

1983

# Studies of properties of derivatives of 1-phospha-5-aza-2,6,9-trioxabicyclo[3.3.3]undecane and structurally related molecules

Leslie Earl Carpenter II  
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STUDIES OF PROPERTIES OF DERIVATIVES OF 1-PHOSPHA-5-AZA-2,6,9-  
TRIOXABICYCLO(3.3.3)UNDECANE AND STRUCTURALLY RELATED  
MOLECULES

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Studies of properties of derivatives  
of 1-phospha-5-aza-2,6,9-trioxabicyclo[3.3.3]undecane  
and structurally related molecules

by

Leslie Earl Carpenter II

A Dissertation Submitted to the  
Graduate Faculty in Partial Fulfillment of the  
Requirements for the Degree of  
DOCTOR OF PHILOSOPHY

Department: Chemistry  
Major: Inorganic Chemistry

Approved:

Signature was redacted for privacy.

~~In~~ Charge of Major Work

Signature was redacted for privacy.

For the Major Department ~~ment~~

Signature was redacted for privacy.

For the Graduate ~~ate~~ College

Iowa State University  
Ames, Iowa

1983



## TABLE OF CONTENTS

	<u>Page</u>
ABSTRACT.....	xx
PART I: CRYSTAL AND MOLECULAR STRUCTURE OF 3,9-DIMETHOXY- 2,4,8,10-TETRAOXA-3,9-DIPHOSPHA SPIRO[5.5]UNDECANE.....	1
INTRODUCTION.....	2
EXPERIMENTAL.....	4
RESULTS AND DISCUSSION.....	11
PART II: CRYSTAL AND MOLECULAR STRUCTURE OF 2-OXO-2(BIS-( $\beta$ - CHLOROETHYL)AMINO)-4,6-DIMETHYL-1,3,2- OXAZAPHOSPHORINANE.....	14
INTRODUCTION.....	15
EXPERIMENTAL.....	18
RESULTS AND DISCUSSION.....	28
PART III: BICYCLIC TO TRICYCLIC TRANSFORMATIONS IN 1-PHOSPHA- 5-AZA-2,6,9-TRIOXABICYCLO[3.3.3]UNDECANE SYSTEMS.....	33
INTRODUCTION.....	34
EXPERIMENTAL.....	36
RESULTS AND DISCUSSION.....	48
PART IV: $^{17}\text{O}$ NMR OF PHOSPHITES AND PHOSPHATES.....	68
INTRODUCTION.....	69
EXPERIMENTAL.....	74
RESULTS AND DISCUSSION.....	83
PART V: ATTEMPTED SYNTHESIS OF "ATRAPE" CAGES.....	118
INTRODUCTION.....	119
EXPERIMENTAL.....	120
RESULTS AND DISCUSSION.....	127

PART VI: PROTONATION OF 1-PHOSPHA-5-AZA-2,6,9- TRIOXABICYCLO[3.3.3]UNDECANE.....	129
INTRODUCTION.....	130
EXPERIMENTAL.....	131
RESULTS AND DISCUSSION.....	135
 SUMMARY .....	 137
REFERENCES.....	138
ACKNOWLEDGEMENTS.....	154

## LIST OF TABLES

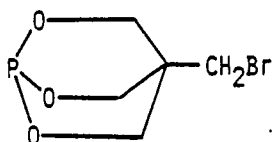
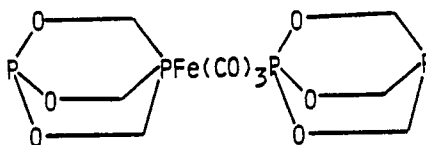
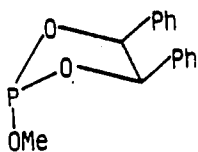
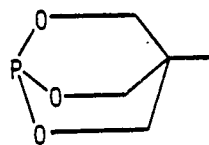
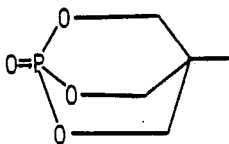
	<u>Page</u>
Table 1. Calculated and observed structure factors for 3,9-dimethoxy-2,4,8,10-tetraoxa-3,9-diphospha-spiro [5.5]undecane .....	6
Table 2. 3,9-Dimethoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro [5.5]undecane final atomic and positional parameters	8
Table 3. 3,9-Dimethoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro [5.5]undecane final thermal parameters.....	9
Table 4. 3,9-Dimethoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro [5.5]undecane intramolecular bond distances and angles.....	10
Table 5. Calculated and observed structure factors for 2-Oxo-2-(bis-( $\beta$ -chloroethyl)amino)-4,6-dimethyl-1,3,2-oxaza-phosphorinane .....	20
Table 6. 2-Oxo-2-(bis-( $\beta$ -chloroethyl)amino)-4,6-dimethyl-1,3,2-oxaza-phosphorinane final atomic and positional parameters.....	24
Table 7. 2-Oxo-2-(bis-( $\beta$ -chloroethyl)amino)-4,6-dimethyl-1,3,2-oxaza-phosphorinane final thermal parameters.....	25
Table 8. 2-Oxo-2-(bis-( $\beta$ -chloroethyl)amino)-4,6-dimethyl-1,3,2-oxaza-phosphorinane intramolecular bond distances and angles.....	26
Table 9. 2-Oxo-2-(bis-( $\beta$ -chloroethyl)amino)-4,6-dimethyl-1,3,2-oxaza-phosphorinane torsional and interplanar angles.....	27
Table 10. $^1\text{H}$ and $^{31}\text{P}$ NMR data for the protonation of phosphatrane oxide ( <u>20</u> ) with trifluoroacetic acid.....	52
Table 11. $^1\text{H}$ and $^{31}\text{P}$ NMR data for the protonation of phosphatrane sulfide ( <u>21</u> ) with trifluoroacetic acid.....	58

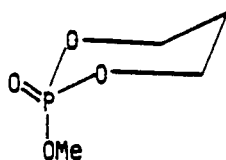
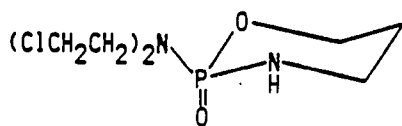
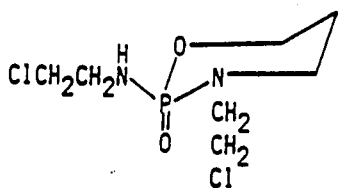
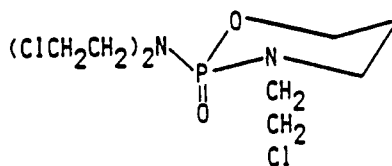
Table 12.	$^1\text{H}$ and $^{31}\text{P}$ NMR data and $\nu_{\text{P=O}}$ for complexes of phosphatrane oxide with $\text{BF}_3$ , $\text{Et}_3\text{SiClO}_4$ and $\text{Zn}(\text{ClO}_4)_2$ .....	64
Table 13.	IR and UV data for cobalt complexes of phosphates...	66
Table 14.	$^{17}\text{O}$ NMR chemical shifts and coupling constants of phosphites.....	84
Table 15.	$^{17}\text{O}$ NMR chemical shifts and coupling constants of phosphates.....	91
Table 16.	$^{13}\text{C}$ and $^{31}\text{P}$ NMR data for cyclic phosphites.....	98
Table 17.	$^{13}\text{C}$ and $^{31}\text{P}$ NMR data for cyclic phosphates.....	105
Table 18.	Dipole moments of cyclic phosphates.....	106
Table 19.	Slopes, intercepts, and correlation coefficients for plots of $\delta^{17}\text{O}$ versus $\delta^{31}\text{P}$ for phosphates.....	112

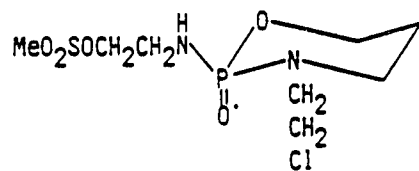
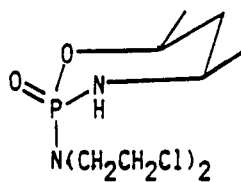
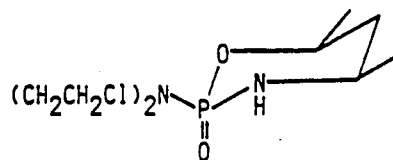
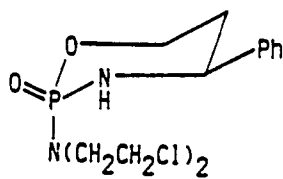
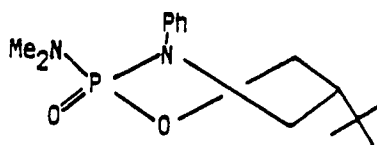
## LIST OF FIGURES

	<u>Page</u>
Figure 1. Computer drawing of 3,9-dimethoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro [5.5]undecane.....	12
Figure 2. Computer drawing of 2-oxo-bis(2- $\beta$ -(chloroethyl) amino)-4,6-dimethyl-1,3,2-oxazaphosphorinane.....	29
Figure 3. $^1\text{H}$ NMR spectrum of methylene group adjacent to nitrogen in initial attempt at protonation of phosphatrane oxide ( <u>20</u> ).....	49
Figure 4. $^1\text{H}$ NMR spectrum of monoprotinated phosphatrane oxide ( <u>20</u> ).....	53
Figure 5. $^1\text{H}$ NMR spectrum of diprotinated phosphatrane oxide ( <u>20</u> ).....	55
Figure 6. $^{31}\text{P}$ NMR spectrum of phosphatrane sulfide as a function of temperature.....	60
Figure 7. Plot of $^{31}\text{P}$ chemical shift versus the $^{17}\text{O}$ chemical shift of the phosphoryl oxygen of phosphates.....	110
Figure 8. Plot of $^{17}\text{O}$ chemical shift of the phosphoryl oxygen of phosphates versus $^1\text{J}_{\text{PSe}}$ of the corresponding selenophosphates.....	114
Figure 9. Plot of $^{31}\text{P}$ chemical shift of cyclic phosphates against $^1\text{J}_{\text{PSe}}$ of the corresponding selenophosphates.....	116

Compounds discussed in thesis:

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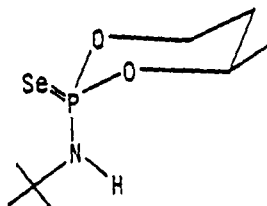
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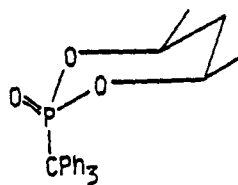


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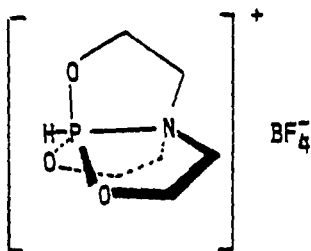
16



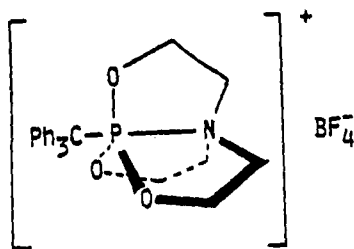
17

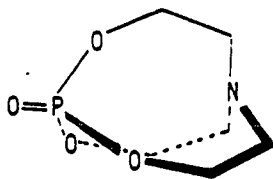
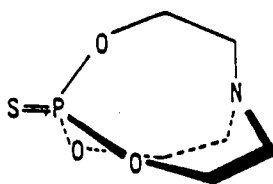
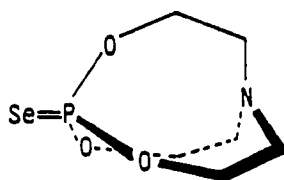
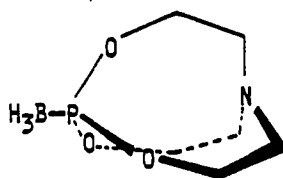
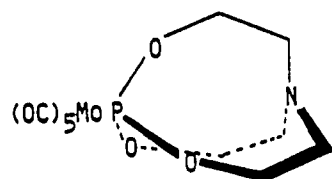


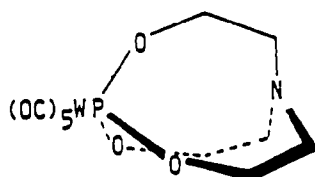
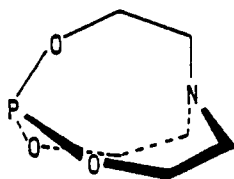
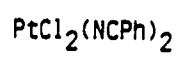
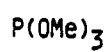
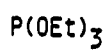
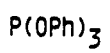
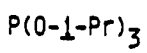
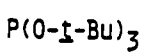
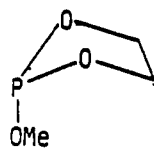
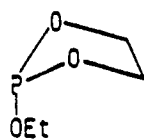
18

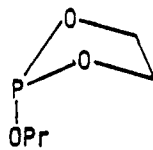
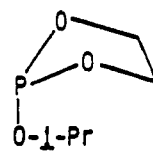
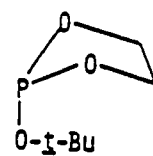
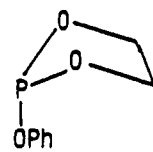
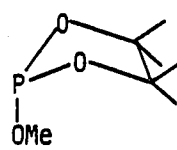
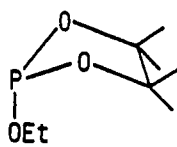


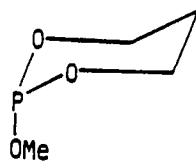
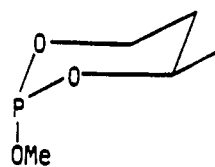
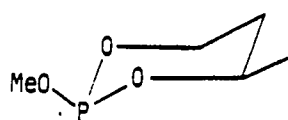
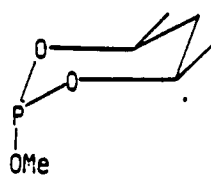
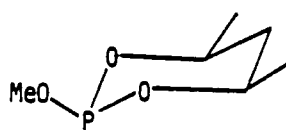
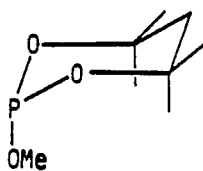
19



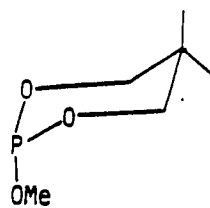
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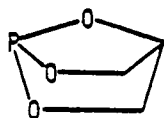
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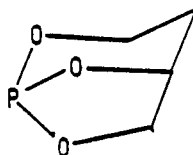
45



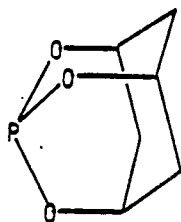
46



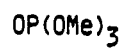
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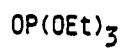
48



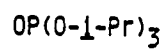
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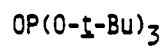
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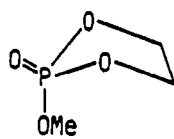
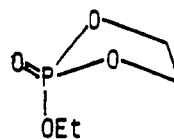
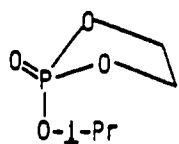
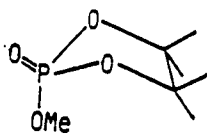
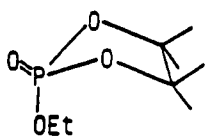
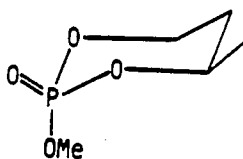


51



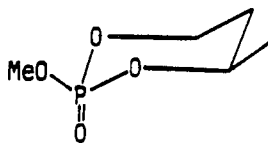
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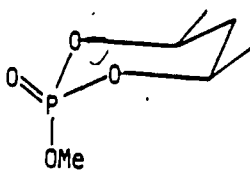
535455565758a

xvii

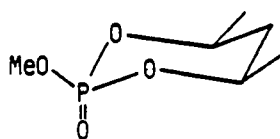
58b



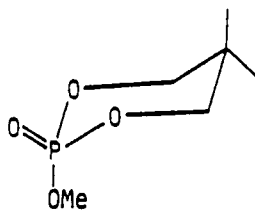
59a



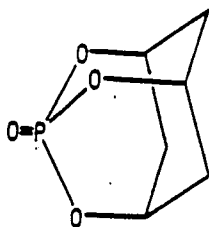
59b



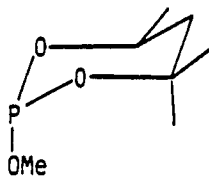
60



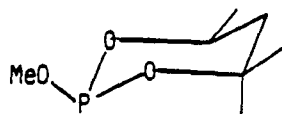
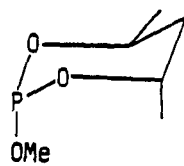
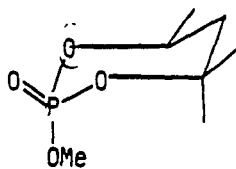
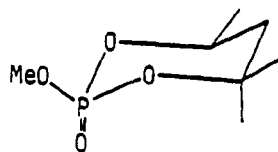
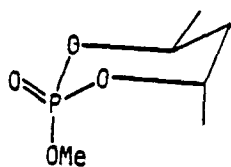
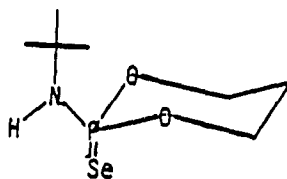
61

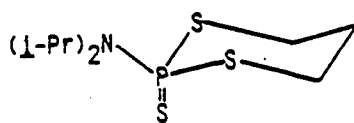
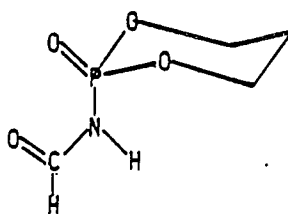


62a





62b6364a64b6566

6768

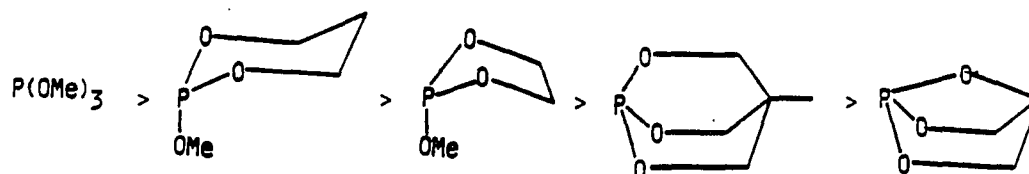
## ABSTRACT

Crystal structure determinations are reported for 3,9-dimethoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5.5]undecane and 2-oxo-2-(bis-( $\beta$ -chloroethyl)amino)-4,6-dimethyl-1,3,2-oxazaphosphorinane. Evidence is presented for transannular bond formation upon protonation of  $OP(OCH_2CH_2)_3N$  and  $SP(OCH_2CH_2)_3N$ . It is also shown that the phosphoryl oxygen or sulfur is diprotonated at high acid to substrate ratios. The  $^{17}O$  NMR data for a series of phosphites and phosphates is correlated with alkyl substitution and ring conformation. A series of unsuccessful attempts to synthesize compounds of the type  $X(OCH_2CH_2)_3P$  ( $X = B, Si, P$ ) are reported. Protonation of  $P(OCH_2CH_2)_3N$  by trialkyloxonium tetrafluoroborate and methyl triflate is investigated to determine the source of the proton.

