement that the reaction in the presence of lutidine gives largely P–O cleavage; the percentages are not appreciably different with a low concentration of lutidine and with tribenzylamine, since 0.05 *M* lutidine does not greatly enhance the reaction rate.

TABLE I

PRODUCTS OF SOLVOLYSIS OF TETRABENZYL PYROPHOSPHATE IN PROPANOL AT 50°

Base	Approximate % yield of Dibenzyl phosphoric acid	Tribenzyl pyrophosphoric acid
Tribenzylamine	25	75
Lutidine (0.05 *M*)	25	75
Lutidine (0.9 *M*)	55	45
Propoxide ion	100	..

Kinetic Data.—The rate constants, determined for the reaction of tetrabenzylpyrophosphate in propanol at 50°, are presented in Table II.

TABLE II

RATES OF SOLVOLYSIS OF TETRABENZYLPYROPHOSPHATE IN PROPANOL AT 50°

Concentrations, mole/l.

Pyrophosphate	Salt[a]	Base		Added reagent		$k_{obs} \times 10^5$, sec.$^{-1}$
0.0201	0.050	0.221	TMA[b]			4.84
.0200	.050	.120	TMA			4.90
.0200	.050	.042	TBA[c]			4.77
.0200		.071	TBA			4.77
.0092		.059	TBA			4.61
.0201		.059	TBA			4.70
.0401		.059	TBA			4.88
.0201	.051	.105	TBA			4.70
.0069	.051	.120	Lutidine			6.46
.0200	.051	.122	Lutidine			6.26
.0521	.051	.122	Lutidine			6.20
.0201	.051	.166	Lutidine			6.89
.0201	.30	.166	Lutidine			5.88
.0201		.062	Lutidine			5.34
.0201		.122	Lutidine			6.21
.0200	.040	.121	Lutidine	$NaClO_4$	0.010	7.29
.0200	.028	.121	Lutidine	$NaClO_4$	0.023	8.35
.0202	.051	.041	Lutidine			5.27
.0200	.051	.084	Lutidine			5.84
.0201	.051	.336	Lutidine			8.42
.0201	.051	.418	Lutidine			9.21
.0201	.051	.054	Collidine			5.81
.0201	.051	.107	Collidine			7.04
.0201	.050	.170	Collidine			8.12
.0201	.051	.260	Collidine			10.11
.0198	.050	.082	Lutidine	Water	0.032	5.89
.0201	.050	.048	Lutidine	Ethanol[d]		7.11
.0201	.050	.160	Lutidine	Ethanol[d]		9.24
.0100		.0110	Propoxide[e]			1.8×10^5[f]

[a] Tetrabutylammonium perchlorate. [b] 2,6,N,N-Tetramethylaniline. [c] Tribenzylamine. [d] As solvent, instead of propanol. [e] At 0°. [f] M^{-1} sec.$^{-1}$.

An inspection of the data in Table II shows that the rate is first order in pyrophosphate and not very sensitive to salt. The addition of more tetra-*n*-butylammonium perchlorate slightly depresses the rate; substitution of sodium for tetrabutylammonium perchlorate slightly increases the rate. A low concentration of water has almost no effect upon the rate, and the rate constants here reported are therefore probably free from error due to adventitious water which may occasionally have been introduced through contact of the propanol solutions with the atmosphere. The rate is essentially constant with variation in the concentrations of tetramethylaniline or of tribenzylamine but increases linearly with increasing concentrations of lutidine and collidine as shown in Fig. 2. The rate is not very sensitive to the change of solvent from propanol to ethanol. On the other hand, reactions carried out in the absence of any base were sharply autocatalytic; no rate constants were obtained for these conditions.

The effect of lithium perchlorate (and other salts) on the reaction rate are recorded in Table III. The rate constant k_{obs} was calculated as if the reaction in the presence of both lithium ion and amine were first order; as explained above, this assumption is approximately valid.

