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THE SYNTHESIS AND DECOMPOSITION OF NOVEL ORGANOPHOSPHORUS COMPLEXANTS*

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ABSTRACT

Aqueous soluble organic diphosphonic acids have been synthesized as aids in the extraction/recovery of metal values from nuclear waste, ground water, or hydrometallurgical processes. The reagents form aqueous soluble complexes at very low pH values (< 1). After use, these compounds do not represent an additional waste management problem as they are readily decomposed to innocuous materials (phosphoric acid and carbon dioxide) by warming and/or by the action of a mild oxidizing agent.

INTRODUCTION

During an on-going investigation of the aqueous complexation chemistry of transition metals, lanthanides, and actinides found in nuclear waste,[1] we required several examples of disubstituted-alkane-1,1-diphosphonic acids. These reagents were expected to complex with a variety of metal ions in the III, IV, V and VI oxidation states to improve the extrac-

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tion/strip chemistry of existing processes utilized in the hydrometallurgical and nuclear industries.

An ideally designed reagent for use in the aqueous phase to alter the chemical order of extraction would have an effective and finite lifetime in very acidic media (pH < 1), after which decomposition to relatively innocuous or environmentally acceptable substances either spontaneously occurs or is easily accomplished with a minimum of reagents or manipulations.

The objective of this paper is to describe the preparation and decomposition studies of a new class of organophosphorus complexants, which meet these criteria. We refer to these complexants as "Thermally Unstable ComplexantS or TUCS."

EXPERIMENTAL

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Phosphorus, carbon and proton NMR spectra were recorded on a General Electric GN 300 Omega spectrometer with a 5mm multinuclear probe, except where otherwise noted. Samples were prepared by dissolving 0.1g of substrate in 1mL of a suitable deuterated solvent (D_2O or $CDCl_3$). Carbon and proton spectra were referenced to internal tetramethylsilane (TMS) or to an external capillary containing $CDCl_3$/TMS. An external capillary containing 85% phosphoric acid was used as a reference for the phosphorus chemical shifts. The proton-decoupled ^{31}P spectra were recorded at 121.7 MHz using a 90° pulse width of 6 μsec, a predelay of 10 sec, and a spectral width of 20000 Hz. The proton-decoupled ^{13}C spectra were recorded at 75.6 MHz with quadrature phase detection and a two-level decoupling pulse sequence to minimize dielectric heating of the sample. A 90° pulse width of 10 μsec, a predelay of 20sec, and a spectral width of 24000 Hz were used. Time domains utilized for all spectra were either 8 or 16K data points. Thermal gravimetric analyses were performed using Mettler Thermoanalyzer 2 (Type T2WR) regulated with a nitrogen sweep as indicated.

Vinylidene-1,1-diphosphonic Acid (4). 1-Hydroxyethane-1,1-diphosphonic acid (**5**, HEDPA), received as a 70% aqueous solution from Albright & Wilson, Inc. (Richmond, VA) was purified from glacial acetic acid. After drying the crystalline salt *in vacuo* at 40 °C overnight to remove residual acetic acid, HEDPA was contacted with four equivalents of NaOH(aq). After stirring for 30 minutes, the solvent was removed *in vacuo* at 50 °C to provide the solid tetrasodium salt of HEDPA. The tetrasodium salt (240g) was introduced into

a 6.5 cm X 75 cm glass tube in two batches. The glass tube was connected to a rotary motor that was set to rotate the tube at 5 rpm. After establishing a vacuum of approximately 25 mm Hg using a vacuum pump, the glass tube was inserted into a 3 inch tube furnace. The temperature was slowly raised to 400 °C and maintained for 3 hours. After cooling the tube to room temperature, the resultant tan-colored solid (180g), which included 60 wt% by ^{31}P NMR and ion chromatography of the title compound, was dissolved in 330 mL of water at 95 °C. Methanol was slowly added until the hot aqueous solution became turbid. Heating was maintained until the aqueous solution clears. The solution was covered and allowed to cool undisturbed. The resulting white solid was isolated by filtration and provided 185.5g of the tetrasodium salt of the title compound as a decahydrate. A solution containing 36.7 g of the tetrasodium salt of VDPA in 100 mL of water was passed slowly through a column containing 133 g of Dowex™ AG MP-50, an acidic ion exchange resin available from BioRad. An additional 100 mL of water was added to elute the free acid of VDPA.

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1,2-Dihydroxyethane-1,1-diphosphonic Acid (3). The aqueous solution of the free acid of VDPA from the above experiment was charged with 1.6g of sodium tungstate and 54 mL of 30% H_2O_2. The resultant solution was warmed to 60 °C for 3 hours. After cooling to room temperature, dilute aqueous NaOH was added dropwise until a pH of 6.2 was obtained. The solvent was concentrated *in vacuo* to provide a syrup. Approximately 50 mL of acetone was introduced and the resulting mixture was stirred for 1 hour. The solvent was decanted and another 50 mL of fresh acetone was introduced. After decanting the solvent, the white oily solid was dried *in vacuo* at 50 °C overnight to provide 25g (95%) of the title compound (85% pure).

