The phosphorus nmr spectrum consists of a triplet of doublets centered at −137.8 ppm (85% H_3PO_4). This is consistent with the existence of a PF_2NH group. The phosphorus signal is split into a triplet by the two equivalent fluorine nuclei (J_{P-F} = 1172 Hz). Each member of this triplet is then split into a doublet by the "d" proton nucleus attached to the nitrogen (J_{PNH_d} = 47 Hz). A comparable chemical shift value of −143 ppm (85% H_3PO_4) has been reported for $PF_2N(CH_3)_2$. The assignments are also supported by agreement of the J_{P-F} coupling from the ^{19}F spectrum.

Reaction of P_2F_4 with $(CH_3)_2NCH_2CH{=}CH_2$. Since a free-radical process was evident in the formation of $PF_2CH_2CHPF_2CH_2PF_2$ and an apparent N-H bond cleavage with formation of amine salts occurred in the formation of $PF_2NHCH_2CH{=}CH_2$, the interaction of P_2F_4 with $(CH_3)_2NCH_2CH{=}CH_2$ was investigated as it was thought that by elimination of the N-H bond as a reaction site, the reaction could proceed by free-radical addition. However, this was not found to be the case. Results indicate a non-free-radical reaction yielding an unidentified brown solid, unreacted $(CH_3)_2NCH_2CH{=}CH_2$, and PF_3.

Acknowledgments. We thank A. Srinivasan and G. Kodama for assistance in obtaining nmr data. Some of the spectra were obtained using equipment of the University of Utah. Financial support of the College of Science and University Research Council at Utah State University, the U. S. Army Research Office (Durham), and the Research Corp. is greatly appreciated.

Registry No. P_2F_4, 13824-74-3; $PF_2CH_2CH{=}CH_2$, 52124-33-1; $PF_2CH_2CHPF_2CH_2PF_2$, 52124-34-2; B_2H_6, 19287-45-7; $F_2PCH_2CHPF_2CH_2PF_2\cdot 3BH_3$, 52124-35-3; $F_2PCH_2CHPF_2CH_2PF_2\cdot 2BH_3$, 52124-36-4; $H_2NCH_2CH{=}CH_2$, 107-11-9; $PF_2NHCH_2CH{=}CH_2$, 52124-37-5.

Contribution from the Research Resources Center and the Department of Biochemistry, University of Illinois at the Medical Center, Chicago, Illinois 60612, and from the Department of Chemistry, Vanderbilt University, Nashville, Tennessee 37235

Cyclic Phosphates with Substitution or with Conjoined or Fused Rings

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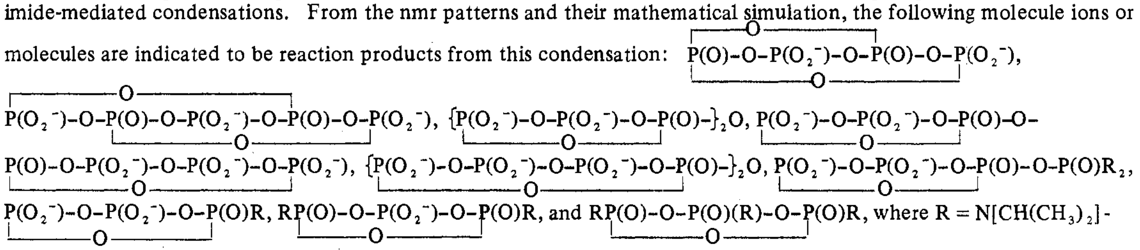

Conditions are reported for optimization of the nine detectable products obtained from orthophosphoric acid by carbodiimide-mediated condensations. From the nmr patterns and their mathematical simulation, the following molecule ions or molecules are indicated to be reaction products from this condensation: $P(O)-O-P(O_2^-)-O-P(O)-O-P(O_2^-)$, $P(O_2^-)-O-P(O)-O-P(O_2^-)-O-P(O)-O-P(O_2^-)$, $\{P(O_2^-)-O-P(O_2^-)-O-P(O)-\}_2O$, $P(O_2^-)-O-P(O_2^-)-O-P(O)-O-P(O)-O-P(O_2^-)-O-P(O_2^-)-O-P(O_2^-)$, $\{P(O_2^-)-O-P(O_2^-)-O-P(O_2^-)-O-P(O)-\}_2O$, $P(O_2^-)-O-P(O_2^-)-O-P(O)-O-P(O)R_2$, $P(O_2^-)-O-P(O_2^-)-O-P(O)R$, $RP(O)-O-P(O_2^-)-O-P(O)R$, and $RP(O)-O-P(O)(R)-O-P(O)R$, where $R = N[CH(CH_3)_2]-[C(O)NHCH(CH_3)_2]$ for condensation with diisopropylcarbodiimide and is the equivalent urea derivative for other carbodiimides. Upon hydrolysis of the condensation product mixtures, the compounds $RP(O_2^-)-O-P(O_2^-)-O-P(O_2^-)R$, $RP(O_2^-)-O-P(O_2^-)-O-P(O_3^{2-})$, and $RP(O_2^-)-O-P(O_3^{2-})$ were produced in addition to some of the usual inorganic chain and ring phosphates. The products obtained by condensation of the tri- and tetrametaphosphoric acids are also discussed.

Although the condensed phosphates[1] make up one of the more important families of chemical compounds (having broad significance to biochemistry[2] as well as many industrial applications[2]), our knowledge of them is still woefully incomplete. In spite of the fact that straight-chain and simple-ring phosphates have been recognized for about a century, individual members of each of these series of compounds up to about the decaphosphate have been separated only quite recently.[3] The situation with respect to oligophosphates containing branching PO_4 groups has until now been almost purely speculative. It has been suggested[4] that the 1,5-μ-oxo-tetrapolyphosphate anion (structure I, given below), must serve as an intermediate in the solvolysis of the P_4O_6 cage molecule. Also, on the basis of hydrolysis products, the orthophosphatyltrimetaphosphate structure (ester IV) was claimed.[5] Unfortunately, because of substituent exchange reactions occurring during the hydrolysis process, this type of structure proof is not very satisfactory for the condensed phosphates and their derivatives. Therefore, we must conclude that, prior to the work described herein, there has been no acceptable evidence for the existence of branched oligophosphates, although it surely seemed reasonable to assume that they exist.

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(1) J. R. Van Wazer, "Phosphorus and Its Compounds," Vol. I, Wiley-Interscience, New York, N. Y., 1958.

(2) J. R. Van Wazer, "Phosphorus and Its Compounds," Vol. II, Wiley-Interscience, New York, N. Y., 1961. Also see any general text on biochemistry.

(3) (a) E. J. Griffith and R. L. Buxton, *J. Amer. Chem. Soc.*, 89, 2884 (1967), and references therein, for chain phosphates; (b) T. Glonek, J. R. Van Wazer, M. Mudgett, and T. C. Myers, *Inorg. Chem.*, 11, 567 (1972), for ring phosphates. Small amounts of both rings and chains through the decaphosphate have been isolated in our laboratory by eluting various phosphate condensation products from an anion-exchange column.

(4) *E.g.*, G. Burkhardt, M. P. Klein, and M. Calvin, *J. Amer. Chem. Soc.*, 87, 591 (1965). For a proper interpretation of this chemistry, see J. R. Van Wazer and S. Norval, *ibid.*, 88, 4415 (1966). For another example showing branched phosphates in hypothetical reactions, see p 694 of ref 1.

(5) R. Ratz and E. Thilo, *Justus Liebig Ann. Chem.*, 572, 173 (1951).