PART I: CRYSTAL AND MOLECULAR STRUCTURE OF 3,9-DIMETHOXY-2,4,8,10-  
TETRAOXA-3,9-DIPHOSPHA SPIRO[5.5]UNDECANE

## INTRODUCTION

It has been quite well established that phosphite triesters become significantly less basic upon constraint of the esteratic oxygens.



Evidence for this trend has come from  $BH_3$  competition studies,<sup>1</sup> the magnitude of the coupling constant  $^1J_{P-H}$  upon protonation,<sup>2,3</sup> the position of the B-H stretching frequency in borane phosphite adducts,<sup>4</sup> shifts in  $\nu_{OH}$  of phenol due to hydrogen bonding to phosphorus,<sup>5</sup> and CNDO/2 calculations.<sup>3</sup>

The changes in basicity have been attributed to conformational differences among the alkoxy groups and bond angle differences which occur preferentially at the oxygens rather than phosphorus.<sup>6</sup> The changes in bond angle results in a shift in the hybridization of the oxygen from  $sp^2$  towards  $sp^3$ , decreasing the bonding ability of the alkoxy oxygens and lowering the negative charge on phosphorus.<sup>3,6</sup> Constraint can also function to lower the amount of d p bonding by orienting the oxygen p orbital such that it cannot overlap with the available phosphorus d orbitals.<sup>6</sup> Another consequence of constraint is the lowering of repulsive interactions between the p orbital of the esteratic oxygens and

the phosphorus lone pair.<sup>6</sup>

An important premise in these arguments is that the structural parameters determined for the cage phosphite ester 1 render it essentially strainless.<sup>7</sup> The only other structural data for phosphite esters which have been reported are for a related cage compound 2<sup>8</sup> and the strained five-membered ring structure 3<sup>9</sup>. It was important, therefore, to determine the molecular structure of a strainless phosphite ester in order to evaluate more completely our ideas on the origins of basicity changes in these system. Although electron diffraction data on  $P(OEt)_3$  and  $P(OCHCH_2)_3$  have appeared,<sup>10</sup> the derived structural parameters are too crude for comparison with the results available from the X-ray diffraction experiments cited above.

Compound 4 is crystalline at room temperature and this is uncommon for phosphite triesters - especially those which are strain free. Spirodiphosphite 4 is also the P(III) parent compound of P(V) derivatives which function as fire retardants in polymers.<sup>11</sup>

## EXPERIMENTAL

Compound 4 was obtained from Borg Warner Chemicals. A colorless crystal of 4 in the form of a thin hexagonal plate (~0.3 mm x 0.33 mm x 0.1 mm) obtained on sublimation at 76° and 0.01 torr, was mounted in a 0.33 mm Lindemann capillary. The capillary was sealed to prevent hydrolysis by atmospheric moisture. The crystal was found to be monoclinic with  $a = 10.87(4)$ ,  $b = 5.74(1)$ ,  $c = 18.76(7)$  Å and  $\beta = 99.7(6)^\circ$  with four molecules of 4 per unit cell. A density of 1.47 g/cm<sup>3</sup> was computed based on a cell volume of 1153.8 Å<sup>3</sup>. Systematic absences (hk1:  $h + k = 2n + 1$ ; h01:  $l = 2n + 1$ ) indicated space group  $C_{2/c}$  which was confirmed by subsequent solution and refinement of the structure.

Using an automated four-circle diffractometer, designed and built in the Ames Laboratory equipped with a scintillation counter and interfaced to a PDP-15 computer, data were collected at room temperature with graphite monochromated Mo  $K_\alpha$  radiation ( $\lambda = 0.70954$  Å) employing a procedure described previously.<sup>12</sup> Six octants were examined within a sphere of  $2\theta < 50^\circ$  yielding 3665 measured intensities. There was no significant crystal decomposition as judged by repeated measurements of three standard reflections. Corrections for Lorentz-polarization effects and averaging of equivalent data yielded 744 observed reflections ( $F_o \geq 3 \sigma(F_o)$ ). Lattice constants were obtained by a least squares refinement of the precise  $\pm 2\theta$  ( $|2\theta| > 25^\circ$ ) measurements of 12 strong independent reflections.

The program MULTAN<sup>13</sup> was used to locate all of the non-hydrogen

atoms. Isotropic refinement of these positions by full matrix least squares techniques<sup>14</sup> led to a conventional R factor of 0.123 and a weighted R factor of 0.133. Ring hydrogen positions were calculated and the hydrogen positions for the terminal methyl groups were obtained from an electron density difference map. Anisotropic refinement then gave a conventional R factor of 0.077 and a weighted  $R_w$  factor of 0.090. The calculated and observed structure factors, final atomic and positional parameters, final thermal parameters and intermolecular bond distances and angles appear in Tables 1, 2, 3 and 4, respectively.



Table 1

Calculated and observed structure factors for 3,9-dimethoxy-2,4,8,10-tetraoxa-3,9-diphospha-spiro[5.5]undecane

h k l		FO		FC		h l		FO		FC		h l		FO		FC	
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
-12	0	11	10	0	12	25	27	-11	9	10	11	-3	16	35	37	0	0
-12	0	0	7	0	10	133	130	-9	1	64	62	-3	18	20	22	0	0
-10	2	63	61	0	15	6	0	-9	2	15	14	-3	19	14	16	0	0
-10	4	10	9	0	16	56	56	-9	3	61	57	-3	20	0	0	0	0
-10	6	20	24	0	18	33	33	-9	5	30	36	-1	1	129	142	0	0
-10	8	30	30	0	20	15	16	-9	7	6	6	-1	2	29	30	0	0
-10	10	15	13	1	0	150	160	-9	9	82	98	-1	3	177	190	0	0
-10	12	23	22	2	2	304	351	-9	10	12	14	-1	4	74	76	0	0
-10	14	15	15	2	4	134	132	-9	13	20	10	-1	5	62	63	0	0
-10	16	25	25	2	6	59	68	-9	14	0	15	-1	6	16	16	0	0
-8	1	53	0	2	0	100	101	-9	15	22	22	-1	7	195	202	0	0
-8	2	171	168	2	10	58	55	-9	17	21	19	-1	0	42	30	0	0
-8	4	71	63	2	12	69	64	-7	2	44	15	-1	0	42	50	0	0
-8	6	67	61	2	14	43	41	-7	3	111	104	-1	10	17	12	7	0
-8	7	4	0	2	16	47	45	-7	4	6	6	-1	11	32	31	7	1
-8	10	52	51	2	18	5	7	-7	5	22	10	-1	12	43	44	7	2
-8	12	13	16	2	20	5	7	-7	6	14	14	-1	13	93	97	7	3
-8	14	25	23	4	0	4	6	-7	7	45	46	-1	14	17	17	7	0
-8	16	41	39	4	2	60	62	-7	8	5	3	-1	15	31	31	7	0
-8	18	20	27	4	4	30	21	-7	9	29	27	-1	16	10	12	7	7
-6	1	3	0	4	4	45	51	-7	11	41	40	-1	17	32	30	7	0
-6	2	17	19	4	12	58	59	-7	12	20	19	-1	21	21	21	7	10
-6	4	110	113	4	14	4	11	-7	13	27	29	1	0	96	101	7	11
-6	6	4	7	4	16	21	19	-7	14	11	12	1	1	293	326	7	14
-6	8	22	22	4	18	22	22	-7	15	6	6	1	2	37	38	7	16
-6	10	24	26	4	0	52	51	-7	17	32	30	1	3	12	14	9	0
-6	12	14	12	4	2	15	12	-5	1	73	79	1	4	154	144	9	1
-6	14	33	32	4	4	7	0	-5	2	67	67	1	5	77	78	9	2
-6	16	26	25	6	4	63	41	-5	4	49	45	1	6	4	7	5	0
-4	2	40	43	6	10	55	53	-5	5	26	27	1	7	161	156	9	6
-4	4	50	56	6	12	0	0	-5	6	28	32	1	0	36	37	9	7
-4	6	26	24	6	14	14	20	-5	7	18	21	1	0	95	79	9	9
-4	8	41	41	6	16	15	15	-5	8	16	15	1	10	30	34	9	11
-4	10	14	15	8	0	15	17	-5	10	4	7	1	11	96	92	11	0
-4	14	50	49	8	2	50	47	-5	11	22	21	1	12	11	11	3	9
-4	16	5	6	8	4	76	73	-5	12	31	29	1	13	13	13	11	4
-4	18	14	12	4	6	16	17	-5	13	10	10	1	15	70	72	11	5
-4	20	5	7	8	8	47	47	-5	14	35	35	1	16	20	17	11	7
-4	22	9	10	8	10	14	17	-5	15	34	31	1	19	13	13	11	7
-2	2	67	62	8	12	57	55	-5	16	37	37	1	20	7	12	11	7
-2	4	40	46	8	14	5	9	-5	17	5	0	1	21	20	19	11	7
-2	6	37	34	10	0	43	43	-5	18	4	5	3	0	64	60	-12	3
-2	8	10	10	10	2	30	31	-5	21	10	11	3	1	42	44	-12	4
-2	10	67	69	10	4	4	6	-3	1	110	111	3	2	77	69	-12	5
-2	12	97	92	10	6	41	40	-3	2	251	274	3	4	5	7	-12	7
-2	14	14	14	10	8	13	15	-1	1	96	90	3	5	43	46	-12	8
-2	16	36	37	10	10	7	13	-3	4	12	0	3	6	17	17	-10	2
-2	20	17	16	12	2	13	12	-3	3	45	47	3	7	39	34	-10	3
-2	22	6	10					-3	6	40	50	3	8	27	20	-10	4
0	2	120	122					-3	7	13	15	3	9	30	37	-10	6
0	4	205	216					-3	8	3	1	3	10	15	15	-10	7
0	5	4	0	-11	1	23	22	3	4	27	20	3	11	40	47	-10	8
0	6	133	139	-11	2	5	9	-3	10	19	14	3	12	46	47	-10	10
0	7	5	0	-11	3	5	6	-3	11	50	46	3	13	33	33	-10	12
0	8	95	93	-11	4	27	25	-3	12	27	20	3	14	42	40	-10	15
0	9	6	0	-11	5	22	20	-3	13	20	20	3	15	27	25	-8	1

Table 1 (Continued)

6 2	33	29	-5 6	25	27	3 5	135	124	-6 14	5	7	4 1	10	11	1 7	6	7
6 3	6	6	-5 7	87	87	3 6	90	81	-6 15	6	7	4 2	36	35	1 8	65	59
6 4	71	78	-5 8	75	75	3 7	46	47	-4 1	32	33	4 3	12	13	1 9	4	2
6 5	8	6	-5 9	68	69	3 8	25	24	-4 2	43	44	4 4	23	22	1 14	12	14
6 6	42	40	-5 10	5	4	3 9	37	35	-4 4	25	24	4 5	44	42	3 2	15	13
6 7	48	45	-5 11	30	27	3 10	12	11	-4 5	19	19	4 6	86	78	3 3	6	3
6 8	22	20	-5 12	7	8	3 11	14	14	-4 7	35	33	4 7	20	17	3 4	23	22
6 10	30	29	-5 14	21	21	3 12	33	33	-4 8	74	74	4 8	15	16	3 5	8	11
6 11	30	29	-5 15	22	20	3 13	15	17	-4 9	26	25	4 9	12	14	3 6	14	12
6 12	13	14	-5 16	4	9	3 15	13	15	-4 10	30	31	4 10	15	15	3 7	6	8
6 13	6	13	-5 18	9	10	3 16	12	15	-4 11	7	8	4 12	16	19	3 8	10	17
6 14	26	26	-3 1	41	40	5 0	54	52	-4 12	16	16	4 13	10	17	3 10	4	6
6 15	21	19	-3 2	59	58	5 1	10	11	-4 14	7	6	4 14	9	10	3 11	16	14
8 0	24	23	-3 3	12	14	5 2	17	18	-4 15	14	15	6 0	24	25	3 12	10	11
8 1	7	11	-3 5	63	64	5 3	66	63	-4 16	9	12	6 1	10	15	3 13	14	13
8 3	4	1	-3 6	43	43	5 5	46	47	-2 1	10	10	6 2	14	15	5 0	5	7
8 4	44	52	-3 7	12	12	5 6	68	65	-2 2	7	9	6 3	33	38	5 1	17	18
8 5	25	26	-3 8	54	57	5 7	89	88	-2 3	31	31	6 5	10	10	5 2	12	15
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8 10	13	14	-3 12	30	32	5 13	38	29	-2 7	41	43	6 9	5	4	5 7	4	3
8 12	13	14	-3 13	22	21	5 14	22	24	-2 8	20	18	6 1	19	19	6 9	4	7
10 2	15	14	-3 15	20	19	6 16	5	4	-2 9	25	26	6 8	20	33	7 0	13	16
10 4	17	17	-3 16	19	21	7 0	17	19	-2 10	35	33	6 6	11	7	4	26	31
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10 7	6	11	-1 1	7	12	7 6	15	20	-2 12	5	3	10 1	11	12			
10 9	7	8	-1 2	9	7	7 7	21	21	-2 15	6	7						
12 0	5	9	-1 3	14	13	7 8	17	14	-2 16	7	9						
12 1	4	5	-1 5	47	49	7 11	5	10	-2 17	7	10						
			-1 6	9	2	7 12	4	10	0 0	8	11						
			-1 7	22	22	7 13	8	10	0 1	10	10						
			-1 8	10	9	9 3	5	9	0 2	11	8						
			-1 9	17	16	9 5	8	10	0 3	52	47						
			-1 10	23	23	9 8	10	11	0 4	14	15						
			-1 11	12	11	11 0	5	4	0 6	15	13						
			-1 14	20	20	11 1	7	9	0 7	29	31						
			-1 15	4	9	11 2	12	13	0 9	26	27						
			-1 16	7	8	11 3	16	19	0 11	24	23						
			-1 17	8	12				0 12	14	14						
			-1 19	17	16				0 13	4	10						
			1 0	51	50				0 14	4	4						
			1 1	13	10				-10 1	7	10						
			1 3	50	46				0 15	5	7						
			1 4	47	48				0 16	7	10						
			1 4	47	48				0 17	11	13						
			1 5	18	10				2 0	8	13						
			1 6	6	7				-10 3	12	11						
			1 7	46	46				2 3	30	36						
			1 9	4	0				-10 9	24	20						
			1 10	24	23				-8 11	14	17						
			1 12	5	1				-8 13	6	7						
			1 13	28	24				-6 1	10	10						
			1 14	19	19				-6 3	8	7						
			1 15	4	3				-6 4	16	19						
			1 16	5	5				-6 5	13	14						
			1 17	17	17				-6 6	32	30						
			1 18	51	51				-6 7	31	27						
			1 19	65	59				-6 8	27	29						
			1 20	43	43				-6 10	23	23						

Table 2

3,9-Dimethoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro  
[5.5]undecane final atomic and positional parameters

	x	y	z
P	0.5781(2)	0.7894(4)	0.1066(1)
O1	0.4691(4)	0.6085(9)	0.1177(2)
O2	0.6071(5)	0.9147(8)	0.1844(2)
O3	0.7000(4)	0.6220(10)	0.1152(2)
C1	0.4810(6)	0.473(1)	0.1832(4)
C2	0.6166(5)	0.778(1)	0.2500(3)
C3	0.5000	0.6250	0.5000
C4	0.7117(9)	0.468(2)	0.0566(4)
H1-C1	0.3995	0.3735	0.1821
H2-C1	0.5583	0.3606	0.1856
H1-C2	0.6955	0.6696	0.2542
H2-C2	0.6264	0.8911	0.2946
H1-C4	0.6451	0.3351	0.0537
H2-C4	0.6995	0.5624	0.0079
H3-C4	0.8038	0.4034	0.0635

Table 3

3,9-Dimethoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro  
[5.5]undecane final thermal parameters<sup>a</sup>

	$\beta(1,1)$	$\beta(2,2)$	$\beta(3,3)$	$\beta(1,2)$	$\beta(1,3)$	$\beta(2,3)$
P	0.0108(2)	0.0417(7)	0.00346(6)	0.0029(3)	0.00028(7)	0.0010(2)
O1	0.0092(4)	0.048(1)	0.0036(2)	0.0003(7)	-0.0004(2)	-0.0014(4)
O2	0.0129(4)	0.028(1)	0.0040(2)	-0.0018(7)	0.0013(2)	0.0003(4)
O3	0.0101(5)	0.051(2)	0.0036(2)	-0.0046(8)	0.0002(2)	-0.0020(5)
C1	0.0096(6)	0.029(2)	0.0046(3)	-0.002(1)	0.0005(3)	-0.0025(6)
C2	0.0082(6)	0.032(2)	0.0035(2)	-0.0031(9)	0.0001(3)	-0.0007(6)
C3	0.0072(7)	0.024(2)	0.0034(3)	0.0	0.0003(3)	0.0
C4	0.0154(1)	0.078(5)	0.0042(2)	0.012(2)	0.0010(4)	-0.004(1)

<sup>a</sup>The  $\beta_{ij}$  are defined by:  $T = \exp\{-(h^2\beta_{11} + k^2\beta_{22} + l^2\beta_{33} + 2hk\beta_{12} + 2hl\beta_{13} + 2kl\beta_{23})\}$ . The isotropic temperature factors for all hydrogen atoms were set equal to  $3.0\text{\AA}^2$ .