1-Carboxy-1-hydroxymethanediphosphonic Acid (2). Methyl oxalyl chloride (Aldrich, 10 mL, 110 mmol) was cooled to 0 °C under nitrogen. Trimethylphosphite (Aldrich, 12.8 mL, 100 mmol) was added dropwise over 45 min while maintaining the temperature at 0 °C. The resultant solution was allowed to slowly warm to room temperature over 2 hours. The resultant trimethyl ester of oxalphosphonate (98% yield) was characterized by NMR (see text), but was not isolated. After adding 30 mL of diethyl ether and cooling to 0 °C, a solution of dimethylphosphite (Aldrich, 9.6 mL, 100 mmol) and di-*n*-butylamine (Aldrich, 1.4 mL, 8.5 mmol) in 50 mL of diethyl ether was added dropwise over 2 hours. The resultant solution was warmed slowly to room temperature overnight. The solvent was concentrated under a stream of nitrogen to provide an oil (26 g, 70 %) identified as the penta-methyl ester of the title compound.

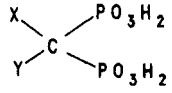
To a cool (0 °C), stirred solution of the penta methyl ester (5 g, 16.3 mL) in 10 mL of carbon tetrachloride was added dropwise a solution of iodotrimethylsilane (8.2 mL, 58.1 mmol). The resultant solution was vigorously stirred while warming to room temperature. Water (6 mL) was introduced and stirring was continued an additional hour. The organic and aqueous phases were separated and the aqueous phase was washed with 2 X 10 mL of carbon tetrachloride. The aqueous phase was concentrated *in vacuo* to provide the title compound in 60% yield.

NOTE: The title compound slowly decomposes to phosphoric acid and carbon dioxide with the concomitant pressure buildup. Appropriate precautionary steps should be exercised during its synthesis and storage.

DISCUSSION

PART I: THE SYNTHESIS OF DIPHOSPHONIC ACID COMPLEXANTS.

The design of an acidic organic compound that would effectively complex a metal ion and remain in solution in aqueous media containing acid concentrations between 1 and 7 M is a very imposing problem. Of the various acidic organic functional groups only geminally-substituted diphosphonic acids (**1**), with pK_a values $\leq$ 1.4, appear to be sufficiently acidic to accomplish complexation at these acidities. Structure **1** represents a generic gem-diphosphonic acid molecule for the candidate complexants, where X and can be functional groups that are manipulated to decrease the pK_a values as well as weaken the P-C bonds to introduce a degree of instability.



	X	Y
1	X	Y
2	CO_2H	OH
3	CH_2OH	OH
4	H_2C-	
5	CH_3	OH
6	$-CH_2O-$	

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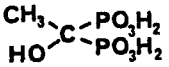
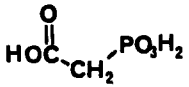
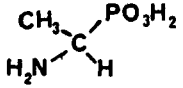
The ease of decomposition of several commercially available diphosphonic and mono-phosphonic acids was examined in 8M HNO_3 at 100 °C to identify potential candidates for X and Y. The structures and the results of the ^{31}P NMR data are given in Table 1. These data suggest that a β-carboxylate or carboxylate precursor, such as an alcohol, substituent in a α-hydroxyethane-diphosphonic acid system (i.e., **2**, where X = CO_2H, Y = OH) should generate a structure with the desired acidity and a degree of instability.

Table 1. The Degradation of Commercially Available Mono- and Diphosphonic Acids.[1]

Structure	% Decomposition[2]	Chemical Shift (δ,ppm)[3]
	50 (18hr)	20.6
	100 (4hr)	17.2
	0 (22hr)	14.6
	10 (28hr)	24.5

1 Decomposition experiments were conducted in refluxing 8M HNO_3 D_2O with a concentration of substrate that was sufficient for NMR spectrometry (approximately 8mg/mL).

2 Estimated by integrating the ^{31}P resonances for the sample and H_3PO_4 (δ 3.10ppm) for 10 mL aliquots withdrawn every hour. The time indicated is the time at which no further change in the value for the integration had been noted for three consecutive aliquots.

3 The spectra were recorded on a Bruker AM-300 spectrometer equipped with a 10mm multinuclear probe. An external capillary containing 85% phosphoric acid was used as a reference for the chemical shifts, which are recorded in parts per million (ppm) downfield. The proton decoupled spectra were obtained at 121.5 MHz using a 90° pulse width of 16 μsec, a spectral width of 15151.51 Hz and a filter width of 19000 Hz. An exponential line broadening of 0.3 Hz was applied to the FID.

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No literature references to structure **2**, where X = CO_2H and Y = OH, were found. However, a number of citations[2,3] in the patent literature indicated that the carboxylate precursors **3** (X = $HOCH_2$, Y = OH) and **4** (X = Y = H_2C=) were available. In addition, the synthetic utility of vinylidene-1,1-diphosphonic acid (**4**) was amply documented by the number of derivatives prepared through the epoxide.[5a]

Although the literature contains a number of synthetic methods for the preparation of α-substituted diphosphonic acids[4] and esters,[5] 1-hydroxyethane-1,1-diphosphonic acid (**5**, HEDPA) is an ideal starting material as this structure incorporates the *principle of conservation of synthetic effort.* HEDPA (**5**) is an inexpensive, readily-available organo-phosphorus compound that contains two of the three desired functional groups. Only functionalization at the β-carbon is required to complete the synthesis. We have shown that HEDPA (**5**) is not a completely satisfactory complexant for many of the applications envisioned for these reagents.[6]

HEDPA (**5**) is received as a 60 - 70 % aqueous solution from Albright & Wilson (Richmond, VA) and is purified by crystallization using glacial acetic acid according to the Merck Index.[7]

The Preparation of Vinylidene-1,1-Diphosphonic Acid.