TABLE III

EFFECT OF METAL SALTS ON THE SOLVOLYSIS OF TETRABENZYLPYROPHOSPHATE

Pyrophosphate	$LiClO_4$	Base		T, °C.	$k_{obs}' \times 10^5$, sec.$^{-1}$
0.0201	....	TBA	0.071	50	4.77
.0201	....	Lutidine	.122	50	6.21
.0106	0.0351	TBA	.0627	50	7.38
.0106	.0342	TBA	.0318	50	7.74
.0201	.01025	TBA	.0594	50	5.00
.0200	.0341	TBA	.0593	50	7.54
.0200	.0428	TBA	.0593	50	8.56
.0200	.0141	Lutidine	.249	50	13.04
.0201	.0429	Lutidine	.250	50	24.6
.0201	.0640	Lutidine	.250	50	32.8[a]
.0201	.0660	Lutidine	.250	50	33.3
.0201	.0887	Lutidine	.253	50	41.9
.0201	.105	Lutidine	.250	50	48.0
.0201	.1330	Lutidine	.250	50	54.4
.0201	.0347	Lutidine	.168	50	17.0
.0201	.0665	Lutidine	.168	50	25.6
.0200	.0925	Lutidine	.168	50	32.3
.0200	.0127[b]	Lutidine	.120	0	3.0
.0200	.0265[b]	Lutidine	.120	0	3.7

[a] 0.06 *M* in water. [b] $Ca(ClO_4)_2$ in place of $LiClO_4$.

The large reaction rate with propoxide ion, and the very modest increase in the rate with lutidine and collidine, raises the question as to whether the catalysis by these bases might not be caused by the trace of propoxide ions present in any solution of an amine in propanol. However, such

$$B + PrOH \rightleftharpoons BH^+ + PrO^- \qquad (6)$$

an interpretation is inconsistent with the fact that the rate of the reaction is well-behaved; were propoxide important, the rate constant would decrease sharply during any particular experiment, as the concentration of dibenzylphosphoric acid

increased. Further, very crude indicator measurements have shown[17] that the concentration of propoxide ions is far too small to be responsible for the reaction.

Isotope Effect.—The isotope effect upon the reaction rate was determined by comparing the reaction rate in C_3H_7OD with that in C_3H_7OH. The individual rate constants in the deuterated solvent are presented in Table IV.

TABLE IV

RATES OF SOLVOLYSIS OF TETRABENZYLPYROPHOSPHATE IN PROPANOL-OD AT 50°

Concentrations, mole/l.

Pyrophosphate	Base		Added reagent		$k_{obs} \times 10^5$, sec.$^{-1}$
0.0201	TBA[a]	0.0592			3.87
.0200	TBA[a]	.0594			4.08
.0200	Lutidine	.0526			4.40
.0201	Lutidine	.0837			4.50
.0203	Lutidine	.134			4.78
.0198	Lutidine	.177			4.74
.0201	Lutidine	.198			4.64
.0202	Lutidine	.213			4.97
.0201	Collidine	.0790			4.54
.0202	Collidine	.125			4.96
.0200	Collidine	.155			5.07
.0202	Collidine	.197			5.31
.0205	Collidine	.131			5.55
.0201	Collidine	.202			5.58
.0200	TBA[a]	.0594	$LiClO_4$	0.0296	5.85
.0201	TBA[a]	.0594	$LiClO_4$	.0329	6.01
.0200	Lutidine	.168	$LiClO_4$	.0354	10.05
.0200	Lutidine	.168	$LiClO_4$	.0609	13.32
.0201	Lutidine	.168	$LiClO_4$	.1306	24.0

[a] Tribenzylamine.

TABLE V

SUMMARY OF KINETIC DATA

Rate constant	Ethanol	Propanol C_3H_7–OH	Propanol C_3H_7–OD	k_H/k_D
$10^5 k_1$ (solvolysis), sec.$^{-1}$	6.58	4.84	4.12	1.18
$10^5 k_2$ (lutidine catalysis), M^{-1} sec.$^{-1}$	18.9	11.3	3.33	3.39
$10^5 k_2$ (collidine catalysis), M^{-1} sec.$^{-1}$		20.8	6.38	3.24

Discussion

The product analyses show that the solvolysis of tetrabenzylpyrophosphate in propanol proceeds with both carbon–oxygen and with phosphorus–oxygen cleavage as shown in eq. 1 and 2. These two processes will be discussed in turn.