Table 4

3,9-Dimethoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro  
[5.5]undecane intramolecular bond distances and angles

Distances (Å)		Angles (°)	
P-01	1.616(5)	O1-P-02	101.9(3)
P-02	1.611(5)	O1-P-03	102.1(3)
P-03	1.624(5)	O2-P-03	98.2(3)
O1-C1	1.443(8)	P-01-C1	119.6(4)
O2-C2	1.448(7)	P-02-C2	120.2(4)
O3-C4	1.431(10)	P-03-C4	117.8(5)
C1-C2	1.514(7)	O1-C1-C3	111.9(5)
C3-C2	1.543(6)	O2-C2-C3	111.6(4)
		C1-C3-C2	109.1(4)

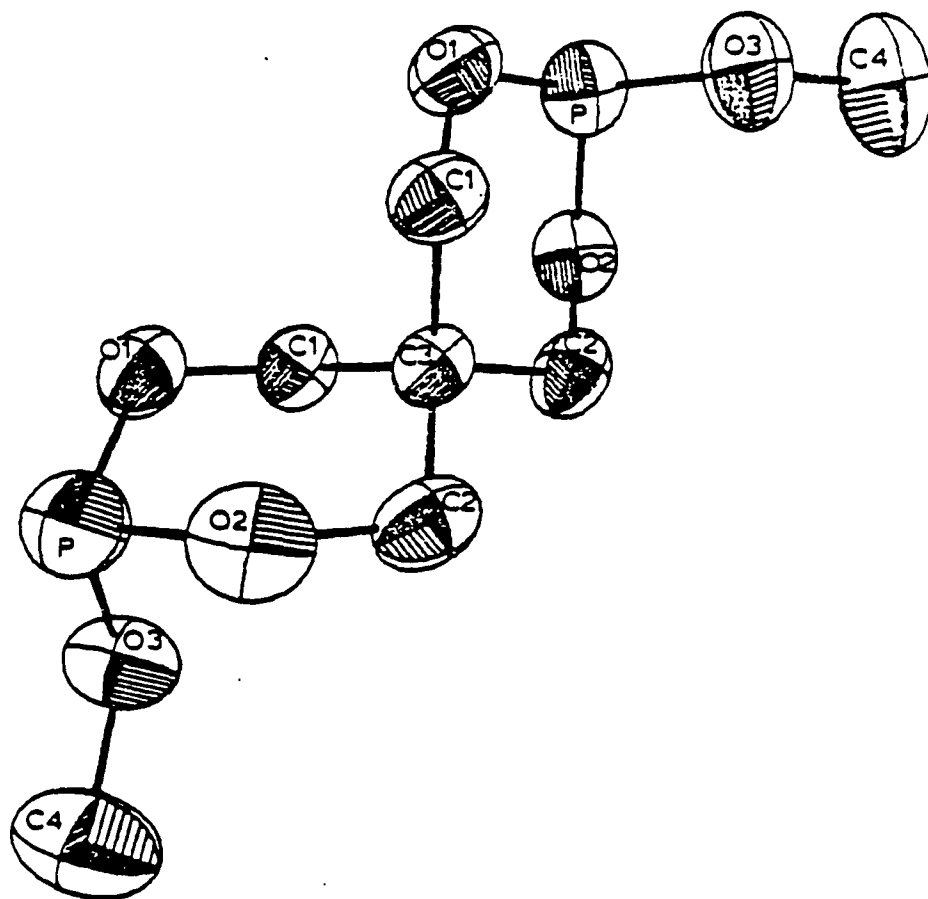
## RESULTS AND DISCUSSION

The computer-drawn<sup>15</sup> structure of 4 stemming from the solution and refinement of the diffraction data is shown in Figure 1. Both methoxy groups are axial in the solid state of 4 as has been suggested from earlier solution NMR studies<sup>16</sup> and more recently from an analysis of dipole moment data of 4 and a monocyclic analog.<sup>17</sup>

From Table 4, the average exocyclic OPO angle in 4 ( $101.1^\circ$ ) compares well with the endocyclic OPO angle of  $101.8^\circ$ . Similarly, the exocyclic POC angle ( $117.8^\circ$ ) is close to the average endocyclic angle of  $119.9^\circ$ . The similarity in these angles and the PO bond lengths ( $1.63 \overset{\circ}{\text{A}}$  average) in 4 with those reported earlier in 1<sup>7</sup> (OPO =  $100.1^\circ$ , POC =  $117.5^\circ$  and PO =  $1.61 \overset{\circ}{\text{A}}$ ) strongly substantiates our earlier conclusion that the bicyclic cage phosphite is essentially strainless.<sup>7</sup>

Oxidation of 5 leads to  $\text{OP}(\text{OCH}_2)_3\text{CMe}$  6 whose structure reveals only a decrease in the POC bond angle ( $115^\circ$ ) compared to acyclic phosphates ( $117\text{-}120^\circ$ ).<sup>7</sup> On the other hand, oxidation of 4 to the diphosphate  $\text{MeO}(\text{O})\text{P}(\text{OCH}_2)_2\text{C}(\text{CH}_2\text{O})_2\text{P}(\text{O})\text{OMe}$  (7) can be expected to proceed without significant strain introduction since the related compound 8 possesses both angles and lengths<sup>18</sup> closely resembling those in acyclic phosphates. Thus, barring steric factors stemming from bulky phosphorus substituents, pentavalent phosphorus derivatives of 4 can reasonably be assumed to be quite strain free.

Figure 1. . Computer drawing of 3,9-dimethoxy-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5.5]undecane





PART II: CRYSTAL AND MOLECULAR STRUCTURE OF 2-OXO-2(BIS-( $\beta$ -CHLOROETHYL)  
AMINO)-4,6-DIMETHYL-1,3,2-OXAZAPHOSPHORINANE

## INTRODUCTION

Phosphamides of the type 9-12 are very effective anti-tumor agents.<sup>19</sup> In order to gain insight into the metabolic pathways taken by these systems, a large number of studies have been directed at understanding their stereochemical behavior in the solid state and in solution.<sup>19-24</sup> As part of the latter investigation on cyclophosphamide 9, White et al. compared several solution spectroscopic properties of 13a and 13b which are rigid analogs of the chair forms of 9.<sup>24</sup>

The protons of both methyl groups couple to the phosphorus in each of the isomers 13a and 13b. This coupling has been shown to be  $1.8 \pm 0.2$  and  $2.5 \pm 0.2$  Hz, respectively.<sup>24</sup> Earlier investigation of 1,3,2-dioxaphosphorinane systems showed that the coupling between phosphorus and equatorial methyl groups in the 4 and 6 positions fell in the range 1.5-3.0 Hz. Methyl groups which were axially oriented showed no coupling.<sup>25</sup>

Both configurational isomers, 13a and 13b, show two bands in the N-H stretching region of the infrared spectrum, a sharp band at high frequency and a broad band at lower frequency.<sup>24</sup> These bands have been assigned to the free and hydrogen bonded N-H stretching mode, respectively.<sup>26</sup> The frequencies of the free N-H stretch differ significantly between the two conformers. Based upon the data from the IR and proton NMR spectra, it appears that each isomer exists in a rigid configuration and that the two differ in the stereochemistry at phosphorus.<sup>24</sup>

Prior NMR studies of isomeric 2-oxo-2-R-cis-4,6-dimethyl-1,3,2-dioxaphosphorinanes have shown that, usually, the isomer with an equatorial R group possesses a greater downfield chemical shift in the  $^{31}\text{P}$  NMR spectrum,<sup>6</sup> and that lower field chemical shifts are associated with the axial methinyl protons in the 4 and 6 positions.<sup>27</sup> The stereochemistry of the two isomers, 13a and 13b, were assigned on this basis.

Further evidence for these stereochemical assignments was provided by a lanthanide induced shift (LIS) study. The results were analyzed using the program PDIGM<sup>28</sup> which moves the europium relative to the substrate and compares observed and calculated LIS values. The program expresses the similarity between the two values in terms of an agreement factor, R, for each europium position. These data supported the above stereochemical assignments.

The IR spectrum of 9 shows two bands for the free N-H stretch. The positions and intensities of these bands imply that there are two configurational isomers present and that the major conformer resembles 13a.<sup>24</sup> The values of  $^3J_{\text{POCH}}$  for 9 are significantly larger than the values of  $^3J_{\text{POCH}}$  for 13a and 13b.<sup>24</sup> Since conformer interconversion is rapid on the NMR time scale and from the dependence of  $^3J_{\text{POCH}}$  on the POCH dihedral angle,<sup>29</sup> one can conclude that the larger values of  $^3J_{\text{POCH}}$  in 9 are due to a weighted average of conformers in the chair form having opposite configurations at phosphorus. If  $J_{\text{POCH},(\text{ax})}$  is taken to be the average of the values for 13a and 13b (2.2Hz) and  $J_{\text{POCH},\text{eq}} = J_{\text{POCH},(\text{A})} + J_{\text{POCH},(\text{B})} - J_{\text{POCH},(\text{ax})}$  (20.2 Hz), a conformer ratio A:B of 6:1 is

obtained for compound 9.<sup>24</sup> If 13a and 13b are taken to represent extreme chair conformers of 9<sup>25</sup> and the methyl groups do not have a significant effect on  $\delta^{31}\text{P}$ , then the  $^{31}\text{P}$  NMR data also imply a conformer ratio of about 6:1 in  $\text{CDCl}_3$ .

The conclusion that compound 9 tends to exist in a chair conformer having an axial P=O group is dependent on the assumption that the stereochemistry at phosphorus in 13a and 13b is as shown. In order to confirm this result, a structural determination of 13b by X-ray diffraction was undertaken.

## EXPERIMENTAL

Compound 13b was prepared as described earlier<sup>24</sup> and recrystallized from ethyl acetate/Skelly B. A crystal (~0.3 mm x 0.1 mm x 0.1 mm) was removed from a cluster of needles and mounted on a glass fiber. The crystal was found to be monoclinic with  $a = 11.11(2)$ ,  $b = 7.808$ ,  $c = 16.88(3)$  Å and  $\beta = 105.3(3)^\circ$  with four molecules per unit cell. A density of  $1.29 \text{ g/cm}^3$  was calculated based on a unit cell volume of  $1413(2)$  Å<sup>3</sup>. Systematic extinctions ( $0k0$ ,  $k = 2n + 1$ ;  $h\ 1$ ,  $h + 1 = 2n + 1$ ) indicated space group  $P2_1/n$  which was confirmed by subsequent solution and refinement of the structure.

Using an automated four-circle diffractometer designed and built in the Ames Laboratory equipped with scintillation counter and interfaced to a PDP-15 computer, data were collected at room temperature with graphite monochromated Mo  $K_\alpha$  radiation ( $\lambda = 0.7095$  Å) employing a procedure previously described.<sup>12</sup> Four octants were examined within a sphere  $2\theta < 45^\circ$  yielding 4284 measured intensities. During data collection, the intensities of three standard reflections were monitored every 75 reflections to check for instrument and crystal stability. Whenever a significant drop in the intensity of one or more reflections was observed, all three of the reflections were relocated and their integrated intensities redetermined. A 25% decay in standard intensities was found when data collection was completed. All intensities were corrected for decay through a least squares fitting of a third order polynomial to the measured standard intensity sum as a function of

reflection count. After decay correction, the corrections for Lorentz-polarization effects and averaging of equivalent data yielded 1359 observed reflections ( $F_o \geq 3\sigma(F_o)$ ). Due to the small size of  $\mu$  ( $5.4 \text{ cm}^{-1}$ ), no absorption correction was deemed necessary. Lattice constants were obtained by a least squares refinement of the precise  $\pm 2\theta$  ( $|2\theta| > 25^\circ$ ) measurements of 12 strong independent reflections.

The program MULTAN<sup>13</sup> was used to locate the position of the phosphorus atom. The remaining non-hydrogen atomic positions were subsequently obtained from electron density maps.<sup>12</sup> Anisotropic refinement of these parameters by full matrix least squares techniques<sup>30</sup> led to a conventional R factor of 0.134 and a weighted  $R_w$  factor of 0.161. The positions of the hydrogen atoms were located from an electron density difference map. Anisotropic refinement then gave a conventional R factor of 0.106 and a weighted  $R_w$  factor of 0.128. Large thermal motion of C1<sub>2</sub> and C<sub>9</sub> precluded achievement of lower R and  $R_w$  values. However, the distance between C1<sub>2</sub> and C<sub>8</sub> is in the expected range and is close to that between C1<sub>1</sub> and C<sub>6</sub>. The calculated and observed structure factors, final atomic and positional parameters, final thermal parameters, intramolecular bond distances and angles, and torsional and interplanar angles appear in Tables 5, 6, 7, 8, and 9, respectively.