Attempts to prepare the olefin by dehydration of HEDPA (**5**) using standard methods failed. Refluxing with concentrated sulfuric, hydrochloric, or hydrobromic acids produced intractable tars. It is conceivable that dehydration to vinylidene diphosphonic acid, followed by polymerization occurred under these conditions. We recovered unchanged starting material from attempts to dehydrate under milder conditions (mineral acids at 0, 25, or 50 °C). Elimination of the methanesulfonyl ester (generated *in situ*) by reacting HEDPA with methanesulfonyl chloride in an excess of triethylamine at reflux also resulted in unchanged HEDPA. The latter reaction would be more likely to succeed using the tetra-alkyl ester of HEDPA. However, esters of this type have been reported to be unstable[4b] and no attempt to prepare an ester derivative was made.[8]

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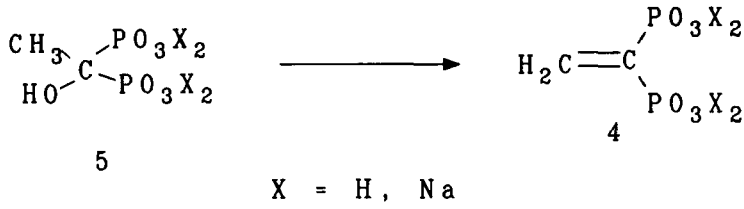

5 4

X = H, Na

The thermolytic dehydration of various salts of 1-hydroxyalkyl-1,1-diphosphonic acids has been described in the patent literature.[9] The ^{31}P NMR spectrum of the crude product after heating the tri-sodium salt of HEDPA with an excess of di-sodium orthophosphate at 290 °C for 2.5h indicated that a mixture of sodium pyrophosphate (~50%, δ -4.97ppm), starting Na_3HEDPA (~50%, δ 20.0ppm), and only traces of the desired vinylidene diphosphonic acid (δ 12.1ppm) had been formed. The results from similar experiments with an excess of sodium hydroxide or calcium hydroxide as dehydrating agents were equally disappointing.

Thermogravimetric analyses of the various sodium salts of HEDPA have been reported,[4b] but did not include the thermal dehydration of HEDPA to vinylidene-1,1-diphosphonic acid (**4**). Because we required a more efficient method of preparing VDPA than previously reported we reexamined the thermogravimetric analysis data for the di, tri, and tetra-sodium salts of HEDPA. We extended the earlier study by examining the thermolysis residues using ^1H and ^{31}P NMR. The spectral assignments for HEDPA are ^{31}P: δ 20.0ppm, ^1H: δ 1.45ppm (triplet J = 13.7Hz) and for VDPA (**4**) ^{31}P: δ 12.1ppm; ^1H: δ 6.12ppm (doublet of doublets J = 34.8, J´ = 31.9 Hz).

The ^1H NMR spectral data was very useful for determining the HEDPA:VDPA product distribution under conditions where the dehydration reaction appeared to be moderately efficient (i.e., the tetrasodium salt at 350, 400 or 450 °C under a vacuum (Table 2). The ^1H data provided no information concerning the amount of decomposition occurring. Because the integral ratio for HEDPA to VDPA in the ^1H and the ^{31}P NMR spectra were nearly identical[10] and the phosphorus data is useful for determining the amount of decomposition, only the ^{31}P NMR data are listed in Table 2.

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Table 2: The thermogravimetric analysis of the salts of HEDPA.

Salt[1]	Conditions	^{31}P (ppm)[2]	Comments
Na_2	350 °C/N_2	??[3]	Very decomposed.
Na_3	300 °C/N_2	20.00(trace)	Mostly decomposed.
Na_3	325 °C/N_2	-5.06(major)	Mostly decomposed.[4]
Na_3	350 °C/N_2	-5.06(major)	Mostly decomposed.[4]
Na_3	330 °C/air	20.0(trace)	Mostly decomposed.[4]
Na_3	320 °C/vacuum	20.0/11.9	7:1 HEDPA:VDPA
Na_4	240 °/N_2	20.0/12.1(trace)	Recovered HEDPA
Na_4	350 °/vacuum	20.0/12.1	1:1 HEDPA:VDPA
Na_4	400 °/vacuum	20.0/12.1	1:3 HEDPA:VDPA
Na_4	450 °/vacuum	12.1(major)	Some decomposition.[4]
Na_4	240 °/air	??[3]	Very decomposed.[4]
Na_4	300 °/air	??[3]	Very decomposed.[4]
Na_4	380 °/air	??[3]	Very decomposed.[4]

[1] The salt was prepared by adding the calculated number of equivalents of NaOH (aq), evaporating the solvent in vacuo at 50 °C. The product was dried in a vacuum oven at 100 °C overnight.