The carbon–oxygen cleavage is an uncatalyzed reaction and leads largely to the production of benzyl propyl ether and tribenzylpyrophosphate. The rates of this reaction may be compared to those for the solvolysis of other benzyl esters. The rate constant of solvolysis of tetrabenzylpyrophosphate, with C–O cleavage, in propanol at 50° is about 4×10^{-5} sec.$^{-1}$; the rate constant in ethanol at 50° is about 5×10^{-5} sec.$^{-1}$. The corresponding constant for benzyl chloride at 50° in absolute ethanol[18] is 3×10^{-7} sec.$^{-1}$, that for benzyl bromide at 77° in 80% aqueous alcohol[19] is about 20×10^{-5} sec.$^{-1}$, that for benzyl tosylate in absolute ethanol[18] at 25° is 5×10^{-5} sec.$^{-1}$ and that for benzyl nitrate at 50° in 60% aqueous dioxane[20] is 0.16×10^{-5} sec.$^{-1}$. Both the rates for the pyrophosphate and for the tosylate have been measured in ethanol; when allowance is made for the difference in temperature, the rate for the solvolysis of the pyrophosphate is probably about a fifth as great as that for the tosylate. The rate for benzyl pyrophosphate is much greater than that for benzyl chloride. If the mechanisms for all these solvolytic reactions are similar, then the pyrophosphate is a remarkably efficient "leaving group." Further investigation will be required to elucidate this point.

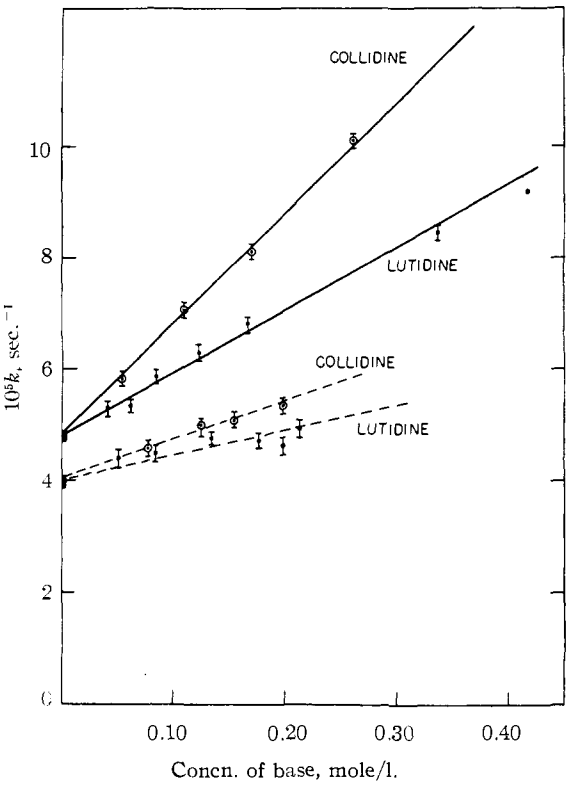


Fig. 2.—Rate of solvolysis of tetrabenzylpyrophosphate at 50°. The solid lines refer to reaction in C_3H_7OH as solvent; the dotted lines to reaction in C_3H_7OD as solvent.

The mechanism of the reaction which results in P–O cleavage has been more firmly established. Propoxide ion cleaves tetrabenzylpyrophosphate exclusively at the P–O bond, and the reaction which is catalyzed by the sterically hindered pyridines (*sym*-collidine and 2,6-lutidine) leads largely to the products of P–O scission. *A priori* two mechanisms for the amine catalyzed reaction must be considered. One possibility[2] is that the amine itself directly attacks the phosphorus, according to the equations

$$(C_6H_5CH_2O)_2PO{\cdot}O\ PO{\cdot}(OCH_2C_6H_5)_2 + R_3N \longrightarrow (C_6H_5CH_2O)_2\ PO_2^- + (C_6H_5CH_2O)_2\ PO{\cdot}\overset{+}{N}R_3 \quad (7)$$

(17) G. Dudek, unpublished results.