Table 5. Calculated and observed structure factors for 2-oxo-2-(bis-( $\beta$ -chloroethyl)amino)-4,6-dimethyl-1,3,2-oxazaphosphorinane

L = -15				7 1 107 127	8 3 107 -109	9 4 171 171	5 3 141 153	4 0 145 160	
H K	FO	FC		7 3 98 79	8 5 118 -135	9 7 114 135	5 8 184 -238	4 -12 139 139	L = -8
1 -3	96 -128			7 7 105 -153	8 6 130 101	10 1 128 134	6 0 634 596	4 -11 169 161	H K
2 4	86 -103				9 1 115 -117	10 3 103 103	6 2 189 185	4 -9 151 134	FO
3 -4	80 109				9 6 74 84	10 5 85 65	6 3 232 218	4 -8 144 -127	FC
4 1	78 -77						6 4 207 -221	4 -6 332 -310	
4 -3	97 105						6 5 131 139	4 -5 94 -73	
4 -2	76 -89						6 8 87 -61	4 -3 347 -360	
8 1	74 -82						6 9 130 -125	4 -2 213 195	
L = -12				0 -11 111 105	11 1 126 -131		7 1 104 -91	4 -1 254 -236	
				0 -10 103 106			7 2 107 -94	5 1 88 -70	
L = -14				0 -9 131 120			7 3 187 -173	5 2 99 -102	
H K	FO	FC		0 -8 93 -88			7 4 121 137	5 4 248 -234	
0 -8	89 97			0 -7 189 214			7 5 204 239	5 3 134 -135	
0 -6	99 110			0 -6 146 -162			8 0 335 340	5 8 190 -198	
0 -4	114 131			0 -4 112 -140			8 1 281 293	6 0 313 300	
0 -3	126 139			0 -3 294 -400			8 2 131 -129	6 1 304 304	
1 -2	91 -83			1 -10 114 -135			8 3 221 243	6 2 134 167	
2 -6	104 121			1 -5 103 -107			8 6 92 -86	6 3 207 216	
2 -3	83 93			1 -2 95 96			8 8 112 -123	6 5 109 82	
3 -7	114 118			1 -1 124 137			8 9 89 -93	6 6 140 -135	
3 -5	127 161			2 0 163 168			9 1 190 217	6 8 157 -167	
3 -2	85 104			2 6 83 -111			9 2 96 -108	7 1 306 288	
3 -1	119 -141			2 -11 103 124			9 4 148 161	7 2 539 -533	
4 -4	103 103			2 -10 131 -146			10 2 167 183	7 3 266 284	
5 1	184 -191			2 -9 90 82			10 3 111 120	7 4 156 -137	
5 3	78 -78			2 -4 190 -214			10 9 83 -100	7 6 90 -81	
6 3	88 86			2 -3 177 -181			11 3 88 98	7 7 178 -180	
6 4	76 -72			2 -1 164 -183			11 4 91 -100	7 8 117 116	
6 5	94 136			3 8 88 -81				7 9 93 -100	
7 1	76 -77			3 -10 79 -58				7 11 120 113	
L = -13				3 -9 98 -120				7 13 75 58	
H K	FO	FC		3 -5 111 -115				8 0 569 -535	
1 9	79 93			3 -4 151 134				8 1 202 202	
1 -10	91 100			3 -3 107 120				8 2 242 237	
1 -7	119 111			3 -1 234 237				8 3 80 88	
1 -6	97 97			4 0 190 -200				8 4 230 229	
1 -5	234 247			4 10 95 -76				8 5 230 -271	
1 -3	97 139			4 11 74 78				8 11 94 -76	
1 -2	163 -198			4 -6 138 129				9 3 89 106	
1 -1	146 -149			4 -5 115 -92				9 4 103 -95	
2 0	122 118			4 -4 206 -239				9 5 232 -241	
2 10	96 92			4 -3 87 -55				9 6 95 -122	
2 -9	85 72			5 1 278 267				9 7 164 -145	
2 -3	207 -222			5 2 107 -118				9 8 110 104	
3 -9	96 92			5 4 102 133				9 10 111 102	
3 -4	83 -90			5 7 112 -127				10 1 139 -154	
4 0	92 97			5 8 88 57				10 2 140 136	
4 4	90 111			6 0 180 196				10 4 95 112	
4 -3	130 -159			6 1 99 -120				10 5 129 -146	
4 -2	89 95			6 3 92 -124				10 6 115 139	
4 -1	148 -160			6 4 87 -94				10 7 92 -70	
5 2	104 194			6 6 107 76				10 8 146 171	
5 4	81 -67			6 8 83 117				10 9 79 100	
5 5	86 -106			7 2 232 -234				11 4 93 -83	
6 0	177 176			7 3 120 137				11 7 107 -102	
6 1	124 126			7 4 80 105				12 2 91 -102	
6 5	113 144			8 1 87 -98				12 4 86 94	
				8 2 118 -134				12 5 94 -106	
								4 -3 277 -248	

Table 5 (Continued)

4 -2 370 -343	1 -6 461 442	6 9 91 86	0 -3 493 460	5 12 123 -139	1 -7 378 383	6 6 143 -160
4 -1 92 91	1 -3 191 -196	6 10 123 -107	0 -4 129 -82	5 13 117 -117	1 -6 257 -226	6 7 104 -121
3 1 471 448	1 -4 132 122	6 11 97 82	0 -3 543 330	6 0 93 88	1 -4 641 -649	6 8 407 -393
3 2 220 -198	1 -3 136 120	6 12 89 -78	0 -2 681 -664	6 1 300 -466	1 -3 526 -439	6 9 96 -96
3 4 159 -142	1 -2 359 331	6 14 87 -88	0 -1 473 -474	6 2 126 -101	2 0 988 1036	6 11 99 -80
3 7 153 -156	1 -1 253 236	7 1 150 -166	1 -16 99 -93	6 3 136 143	2 14 90 -65	6 12 141 147
3 8 133 114	2 0 76 37	7 2 94 70	1 -15 107 -119	6 6 186 -184	2 -13 224 210	6 14 146 181
3 9 210 -213	2 -12 180 -169	7 3 121 101	1 -13 83 -48	6 8 99 -87	2 -12 199 199	7 1 367 357
3 10 163 177	2 -11 98 -68	7 4 93 94	1 -12 198 -182	6 9 169 -187	2 -11 252 244	7 2 347 -368
6 0 448 -434	2 -9 456 -456	7 5 172 137	1 -11 99 -70	6 10 93 -60	2 -9 251 237	7 3 77 69
6 1 134 134	2 -7 140 -144	7 6 183 182	1 -8 81 79	6 14 120 128	2 -8 359 -343	7 4 185 -218
6 2 249 -232	2 -6 83 72	7 7 161 162	1 -7 236 244	7 1 296 -295	2 -7 266 237	7 5 91 -60
6 3 304 -297	2 -4 223 195	7 8 177 -197	1 -6 384 -330	7 2 185 179	2 -6 156 149	7 6 132 143
6 4 98 103	2 -3 113 135	7 9 188 227	1 -5 190 -178	7 11 94 82	2 -5 142 147	7 8 372 375
6 5 388 -356	2 -2 630 -637	7 10 172 -212	1 -4 611 -592	8 0 428 414	2 -4 271 282	7 9 93 -106
6 6 107 67	2 -1 140 131	7 13 81 -62	1 -3 466 449	8 1 161 162	2 -3 502 507	7 10 281 304
6 7 130 124	3 8 80 37	8 0 93 -70	1 -2 456 -491	8 2 146 -143	2 -2 817 811	7 11 86 92
6 10 83 -103	3 -13 89 81	8 1 314 -298	1 0 186 183	8 3 312 291	2 -1 463 -467	7 12 176 210
6 14 78 -60	3 -12 148 -136	8 2 194 -186	2 0 137 143	8 4 226 -216	3 -13 86 94	7 13 84 67
7 1 213 207	3 -10 393 -347	8 3 88 106	2 1 68 69	8 5 285 272	3 -13 112 -119	7 14 92 117
7 4 80 -102	3 -9 193 -160	8 8 133 -148	2 -14 102 -107	8 6 188 -167	3 -12 206 198	8 0 74 -62
7 8 103 -110	3 -7 257 243	9 1 313 -328	2 -13 193 222	8 8 183 -187	3 -10 488 449	8 1 111 107
7 10 132 126	3 -6 106 96	9 2 362 361	2 -12 316 -305	8 9 104 103	3 -9 77 62	8 3 242 -215
8 0 406 -405	3 -5 73 33	9 4 230 245	2 -9 75 75	8 13 78 87	3 -8 154 145	8 5 163 -169
8 1 247 -247	3 -4 117 113	9 5 159 148	2 -8 344 341	8 14 103 131	3 -6 262 247	9 1 171 -144
8 3 208 -198	3 -3 65 90	9 6 96 -117	2 -6 499 492	9 1 220 202	3 -5 477 457	9 2 143 -134
8 4 98 -134	3 -2 233 223	9 10 144 -134	2 -5 1038 989	9 2 113 -88	3 -4 207 -200	9 3 113 99
8 5 220 -230	3 -1 193 204	10 0 418 390	2 -4 203 -177	9 3 151 148	3 -3 482 -443	9 4 440 -402
8 6 184 185	4 0 336 -327	10 1 91 79	2 -3 492 474	9 5 108 -108	3 -2 383 369	9 5 156 -152
8 8 97 90	4 -14 132 -146	10 2 87 47	2 -2 428 -403	9 8 129 103	3 -1 509 -541	9 6 128 134
9 1 107 103	4 -13 127 -112	10 3 188 176	3 -16 75 -50	9 10 84 85	4 0 361 -394	9 7 205 -217
9 2 228 211	4 -12 93 -91	10 4 126 -131	3 -14 113 -112	10 0 377 377	4 -14 156 151	9 8 174 154
9 3 256 -278	4 -11 291 -264	10 5 100 114	3 -11 106 -100	10 2 320 329	4 -12 291 266	9 10 191 215
9 4 93 -80	4 -10 99 118	10 6 288 -300	3 -10 216 218	10 3 125 126	4 -9 237 214	10 0 92 -59
9 7 86 103	4 -9 448 -416	11 3 243 240	3 -8 201 188	10 4 82 -74	4 -8 610 -585	10 1 117 -103
9 8 137 -160	4 -7 147 -144	11 5 123 113	3 -7 460 439	11 1 173 165	4 -7 314 297	10 2 93 -63
10 0 198 148	4 -6 340 322	12 0 83 73	3 -6 380 -338	11 2 225 -223	4 -6 582 -561	10 3 269 -257
10 1 136 -129	4 -5 74 83	12 1 108 122	3 -5 139 143	11 4 342 -348	4 -5 238 -224	10 6 303 323
10 2 88 -74	4 -4 212 200	12 2 87 46	3 -4 710 -663	11 6 124 116	4 -4 277 249	10 7 103 -108
10 3 344 -365	4 -3 136 -123	12 3 149 167	3 -2 609 -588	11 7 86 -78	4 -3 337 -327	10 8 124 137
10 6 155 187	4 -2 381 -371	12 4 112 -139	3 -1 229 -223	11 12 78 109	4 -2 358 344	10 14 79 -123
11 1 198 -201	4 -1 164 -146	12 6 189 -226	4 0 323 320	12 6 87 108	4 -1 73 -36	11 1 116 -120
11 3 101 -113	3 1 73 -70	12 8 78 -37	4 -9 94 70	12 7 78 -101	3 1 280 -290	11 2 173 -182
11 4 113 110	3 2 203 190	13 1 158 143	4 -8 553 520	13 1 262 232	3 2 328 303	11 3 100 -97
11 5 88 73	3 3 173 -156	13 4 142 -163	4 -7 93 34	13 2 198 -205	3 3 438 -392	11 4 193 -194
11 7 92 89	3 4 105 74	14 0 96 84	4 -6 85 -81	13 3 95 -92	3 4 134 -139	11 10 84 -124
11 10 116 -127	3 6 94 -86	14 2 103 87	4 -4 103 -103	13 4 111 -127	3 5 269 -263	12 0 562 -511
12 0 127 -107	3 7 139 161		4 -3 298 289	14 1 137 -163	3 6 168 -147	12 1 89 -49
12 3 80 81	3 8 96 49		4 -2 776 779		3 7 185 -199	12 2 204 -216
13 4 114 127	3 10 132 149		4 -1 493 -484		3 8 219 215	12 4 129 122
	3 12 101 -99		3 1 247 -240		3 9 94 -93	12 6 103 99
	3 13 102 -121		3 2 61 -73		3 12 91 -107	13 2 140 131
L = -7	6 0 363 -367		3 4 418 429		1 -15 107 -176	13 4 160 176
H K FO FC	6 1 112 -86		3 6 157 156		1 -14 100 -91	14 1 106 -115
1 -14 120 129	6 2 249 243		3 8 163 164		1 -13 163 -170	15 1 133 -132
1 -12 104 -95	6 3 97 -98		3 9 213 -122		1 -11 120 -138	15 2 132 143
1 -11 207 211	6 4 98 -81		3 9 121 242		1 -10 218 197	
1 -10 421 -421	6 5 149 -133		3 10 259 -267		1 -9 136 108	
1 -8 290 -275	6 6 229 212		3 11 81 -48		1 -8 378 350	
1 -7 330 -321						



Table 5 (Continued)

L = -4	4 -9 193 -163	10 6 220 216	4-12 95 -78	9 2 428 393	1 -4 286 -267	6 5 118 -106
H K FO FC	4 -8 503 440	10 7 100 -67	4-11 273 -256	9 3 136 146	1 -3 155 144	6 6 463 -470
0 0 2401 2625	4 -7 230 -216	10 10 116 154	4-10 140 -139	9 4 126 144	1 -2 181 258	6 7 248 -244
0-18 93 -103	4 -6 235 239	11 1 237 -208	4 -9 121 -155	9 7 228 218	1 -1 588 -647	6 8 179 -190
0-15 163 -170	4 -5 917 -822	11 2 96 83	4 -7 80 83	9 8 228 -238	2 0 543 -650	6 9 112 -104
0-14 85 83	4 -4 292 -262	11 4 301 306	4 -6 1201 1176	9 9 83 -86	2-14 184 -187	6 11 172 -183
0-13 186 179	4 -3 881 -837	12 0 227 -227	4 -4 119 139	9 10 292 -309	2-10 301 -273	6 12 278 301
0-12 269 268	4 -2 321 -315	12 2 208 -204	4 -2 857 -945	9 12 191 -248	2 -8 249 -230	6 13 196 -255
0 -9 439 407	4 -1 737 759	12 3 102 98	4 -1 274 -288	10 0 192 187	2 -7 228 198	6 14 91 92
0 -8 276 -263	3 1 645 661	12 5 108 -111	3 1 210 -217	10 1 120 74	2 -6 526 474	7 1 95 -86
0 -7 360 -349	3 2 635 -627	12 6 103 -98	3 2 342 353	10 2 231 245	2 -5 476 427	7 2 104 92
0 -6 88 77	3 3 676 663	13 1 101 -77	3 3 316 324	10 3 247 222	2 -4 508 -548	7 3 105 -71
0 -5 212 -203	3 4 429 -416	13 2 273 258	3 4 349 337	10 4 239 -224	2 -3 736 -779	7 4 276 255
0 -4 313 -298	3 5 181 -167	13 4 113 120	3 5 610 605	10 5 145 -124	2 -2 2403 -2694	7 5 68 56
0 -3 390 -369	3 6 123 -126	14 0 266 256	3 6 65 51	10 6 137 -134	2 -1 290 318	7 7 258 256
0 -2 898 831	3 7 110 -101	15 1 118 -130	3 7 371 -356	10 7 85 106	3-18 75 -54	7 8 129 -123
0 -1 319 -313	3 8 407 389		3 8 192 206	10 8 118 -131	3-16 104 -127	7 10 78 -89
1 13 103 66	3 10 183 189	L = -3	3 9 217 211	10 9 171 202	3-14 107 -87	7 11 101 -98
1-16 98 88	3 12 94 94	H K FO FC	3 10 231 -255	10 12 115 128	3-12 118 113	8 0 207 197
1-10 88 51	3 16 115 -136	1-18 79 84	3 11 86 125	11 4 98 103	3-11 114 -111	8 1 117 -113
1 -8 168 -171	6 0 595 -583	1-16 133 157	3 12 163 -169	11 7 119 122	3-10 178 156	8 2 201 206
1 -7 364 -332	6 2 179 -159	1-11 135 120	3 14 99 76	12 0 237 225	3 -9 263 241	8 3 373 371
1 -6 480 457	6 3 757 -749	1-10 326 -295	3 15 96 -139	12 1 90 76	3 -8 158 128	8 4 325 -284
1 -4 725 697	6 4 140 149	1 -9 86 99	6 1 985 963	12 2 93 100	3 -7 477 -459	8 5 186 186
1 -3 218 201	6 5 159 135	1 -8 121 -114	6 3 406 -420	12 3 108 125	3 -6 140 -157	8 6 311 -305
1 -2 473 468	6 6 662 629	1 -7 342 -335	6 4 550 555	12 4 103 -93	3 -5 292 285	8 8 372 -382
1 -1 229 -230	6 8 258 231	1 -6 251 247	6 5 333 -328	12 8 145 -163	3 -4 639 -628	8 14 110 125
2 0 1214 -1340	6 10 173 -174	1 -5 322 -344	6 6 679 662	13 7 91 -92	3 -3 320 -376	9 1 223 203
2-17 86 -81	6 11 106 -116	1 -4 375 399	6 8 418 414	14 0 294 285	3 -2 2123 -2176	9 2 343 -320
2-14 121 128	6 12 188 -177	1 -3 231 266	6 9 74 65	14 2 125 141	3 -1 939 -1019	9 3 120 122
2-13 93 -56	7 1 599 -597	1 -2 586 -483	6 10 219 -220	14 3 80 -74	4 0 926 923	9 7 119 122
2-12 102 89	7 2 78 -53	1 -1 562 -625	6 11 193 175	15 1 93 -91	4-16 100 -127	9 9 99 111
2-11 137 136	7 3 391 366	2 0 547 -601	6 12 134 -158	15 2 252 -264	4-14 111 125	9 10 107 113
2-10 103 -86	7 4 273 257	2-15 146 154	6 13 213 -293	15 6 96 -86	4-13 99 96	9 11 115 -149
2 -8 88 -61	7 6 152 -142	2-14 180 -169	6 14 137 -139		4-12 75 -36	10 0 428 414
2 -6 650 -627	7 7 236 -251	2-13 165 -141	6 15 80 62	L = -2	4-10 111 -111	10 3 115 120
2 -5 481 -444	7 8 164 146	2 -9 321 -330	6 16 98 -110	H K FO FC	4 -7 501 457	10 4 196 202
2 -4 375 -346	7 10 140 172	2 -8 387 354	7 1 191 -190	0 0 1111 -1237	4 -6 227 207	10 5 169 186
2 -3 117 -115	7 12 116 121	2 -7 123 118	7 2 343 328	0-18 114 125	4 -5 152 -161	10 6 184 -201
2 -2 585 589	7 15 85 84	2 -6 296 344	7 3 412 391	0-15 224 223	4 -4 613 -578	10 9 142 -161
2 -1 475 -482	7 16 78 -105	2 -5 136 138	7 4 385 375	0-14 130 -120	4 -3 89 -118	10 10 103 -121
3-16 118 124	8 0 169 -152	2 -4 491 -503	7 5 453 433	0-13 137 -128	4 -2 979 991	10 11 87 97
3-15 111 122	8 1 263 -261	2 -3 459 -450	7 6 192 162	0-12 253 -239	4 -1 1121 -1200	11 1 199 191
3-14 217 201	8 2 144 -159	2 -2 481 413	7 8 434 -426	0-11 136 136	3 2 332 330	11 2 99 -103
3-13 174 171	8 3 132 -146	2 -1 1035 1169	7 9 98 90	0 -9 282 -255	3 3 245 242	11 3 112 120
3-11 77 -60	8 4 275 261	3-14 147 167	7 10 517 -557	0 -8 918 898	3 4 520 539	11 4 178 -173
3-10 287 -273	8 6 300 294	3-12 103 -88	7 11 111 124	0 -6 725 696	3 6 371 -357	11 5 80 86
3 -8 192 -186	8 8 254 261	3-11 81 84	7 12 110 -122	0 -4 917 -888	3 7 181 -179	11 7 89 -100
3 -7 266 -261	8 11 134 187	3-10 88 -78	8 0 326 308	0 -3 895 -941	3 8 255 -238	11 9 176 214
3 -6 910 860	8 12 148 -142	3 -9 197 196	8 1 319 268	0 -2 383 -305	3 9 385 376	11 10 167 190
3 -5 246 -221	8 14 94 -133	3 -7 119 -150	8 2 323 304	0 -1 1177 1347	3 10 423 -407	11 12 101 194
3 -4 1031 1069	9 1 363 -341	3 -6 307 -507	8 4 178 153	1-16 159 -163	3 12 162 -173	12 0 85 81
3 -3 229 186	9 3 99 -109	3 -5 634 596	8 5 142 154	1-11 138 -114	3 13 161 -190	12 1 130 121
3 -2 219 230	9 7 115 -142	3 -4 405 416	8 6 132 120	1-10 96 92	3 14 90 76	12 2 134 136
3 -1 439 -457	9 8 114 -87	3 -3 343 393	8 8 104 -104	1 -9 71 52	3 16 83 69	12 3 163 -150
4 0 316 356	9 10 160 -176	3 -2 981 603	8 9 243 271	1 -8 501 466	6 0 328 319	12 5 131 122
4-13 269 -244	10 0 283 -290	3 -1 431 460	8 11 189 215	1 -7 300 -258	6 1 308 -206	12 7 326 -318
4-11 249 -230	10 1 205 -173	4 0 465 -467	8 12 95 106	1 -6 944 -938	6 2 171 166	12 9 167 -175
4-10 137 -123	10 2 262 -273	4-14 230 -245	8 14 103 -124	1 -5 172 165	6 4 95 -80	12 11 202 -215