The work reported herein is part of a continuing study[3b,6,7] which has been under way for more than 5 years concerning the application to inorganic phosphorus chemistry of the numerous reagents for the condensation and esterification of phosphoric acids which have been developed by biochemists, particularly for use in the synthesis of nucleotide cofactors and polynucleotides. During this time there has been a significant improvement in the resolving power of ^{31}P nuclear magnetic resonance (nmr) spectrometers which has revealed the middle- and branch-group regions of the ^{31}P spectra of mixtures of phosphates as well as of their derivatives to be particularly rich in fine structure. Observation of many hundreds of spectra of condensed phosphates has shown that certain peaks consistently appear in a given ratio with respect to certain other phosphate spectral peaks so that it became clear that such groups of related resonances must be attributable to individual molecules. The characterization and interpretation of the groups of related ^{31}P nmr resonances appearing in the products resulting from condensation with carbodiimides are the subject of this paper.

Experimental Section

Crystalline orthophosphoric acid was made in the standard manner[1] as were the various linear[1,3] and cyclic[3,8] condensed phosphates. Diisopropyl-, di-*p*-tolyl-, and dicyclohexylcarbodiimide, tri-*n*-butylamine, *p*-toluenesulfonic acid, and tetra-*n*-butylammonium hydroxide as well as the ureas corresponding to hydration of the carbodiimides were purchased from the Aldrich Chemical Co. The anhydrous pyridine[9] and anhydrous tetramethylurea[6] were prepared as described previously. Dimethyl sulfoxide (Aldrich) was purified by rotary evaporation at 30° and then dried with a molecular sieve (Linde, Type 4-A).

Ion exchange using Dowex 50 resin was employed to place the desired cation on the selected phosphate.[3b] The ^{31}P nuclear magnetic resonance measurements[3,10,11] were carried out on a Bruker HFX-5 spectrometer at 36.5 MHz, and the ^{1}H measurements were done on the same instrument at 90.0 MHz. Heteronuclear ^{1}H field frequency stabilization was used in most of the routine ^{31}P measurements, as well as for ^{31}P–^{31}P indor studies,[7] and ^{19}F field frequency stabilization was employed for heteronuclear decoupling between the ^{1}H and ^{31}P nuclei. The spectrometer is equipped with proper facilities for signal averaging including the taking of signal-averaged ^{31}P–^{31}P indor spectra. It should be noted that the modern techniques of signal averaging employed in this work allow a concentration as low as 10^{-4} *M* in phosphorus to be observed[12] for any given nmr peak. And furthermore, with our setup this signal averaging does not have to cover the entire spectrum. Thus, a concentration of 10^{-4} *M* in P is readily measured for an nmr peak on an equilibrated sample after 3 days of averaging when a 10-Hz range is employed, as is done for example in looking for the presence of traces of orthophosphate in mixtures. Chemical shifts are reported with respect to 85% H_3PO_4 for ^{31}P and with respect to tetramethylsilane for ^{1}H, with upfield shifts being positive for ^{31}P and negative for ^{1}H as is customary.

Reactions were often run in 40-ml centrifuge tubes fitted with Teflon-lined caps. After the initial heat of condensation had dissipated in the carbodiimide condensation reactions, the reaction tube was centrifuged to compact the urea which had formed, and the clear supernatant solution was then withdrawn for nmr analysis, without being concentrated or diluted.

Since all of these reactions are very sensitive to moisture, extreme care must be used in every step to keep out traces of water! We have found that when the operations are performed rapidly with use of tightly stoppered containers by an experienced operator, a drybag flushed by dry nitrogen is considerably more effective in avoiding contamination by moisture than is the usual drybox. A good test of the drybag technique for this work is found in making without an excess of condensing agent replicate preparations of equilibrium mixtures, which are found to exhibit essentially equivalent nmr patterns when prepared under conditions where the water of composition of the reaction products has not been increased by improper handling.

The five reaction mixtures which are discussed in detail were prepared as follows.

Mixture 1. Melted dicyclohexylcarbodiimide (20.6 g, 100 mmol) was layered above a solution of 4 g (40 mmol) anhydrous phosphoric acid in 20 ml of tetramethylurea. The reaction vessel was sealed, vigorously shaken for 2 min, and then centrifuged at 2500 rpm for 40 min.

Mixture 2. Anhydrous tris(tri-*n*-butylammonium) trimetaphosphate (1.3 mmol) was dissolved in 40 ml of tetramethylurea, and 10 mmol (1.6 ml) of diisopropylcarbodiimide, DIC, was added. The reaction vessel was sealed and allowed to stand for 48 hr. The reaction proceeded without evolution of heat or formation of precipitated urea.

Mixture 3. Tetrakis(tri-*n*-butylammonium) tetrametaphosphate (1 mmol) was taken up in 4 ml of dimethyl sulfoxide (DMSO), and DIC (10 mmol) was added. The reactants were promptly mixed and allowed to stand for approximately 1 hr. This reaction proceeded rapidly without evolution of heat and, if the reactants were thoroughly dried, without formation of precipitates.

Mixture 4. DIC (6.2 ml, 40 mmol), diisopropylurea (DIU, 2.9 g, 20 mmol), and 10 ml of tetramethylurea were stirred together for 1 hr, after which crystalline orthophosphoric acid (1 g, 10 mmol) in 3 ml of tetramethylurea was introduced. The reaction vessel was sealed, vigorously agitated, and allowed to stand for 15 min.

Mixture 5. This reaction was initiated by suspending 0.71 g of phosphorus pentoxide (H form[1]) in 20 ml of an anhydrous solvent composed 4:1 by volume of tetramethylurea and tri-*n*-butylamine and adding 0.027 ml of water (theoretical degree of condensation 2.7).[6] The product was obtained after stirring for $^1/_2$ hr and decanting from the insoluble phosphatic residue.

General Hydrolytic Procedure. A volume of a reaction mixture containing about 10 m*M* P was quickly poured into 400 ml of a vigorously agitated two-phase mixture consisting of equal parts of 1 *M* aqueous triethylammonium bicarbonate and ethyl ether. The aqueous phase was separated, extracted twice with additional volumes of ethyl ether to remove the unreacted carbodiimide, the free amine, and other nonpolar constituents, concentrated to a thick syrup on a rotary evaporator at 24°, and purged[3b] of the residual bicarbonate salt by three successive evaporations of 100 ml of methanol. The residue was dissolved in 100 ml of H_2O (or more, if necessary) and the solution passed through a column (2.5 × 25 cm) containing 70 ml of diethylaminoethylcellulose in the bicarbonate form. After being washed with at least 1 l. of H_2O, the phosphates were eluted with 500 ml of 1 *M* aqueous triethylammonium bicarbonate, concentrated by rotary evaporation, and again purged of the residual bicarbonate with methanol. The triethylammonium phosphates were then converted to the sodium salts for ^{31}P nmr analysis by passing an aqueous solution of the triethylammonium salt (0.1 *M* in P) through a column (1.5 × 20 cm) containing 30 ml (*ca.* 60 mequiv) of Dowex 50-X8-200 in the protonic form and *immediately* neutralizing the effluent with 0.1 *M* sodium hydroxide. After rotary evaporation, the concentrated solution was taken up in a sufficient volume of 0.1 *M* sodium EDTA at pH 7 to yield a solution 0.1 *M* in P. We have found[3b] that the acid-column treatment does not result in measurable degradation of chain- or ring-phosphate salts when the operation (including neutralization) is carried out quickly (<1 min).

Results and Discussion

Our studies have shown that an excess of a carbodiimide giving a relatively insoluble urea hydration product consistently drives the condensation of orthophosphoric acid and of the straight-chain and simple-ring phosphoric acids quite far into the ultraphosphate region, generally about halfway between the metaphosphate and the phosphoric anhydride compositions. For the several hundred condensations of this type which have been carried out in our labora-

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(6) T. Glonek, J. R. Van Wazer, and T. C. Myers, *Bioinorg. Chem.*, 1, 1, 23 (1971).

(7) T. Glonek, T. C. Myers, P. Z. Han, and J. R. Van Wazer, *J. Amer. Chem. Soc.*, 92, 7214 (1970).