[2] NMR data were recorded as previously discussed in Table 1. The units are parts per million downfield from an external reference capillary containing 85% phosphoric acid.

[3] ?? indicates that no identifiable phosphorus peaks were in the NMR spectrum.

[4] Samples indicated by various degrees of decomposition were dark brown to black in color. The ^{31}P NMR spectra contained several peaks which could not be identified.

The data suggest that the thermal dehydration of either the tri- or tetra-sodium salts of HEDPA between 320 and 450 °C as potentially useful reactions to investigate further for the formation of VDPA. The conversion to VDPA with minimal decomposition was observed for the thermolysis of Na_3HEDPA and Na_4HEDPA using a vacuum of 25mm Hg. We believe that the vacuum assists in the removal of water and air, which appear to be involved in the formation of the pyrophosphate by-product. This view is supported by the data in Table 2 which clearly indicates that the presence of air promotes decomposition during the thermolysis of HEDPA salts as an

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increased number of unidentifiable ^{31}P peaks are observed under these conditions.

We investigated the thermolysis time on a preparative scale for the tri-sodium and tetra-sodium salts at three temperatures (300, 350, and 400 °C) under vacuum. The products obtained after 1.5, 3, 6, 7, 9, 18 and 48 hours were analyzed by NMR and ion chromatography. The results are listed in Table 3. These data clearly indicate that the tetra-sodium salt provides the product with lesser amounts of degradation than the tri-sodium salt. Heating to 400 °C for 3 hours provided a similar yield of VDPA with less degradation than obtained at the lower temperatures. An increase in the reaction time at 400 °C does not appreciably improve the yield of VDPA and promotes the formation of the degradation products.

Table 3: Results from the preparative scale thermolysis of Na_3HEDPA and Na_4HEDPA.

Salt[1]	Temperature (°C)	Time(hr)	Yield[2]	Comment
Na_3	300[3]	3	57	Decomposed
Na_3	350[3]	3	0	Very decomposed
Na_3	400[3]	3	0	Very decomposed
Na_4	300[3]	3	11	Largely Na_4HEDPA
Na_4	350[3]	3	11	Largely Na_4HEDPA
Na_4	350[3]	5	25	Na_4HEDPA recovered
Na_4	350[3]	18	44	Balance decomposed
Na_4	350[3]	48	42	Very decomposed

[1] The salt was prepared by adding the calculated number of equivalents of NaOH (aq), evaporating the solvent in vacuo at 50 °C. The product was dried in a vacuum oven at 100 °C overnight.

[2] The yield of Na_xVDPA (^1H: δ6.10ppm; ^{31}P: δ12.11ppm) was estimated by integrating the NMR resonances. The data agree (±5%) with the yield as determined by ion chromatography.

[3] The experiment was conducted on 5g of salt in a tube furnace. The tube was evacuated to 25mm of Hg and rotated at 5rpm using a rotary evaporator motor.

(continued)

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Table 3 (continued): Results from the preparative scale thermolysis of Na_3HEDPA and Na_4HEDPA

Salt[1]	Temperature (°C)	Time(hr)	Yield[2]	Comment
Na_4	400[3]	1.5	38	Largely Na_4HEDPA
Na_4	400[3]	3	60	35% Na_4HEDPA
Na_4	400[3]	6	60	35% Na_4HEDPA
Na_4	400[3]	18	74	Balance decomposed
Na_4	350[4]	3	19	Very decomposed Na_4HEDPA present
Na_4	400[5]	3	59	Very decomposed
Na_4	400[5]	7	48	Very decomposed
Na_4	400[5]	9	53	Very decomposed

[3] The experiment was conducted on 5g of salt in a tube furnace. The tube was evacuated to 25mm of Hg and rotated at 5rpm using a rotary evaporator motor.

[4] The experiment was conducted as above without rotating the tube.

[5] The experiment was conducted as above expect that the tube was rotated at 25rpm.

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We have also investigated the rotation speed of our glass reaction tube. At rotation speeds approaching 25 rpm lesser amounts of the starting material are converted into the product than at a slower rotation speed. However, no rotation of the tube generates very little product and a significant rise in the amount of degradation products. We believe that slower rotation speeds promote more efficient heat transfer through the solid; While, the faster rotation speeds and no rotation do not allow for adequate mixing of the solid and a resultant decrease in the efficacy of heat transfer throughout the reactant. This results in local overheating and a greater degree of degradation of the starting material or the product.

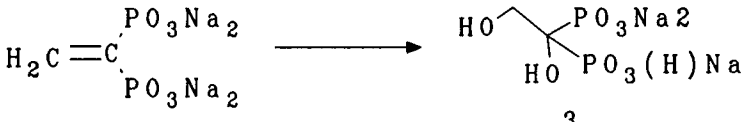
We have determined that the optimum conditions for the preparation of VDPA via the thermal dehydration of HEDPA are to maintain the tetrasodium salt of HEDPA at 400 °C in a tube furnace for three hours under a vacuum (25 mm Hg) while rotating the tube at 5 rpm. We use these conditions to routinely dehydrate up to 200g of Na_4HEDPA in a single experiment. The crude product contains 60-65% (by weight) of Na_4VDPA, 30-35% (by weight) of Na_4HEDPA, and 5-10% (by weight) of sodium pyrophosphate as determined by ^{31}P NMR spectrometry and ion chromatography.