Table 5 (Continued)

14 0 182 -162	5 2 128 130	10 6 423 410	4 0 495 524	L = 1	L = 11
14 6 107 87	5 3 184 -186	10 8 176 199	4-16 164 170	H K FO FC	H K FO FC
14 8 126 170	5 4 341 -339	10 11 143 -210	4-14 136 -151	7 6 74 -62	1 1 78 72
15 1 88 -75	5 5 382 -375	10 12 121 -179	4-12 270 244	11 3 81 -51	3 2 84 -52
15 2 151 -143	5 6 75 -59	11 4 94 -85	4-10 357 -323	15 4 99 -93	3 3 78 54
16 0 181 -179	5 7 516 -505	11 5 129 128	4-R 241 246		4 -1 92 70
16 2 94 -94	5 8 290 -264	11 6 105 -99	4 -6 315 314	L = 2	7 2 79 -32
	5 9 76 74	11 8 101 82	4 -4 956 -979	H K FO FC	9 3 74 -62
	5 10 77 81	12 0 515 -503	5 2 292 -316	0 17 96 -83	
L = -1	5 11 78 -79	12 2 186 -180	5 4 209 -230	4 8 64 -26	L = 12
H K FO FC	5 12 137 177	12 3 108 88	5 6 478 454	7 14 78 -105	H K FO FC
1-10 94 -112	5 14 98 -91	12 5 151 -169	5 8 134 157	7 15 83 -136	0 -1 103 139
1-16 236 -245	6 1 191 196	12 6 245 241	5 10 324 352	8 12 93 88	2 -5 91 60
1-13 176 -167	6 2 265 -267	12 7 85 82	5 12 396 423		9 7 69 -68
1-12 84 75	6 3 140 -140	12 8 168 185	6 0 334 -319	L = 3	10 2 76 -88
1 -9 86 70	6 4 1032-1019	13 2 103 80	6 2 58 38	H K FO FC	
1 -7 112 -113	6 5 262 -257	13 4 240 250	6 4 153 -144	9 1 67 -61	L = 13
1 -6 306 -485	6 6 355 -345	13 5 105 102	6 6 313 497		H K FO FC
1 -5 1042-1005	6 7 194 -172	14 1 117 100	6 12 113 -94	L = 4	4 -9 90 69
1 -4 658 -734	6 8 413 -405	14 2 126 -118	7 4 317 301	H K FO FC	
1 -3 1152 1326	6 10 120 -110	14 4 139 -143	7 6 246 -236	2-15 78 46	L = 14
1 -2 1676-1984	6 11 173 -186	14 6 93 71	7 8 239 255	8 5 47 -32	H K FO FC
1 -1 422 -649	6 12 337 374	14 8 90 74	7 10 88 101	9 4 92 -58	3 -8 80 100
2 0 1793 2368	6 16 107 154	15 2 125 111	8 0 453 402		4 0 89 -90
2-14 214 199	7 1 222 -206	16 1 113 133	8 2 475 -412	L = 5	4 2 87 -64
2 -9 185 -156	7 2 331 -334		8 4 487 495	H K FO FC	5 -7 81 -92
2 -8 367 -317	7 3 139 -119	L = 0	8 6 74 75	1 -2 59 -16	4 3 74 72
2 -7 154 170	7 4 333 -347	H K FO FC	8 8 319 324	12 3 82 -67	
2 -6 339 354	7 8 341 339	0-18 111 -136	8 12 228 -252	14 4 86 -80	
2 -5 449 437	7 9 147 -166	0-16 181 -169	9 2 98 -72	15 3 76 78	
2 -4 474 -567	7 10 394 421	0-14 319 315	9 4 214 -215		
2 -3 1097-1129	7 12 221 261	0-12 113 106	9 8 338 -352	L = 6	
2 -2 338 -319	7 13 107 130	0-10 94 84	9 10 217 -250	H K FO FC	
2 -1 133 -80	7 15 84 94	0 -8 181 159	9 12 112 -129	6 12 87 68	
3 15 84 86	7 16 82 -108	0 -6 993 974	10 0 507 -479	14 0 97 -91	
3-14 99 -127	8 0 106 -114	0 -2 594 471	10 2 259 -238	14 2 85 -85	
3-12 320 309	8 1 238 246	1-16 137 159	10 6 339 326		
3-10 405 381	8 2 79 75	1-12 211 197	10 8 139 165	L = 7	
3 -9 488 454	8 3 238 260	1-10 218 186	11 4 370 355	H K FO FC	
3 -8 153 160	8 4 182 -105	1 -8 107 105	11 6 388 409	2 -8 79 -78	
3 -7 221 -213	8 5 195 171	1 -6 185 -179	11 8 341 -407		
3 -6 375 327	8 6 79 -81	1 -4 1350 1409	12 0 209 -187	L = 8	
3 -5 220 -225	8 8 142 160	1 -2 1336 1470	12 2 163 157	H K FO FC	
3 -3 498 513	8 9 77 -78	2 0 1318 1255	12 4 141 -130	1 -6 88 -77	
3 -2 793 -816	8 13 111 103	2-14 333 313	12 6 117 -116	7 2 76 54	
3 -1 720 694	9 1 119 103	2-12 132 89	12 8 98 144	8 2 85 -87	
4 0 1044-1060	9 2 165 -158	2-10 169 -164	12 10 94 -115		
4-16 111 123	9 3 293 251	2 -8 409 -419	13 2 91 86	L = 9	
4-14 272 267	9 4 360 -353	2 -6 146 -120	13 4 267 257	H K FO FC	
4-12 297 279	9 5 205 -210	2 -4 873 -839	13 6 262 298	3 2 75 43	
4-10 249 -226	9 6 137 -150	2 -2 708 736	13 8 123 -139	4-14 90 -95	
4 -9 75 -92	9 7 205 -192	3-18 98 104	14 0 159 165		
4 -8 298 -277	9 8 457 433	3-16 147 159	14 2 245 242	L = 10	
4 -7 135 121	9 10 264 278	3-14 160 129	14 8 92 -134	H K FO FC	
4 -6 947 -921	9 11 104 123	3-12 137 -140	15 2 141 -152	4-13 86 105	
4 -4 780 -858	10 2 239 -230	3-10 481 -642	15 4 218 229	8 3 85 -97	
4 -3 554 -547	10 3 104 -110	3 -8 243 250		9 10 78 85	
4 -2 136 112	10 4 193 179	3 -6 403 -406		10 0 98 99	
4 -1 273 300	10 5 280 -286	3 -4 1307 1343			
5 1 333 -321					

Table 6

2-Oxo-2-(bis-( $\beta$ -chloroethyl)amino)-4,6-dimethyl-  
1,3,2-oxaza-phosphorinane  
final atomic and positional parameters

	x	y	z
C1 <sub>1</sub>	0.0509(3)	0.2555(4)	0.4654(2)
C1 <sub>2</sub>	-0.1697(5)	0.8356(8)	0.2653(5)
P <sup>2</sup>	0.1017(2)	0.5531(2)	0.2006(1)
N1	0.0604(6)	0.5866(8)	0.2866(4)
N2	0.1039(6)	0.3482(8)	0.1855(4)
O1	0.2185(5)	0.6442(8)	0.2017(3)
O2	-0.0050(5)	0.6227(6)	0.1267(3)
C1	-0.1224(8)	0.525(1)	0.1055(6)
C2	-0.0081(8)	0.250(1)	0.1424(5)
C3	-0.0953(9)	0.353(1)	0.0763(5)
C4	-0.2102(9)	0.629(1)	0.0393(7)
C5	0.041(1)	0.083(1)	0.1092(6)
C6	0.016(1)	0.455(1)	0.3365(6)
C7	0.117(1)	0.394(1)	0.4015(7)
C8	0.074(1)	0.762(1)	0.3239(7)
C9	-0.027(2)	0.867(2)	0.309(1)
H-C <sub>1</sub>	-0.1562	0.5343	0.164
H-C <sub>2</sub>	-0.0468	0.2156	0.180
H1-C <sub>3</sub>	-0.0312	0.3562	0.022
H2-C <sub>3</sub>	-0.1562	0.2655	0.039
H1-C <sub>4</sub>	-0.2406	0.7656	0.063
H2-C <sub>4</sub>	0.8310	0.6560	-0.028
H3-C <sub>4</sub>	0.7029	0.5940	0.023
H1-C <sub>5</sub>	0.1090	0.0310	0.164
H2-C <sub>5</sub>	-0.0218	0.0053	0.071
H3-C <sub>5</sub>	0.0000	0.1090	0.094
H1-C <sub>6</sub>	-0.0781	0.5156	0.352
H2-C <sub>6</sub>	-0.0156	0.3906	0.297
H1-C <sub>7</sub>	0.1406	0.5187	0.438
H1-C <sub>8</sub>	0.1093	0.8281	0.273
H1-C <sub>9</sub>	-0.0937	1.0031	0.320
H-N <sub>2</sub>	0.156	0.328	0.219

Table 7

2-Oxo-2-(bis-( $\beta$ -chloroethyl)amino)-4,6-dimethyl-  
1,3,2-oxaza-phosphorinane  
final thermal parameters<sup>a</sup>

	$\beta(1,1)$	$\beta(2,2)$	$\beta(3,3)$	$\beta(1,2)$	$\beta(1,3)$	$\beta(2,3)$
C11	0.0253(5)	0.048(1)	0.0081(1)	0.0063(5)	0.0061(2)	0.0084(3)
C12	0.0262(7)	0.077(2)	0.0291(7)	0.015(1)	0.0066(6)	-0.016(1)
P	0.0112(2)	0.0174(4)	0.0042(1)	-0.0005(2)	0.0012(1)	-0.0002(1)
N1	0.0149(8)	0.019(1)	0.0051(3)	-0.0022(9)	0.0039(4)	-0.0007(5)
N2	0.0112(7)	0.016(1)	0.0048(3)	-0.0015(8)	0.0014(4)	-0.0016(5)
O1	0.0104(6)	0.027(1)	0.0064(3)	-0.0052(8)	0.0018(3)	-0.0019(5)
O2	0.0116(6)	0.020(1)	0.0053(2)	-0.0002(7)	0.0001(3)	0.0018(4)
C1	0.010(1)	0.032(2)	0.0055(4)	-0.002(1)	-0.0002(5)	0.0022(9)
C2	0.015(1)	0.020(1)	0.0045(4)	-0.003(1)	0.0029(6)	-0.0012(7)
C3	0.014(1)	0.026(2)	0.0043(4)	-0.004(1)	-0.0000(5)	0.0006(8)
C4	0.010(1)	0.039(3)	0.0088(7)	0.000(1)	-0.0001(7)	0.005(1)
C5	0.024(1)	0.024(2)	0.0072(6)	-0.003(1)	-0.0004(8)	-0.0054(9)
C6	0.017(1)	0.030(2)	0.0055(5)	-0.000(1)	0.0015(7)	-0.0021(9)
C7	0.019(1)	0.037(3)	0.0063(5)	0.001(1)	0.0015(8)	0.001(1)
C8	0.023(1)	0.024(2)	0.0096(7)	-0.001(1)	0.006(1)	0.001(1)
C9	0.053(3)	0.041(4)	0.022(2)	0.003(3)	-0.004(2)	-0.006(2)

<sup>a</sup>The  $\beta_{ij}$  are defined by:  $T = \{ \exp [ - ( h^2 \beta_{11} + k^2 \beta_{22} + l^2 \beta_{33} + 2hk \beta_{12} + 2hl \beta_{13} + 2kl \beta_{23} ) ] \}$ . The isotropic temperature factors for all hydrogen atoms were set equal to 5.0 Å<sup>2</sup>.

Table 8

2-Oxo-2(bis-( $\beta$ -chloroethyl)amino)-4,6-dimethyl-  
1,3,2-oxaza-phosphorinane  
intramolecular bond distances (Å) and angles ( $^{\circ}$ )

P-O <sub>1</sub>	1.475(6)	C <sub>6</sub> -H <sub>1</sub> C <sub>6</sub>	1.23
P-O <sub>2</sub>	1.573(7)	C <sub>6</sub> -H <sub>2</sub> C <sub>6</sub>	0.84
P-N <sub>1</sub>	1.654(8)	C <sub>7</sub> -H <sub>1</sub> C <sub>7</sub>	1.14
P-N <sub>2</sub>	1.621(9)	C <sub>8</sub> -H <sub>1</sub> C <sub>8</sub>	1.15
N <sub>2</sub> -C <sub>2</sub>	1.48(1)	C <sub>9</sub> -H <sub>1</sub> C <sub>9</sub>	1.33
O <sub>2</sub> -C <sub>1</sub>	1.47(1)	O <sub>1</sub> -P-O <sub>2</sub>	108.63(37)
C <sub>1</sub> -C <sub>3</sub>	1.48(1)	O <sub>1</sub> -P-N <sub>2</sub>	115.35(39)
C <sub>1</sub> C <sub>4</sub>	1.51(1)	O <sub>1</sub> -P-N <sub>1</sub>	111.05(39)
C <sub>2</sub> -C <sub>3</sub>	1.50(1)	N <sub>1</sub> -P-N <sub>2</sub>	108.25(35)
C <sub>2</sub> -C <sub>5</sub>	1.57(1)	N <sub>1</sub> -P-O <sub>2</sub>	108.39(36)
N <sub>1</sub> -C <sub>6</sub>	1.49(1)	N <sub>2</sub> -P-O <sub>2</sub>	104.82(31)
N <sub>1</sub> -C <sub>8</sub>	1.50(1)	P-N <sub>1</sub> -C <sub>6</sub>	126.55(58)
C <sub>6</sub> -C <sub>7</sub>	1.43(1)	P-N <sub>1</sub> -C <sub>8</sub>	119.51(65)
C <sub>8</sub> -C <sub>9</sub>	1.35(2)	P-N <sub>2</sub> -C <sub>2</sub>	122.91(53)
C <sub>7</sub> -C <sub>11</sub>	1.81(1)	P-O <sub>2</sub> -C <sub>1</sub>	116.59(52)
C <sub>9</sub> -C <sub>12</sub>	1.58(2)	N <sub>2</sub> -C <sub>2</sub> -C <sub>3</sub>	112.41(70)
		N <sub>2</sub> -C <sub>2</sub> -C <sub>5</sub>	106.22(72)
		O <sub>2</sub> -C <sub>1</sub> -C <sub>3</sub>	107.74(75)
		O <sub>2</sub> -C <sub>1</sub> -C <sub>4</sub>	105.00(71)
		C <sub>1</sub> -C <sub>3</sub> -C <sub>2</sub>	112.59(70)
		C <sub>5</sub> -C <sub>2</sub> -C <sub>3</sub>	113.29(71)
		C <sub>4</sub> -C <sub>1</sub> -C <sub>3</sub>	112.80(77)
		C <sub>6</sub> -N <sub>1</sub> -C <sub>8</sub>	113.83(78)
		N <sub>1</sub> -C <sub>6</sub> -C <sub>7</sub>	110.70(86)
		N <sub>1</sub> -C <sub>8</sub> -C <sub>9</sub>	119.16(1.01)
		C <sub>6</sub> -C <sub>7</sub> -C <sub>11</sub>	107.24(80)
		C <sub>8</sub> -C <sub>9</sub> -C <sub>12</sub>	132.08(1.22)

Table 9

2-Oxo-2-(bis-( $\beta$ -chloroethyl)amino)-4,6-dimethyl-  
1,3,2-oxaza-phosphorinane  
torsional<sup>a</sup> and interplanar angles ( $^{\circ}$ )

$O_1-P-N_2-C_1$	-148.4	$O_2-P-N_2$ to $C_1-O_2-N_2-C_2$	31.8
$O_1-P-O_2-C_1$	168.4	$C_1-C_3-C_2$ to $C_1-O_2-N_2-C_2$	51.9
$P-N_2-C_2-C_3$	32.8	$O_2-N_2-C_2$ to $C_1-O_2-N_2$	14.9
$P-O_2-C_1-C_3$	-64.9	$O_2-N_2-C_2$ to $C_1-O_2-N_2-C_2$	8.7
$C_6-N_1-P-N_2$	-7.8	$C_2-N_2-O_2$ to $C_1-O_2-N_2-C_2$	8.6
$C_6-N_1-P-O_2$	105.6	$O_2-P-N_2$ to $O_2-N_2-C_2$	24.3
$C_8-N_1-P-N_2$	168.5	$O_2-P-N_2$ to $C_2-N_2-O_2$	39.0
$C_8-N_1-P-O_2$	-78.4		

<sup>a</sup>The angle a-b-c-d is positive when the angle is clockwise as viewed down the b to c axis and minus when this angle is counterclockwise.