(8) S. Y. Kalliney, *Top. Phosphorus Chem.*, 7, 255 (1972).

(9) M. Smith and H. G. Khorana, *J. Amer. Chem. Soc.*, 80, 1141 (1958).

(10) T. Glonek, M. Lunde, M. Mudgett, and T. C. Myers, *Arch. Biochem. Biophys.*, 142, 508 (1971).

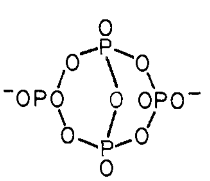
(11) T. Glonek, T. O. Henderson, R. L. Hilderbrand, and T. C. Myers, *Science*, 169, 192 (1970).

(12) T. O. Henderson, T. Glonek, R. L. Hilderbrand, and T. C. Myers, *Arch. Biochem. Biophys.*, 149, 484 (1972).

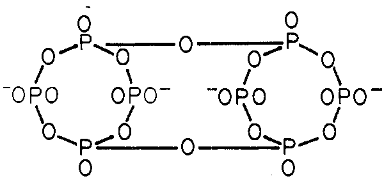
tories, as well as for the reverse decondensation reactions of phosphorus pentoxide, ^{31}P nmr has shown consistently that only nine phosphorus compounds (as identified by recognizable sets of peaks within which there are always fixed area ratios) are to be found in the ultraphosphate reaction product mixtures. Although the possibility certainly exists that there may be as yet unidentified additional components exhibiting considerable multiplicity in their ^{31}P nmr patterns, we have not yet hit upon a combination of reagents and/or experimental technique which would cause such species to account for more than 3-5% of the total phosphorus.

In the course of these studies, we have discovered the experimental parameters which give much higher relative amounts of one or another of the observed molecules than are usually found. These optimized preparations are described in the Experimental Section as mixtures 1-5. The ^{31}P nmr patterns of these mixtures are presented in Figure 1. Note that the spectral scale of this figure covers only the range of the middle (or difunctional) PO_4 resonances and branch (or trifunctional) PO_4 group resonances, since nothing was seen elsewhere in the ^{31}P spectra upon time averaging. This means that less than 0.1% of the total phosphorus could be present as orthophosphate and less than about 1% as phosphate end groups, which are found in the range of 10-14 ppm. Even in spectra where end-group resonances were to be seen, we saw no evidence for molecules containing both branch and unsubstituted end groups, although this does not mean that structures such as the isotetrapolyphosphate anion are necessarily nonexistent.

Structure Identifications. One of the more commonly observed groups of ^{31}P nmr resonances corresponding to an individual molecule is the set of resonances which dominate reaction mixture 1. We have analyzed this spectral pattern in a communication[7] but were at that time unable to differentiate between structures I and II. Note that structure II is probably a feasible one, since it can be assembled with a molecular model. Briefly, the argument for either of these structures results from the fact that at a normal spectral expansion, such as is shown in Figure 1, the nmr resonance corresponds to a triplet in both the middle- and branch-group regions of the nmr spectrum as would be expected from each middle group bonded to two branch groups and each branch group bonded to two middle groups. Furthermore, there is no change in the spectrum with proton decoupling; and homonuclear ^{31}P indor shows that there is indeed coupling between the phosphorus giving three middle-group resonances and that giving the three branch-group resonances. These results, plus the relatively narrow nmr line widths, are in accord with either structures I or II.



I



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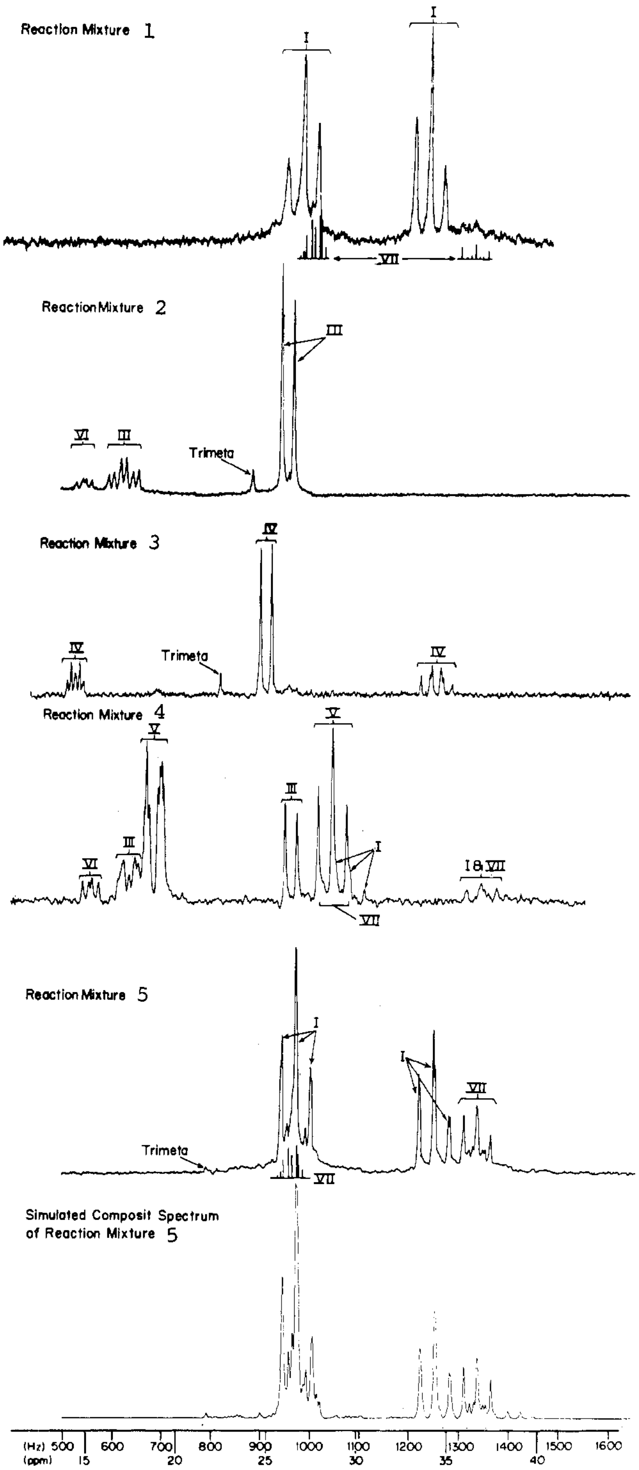

Figure 1. ^{31}P nmr spectra of mixtures 1-5. Chemical shifts are given relative to external 85% orthophosphoric acid. The magnetic field increases from left to right. The simulated composit spectrum was calculated using a mathematical model compiled from data obtained from mixture 5.

At higher resolution, such as is shown in Figure 2, the observed spectrum corresponding to compounds I or II is seen to be more complex than an approximately 1:2:1 triplet. The detailed structure of the high expanded spectrum (the branch-group region of which is shown in Figure 2) was beautifully fit by computer simulation[13-15] for structure I using δ_m 28.9 ppm (1052 Hz), δ_b 36.5 ppm (1327 Hz), and J_{mb} = 30.4 Hz, with **m** and **b** corresponding to the middle and branch groups in the structure. Thus, the 22 transitions corresponding to structure I (the 1,5-μ-oxo-tetrameta-

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(13) J. D. Swalen and J. W. Copper, "NMRIT-IV, NMR Iterations," Program 126, Quantum Chemistry Program Exchange, Indiana University, 1972.

(14) J. D. Swalen and J. W. Cooper, "NMREN1, NMR Energy Levels," Program 127, Quantum Chemistry Program Exchange, Indiana University, 1972.

(15) J. D. Swalen, "NMRPLT, NMR Spectrum Plotting," Program 36, Quantum Chemistry Program Exchange, Indiana University, 1972.