The tetra-sodium salt of VDPA is separated from the starting material and any degradation products by dissolving the crude product in a minimum of hot water, followed by precipitation with methanol. The product obtained after two crystallizations is 95+% pure by ^{1}H and ^{31}P NMR. It is not uncommon for the crystallized product to contain traces of sodium phosphate and sodium pyrophosphate.

The free acid of VDPA is obtained by ion exchange using Dowex™ AG MP50 ion exchange resin on the hydrogen cycle, followed by concentration of water at reduced pressure. VDPA (**4**), as isolated in this manner, is used with no further purification in subsequent investigations.[1] If desired the tetra-basic acid of VDPA can be further purified by slow crystallization from water.

The Preparation of 1,2-Dihydroxyethane-1,1-diphosphonic Acid

The oxidation of the tri-basic acid of vinylidene-1,1-diphosphonic acid using hydrogen peroxide and sodium tungstate (catalyst) according to the method of Kerst[2a] provided phosphoric acid as the only phosphorus containing product (^{31}P: δ 3.10ppm). We assumed that either over-oxidation of the expected epoxide (**6**) or variations in pH during the workup of the reaction was promoting the preparation of phosphoric acid, we slowly introduced sodium carbonate until a pH of 6 - 7 was obtained, while cooling the reaction mixture in an ice bath. The introduction of carbonate neutralizes the phosphonic acid groups and has been noted by us to decompose any excess peroxide. The subsequent addition of acetone precipitated a viscous oil, identified by its NMR spectral data as 1,2-dihyroxyethane-1,1-diphosphonic acid, trisodium salt (**3**). The ^{1}H NMR data displayed a triplet (J = 6.00 Hz) at δ 3.11ppm. The phosphorus signal was observed at δ 13.6ppm. The phosphorus data was used to establish the purity of the compound as > 95%, in good agreement with the acid-base titration data.[1]



4 3

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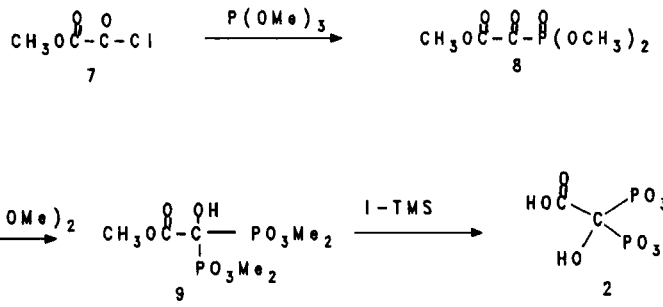
Several attempts to convert the tri-sodium salt into the free acid using an ion exchange procedure (*vide supra*) significantly decomposed the sample as evident by the generation of phosphoric acid. The ^{31}P NMR spectrum of the aqueous solution from the column contained a peak at δ 3.10ppm, which was not present in the starting salt. Furthermore, we eliminated the possibility of that the δ 3.10 ppm peak came from the ion exchange material as it was not observed when using the ion exchange column material for the conversion of other acid salts; such as Na_4VDPA. This led us to suspect the stability of the acidic form of DHEDPA (**3**). Apparently, the trisodium salt of DHEDPA (**3**) is a stable species. The instability aspects of the chemistry of 1,2-dihydroxyethane-1,1-diphosphonic acid will be addressed more fully in Part II The Decomposition of Diphosphonic Acid Complexants section of this paper (*vide infra*).

The Preparation of 1-Carboxy-1-hydroxymethanediphosphonic Acid (2)

The oxidation of 1,2-dihydroxyethane-1,1-diphosphonic acid (**3**) to carboxyhydroxymethanediphosphonic acid (**2** X = CO_2H and Y = OH) was not attempted due to the observed instability of DHEDPA in acidic aqueous solutions. Therefore, an alternate synthetic route, which did not involve the intermediacy of VDPA (**4**) and DHEDPA (**3**) was required.

Structural analysis of **2** suggested a short synthetic route that utilized organo-phosphorus chemistry previously developed for the synthesis of diphosphonic acid esters.[4,5,11] The trimethyl ester of oxalophosphonate (**8**) was prepared in 98% yield by reacting methyl oxalyl chloride (**7**) with trimethylphosphite. The carbon and phosphorus NMR spectra were used to assign the structure. The resonances at δ 161.26ppm (doublet, $J_{C\text{-}P}$ = 285 Hz) and at δ 181.36ppm (singlet) were assigned to the ketone carbonyl and ester carbonyl, respectively. The phosphorus signal resonated at δ 3.37ppm.