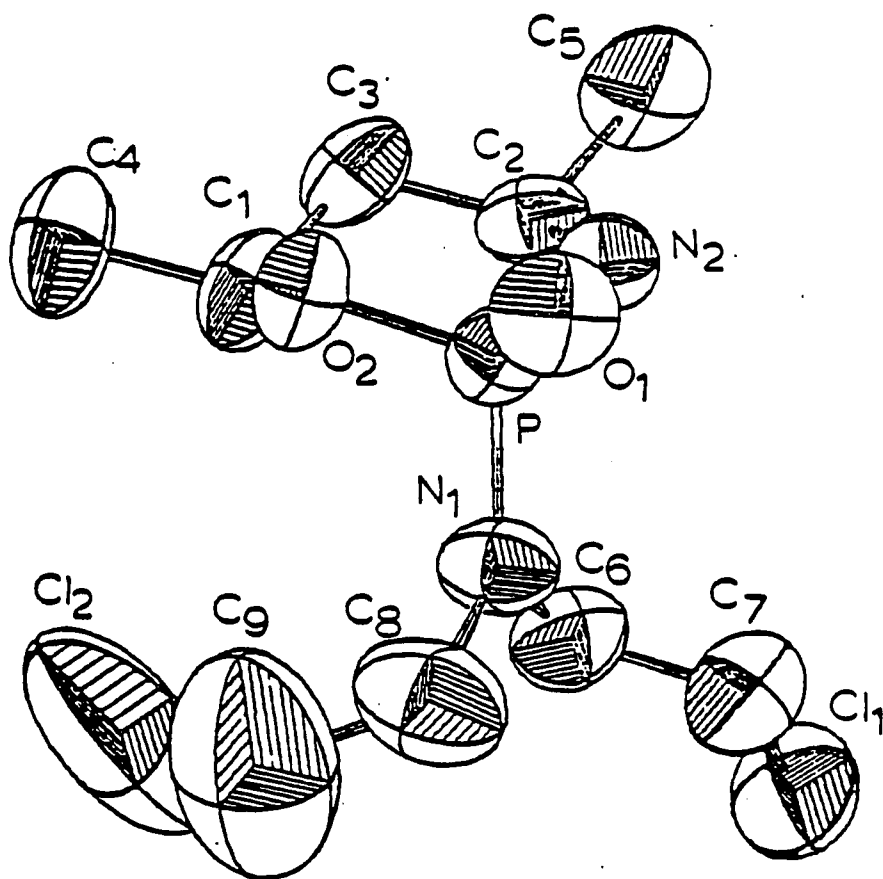
## RESULTS AND DISCUSSION

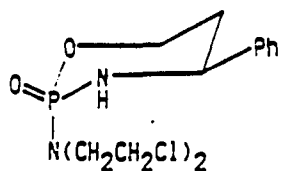
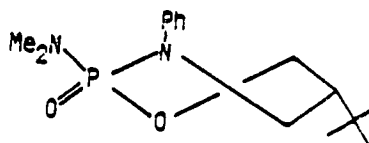
From Figure 2 it is seen that the solid phase structure 13b possesses the same stereochemistry as that assigned to it on the basis of solution studies.<sup>24</sup> In 2-R-2-oxo-1,3,2-dioxaphosphorinane systems there is a marked tendency for configurations with equatorial dialkylamino groups to dominate in solution, whereas this tendency is less pronounced where R is an alkylamino function.<sup>19</sup> These observations are reflected in the solid phase for R = piperidino and anilino which are found to be equatorial and axial, respectively.<sup>19</sup> In 2-R-2-oxo-1,3,2-oxazaphosphorinanes, the situation is not quite as straightforward. The proclivity of the  $(\text{ClCH}_2\text{CH}_2)_2\text{N}$  group in 9 to be equatorial in solution<sup>24</sup> is realized in the solid phase structure.<sup>19</sup> The similarity of 11 to 9 coupled with the finding that the  $(\text{ClCH}_2\text{CH}_2)_2\text{N}$  group is equatorial in the solid phase for 11<sup>19</sup> suggests that 11 also exists mainly in this configuration in solution. Unexpectedly, however, the  $\text{ClCH}_2\text{CH}_2\text{NH}$  group in racemic 10 is equatorial in the solid phase,<sup>19a</sup> whereas it has recently been found in the X-ray structural determination of the S(-) enantiomer<sup>23</sup> to be axial. Apparently, the predilection of the  $\text{ClCH}_2\text{CH}_2\text{NH}$  group for a particular stereochemistry is not very strong and this is probably also the case in solution.

Biasing the ring with carbon substituents as in 13a, 14 and 15 produces some interesting consequences. The overriding tendency for the methyl, phenyl and t-butyl groups to be equatorial in these compounds forces the  $(\text{ClCH}_2\text{CH}_2)_2\text{N}$  substituent to adopt a relatively unfavorable

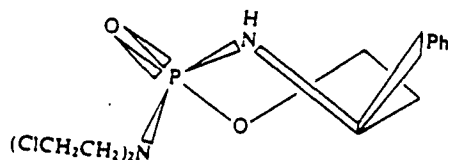
Figure 2. Computer drawing of 2-oxo-bis(2-β-(chloroethyl)amino)-4,6-dimethyl-1,3,2-oxazaphosphorinane





1415

axial stereochemistry in 13b and 14.<sup>31</sup> This problem appears to be alleviated in 15 by the adoption of a twist-boat configuration which allows the Me<sub>2</sub>N group to be pseudo equatorial.<sup>22</sup> Although a similar option appears to exist for 14 as shown below, a twist-boat configuration

14

for 13b would place one methyl group in a sterically unfavorable pseudo axial position.

Forcing bulky phosphorus substituents into the axial position in chair-form phosphorinane rings as in 13b, 14, 16<sup>32</sup> and 17<sup>19</sup> has given rise to two principal compensating conformation changes. In the equatorial position of 9-11, the C<sub>2</sub>N plane of the mustard group is nearly perpendicular to the OPN plane of the ring.<sup>19,33</sup> This phenomenon also occurs in acyclic systems of the type O=PX<sub>2</sub>(NMe<sub>2</sub>).<sup>6</sup> In 13b and 14, the

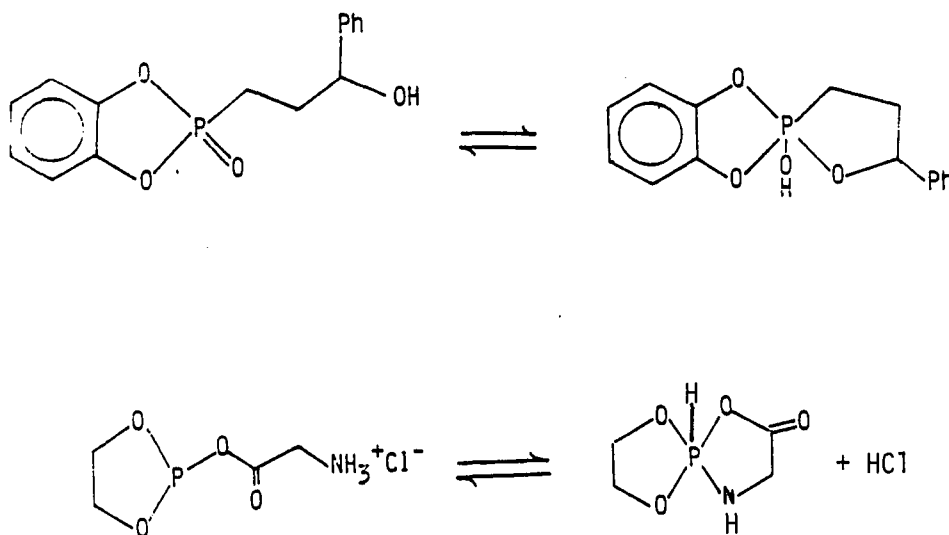
$C_2N$  plane of the mustard group rotates in order to prevent a  $ClCH_2CH_2$  moiety from interacting with axial hydrogens under the ring. The same is true for the HNC plane in 16.<sup>34</sup> In 17 the more bulky  $Ph_3C$  group lacks the proper symmetry to exercise this choice, and instead causes the ring to flatten to a "chaise longue" conformation. Thus, the angle between the OPO and  $(OC)_2$  planes of the ring is  $3.7^\circ$  in 17 whereas in other 2-R-2-oxo-1,3,2-dioxaphosphorinanes where R is non-bulky, this angle ranges from  $33.5$  to  $40^\circ$ .<sup>19</sup> In 13b this angle is about  $32^\circ$ .

The tendency for the exocyclic nitrogen to possess a planar geometry when equatorial in phosphamides is well-documented.<sup>19b</sup> Apparently, this is also the case when the nitrogen substituent is axial as shown from Figure 2 for 13b and as is suggested from the depiction in reference 23 of the structure of the S(-) enantiomer of 10. In both structures, this plane is not perpendicular to the ring OPN plane as is the case when the exocyclic N substituent is equatorial. Thus, in structure 13b the exocyclic  $NC_2$  plane and the PN endocyclic bond make an angle of  $7.8^\circ$  and a similar conformation appears to be adopted by the exocyclic NHC moiety of the S(-) enantiomer of 10 in the solid state.<sup>23</sup> 1,3 syn-diaxial interactions may be too severe in structures such as 13b for stabilization of the electronically favored conformation in which the exocyclic  $NC_2$  plane is perpendicular to the ring NPO plane.

PART III: BICYCLIC TO TRICYCLIC TRANSFORMATIONS IN 1-PHOSPHA-5-AZA-  
2,6,9-TRIOXABICYCLO[3.3.3]UNDECANE SYSTEMS

## INTRODUCTION

Five-coordinate intermediates have often been postulated in the reaction of nucleophiles with tetra-coordinate phosphorus compounds.<sup>35-39</sup> In support of this hypothesis, several examples of equilibria between four and five coordinate phosphorus compounds have been reported,<sup>40-45</sup> for example:



Milbrath and Verkade reported the synthesis of a series of phosphatrane<sup>46</sup> derivatives<sup>47</sup> 18-25. Solution studies of these compounds indicated that 18 and 19, in which the phosphorus is polarized by a positively charged Lewis acid, possessed a tricyclic structure containing a transannular P-N bond, whereas the structure in the chalconide (20-22), the borane 23, and the pentacarbonyl metal complexes, 31 and 32, was a

bicyclic.<sup>47</sup> X-ray structure determinations of 18,<sup>48</sup> 21,<sup>49</sup> and 23<sup>50</sup> confirmed the geometrical assignments. On the basis of CNDO/2 calculations, van Aken and co-workers concluded that protonation of the phosphoryl oxygen of 20 would lead to the formation of a P-N transannular bond.<sup>51</sup> We, on the basis of this result, decided to perform a series of experiments to investigate the conditions that might lead to the formation of a transannular bond in phosphatranes and phosphatrane chalconides.

## EXPERIMENTAL

## Techniques

Materials

All solvents were reagent grade or better. Toluene was purified by refluxing with and distilling from sodium or sodium-potassium alloy. Chloroform and acetonitrile were dried by refluxing with and distilling from  $P_4O_{10}$ . Methylene chloride was dried by refluxing over and distillation from 4A molecular sieves. Acetic anhydride was distilled prior to use.

Triethanolamine was dried by azeotropic distillation with benzene, followed by vacuum distillation of the alcohol. Ethanol was dried by refluxing with and subsequently distilling from magnesium ethoxide. 1,1,1-Tris-(hydroxymethyl)ethane (technical grade) and triphenylcarbinol were both obtained from Aldrich Chemical Company and used as received.

Phosphorus trichloride was distilled just prior to use. Trimethylphosphite was refluxed over and distilled from sodium. Tris-(dimethylamino) phosphine (90+%) was purified by vacuum distillation.

Zinc perchlorate hexahydrate and cobalt perchlorate hexahydrate were obtained from the G. Fredrick Smith Chemical Company and were used as received. Dinitrogen tetroxide was dried by passage through a tube of  $P_4O_{10}$  immediately prior to use. Triethyl orthoformate and boron trifluoride etherate were purchased from Aldrich Chemical Company and used as received. Triply sublimed sulfur (Fisher Chemical Company), potassium superoxide (Alfa Chemical Company), triethylsilane (Petrarch

Systems, Inc.), and 70% perchloric acid (Mallinckrodt) were all used without further purification.

### NMR Spectroscopy

Proton NMR spectra were obtained on either a Varian HA-100 or a Nicolet NT-300 spectrometer. Samples run on the Varian HA-100 instrument contained  $\text{Me}_4\text{Si}$  as an external standard, sealed in a 1 mm capillary tube held coaxially in the sample tube by a Teflon vortex plug. The proton resonance of tetramethylsilane or trifluoroacetic provided the lock signal for the instrument. The Nicolet NT-300 machine was operated in the FT mode while locked on the  $^2\text{H}$  resonance of the deuterated solvent.

$^{13}\text{C}$  NMR spectra were obtained on a JEOL FX90Q spectrometer operating at 22.50 MHz in the FT mode while locked on the  $^2\text{H}$  resonance of the deuterated solvent. The carbon atoms of the solvents were used as references.

$^{31}\text{P}$  NMR spectra were obtained on solutions in 10-mm tubes with a Bruker HX-90 spectrometer operating at 36.434 MHz in the FT mode while locked on the  $^2\text{H}$  resonance of the deuterated solvent. The external standard was 85%  $\text{H}_3\text{PO}_4$  sealed in a 1-mm capillary tube held coaxially in the sample tube by a Teflon vortex plug. For samples run in trifluoroacetic acid, the lock solvent,  $\text{C}_6\text{D}_6$ , was placed in a 5 mm sample tube, held coaxially in the 10 mm tube by two Teflon rings. The  $\text{H}_3\text{PO}_4$ , used as an external standard, was sealed in a 1-mm capillary tube, held coaxially in the 5-mm sample tube by a Teflon vortex plug. The



spectrometer was interfaced with a Nicolet Instruments 1080 minicomputer system.

### Infrared Spectroscopy

Infrared spectra were obtained using a Perkin Elmer 281 double beam spectrophotometer using NaCl optics.

### Visible and Ultraviolet Spectra

Spectra were obtained in the visible and ultraviolet regions on a Beckman DU-8 recording spectrophotometer.

### Sample Preparation

#### Triethylsilyl Perchlorate

This compound was prepared as previously described.<sup>52</sup>

#### 1-Phospha-5-aza-2,6,9-trioxabicyclo[3.3.3]undecane (26)

This compound was prepared by a modification of the method of Milbrath and Verkade.<sup>47</sup> A 1 L. three-necked round bottom flask, equipped with a reflux condenser and two bent adapters with rubber septa, was set up hot from the oven and under a nitrogen flush. A solution of 7.5 g (50 mmole) of  $N(\text{CH}_2\text{CH}_2\text{OH})_3$  in 20 ml  $\text{CHCl}_3$  was diluted to 50 ml with toluene and placed in a 50-ml syringe. Tris(dimethylamino)phosphine (9.0 g, 55 mmole) was dissolved in enough toluene to make 50 ml of solution and

placed in a second 50-ml syringe. The syringes were mounted in a Harvard Apparatus Company dual syringe drive and the needles were inserted through the septa in the bent adaptors. 750 ml of dry toluene were placed in the flask and brought to reflux. The syringe drive was started and the reactants added simultaneously over a 24 hour period. Shorter addition times resulted in a lower yield. Addition times which were much longer than 24 hours resulted in no product being obtained. The trivalent compound could not be isolated, but was derivatized as described below prior to work up.