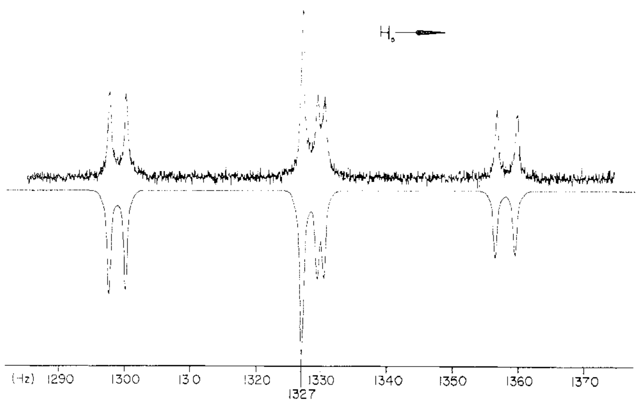
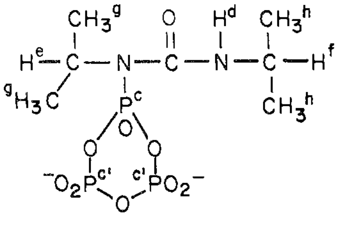


Figure 2. Actual (top) and theoretical[6,13] (bottom) spectra of the branch-group multiplet of 1,5-μ-oxo-tetrametaphosphate. The multiplet in the branch region is constructed from ten transitions with the major resonance signal arising from the coincidental overlay of four of these. The signal width at half-height was taken as 0.7 Hz for the theoretical spectrum. The actual spectrum was taken with time averaging of four scans, using 16.38 sec/scan.

phosphate anion) led to an exact fit of the fine structure observed in both the middle- and branch-group spectral region. On the other hand, computer simulation of the nmr pattern corresponding to structure II always led to thousands of transitions; and this was found to result in appreciable broadening of the multiplet bands when any reasonable set of coupling constants and chemical shift values was employed in setting up the model. Since at best the nmr pattern is only poorly approximated by the eight-spin system of structure II, whereas it is beautifully accounted for by the four-spin system of structure I, we offer this computer simulation as a structure proof for I. The simulated nmr patterns of structure I and of structures III-VII are shown in Figure 3 at a scale commensurate with that of Figure 1.

The set of resonance lines denoted by III in the spectrum of mixture 2 is also a commonly observed nmr pattern. For example, it is the major product formed when orthophosphoric acid is condensed with an excess of both diisopropylcarbodiimide and tri-*n*-butylamine. As shown in Figure 1 the spectrum of compound III consists of a downfield sextet and an upfield doublet of exactly twice the peak area of the sextet, with both multiplets being in the middle-group region. Heteronuclear proton decoupling reduces the sextet to a 1:2:1 triplet. These findings tentatively indicate the presence of a single organic substituent on a trimetaphosphate cyclic anion. With care being taken to exclude moisture, it was found possible to purify the compound giving rise to these signals. This was accomplished by precipitation with ether of the phosphatic material from mixture 2 to produce a sample which upon dissolution in scrupulously dry deuteriochloroform exhibited only the signals corresponding to III, even after extensive signal averaging, while showing no signs of the organic components of the reaction mixture, except for a small and variable amount of diisopropylurea.



III

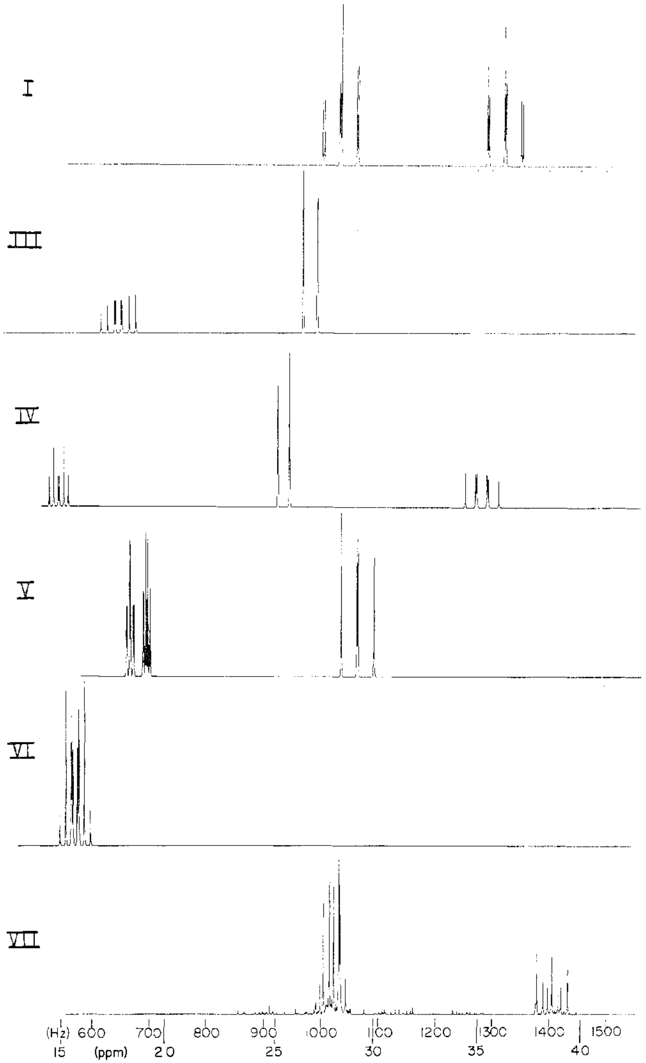


Figure 3. Computer-simulated spectra of molecules I, III, IV, V, VI, and VII, as displayed at about the same frequency scale as that of Figure 1. A line width of 0.6 Hz was chosen for this display since this value corresponds to the best resolved spectra obtained for these systems.

As shown in Table I, the nmr data demonstrate that the structure of compound III consists of the *N*-phosphorylurea formed between trimetaphosphate and one of the nitrogen atoms of diisopropylurea. According to this interpretation, all of the hydrogens of the urea except that labeled e are too far away from the c phosphorus atom to cause splitting and the value of 11.2 Hz for the PNCH coupling between atoms c and e is in accord with observations[16] on similar molecules, *e.g.*, *N*-isopropylphosphorylamides. The proton spectra of hydrogen atoms d-h show the proper relative areas and the expected multiplicity for structure III, as indicated by Table I. Furthermore, continuous-wave proton decoupling proves that these protons are indeed coupled to their nearer-neighbor protons as expected. Since the spin system of hydrogens e and g is not connected with the spin system of hydrogens d, f, and h, it is necessary to carry out a chemical reaction on compound III in order to complete its structure proof by nmr. Thus, dissolution of the sample in water produced as sole products the simple trimetaphosphate anion (a single resonance in the ^{31}P spectrum) and crystals of

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(16) V. Mark, C. H. Dungan, M. M. Crutchfield, and J. R. Van Wazer, *Top. Phosphorus Chem.*, 5, 227 (1967). We have determined the PNCH coupling in hexamethylphosphoramide, $P(O)[N(CH_3)_2]_3$, to be 9.0 Hz.

Table I. Nmr Data Relating to Structure III

Nucleus obsd	Group	Undecoupled multiplicity	Rel area	Shift, δ,[a] ppm	Decoupled from	Spin system	Coupling const, J, Hz
^{31}P	c	Triplet of doublets	1	16.3	c′[b]	POP	24.5
					e	PNCH	11.2
	c′	Doublet	2	25.4	c		
^{1}H	d	Broad doublet	1	8.1	f	HNCH	6.9
	e	Doublet of septets	1	4.2	c		
					g	HCCH	6.6
	f	Doublet of septets	1	3.8	d		
					h	HCCH	6.5
	g	Doublet	6	1.3	e	HCCH	6.7
	h	Doublet	6	1.1	f		

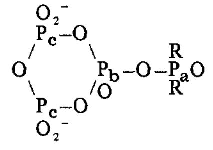
[a] Relative to external 85% orthophosphoric acid for ^{31}P spectra and internal tetramethylsilane for ^{1}H spectra. [b] Shown by indor.

diisopropylurea (characterized by the ^{1}H spectrum and a mixture melting point).