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The successful preparation of (**11**) set up the pivotal reaction for this synthetic approach. We anticipated that a base-initiated reaction[5e] of a nucleophile (dialkylphosphite) with the ketonic carbonyl center could occur in the presence of an ester carbonyl group. An electronic argument suggests that the ketonic carbonyl is the preferential site for nucleophilic attack. However, the ester carbonyl is the less hindered carbonyl center. Molecular models, generated using the program *Alchemy* (Tripos Associates) on an IBM AT personal computer,[12] clearly demonstrate the different steric environments (Figure 1). The space filling models in Figure 1 attempt to demonstrate a graphical representation of the approach, represented by the arrows, that a nucleophile "Nu:" must take to react at the ketonic carbonyl carbon (**Pathway A**) or the ester carbonyl carbon (**Pathway B**). The approach directed at the ester carbonyl is the pathway with the lesser degree of steric hindrance, compared to pathway B toward the ketone carbonyl. It is apparent from the models that the nucleophile in approaching along pathway A must pass nearer to the phosphonate alkyl groups in the molecule. The more hindered approach to react with the ketone necessitates a higher degree of order in the transition state and, therefore, a corresponding increase in the energy of activation for nucleophilic addition.

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However, exclusive addition to the electronically-favored ketone carbonyl occurred. We isolated 1-hydroxydiphosphonate **9** in 86% yield from the reaction of dimethylphosphite with **8**. This reaction was conducted using di-*n*-butylamine at 0 °C as per Nicholson and Vaughn.[5e] Furthermore, we were unable to detect the presence of any bis-phosphonate other than the desired geminally-substituted product in the NMR data. The structure **9** was assigned based upon the carbon and phosphorus NMR data. The carbon spectrum displayed the resonance for the ester carbonyl carbon at δ 181.5 ppm. A triplet ($J_{P\text{-}C\text{-}P}$ = 536 Hz) at δ 19.5ppm has been assigned to the quaternary carbon. By way of negative evidence, the doublet at δ 161.26 ppm, previously assigned to the ketone carbonyl in **8**, is missing from the spectrum. The phosphorus signal was observed at δ 10.85ppm. The latter resonance compares favorably to the reported signal for carboxymethane diphosphonate (**10**) at δ 11.0ppm.[13] The reported attempted hydrolysis of **10** using refluxing hydrochloric acid did not generate the expected free acid, but methylene diphosphonate and CO_2 were isolated.

As we were uncertain of the stability of carboxy-hydroxymethane-diphosphonic acid (**2**) or its ester, we utilized iodotrimethylsilane, the mildest available reagent for the conversion of alkylphosphonates into phosphonic acids.[14] Our initial attempts to de-alkylate **9** used stoichiometric amounts of TMSI in order to completely dealkylate the penta-ester. Unexpectedly, the reactions with either 5 or 4 equivalents of TMSI yielded dark, resinous

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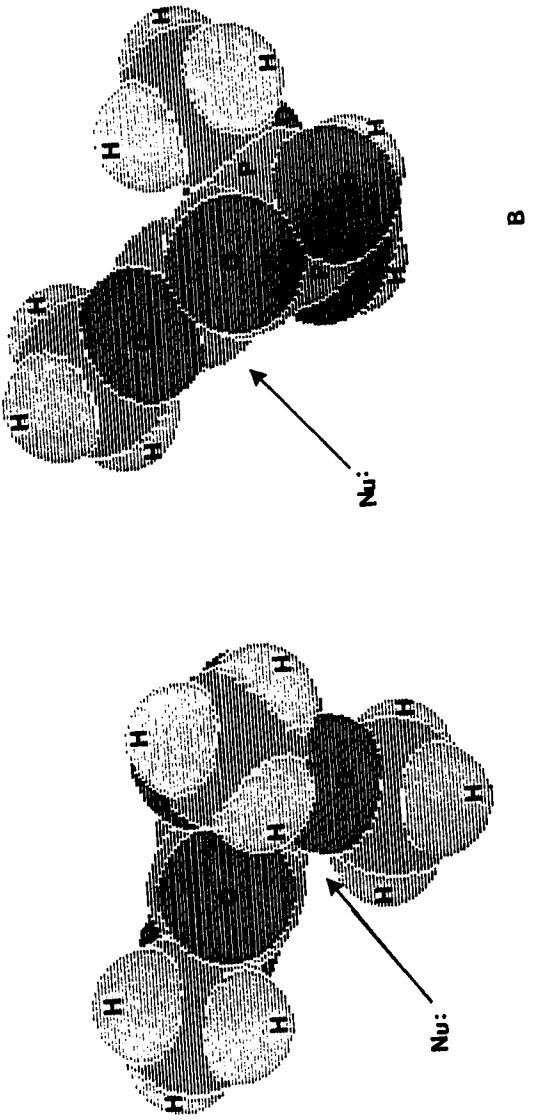

Figure 1: Alchemy generated molecular model of nucleophilic addition to the carbonyl groups.

materials, which proved to be intractable. Resigned to the probability that we would only partially dealkylate the ester, we were somewhat surprised that the utilization of a further sub-stoichiometric amount of iodotrimethylsilane (3.5 equivalents) completely de-alkylated **9**. The addition of water to the crude reaction solvent (carbon tetrachloride) was sufficient to hydrolyze the intermediate trimethylsilyl esters, generated during the reaction, without isolating them. The free penta-basic acid (**2**) was obtained in 60% yield after the concentration of the aqueous phase.