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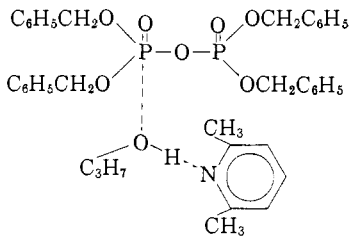
$$(C_6H_5CH_2O)_2\,PO{\cdot}\overset{+}{N}R_3 + C_3H_7OH \longrightarrow (C_6H_5CH_2O)\,PO{\cdot}OC_3H_7 + R_3\overset{+}{N}H \quad (8)$$

A second possibility is that the reaction consists of a direct attack by propanol upon the phosphorus–oxygen bond and that the reaction rate is enhanced by the simultaneous attack of the base on the proton of the alcohol. If this mechanism is correct, the activated complex for the reaction would have the structure



Probably both mechanisms obtain in special cases (see below). But the reactions catalyzed by collidine and lutidine are most probably of the second type. For the data of Table IV and of Fig. 2 show that the catalysis by collidine and lutidine is diminished by a factor of about three when the reactions are carried out in C_3H_7OD rather than in C_3H_7OH as solvent. Presumably, therefore, a hydrogen–oxygen bond is broken in the rate-controlling step of the reaction. Since the reaction rate depends upon the concentration of the nitrogen base present in the solution, the activated complex shown above is most probably correct. This mechanism is at least roughly analogous to that postulated by Cunningham[21] for the action of chymotrypsin and might perhaps also serve as a model for a similar mechanism[22] for the action of phosphoglucomutase. However, pyridine, which is a weaker base than its homologs, causes a greater increase in rate. The details of this reaction have not yet been worked out, but the fact that the weaker base is the stronger catalyst suggests a different mechanism, which may prove to be a direct attack[2] of the base on phosphorus. However, neither the work with pyridine nor that with other unhindered bases (*e.g.*, imidazole) is yet complete.

Finally, the reaction in the presence of pyridine (and other) bases is strongly catalyzed by polyvalent cations. The salt effect on the reaction by sodium and potassium ions is not marked (see Table II) and that by the tetrabutylammonium ion is negligible. But lithium perchlorate strongly increases the rate, and ions such as calcium and magnesium are strong catalysts. These metal ion effects parallel those reported by Lowenstein[23] for the phosphorolysis of adenosine triphosphate and are analogous to enzymatic reactions of ATP, where magnesium ion is required for activity. The mechanisms of these processes are under investigation.

NOTE ADDED IN PROOF.—Professor H. C. Brown suggested, as an alternative explanation for the results with C_3H_7OD, that the amine might be much more strongly hydrogen-bonded in the deuterated than in the normal solvent. The kinetic results would then follow provided only the free-base were catalytically active. However, Mr. Robert Blakely has now found that the heats of solution of pyridine and of 2,6-lutidine in D_2O differ by less than 50 calories from the corresponding values in water. The alternative explanation is therefore considered untenable.

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Preparation and Properties of Pentafluoroselenium Hypofluorite (F_5SeOF) and Bis-(pentafluoroselenium) Peroxide ($F_5SeOOSeF_5$)

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The fluorination of selenium dioxide and of selenium oxychloride has been found to give rather small yields of the new compounds, pentafluoroselenium hypofluorite (F_5SeOF) and bis-(pentafluoroselenium) peroxide ($F_5SeOOSeF_5$). The former is highly reactive. It boils at about −29° and melts at about −54°. The latter is relatively inert chemically. It melts at −62.8° and boils at 76.3°.

Although only one oxyfluoride of selenium, $SeOF_2$, has been described in the literature,[1–5] it appears probable that its close relationship to sulfur should permit selenium to form several oxyfluorides. Recent studies of the synthesis of SF_5OF, SO_3F_2, SOF_4 and $S_2O_6F_2$ by the fluorination of SO_3, SOF_2 and SO_2[6–9] suggest that similar fluorinations of SeO_2, $SeOF_2$ or $SeOCl_2$ may lead to the formation of new compounds of selenium, oxygen and fluorine. This expectation is strengthened by the

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