When condensing agents other than diisopropylcarbodiimide are employed, compounds equivalent to structure III are obtained with the pair of isopropyl groups being replaced by other substituents. Such replacement leads to the expected changes in the nmr patterns. Thus, with the *p*-tolylcarbodiimide as the dehydrating agent, c shows up in the ^{31}P spectrum as a simple triplet rather than the triplet of doublets as observed for condensation with diisopropylcarbodiimide (see Table I). In the structure of this *p*-tolylurea derivative there is no hydrogen sufficiently close to the P_c atom to give measurable splitting, so that the triplet due to interaction with the two $P_{c'}$ atoms is the only fine structure observed in the P_c resonance. When dicyclohexylcarbodiimide is employed as the condensing agent, the pattern is the same as that observed with the use of diisopropylcarbodiimide, since again there is a single hydrogen to give coupling along the H-C-N-P chain. When di-*n*-butylcarbodiimide is employed, the ^{31}P spectrum of atom P_c turns out to be a triplet of triplets because of splitting by two hydrogens. In all cases, $J_{\mathrm{PNCH(methylene\ and\ methine)}}$ is equal to 11.2 ± 0.2 Hz. The enol version of structure III, in which there is a P-O-C linkage to the central carbon atom of the urea, is ruled out on the basis of the size of the observed coupling constant (11.2 Hz), which is surely much too large for the chain of atoms P-O-C-N-H.[16]

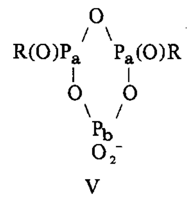
When dimethyl sulfoxide is used as the solvent for the carbodiimide condensation reaction, the three nmr multiplets (of fixed-area ratios) denoted by IV in Figure 1 are found to be present in unusually large amounts; and, when the tetrametaphosphate anion is used as the phosphatic reagent, the conversion becomes nearly quantitative. Proceeding upfield in the spectrum of mixture 3, it is seen that the areas of the three multiplets are in a 1:2:1 ratio. The most upfield of these multiplets lies at the lower end of the branch-group region; and its fine structure reveals a doublet of triplets overlapping in such a way as to appear (on the scale of the figure) as a quartet. Because of its position in the spectrum, the simple doublet at about 25 ppm must arise from ionized middle groups.

The doublet of triplets lying immediately below 15 ppm appears in a spectral region which could be associated with either an end or a middle group. Upon broad-band proton irradiation, this multiplet is reduced to a simple doublet while the other multiplets are unaffected. Continuous-wave decoupling indicates that the P-H coupling in this downfield multiplet is attributable to a methine type of proton, while its multiplicity is characteristic of two such protons. The chemical structure which is in accord with these findings is shown as compound IV, which is the first known example of a phosphate-substituted metaphosphate ring and is also the first demonstrable example of a molecule in which a phosphate end group is bonded to a branch group. This basic phosphate skeleton (*i.e.*, the orthophosphoryltrimetaphosphate anion) has been suggested many times[4,17] as an intermediate in the solvolysis of the P_4O_{10} molecule, where R = $N[CH(CH_3)_2][C(O)NHCH(CH_3)_2]$ for diisopropylcarbodiimide, which was used in this particular experiment. Compound IV usually occurs as a transient intermediate which seems to convert to III. Computer simulation of the nmr pattern of IV has been carried out (see Figure 3), and the simulated spectrum is found to agree perfectly with the experimental one when presented on a much more expanded scale than used for Figures 1 and 3. From this simulation, the following nmr constants were obtained: δ_a 13.5 ppm (491 Hz), δ_b 33.5 ppm (1219 Hz), δ_c 24.1 ppm (877 Hz), δ_H 4.5 ppm (407 Hz), J_{PNCH} = 7.5 Hz, J_{ab} = 17.4 Hz, and J_{bc} = 20.0 Hz, where H is the methine hydrogen of the isopropyl group on the nitrogen connected to the phosphorus.



IV

The set of nmr resonances labeled V in the nmr pattern of mixture 4 in Figure 1 was readily maximized by previously saturating the solvent with the urea obtained from hydration of the carbodiimide. The well-defined triplet labeled V appearing between 25 and 30 ppm in the spectral region corresponding to ionized middle-phosphate groups has been shown by indor to be coupled to the set of peaks also labeled V appearing between 15 and 20 ppm in Figure 1. The upfield group of these peaks exhibits half the area of that of the downfield set, and proton-decoupling experiments similar to those discussed for IV show that the downfield peak of V once again involves coupling between a phosphorus and a methine proton of the isopropyl urea residue. These findings are consistent with structure V. In our vari-



V

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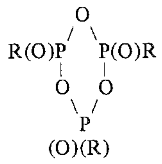
(17) R. K. Osterheld, *Top. Phosphorus Chem.*, 7, 103 (1972).

ous studies, we have noted that this compound usually plays the role of a transient intermediate in carbodiimide condensations—an intermediate which converts to a number of compounds, the principal one of which is III. Computer simulation (see Figure 3) of the nmr spectrum once again yielded a gratifying fit, when the following nmr constants were employed: $\delta_a = 17.8$ ppm (648 Hz), $\delta_b = 28.1$ ppm (1029 Hz), $\delta_H = 4.3$ ppm (391 Hz), $J_{PNCH} = 11.8$ Hz, $J_{ab} = 28.5$ Hz, and $J_{aa} = 28.5$ Hz.

A comparison between the experimental spectrum of molecule V and the computer simulation of it is shown in Figure 4B for the region of the spectrum corresponding to the urea-substituted middle groups of V. Note the good agreement of the simulated and experimental spectra in this region, where the fine structure cannot be interpreted on the basis of simple first-order approximations.

One of the more difficult nmr spectral patterns to maximize is the one labeled VI which seldom appears to a greater amount than is shown in mixture 2 in which III is by far the major constituent. The best pattern corresponding to VI in Figure 1 is seen in the spectrum of mixture 4. This resonance, lying slightly downfield from 15 ppm, is in the spectral region corresponding to substituted-phosphate middle groups or perhaps even to end groups. Hydrogen decoupling, applied as previously described, reduces the multiplet structure of VI to a single sharp peak. We ascribe this overall nmr spectral pattern to the reaction product in which each phosphorus of a metaphosphate ring, presumably a trimetaphosphate, is substituted by a urea nitrogen.



VI

Again, computer simulation (see Figure 2) gave a good fit to the ^{31}P nmr spectrum, using the following parameters: δ_P 14.3 ppm (524 Hz), δ_H 4.3 ppm (385 Hz), J_{PNCH}(effective) = 32.0 Hz, and J_{PP}(effective) = 87.3 Hz, where the spin system involves three equivalent PP couplings. Because of the high symmetry of this molecule the effective J values correspond to a hypothetical single active nucleus of spin $^3/_2$ so that the real coupling constants are $J_{PNCH} = 10.7$ Hz, and $J_{PP} = 29.1$ Hz.

Compounds III, V, and VI represent an increasing substitution of the trimetaphosphate ring structure. It is interesting to note that going from simple trimetaphosphate to VI has little if any effect on the chemical shift of either the unsubstituted (*i.e.*, ionized) phosphate middle group (+25 ppm) or the substituted one (+16 ppm). There is also very little change in the value of the POP (26 Hz) or of the PNCH (11 Hz) coupling constant with increasing substitution. This consistency of the nmr parameters offers additional supporting evidence for the structural assignments given to compounds III, V, and VI.