1-oxo-1-phospha-5-aza-2,6,9-trioxabicyclo[3.3.3]undecane (20)

This compound was prepared and purified by a modification of a literature method.<sup>47</sup> The reaction mixture of 26 was cooled to 45-50°C after which a four-fold molar excess of finely ground K<sub>2</sub>O<sub>2</sub> (14.2 g, 200 mmole) and a catalytic amount of 18-crown-6 ether (0.2 g, 0.75 mmole) was added and the mixture heated to 90-100°C. As the reaction proceeded, gas was evolved. Heating was continued for about 1 hour after gas evolution had ceased.

The mixture was then allowed to cool and was filtered. The filtrate was evaporated on the vacuum line. The resulting yellow viscous oil was taken up in methylene chloride and hexane was added to the cloud point. The beaker was then allowed to stand for 24 to 48 hours during which time crystals of 20 grew on the sides of the beaker and a yellow oil was deposited on the bottom. The yellow oil and remaining solvent were

removed with a Pasteur pipet and the crystals collected. The yellow oil was allowed to stand for an additional 2 to 4 days during which time a second batch of crystals formed in the oil. This mixture was placed on a clay plate to effect separation of the crystals from the very viscous oil. When most of the oil had been absorbed by the clay plate, the crystals were spread out on pieces of filter paper in order to remove the rest of the oil. Further purification was accomplished by recrystallization from a methylene chloride-hexane or chloroform solution cooled to  $-78^{\circ}\text{C}$ . It may also be purified by sublimation at  $120^{\circ}\text{C}$ , 0.1 torr, although a significant amount of material decomposes during sublimation. The overall yield was 7%.

1-Thio-1-phospha-5-aza-2,6,9-trioxabicyclo[3.3.3]-undecane (21)

The reaction mixture of 26 was cooled to  $50-60^{\circ}\text{C}$ , after which, sublimed sulfur (1.8 g, 56 mmole) was added. The mixture was heated to reflux and allowed to cool to room temperature. The mixture was filtered and the filtrate evaporated on the vacuum line. Purification of the resulting yellow oil was accomplished using the same procedure as described for 20. Further purification could be accomplished by recrystallization from a methylene chloride-hexane or acetonitrile-ether solution cooled to  $-78^{\circ}$  or by sublimation at  $125^{\circ}\text{C}$  at 0.1 torr. Once again, a significant amount of material decomposed during sublimation. The yield of the resulting white solid was 6%.

1-Seleno-1-phospha-5-aza-2,8,9-trioxabicyclo[3.3.3]undecane (22)

Red selenium<sup>53</sup> (7.9 g, 100 mmole) was added to a cooled reaction mixture of 26 and the mixture heated to 75-80° for two hours. The product was purified by the procedure described for the other chalconide derivatives, 20 and 21. Again, the white solid produced was recrystallizable from a methylene chloride-hexane solution cooled to -78°.

4-Methyl-2,6,7-trioxa-1-phosphabicyclo 2.2.2 octane (27)

The preparation and purification of this bicyclic phosphite has been described elsewhere.<sup>54</sup>

4-Methyl-2,6,7-trioxa-1-oxo-1-phosphabicyclo[2.2.2]octane (6)

This phosphate was prepared by N<sub>2</sub>O<sub>4</sub> oxidation following "Method B" as described by Cox and Westheimer.<sup>55</sup> The compound was purified by sublimation as previously described.<sup>56</sup>

Adduct of Boron Trifluoride with 1-oxo-1-phospha-5-aza-2,6,9-trioxabicyclo[3.3.3]undecane (20)

Phosphatrane oxide (20) (0.1 g, 0.5 mmole) was dissolved in 3 ml of deuterated acetonitrile. Boron trifluoride etherate (0.07 g, 0.5 mmole) was added via syringe. After <sup>1</sup>H and <sup>31</sup>P NMR spectra were obtained, an additional equivalent of boron trifluoride etherate was added.

Reaction of Triethylsilyl Perchlorate with 1-oxo-1-phospha-5-aza-2,6,9-trioxabicyclo [3.3.3]undecane (20)

Phosphatrane oxide (20) (0.1 g, 0.5 mmole) was dissolved in 3 ml of  $d^3$ -acetonitrile in a 10 mm NMR tube. Triethylsilyl perchlorate (0.1 g, 0.5 mmole) was added via syringe. After obtaining spectral data, an additional 0.1 g of triethylsilyl perchlorate was added. Removal of the solvent on the vacuum line yielded a white solid which proved to be a mixture of the mono and disilylated material. Attempts to separate these products by recrystallization from an acetonitrile-hexane solution proved unsuccessful.

Complex of Triethylphosphate with Cobalt(II) Perchlorate

This complex was made by a modification of the general method of Karayannis et al.<sup>57</sup> Cobalt perchlorate hexahydrate (0.03 g, 0.08 mmole) was heated to 50° in 5 ml of triethyl orthoformate for 1 hour. The solution was then evaporated to dryness on the vacuum line to yield a light pink crystalline material. The solid was then dissolved in 3 ml of nitromethane and 0.1 g of triethylphosphate was added. Addition of the phosphate caused an immediate change in the color of the solution from pink to blue. The nitromethane was then removed in vacuo to yield a deep blue solid.

Complex of 4-Methyl-2,6,7-trioxa-1-oxo-1-phosphabicyclo[2.2.2]octane (6)

with Cobalt(II) Perchlorate

The synthesis of the complex was done in a manner exactly analogous to that just described for the triethylphosphate complex. This material was also obtained as a deep blue solid.

Complex of 1-oxo-1-phospha-5-aza-2,6,9-trioxabicyclo[3.3.3]undecane (20)

with Cobalt(II) Perchlorate

The synthesis of this complex was done in a manner analogous to that used for the triethylphosphate complex (vide supra). Once again a deep blue solid was obtained.

Complex of 1-oxo-1-phospha-5-aza-2,8,9-trioxabicyclo[3.3.3]undecane (20)

with zinc perchlorate

This compound was made using the general method described by Karayannis et al.<sup>57</sup> Zinc perchlorate hexahydrate (0.064 g, 0.17 mmole) was heated to 50° in 5 ml of triethyl orthoformate for 1 hour. Phosphatrane oxide (20) (0.2 g, 1 mmole) was then added. The reaction was stirred for 1 hour and then evaporated to dryness on the vacuum line to yield a pale yellow solid.

Reaction of 1-oxo-1-phospha-5-aza-2,8,9-trioxabicyclo[3.3.3]undecane (20)

with anhydrous phosphoric acid

Phosphatrane oxide (20) (0.1 g, 0.5 mmole) was dissolved in 2 ml of

$d^3$ -acetonitrile. Anhydrous phosphoric acid (0.05 g, 0.5 mmole) was dissolved in 1 ml of  $d^3$ -acetonitrile and added via syringe to the solution of 20. A white solid immediately precipitated from the reaction. A  $^{31}\text{P}$  NMR spectrum of the supernatant indicated that it was devoid of the reactants. The solid was dried on the vacuum line. The solid proved only to be soluble in dimethylsulfoxide.  $^1\text{H}$  and  $^{31}\text{P}$  NMR spectra in this solvent only showed resonances for unreacted 20.

Reaction of 1-oxo-1-phospha-5-aza-2,8,9-trioxabicyclo[3.3.3]undecane (20)  
with antimony pentachloride

Phosphatrane oxide (20) (0.1 g, 0.5 mmole) was dissolved in 3 ml of  $d^3$ -acetonitrile. Antimony pentachloride (.15 g, 0.5 mmole) was added from a syringe, causing a white solid to precipitate immediately. This precipitate proved to be insoluble in a variety of solvents. A violent reaction occurred upon attempting to dissolve the solid in dimethylsulfoxide.

Reaction of 1-oxo-1-phospha-5-aza-2,8,9-trioxabicyclo[3.3.3]undecane (20)  
with phosphorus pentachloride

Phosphatrane oxide (20) (0.1 g, 0.5 mmole) was dissolved in 2 ml of  $d^3$ -acetonitrile. Freshly sublimed phosphorus pentachloride (0.10 g, 0.5 mmole) was dissolved in 1 ml of  $\text{CCl}_4$  and added by syringe to the solution of 20, again causing a white solid to immediately precipitate. This precipitate was also insoluble in a variety of solvents and decomposed on

attempting to dissolve it in dimethylsulfoxide.

cis-Dichlorobis(benzonitrile)platinum(II) (28)

This compound was prepared by the method of Church and Mays.<sup>56</sup>

Attempted synthesis of cis-dichlorobis(1-phospha-5-aza-2,8,9-trioxabicyclo[3.3.3]undecane)platinum(II)

The reaction mixture of 26 was cooled to room temperature and 1.77 g (3.75 mole) of 28 was added. The reaction was stirred for two hours and then filtered. The filtrate was evaporated on the vacuum line and the resulting solid was taken up in methylene chloride. Attempts to separate the monomer by recrystallization from a methylene chloride-hexane solution proved unsuccessful. Thin layer chromatography was used in an attempt to find chromatographic conditions which would permit separation of any monomer that might be present from the polymer, but this was also unsuccessful.

The precipitate from the original reaction was extracted with methylene chloride and the extract evaporated on the vacuum line. The solid which was obtained was subjected to attempts at recrystallization and chromatography as just described, also without success.

Attempted synthesis of tetrakis(1-phospha-5-aza-2,8,9-trioxabicyclo[3.3.3]undecane) silver tetrafluoroborate

To the reaction mixture of 26, which had been cooled to room



temperature, was added  $\text{AgBF}_4$  (0.324 g, 1.66 mmoles) dissolved in 50 ml of dry acetone. The reaction mixture was stirred for 1 hour and filtered. The precipitate was extracted with acetonitrile and the extract evaporated to dryness on the vacuum line. The sticky solid so obtained was dissolved in a minimum of acetonitrile and an attempt was made to recover any monomer that was present by selectively precipitating the polymer with ether. This did not lead to any improvement in the purity of the material, as judged by the  $^1\text{H}$  and  $^{31}\text{P}$  NMR spectra. The original precipitate was then extracted with acetone, and an attempt to obtain the monomer by recrystallization with ether was also unsuccessful. The filtrate from the reaction was evacuated to dryness on the vacuum line. Attempts to obtain the monomer from this solid by recrystallization from acetonitrile/ether and acetone/ether were also unsuccessful.

Attempted synthesis of pentakis(1-phospha-5-aza-2,8,9-trioxabicyclo[3.3.3]undecane) nickel perchlorate

The attempted synthesis of this compound was done by a modification of the procedure described by Coskran and co-workers.<sup>58</sup>  $\text{Ni}(\text{H}_2\text{O})_6(\text{ClO}_4)_2$  (0.548 g, 1.5 mmole) was dissolved in 20 ml of 2,2-dimethoxypropane and the solution was stirred for two hours. This solution was then injected into the room temperature reaction mixture of 26 and stirred for one hour. The reaction mixture was then filtered and the solid extracted with dry acetone. The acetone extract was evaporated to dryness and the solid redissolved in a minimum amount of dry acetone. An attempt to separate out any monomer that might be present by

precipitating out impurities with ether failed. The solid from the original reaction mixture was also extracted with methylene chloride. This extract was treated in a manner similar to that described for the acetone extract, but the  $^1\text{H}$  and  $^{31}\text{P}$  NMR spectra indicated that this also failed to yield any of the desired product. The filtrate from the original reaction mixture was evaporated on the vacuum line and attempts were made to obtain monomer from this solid by recrystallization but also without success.

Attempted synthesis of pentakis(1-phospha-5-aza-2,8,9-trioxabicyclo[3.3.3]undecane) cobalt(I) tetrafluoroborate and hexakis(1-phospha-5-aza-2,8,9-trioxabicyclo 3.3.3 undecane)cobalt (III) tetrafluoroborate

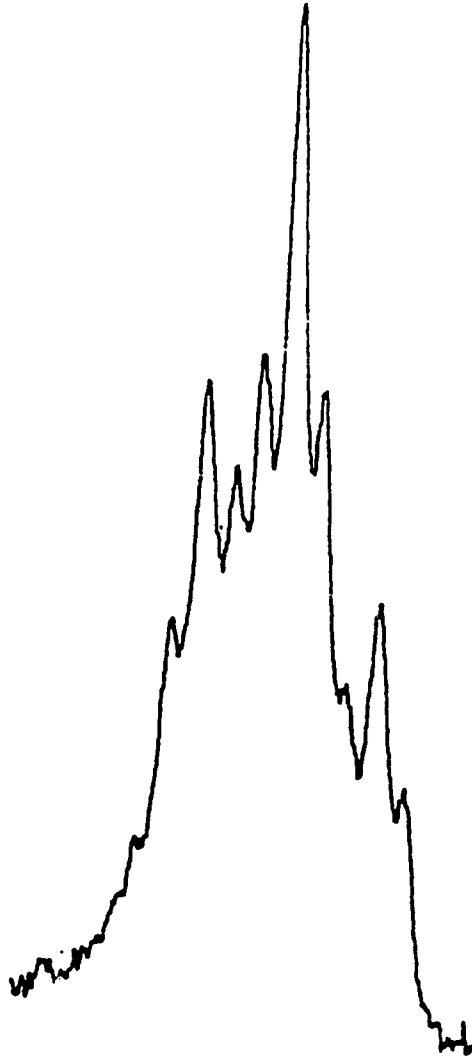
This synthesis was attempted by a modification of the method of Piper and Verkade.<sup>59</sup>  $[\text{Co}(\text{H}_2\text{O})_6] (\text{ClO}_4)_2$  (0.549 g, 1.5 mmole) was dissolved in a solution of 15 ml of acetone and 15 ml of 2,2-dimethoxypropane and stirred for two hours. This solution was then added by syringe to the room temperature reaction mixture of 26 and stirred for 1 hour. The reaction mixture was then filtered and the solid was washed with methylene chloride. The filtrates were combined and evaporated to dryness on the vacuum line. The solid was dissolved in a minimum of methylene chloride and an attempt to obtain monomer by recrystallization from methylene chloride/ether failed to yield any  $[\text{Co}(\underline{33})_5]\text{BF}_4$ . An attempt to obtain  $[\text{Co}(\underline{33})_6](\text{BF}_4)_3$  by recrystallization of the methylene chloride-washed precipitate from the original reaction mixture using acetonitrile/tetrahydrofuran also failed.

## RESULTS AND DISCUSSION

In the initial attempt at protonation, a small amount of phosphatrane oxide (20), was dissolved in trifluoroacetic acid. The proton NMR spectrum of this solution contained the expected doublet of triplets for the methylene group adjacent to the oxygen<sup>47</sup> and a triplet of triplets for the nitrogen methylene group (Figure 3). This splitting pattern for the nitrogen methylene group did not conform to that expected for either the formation or absence of a transannular P-N bond. In the absence of the formation of a transannular bond, one would expect a triplet for the nitrogen methylene group, which is what is observed in all of the bicyclic phosphatranes.<sup>47</sup> If a P-N bond were to form upon protonation of the phosphoryl oxygen, as predicted by van Aken et al.,<sup>51</sup> one would expect to see coupling between these protons and phosphorus, since the four bond coupling would now be reduced to a three bond interaction. This coupling,  ${}^3J_{\text{PNCH}}$ , has been observed in all previous phosphatrane derivatives containing a P-N bond.<sup>47</sup> A rationale for the observed splitting pattern is that formation of the P-N bond permits a phosphorus-hydrogen coupling,  ${}^3J_{\text{PNCH}}$ , which is equivalent to a hydrogen-hydrogen coupling  ${}^5J_{\text{HOPNCH}}$ . Not only did this seem unlikely, this splitting pattern was never reproduced in further protonation experiments.

A second sample of phosphatrane oxide (20) was then dissolved in trifluoroacetic acid in order to obtain  ${}^{31}\text{P}$  NMR spectral data. The  ${}^{31}\text{P}$  NMR spectrum of this sample revealed the presence of two species, both of

Figure 3.  $^1\text{H}$  NMR spectrum of methylene group adjacent to nitrogen in  
initial attempt at protonation of phosphatrane oxide (20)



which displayed signals which were shifted well upfield of phosphatrane oxide (20). The proton NMR spectrum of this sample also indicated the presence of two protonated species, as it contained two overlapping multiplets for the methylene group adjacent to the nitrogen. Therefore, a study in which variation of the acid to substrate ratio was undertaken.

The NMR data for the protonation of phosphatrane oxide (20) at various acid to substrate ratios are collected in Table 10. These results are consistent with two protonations, both of which occur at the phosphoryl oxygen. At the higher concentrations of phosphatrane oxide, the phosphoryl oxygen is protonated, causing the geometry at phosphorus to change from tetrahedral to trigonal bipyramidal by the formation of a phosphorus nitrogen transannular bond. There are two pieces of evidence in the NMR spectra that are consistent with this change in geometry. The first is the appearance of the phosphorus-hydrogen coupling,  ${}^3J_{\text{PNCH}}$ , as explained above (Figure 4). The second is the relatively large upfield chemical shift (-6 ppm) observed upon protonation in this system compared to that observed in the protonation of acyclic phosphates.<sup>60,61</sup> These two previous studies reported a very small change (0-1 ppm) in the  ${}^{31}\text{P}$  NMR chemical shift upon protonation with trifluoroacetic acid.