The structure was assigned based upon the carbon and phosphorus NMR data. The carbon spectrum displayed a singlet at δ 161.44 ppm and a triplet at 19.5 ppm ($J_{P\text{-}C\text{-}P}$ = 536 Hz). We have assigned the former signal to the carboxylate carbonyl and the latter signal to the quaternary carbon. The phosphorus spectrum displayed two signals at δ 10.5ppm (product) and δ 3.10ppm (phosphoric acid). After storage for several days at room temperature, the signal at δ 3.10ppm was the only remaining resonance in the phosphorus spectrum. This result is indicative of complete decomposition of CHMDPA to phosphoric acid.

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Aqueous samples of carboxy-hydroxymethanediphosphonic acid (**2**, CHMDPA) outgas upon opening after storage under a nitrogen atmosphere at -10 °C. Mass spectral analysis of the air space above a sealed aqueous solution of **2** after storage for 24 hours at room temperature indicated that the gaseous product from decomposition was carbon dioxide. The aqueous solution contained phosphoric acid as indicated by ^{31}P NMR. No carbon spectrum was obtainable. At this time we cannot offer a plausible mechanistic explanation for this observation.

The half-life of the apparent auto-decomposition reaction was crudely determined to be approximately 72 hours by integrating the phosphorus NMR data. The decomposition can be accelerated by the addition of 8M HNO_3. The reaction is complete after 5 minutes. The gaseous products were identified by mass spectrometry as CO_2, NO and NO_2. Once again, phosphoric acid was the only phosphorus-containing product in solution and no carbon spectrum was obtainable. Unfortunately, the rapid auto-decomposition of **2** precluded further examination of its complexation chemistry. We have been unable to obtain a sample of known concentration free of phosphoric acid.

PART II: THE DECOMPOSITION OF DIPHOSPHONIC ACID COMPLEXANTS

The Decomposition of VDPA.

We were disappointed by our inability to isolate epoxide **6** (*vide supra*) from the tungstate-catalyzed hydrogen peroxide oxidation of VDPA (**4**). The isolation of **6** is particularly desirable as we can generate a variety of 1,2-disubstituted ethane-1,1-diphosphonic acids with potential TUCS properties via nucleophilic addition to the epoxide's β-carbon. Therefore, we investigated the vanadyl-catalyzed oxidation using hydrogen peroxide of aqueous solutions of VDPA (**4**) by in an effort to prepare epoxide **6**.

Unfortunately, VDPA was recovered unchanged after stirring for 12 hours with H_2O_2 and catalytic vanadyl acetylacetonate ([V] $\sim 10^{-4}$M) at room temperature. Warming the reaction mixture to 60 °C promoted the quantitative conversion of VDPA to phosphoric acid in as little as 3 hours. Identical results were obtained using sodium vanadate ([V] $\sim 10^{-4}$M). This reaction in the absence of the metal ion (hydrogen peroxide at 60 °C) does not promote the decomposition of VDPA. We are currently investigating the role of the metal ion, especially vanadium, in this reaction.

We have also observed the decomposition of VDPA in 3 hours using 8M nitric acid at 100 °C. The only phosphorus-containing compound in the NMR spectrum was phosphoric acid.

Although the vanadium-catalyzed oxidation did not provide an entry to the desired β-substituted α-hydroxyethanediphosphonic acids we required for further study, the facile conversion of VDPA to H_3PO_4 prompted us to consider VDPA as a viable complexant, rather than a synthetic intermediate. However, unlike 1,2-dihydroxyethanediphosphonic acid (*vide infra*), aqueous solutions of VDPA stored at temperatures ranging from room temperature to 50 °C over a pH range from 2 to 12 are stable for up to six months (or longer). This permits long term storage of the reagent for most envisioned applications.

The Decomposition of 1,2-Dihydroxyethanediphosphonic Acid

During the synthesis of 1,2-dihydroxyethanediphosphonic acid (**3**), we observed the formation of phosphoric acid on the ion exchange column (*vide supra*). The facile formation of phosphoric acid of the sodium salt to the free acid suggested that we examine the effect of pH upon the structure of this complexant.[15] The results of our investigation are summarized in Table 4.

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Table 4. The effect of pH upon the decomposition of DHEDPA (3).

pH[1]	Temperature(°C)	Time(hr)	DHEDPA:H_3PO_4[2]
1.94	25	0	-----[3]
"	"	8	-----
"	"	24	trace H_3PO_4
"	"	48	20:1
"	"	120	9:1
"	"	192	4:1
"	"	360	1:1
"	"	768	1:2
"	"	1560	1:7
1.93	50	0	-----
"	"	8	20:1
"	"	48	9:1
"	"	120	3:1
"	"	192	1:1
"	"	360	1:3
"	"	768	1:7
6.08	25	0	-----
"	"	1560	no H_3PO_4
6.02	50	0	------
"	"	1560	no H_3PO_4
7.99	25	0	------
"	"	1560	no H_3PO_4
7.91	50	0	------
"	"	1560	no H_3PO_4
10.99	25	0	------
"	"	1560	no H_3PO_4
10.58	50	0	------
"	"	1560	no H_3PO_4

[1] The pH was obtained by titrating a D_2O solution of DHEDPA with 0.5M DCl/D_2O or 0.5M NaOD/D_2O using a glass electrode.