The nmr resonance labeled VII is clearly seen in mixture 5 and is present in mixture 1. In the spectrum shown for mixture 5, it can be clearly seen that there is a multiplet, with the overall appearance of a triplet with minor resonances appearing between its arms, in the phosphate branch-group region. These peaks were shown by signal-averaged indor to derive from the same molecule as a complex middle-group multiplet composed of at least eight resolvable resonance bands. Since subtraction of the other resonances in the middle-group region gives only an approximate picture of the spectrum of VII in this region, it was necessary to rely on indor to establish the positions of the major resonance bands of the VII middle-group multiplet. The positions of these nmr peaks and their relative intensities are indicated in Figure 1 immediately below the spectra of mixtures 1 and 5, and this information is shown more clearly in Figure 3.

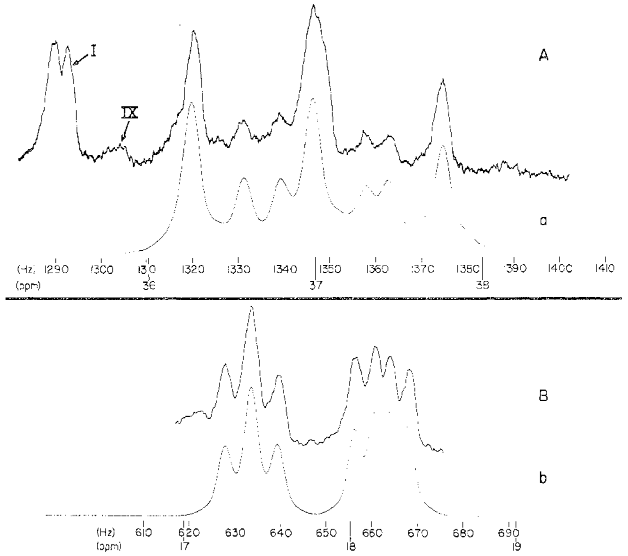
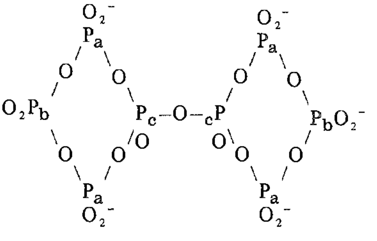


Figure 4. Comparison of actual and calculated spectra for (A) molecule VII in the branch-group region of the spectrum and (B) molecule V in the urea-substituted middle-group region.

Since no carbodiimide or its urea was used in the preparation of mixture 5, it follows that compound VII cannot contain organic substituents (as is the case for III–VI). Furthermore, proton decoupling has no observable effect on the VII spectrum so that compound VII ought to be a purely inorganic phosphate. Computer simulation shows that the VII spectrum is commensurate with the following molecular structure (VII), which might be called the μ-oxo-bis(tetrametaphosphate) anion.

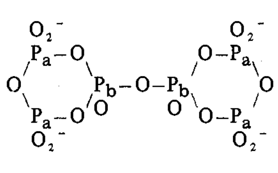


VII

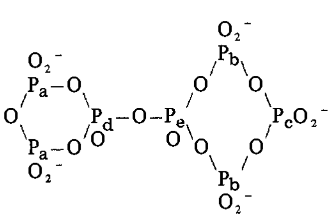
The best fit to the positions and approximate intensities of the middle-group multiplet and the detailed fine structure of the branch-group multiplet is obtained from the following nmr constants: δ_a 26.6 ppm (968.1 Hz), δ_b 26.5 ppm (965.3 Hz), δ_c 37.0 ppm (1346.2 Hz), $J_{ab} = 31.5$ Hz, and $J_{ac} = 27.3$ Hz. It is important to note that the fine structure observed and then simulated in an expanded-scale spectrum of the branch-group region of mixture 5 ensures the validity of the mathematical model. This comparison between the simulated and experimental spectra is presented in Figure 4.

Through the use of signal-averaging and indor techniques we have accumulated considerable evidence for the existence of three other ultraphosphate molecules in the systems of this study, although we have not yet been able to compose an experiment wherein these compounds are produced in high relative amounts. Nevertheless we have been able to simulate their spectra and in so doing account totally for the resonances ascribed to each molecule.

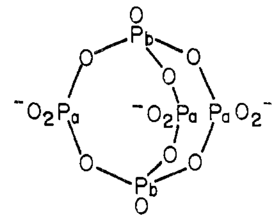
Two molecules are analogs of VII: the monoanhydride of trimetaphosphate, VIII, and a similar mixed anhydride composed of one trimeta- and one tetrametaphosphate ring, IX. The third molecule, X, is related to I but differs in that the bridging oxygen atom of I is substituted by a bridging phosphate middle group.



μ-oxo-bis(trimetaphosphate) anion
VIII



trimetaphosphate-μ-oxo-tetrametaphosphate anion
IX



1,5-μ-orthophosphatyl-tetrametaphosphate anion
X

The nmr spectra of VIII and X approximate that predicted by first-order multiplicity rules, *i.e.*, a doublet in the middle region (P_a) and a triplet in the branch (P_b) for VIII and a triplet in the middle region (P_a) and a quartet in the branch (P_b) for X. However, as in the case of I, X shows additional fine structure in each arm of the multiplets. The nmr pattern of IX is exceedingly complex and at present cannot be established beyond reasonable doubt. The nmr parameters determined for VIII, IX, and X, respectively, are as follows: δ_a 26.4 ppm (958.8 Hz), δ_b 37.0 ppm (1346.6 Hz), J_{ab} = 27.1 Hz; δ_a 27.7 ppm (1007.4 Hz), δ_b 27.6 ppm (1002.8 Hz), δ_c 27.5 ppm (1000.0 Hz), δ_d 34.7 ppm (1262.4 Hz), δ_e 35.0 ppm (1272.8 Hz), J_{ad} = 27.1 Hz, J_{bc} = 31.1 Hz, J_{be} = 27.1 Hz; δ_a 27.3 ppm (989.5 Hz), δ_b 39.0 ppm (1419.5 Hz), J_{ab} = 25.3 Hz.

In Figure 5 the simulated spectra for molecules VIII-X are compared with the experimentally observed resonances for these molecules. The experimental values of the positions and relative areas of these resonances are shown in the form of stick plots, since in all cases there was some overlap with resonances from the other molecules appearing in the mixtures. Fortunately, the relative proportions of the interfering resonances for compound VIII, IX, or X could be varied by changing the reaction conditions. Added credence is given to the stick plots of Figure 5 from the fact that the estimated relative heights of the peaks of compound VIII, IX, or X were found to be essentially unchanged from one reaction mixture to another, even though the amount of interfering signal subtracted from some of these resonances varied. Since the spectra of compounds VIII and X are relatively simple, we think that their structures have been reasonably well demonstrated. In any event, the invariance to their own concentration and to the concentration of other species of the sets of peaks ascribed to molecules VIII-X in the stick plots of Figure 5 strongly indicates the existence of three ultraphosphate molecules based on middle and branch groups.

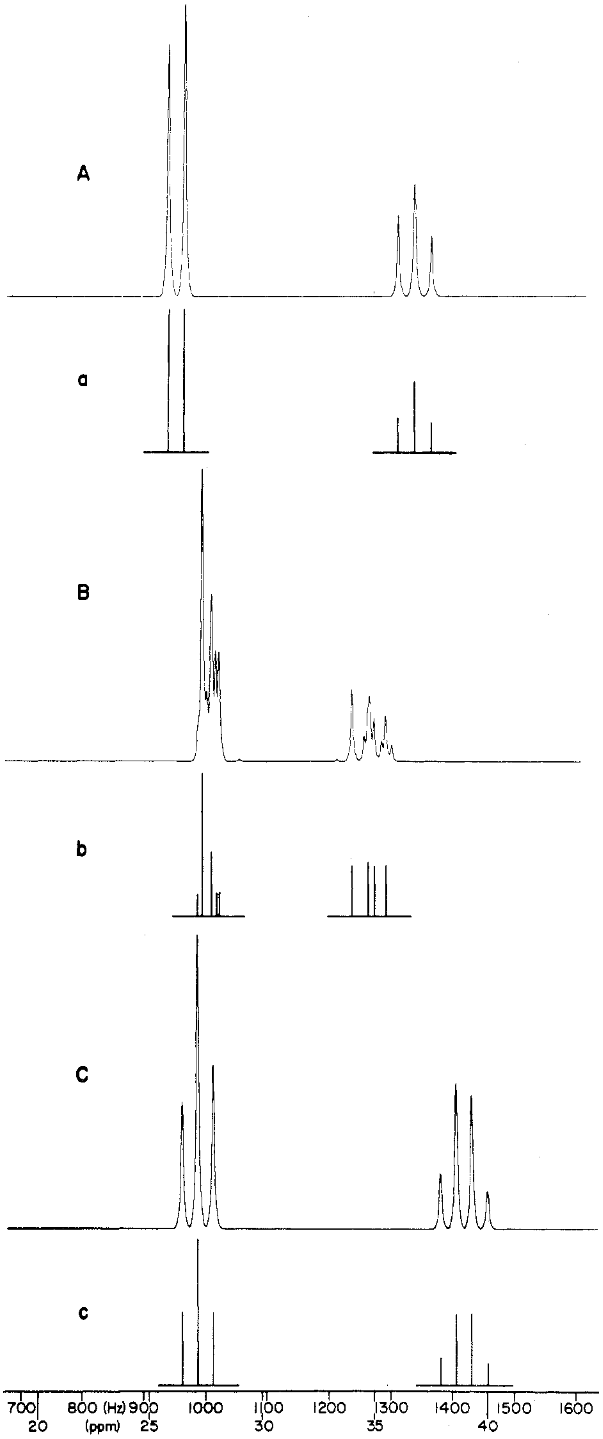


Figure 5. A comparison of the computed spectra (capital letters) with the line positions and intensities (lower case letters) for molecules VIII (A, a), IX (B, b), and X (C, c). The estimated relative experimental intensities shown in the stick plots (denoted by the lower case letters) were confirmed on a series of different samples.

Based upon the aforementioned parameters, the simulated composit spectrum shown in Figure 1 was produced for mixture 5. The appropriate values of the chemical shielding parameters and coupling constants were first determined from an exhaustive nmr snalysis of mixture 5. The set of data corresponding to each molecule was used to generate the set of transitions and their intensities corresponding to each molecule, and these transition sets were then normal-

Table II. Molecular Compositions of Mixtures 1-5 and Their Hydrolysis Products, H1-H5

	Mole percentage of total phosphorus in compd[a]															
Mixture[b]	I	III	IV	V	VI	VII	XI	XII	XIII	O	P	T	Q	TM	QM	LM
1	90					10										
H1														8	83	9
2		83		2	9									6		
H2							4	44	5	9	18			20		
3	3		94											3		
H3										6		3	59	28	4	
4	6	16		66	6	6										
H4							47	3	23	23				4		
5[c]	37[c]					33[c]										
H5										2.5		1.2	2.1	15.6	76.4	2.2

[a] O = ortho-, P = pyro-, T = tripoly-, and Q = tetrapolyphosphate; TM = trimeta- and QM = tetrametaphosphate; LM = larger cyclic phosphates. I-XIII are the compounds described in the text. [b] Hydrolysis products are denoted with an H. [c] Percentages determined from the computer analysis: I, 37.3; VII, 33.3:VIII, 17.0; IX, 8-4; X, 3.3; TM, 0.3; QM, 0.2; pentametaphosphate, 0.2.

ized with respect to their total summed intensities. After normalization, an appropriate percentage (corresponding to the mole per cent of P in that molecule) was taken of each transition set and the sets were plotted together to generate the synthetic spectrum of the mixture. As can be seen in the figure, the composite spectrum agrees well with that which was spectroscopically determined.

Hydrolysis. The percentage of the various phosphatic species obtained from an analysis of the areas of extended-scale nmr patterns corresponding to mixtures 1-5 are presented in Table II along with the same data resulting from hydrolysis of these reaction mixtures. It should be noted that only three phosphorus-containing molecules (XI-XIII) involving organic substituents were shown by hydrogen decoupling to be present in the hydrolysis products. Since these three molecules are found in the hydrolysis product of mixture 4, the nmr spectrum of this hydrolyzed mixture, as observed with broad-band proton decoupling, is depicted in Figure 6.

As was true of all of the hydrolyzed mixtures, the product from the hydrolysis of mixture 4 exhibits no detectable resonances in the branch-group region. The set of resonances labeled XI are observed only in the end-group region of the spectrum and exhibit the form of a classical ab multiplet. In the absence of proton decoupling, each arm of the upfield portion of this multiplet is split into a doublet. As with all of the doublets observed in this study in the 8-10 ppm spectral region, continuous-wave proton decoupling identifies the coupled protons as again being those of methine protons of isopropyl groups when diisopropylcarbodiimide is used as the condensing agent. These nmr results are proof that compound XI consists of a pyrophosphate anion, N substituted on one end only with a diisopropylurea; *i.e.*, XI is $RP(O_2^-)$-O-$P(O_3^{2-})$. The relevant nmr parameters are $\delta_{P(\text{unsubstituted})}$ 5.8 ppm (212 Hz), $\delta_{P(\text{substituted})}$ 9.2 ppm (335 Hz), δ_H 4.3 ppm (391 Hz), $J_{PNCH} = 11.0$ Hz, and $J_{POP} = 21.7$ Hz.

The resonances in Figure 6 corresponding to compounds XII and XIII both show a 2:1 ratio for the end to middle groupings and both compounds give rise to simple pseudo-first-order spectra exhibiting a triplet in the middle-group region and either one (XIII) or two (XII) doublets in the end-group region, as would be expected for a tripolyphosphate skeleton. This straightforward analysis plus the proton-decoupling data demonstrates that XII consists of a tripolyphosphate anion which is N substituted at one end with a diisopropylurea residue; *i.e.*, XII is $RP(O_2^-)$–O–$P(O_2^-)$-O-$P(O_3^{2-})$. Likewise, compound XIII is thus seen to consist of a tripolyphosphate anion similarly substituted on both ends; *i.e.*, XIII is $RP(O_2^-)$-O-$P(O_2^-)$-O-$P(O_2^-)R$. For XII the nmr parameters are $\delta_{P(\text{unsubstituted end})}$ 5.0 ppm (182 Hz), $\delta_{P(\text{substituted end})}$ 9.3 ppm (338 Hz), $\delta_{P(\text{middle})}$ 20.3 ppm (739 Hz), δ_H 4.2 ppm (379 Hz), $J_{PNCH} = 11.1$ Hz, and $J_{POP} = 18.5$ Hz; and for XIII $\delta_{P(\text{end})}$ 9.0 ppm (328 Hz), $\delta_{P(\text{middle})}$ 21.9 ppm (798 Hz), δ_H 4.2 ppm (380 Hz), $J_{PNCH} = 11.0$ Hz, and $J_{POP} = 19.3$ Hz.