[2] The values equal the ratio of the integrated ^{31}P NMR resonances for DHEDPA (δ 12.11ppm) and H_3PO_4 (δ 3.10ppm).

[3] Slashed line indicates that no phosphoric acid was present in the initial NMR spectrum.

Acidic (pH = 2) solutions of DHEDPA (3) at room temperature slowly decompose to phosphoric acid with an approximate half-life of 15 days (estimated by integration of the phosphorus spectrum). The half-life of the

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reaction is decreased to 8 - 9 days upon warming to 50 °C. An aqueous solution of DHEDPA (**3**) at a pH ≥ 6 did not generate phosphoric acid for up to three months at room temperature up to 50 °C.

DHEDPA (**3**) offers us the unique capability of allowing a complexant to slowly decompose to a more environmentally acceptable phosphate by a simple adjustment of pH. Alternatively, the conversion of DHEDPA (**3**) into phosphoric acid can be readily accomplished with 8M HNO_3 at 100 °C in 3 hours. DHEDPA is also readily decomposed under mild oxidative conditions of the acidic form using hydrogen peroxide at 60 °C. A metal ion catalyst is unnecessary.

A detailed examination of the phosphorus NMR data from a D_2O solution of DHEDPA (**3**) at approximately a pH = 2, attained by the addition of hydrochloric acid, allows us to suggest a possible pathway for the decomposition reaction. The ^{31}P NMR data for these solutions contain a phosphorus signal at δ -0.6 ppm (referenced to external 85% phosphoric acid), the resonances previously assigned to the diphosphonic acid (δ 12.11ppm) and phosphoric acid (δ 3.10ppm). We have attributed the high field resonance (δ -0.6ppm) to acetylphosphonate (**12**). Spectral comparison with a sample of **12** confirms the spectral assignment. Authentic acetylphosphonic acid was prepared according to the method of McConnell[5f] followed by the iodotrimethylsilane promoted deesterification of the dimethyl ester. Acetylphosphonic acid has been reported to decompose with P-C bond cleavage.[4a]

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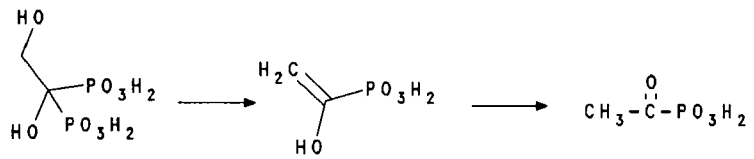

3 11 12

We believe that acetylphosphonate (**12**) is generated from DHEDPA (**3**) by the loss of phosphoric acid through a four-membered intermediate to give enol-phosphonic acid **11**. The enol tautomerizes to acetylphosphonic acid

(**12**). Considering the similarity of this proposal to the Horner-Emmons reaction and the ease which phosphorus forms P-O bonds the speculative pathway is not unreasonable. A similar pH dependent decomposition of 2-hydroxy-1-aminoethanediphosphonic acid (**14**) has been observed by Fukuda.[16] We have examined the products from the decomposition of **14**. The NMR data for the crude product from the reaction between hydroxyacetonitrile (**13**) and phosphorous acid, after acidification, indicated that acetylphosphonic acid (**12**) and phosphoric acid were the phosphorus-containing products. If the decomposition of 2-hydroxy-1-aminoethane-1,1-diphosphonic acid (**14**) proceeds according to our proposal, than we would expect that under acidic conditions conversion to **16** and phosphoric acid as shown. The imine would hydrolyze rapidly to the observed products.

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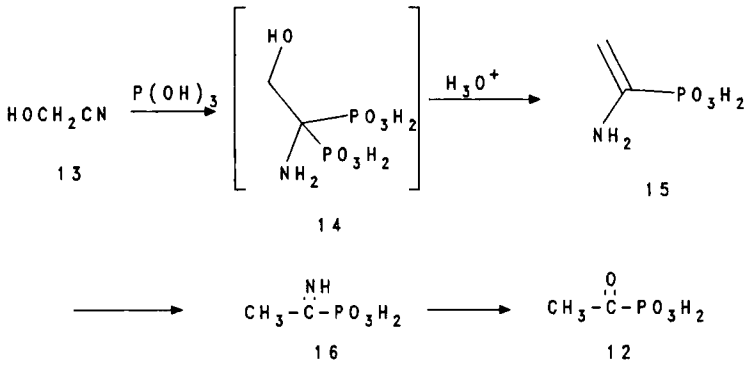

13 14 15 16 12

We may speculate that the induced decomposition of VDPA (**4**) to phosphoric acid via the vanadium (V) catalyzed oxidation with H_2O_2 proceeds through the intermediacy of 1,2-dihydroxyethane-1,1-diphosphonic acid (**3**). We have observed traces of 1,2-dihydroxyethane-1,1-diphosphonic acid (**3**) and acetylphosphonic acid (**12**) in the NMR spectra during the decomposition reactions. However, further investigation into the decomposition is required to establish the intermediacy of DHEDPA (**3**) during the decomposition of VDPA.

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