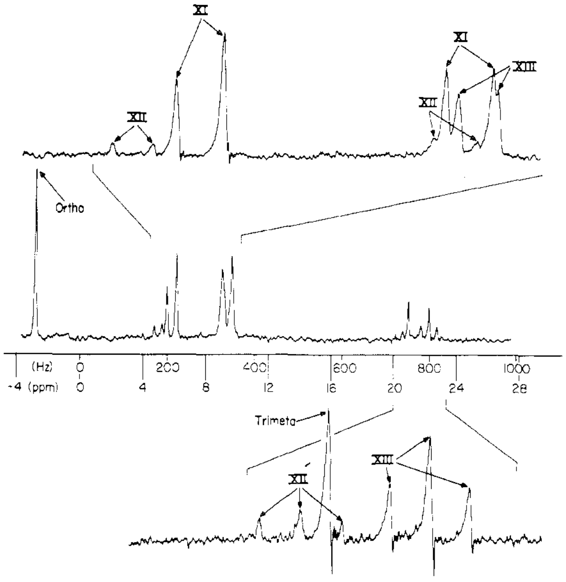
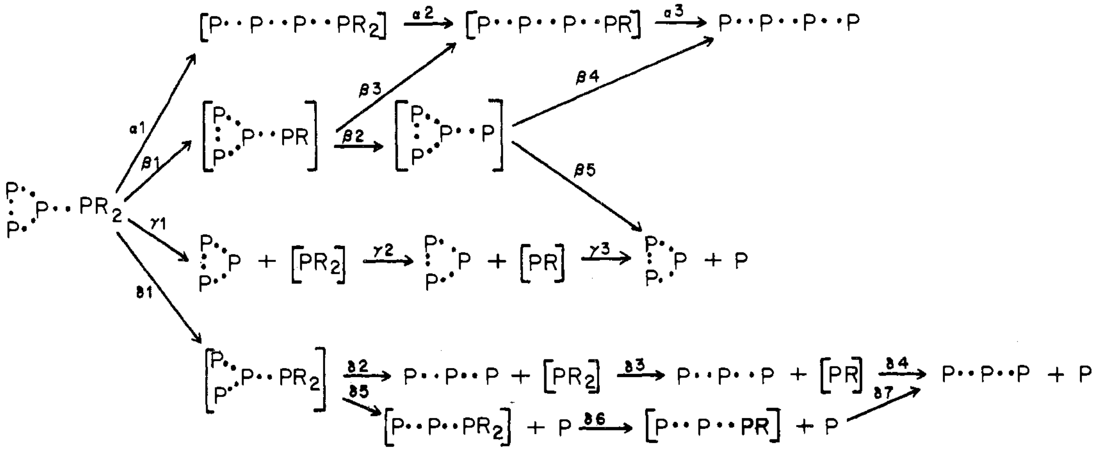


Figure 6. ^{31}P nmr spectra of the hydrolysis product obtained from mixture 4. The top and bottom spectra are expanded views of the end- and middle-group regions, respectively, and all spectra were obtained with ^1H broad-band decoupling.

In all of the hydrolysis reactions investigated in this study, the only species in addition to compounds XI-XIII which were observed in the hydrolysis products are the ortho-, pyro-, tripoly-, and tetrapolyphosphates and the tri- and tetrametaphosphates, as well as small amounts of the larger cyclic phosphates (ranging from the penta- at least to the decametaphosphate[3b]).

It is possible to delineate the probable reaction sequences involved in the standard hydrolysis of mixtures 1-5, using the quantitative data of Table II. Thus, for the hydrolysis of compound IV, Scheme I may be set up. In this scheme the bridging oxygen atoms are indicated by · · and, as previously, R is used to represent the urea substituent. Each step in this sequence represents the reaction of one molecule of water and those species which are not experimentally observed (presumably because of their high hydrolytic reactivity) are shown in brackets. Furthermore, once a straight-chain or simple-ring phosphate skeleton is formed, it is assumed that there will be no further P-O-P scission, although P-N hydrolysis is still accounted for. Reaction

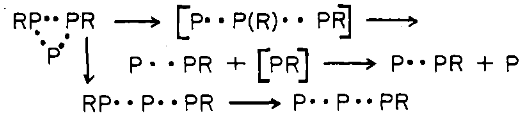
Scheme I

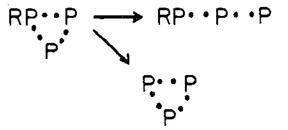


products which do not contain phosphorus are not shown, since this reaction sequence has been set up to account for the observed ^{31}P nmr data.

Since 83% of the hydrolysis products of mixture 1 (which contains 90% of compound I) consists of the tetrametaphosphate anion, it is reasonable to ascribe (within experimental error) all of the tetrametaphosphate (4%) in the hydrolysis product from mixture 3 to the amount of I (3%) originally present. Thus, we have to account for the fact that the hydrolysis product of mixture 3 was observed to contain 59% of tetrapolyphosphate, 28% of trimetaphosphate, 3% of tripolyphosphate, and 6% of orthophosphate. Reaction path α gives the tetrapolyphosphate as do two of the three branches of path β, whereas path γ, as well as the second branch of β, gives the trimetaphosphate plus orthophosphate. Both branches of path δ lead to tripoly- plus orthophosphate. The qualitative lore concerning phosphatic stabilities would indicate that the greatest hydrolytic scission of the starting product, IV, should occur at a P–O–P linkage associated with its single-branch group, so that paths α and γ should be preferred. On a purely statistical basis, the probability of path α ought to be twice that of γ, and this should also be the case for β4 as compared to β5. This simple analysis means that the ratio of tetrapolyphosphate to trimetaphosphate produced by the hydrolysis should be 2:1, and the observed ratio of 2.4:1 is not very far from that. The small amount of tripolyphosphate reported in Table I for this hydrolysis is in accord with the suggested low probability for path δ.

Similar detailed analyses may be carried out for the hydrolysis of the other reaction mixtures. From these analyses, it is seen that the reactions given in eq 1–4 make the major contributions to the hydrolysis of each of the other compounds found in significant amounts in the original reaction mixtures.


(1)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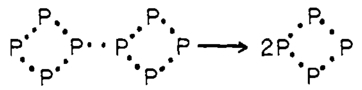
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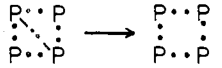
(4)

Discussion

The usual neat or highly concentrated preparations in the ultraphosphate region of composition always exhibit high viscosities and some liquid-phase elasticity (other than compressional), and these properties plus the ^{31}P nmr data give strong evidence for the presence of network macromolecules. In the studies reported herein, the phosphorus concentrations were always sufficiently low so that, according to Le Chatelier's (or Ruggli's[18]) principle, small discrete cyclic molecules were produced instead of network structures.

Compounds I and VII–X are the first discrete ultraphosphate molecules other than P_4O_{10} for which reasonably acceptable structure proofs have been presented. It is hoped that this work gives a sufficiently good introduction to the ^{31}P nmr characterization of ultraphosphates so that other such molecules will be discovered in the near future. In addition, we believe that analogs of these compounds will be found in the numerous condensed systems (other than the condensed phosphates) exhibiting P–O–P bridges. Now that the existence of a wide range of straight-chain and simple-ring phosphates has been well demonstrated,[3] the time is ripe for experimental elucidation of the full range of oligomeric structures exhibiting phosphate branching points.

Acknowledgments. This work was supported in part by grants USPHS-11702 and NSF-GP-28698X, as well as by the General Research-Support Grant awarded to the University of Illinois College of Medicine and a grant from the Research Board of the Graduate College, University of Illinois at the Medical Center.

Registry No. I, 31087-13-5; III, 52195-23-0; IV, 52195-24-1; V, 52195-25-2; VI, 52195-26-3; VII, 52195-16-1; VIII, 52195-17-2; IX, 52195-18-3; X, 52195-19-4; XI, 52195-20-7; XII, 52195-21-8; XIII, 52195-22-9; P, 7723-14-0; dicyclohexylcarbodiimide, 538-75-0; phosphoric acid, 7664-38-2; tris(tri-*n*-butylammonium) trimetaphosphate, 50859-07-9; diisopropylcarbodiimide, 693-13-0; tetrakis(tri-*n*-butylammonium) tetrametaphosphate, 50859-08-0; phosphorus pentoxide, 1314-56-3.

(18) P. Ruggli, *Helv. Chim. Acta*, 29, 796 (1946).