Increasing the ratio of acid to 20, gives rise to a second protonated species as evidenced by the further upfield shift in the  ${}^{31}\text{P}$  NMR spectrum and the increase in the phosphorus-hydrogen coupling,  ${}^3J_{\text{PNCH}}$ , from 1.8 to 5.5 Hz (Figure 5).

The fact that only two types of methylene protons are seen in the  ${}^1\text{H}$  NMR spectrum supports the conclusion that the second protonation occurs

Table 10

$^1\text{H}$  and  $^{31}\text{P}$  NMR data for the protonation of phosphatrane oxide (20) with trifluoroacetic acid

Conc (M)	$\delta^{31}\text{P}$ (ppm)	Peak Ratio <sup>a</sup>	$\delta\text{OCH}_2$ (ppm)	$^3\text{J}_{\text{POCH}}$ (Hz)	$\delta\text{NCH}_2$ (ppm)	$^3\text{J}_{\text{PNCH}}$ (Hz)	$^3\text{J}_{\text{HCCH}}$ (Hz)
1.08	-13.7 -28.2	8 1	4.79(dt) <sub>b</sub>	17.0 <sub>b</sub>	3.88(td) <sub>b</sub>	1.8 <sub>b</sub>	5.5 <sub>b</sub>
0.65	-13.7 -28.2	4 1	4.79(dt) 4.79(dt)	17.0 17.0	3.88(td) 3.93(m)	1.8 4.5	5.5 5.5
0.54	-13.7 -28.3	3 1	4.79(dt) 4.79(dt)	17.0 17.0	3.88(td) 3.93(m)	1.8 4.5	5.5 5.5
0.27	-13.7 -28.3	1 1	4.79 4.79	17.0 17.0	<sub>c</sub> <sub>c</sub>	<sub>c</sub> <sub>c</sub>	5.5 5.5
0.14	-13.7 -28.3	1 4	<sub>b</sub> 4.79	<sub>b</sub> 17.0	<sub>b</sub> 3.93	<sub>b</sub> 4.5	<sub>b</sub> 5.5
0.09	-28.3		4.79	17.0	3.93	4.5	5.5

<sup>a</sup>Determined from integration of  $^{31}\text{P}$  NMR spectrum.

<sup>b</sup>Peaks in the proton NMR spectrum were too small and hidden under the corresponding peaks from the other species to accurately determine these parameters.

<sup>c</sup>Peaks appear as a distorted pentet.

Figure 4.  $^1\text{H}$  NMR spectrum of monoprotonated phosphatrane oxide (20)



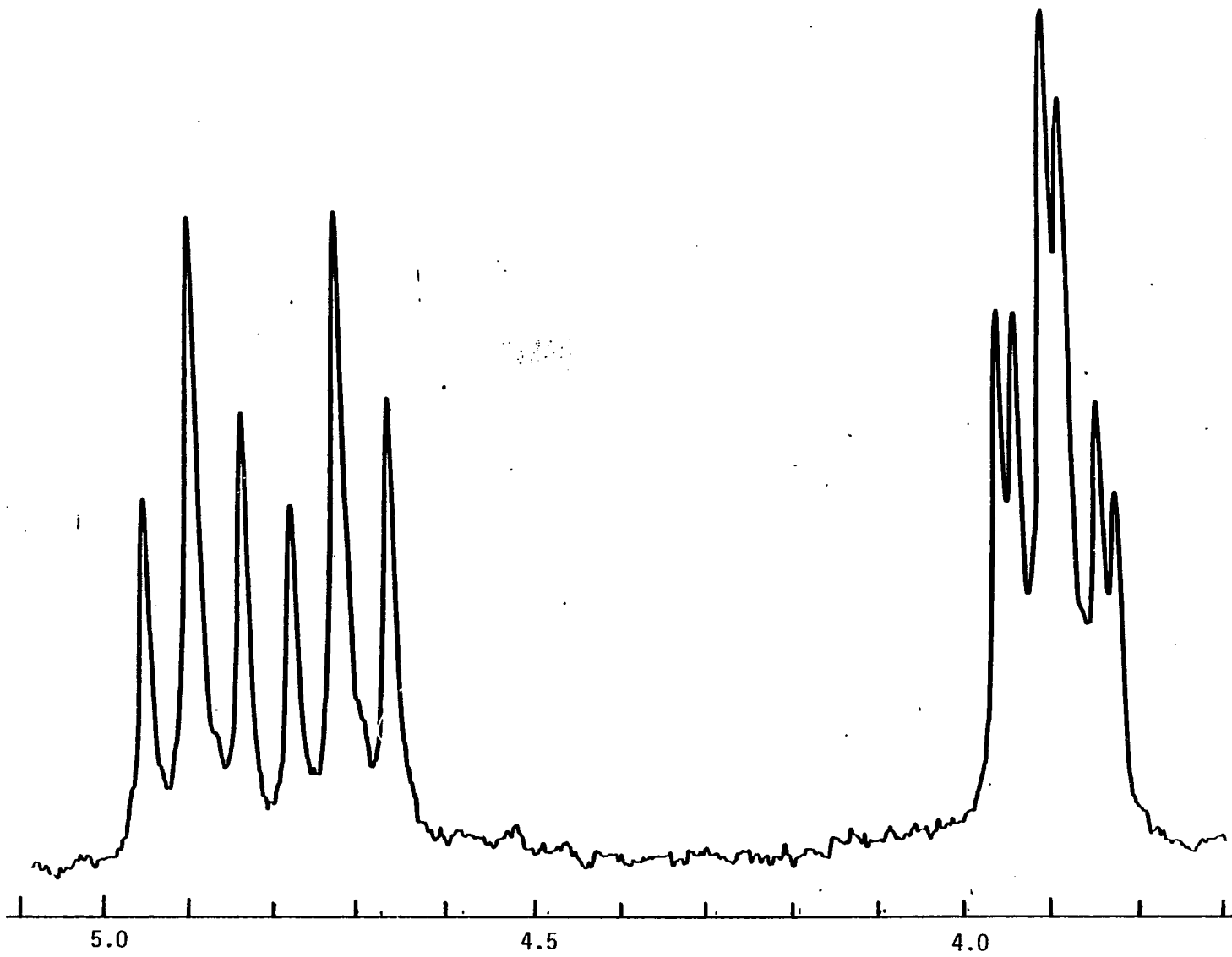
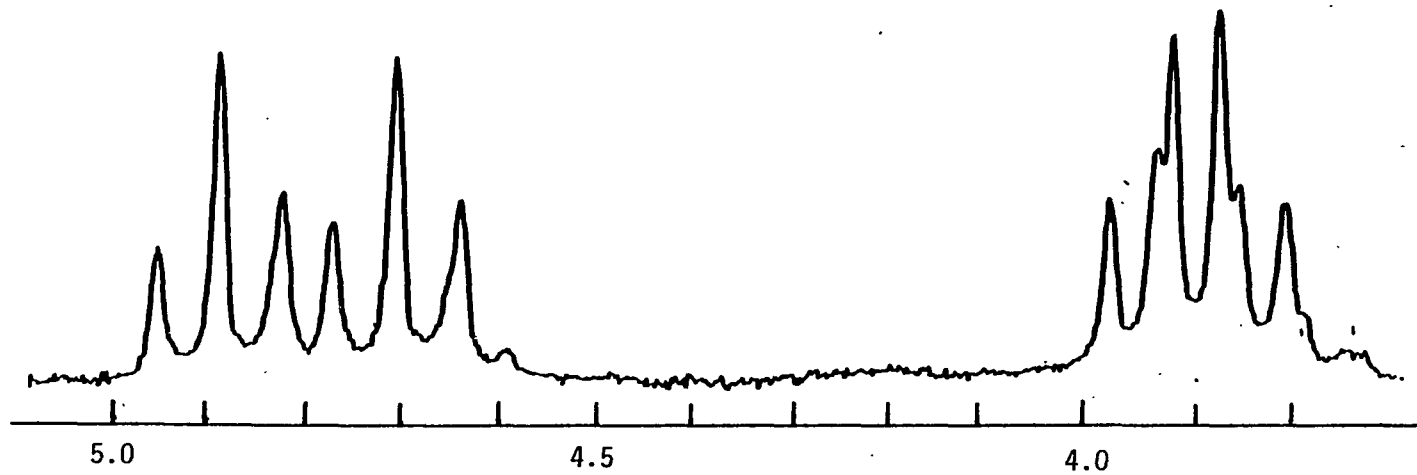


Figure 5.  $^1\text{H}$  NMR spectrum of diprotonated phosphatrane oxide (20)



at the phosphoryl oxygen, since in the absence of exchange, protonation of an esteratic oxygen should give rise to four methylene signals, two for the methylene groups in the bridge containing the protonated esteratic oxygen and two for the methylene groups in the unprotonated bridges. The fact that the  $^1\text{H}$  NMR spectrum is not temperature dependent argues against a rapid exchange between protonation of the various esteratic oxygens.

This second protonation was not expected, as there has not been any previous report of diprotonation of a phosphoryl oxygen. Furthermore, in a related study done concurrently by Buck and co-workers,<sup>62</sup> phosphatrane oxide was protonated by trifluoroacetic acid using methylene chloride as a solvent. In this study only one protonated species was found and the  $^{31}\text{P}$  and  $^1\text{H}$  NMR spectral data coincide with those obtained by us for the monoprotinated species.

In an attempt to confirm that the phosphoryl oxygen was the site of both protonations, we tried to follow the reaction by observing the  $^{17}\text{O}$  NMR spectrum. However, in trifluoroacetic acid, we were unable to observe any signals other than those associated with the acid.

$^1\text{H}$  and  $^{31}\text{P}$  NMR indicated that removing the solvent from the NMR sample of the diprotonated phosphatrane oxide yielded the unprotonated material.

A study of the protonation of phosphatrane sulfide (21) at various acid to substrate ratios was also undertaken. The  $^{31}\text{P}$  and  $^1\text{H}$  NMR data from this study are listed in Table 11. The data indicate that this system behaves in the same manner as phosphatrane oxide. That is, at the

Table 11

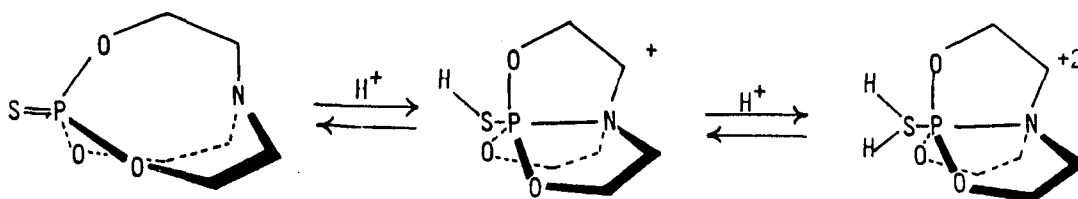
$^1\text{H}$  and  $^{31}\text{P}$  NMR data for the protonation of phosphatrane sulfide (21) with trifluoroacetic acid

Conc (M)	$\delta^{31}\text{P}$ (ppm)	Peak Ratio <sup>a</sup>	$\delta\text{OCH}_2$ (ppm)	$^3\text{J}_{\text{POCH}}$ (Hz)	$\delta\text{NCH}_2$ (ppm)	$^3\text{J}_{\text{PNCH}}$ (Hz)	$^3\text{J}_{\text{NCCH}}$ (Hz)
1.06	65.9	1	b	b	b	b	b
	27.4	37	$\overline{4.89}$	$\overline{18.0}$	$\overline{4.00}$	$\overline{2.0}$	$\overline{5.5}$
	-6.7	8	b	b	b	b	b
0.70	66.3	1	b	b	b	b	b
	25.9	12	4.84	17.0	3.96	1.8	5.5
	-5.8	4	4.88	17.0	4.01	5.5	6.0
0.53	66.7	1	b	b	b	b	b
	24.7	35	$\overline{4.80}$	$\overline{17.0}$	$\overline{3.90}$	$\overline{2.0}$	$\overline{6.0}$
	-5.8	22	4.85	17.0	3.99	5.5	6.0
0.42	23.5	1	4.78	17.0	3.87	2.0	6.0
	-6.1	1	4.83	17.0	3.98	5.5	6.0
0.35	22.7	1	4.75	17.0	3.84	2.0	6.0
	-5.8	2	4.82	17.0	3.96	5.5	6.0
0.18	-6.5	1	4.80	17.0	3.94	5.5	6.0

<sup>a</sup>Determined from integration of  $^{31}\text{P}$  NMR spectrum.

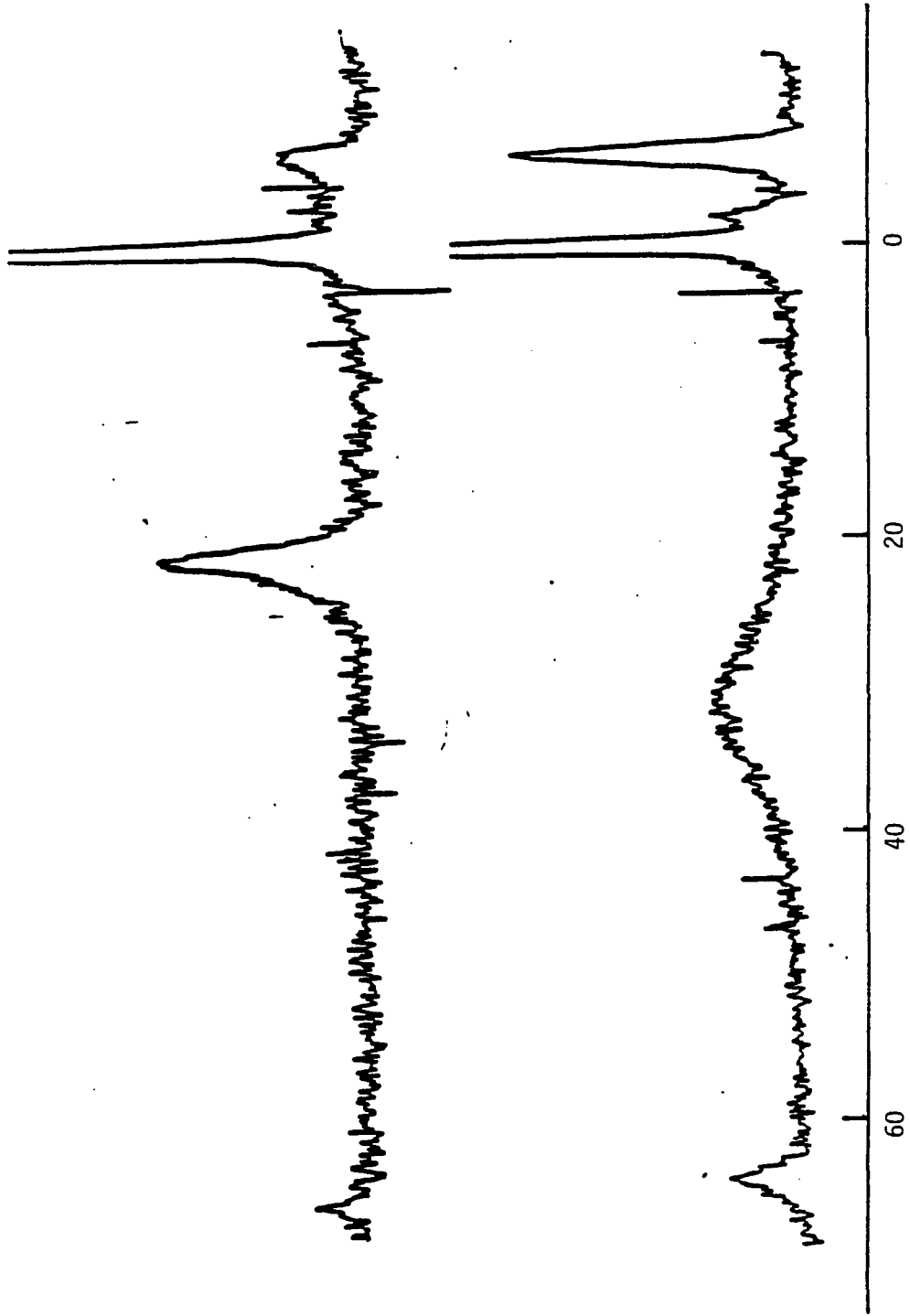
<sup>b</sup>These peaks in the  $^1\text{H}$  NMR spectrum were too small and were hidden under other peaks to accurately determine these parameters.

lower acid to phosphatrane sulfide (21) ratios, the sulfur atom is protonated causing the formation of a P-N bond, and at higher acid to sulfide ratios a second protonation of the sulfur atom occurs. The fact that the magnitude of the upfield chemical shift in the  $^{31}\text{P}$  NMR spectrum upon the protonation of the sulfide is much larger than that observed in the protonation of the phosphate is in accord with previously published protonation data<sup>61</sup> of acyclic compounds, in which phosphates showed small upfield shifts (0-1.2 ppm) and thiophosphates much larger shifts (~-20 ppm) upon protonation. The fact that the upfield shift in this system is even larger (-36 ppm) is again in accord with the change to a pentacoordinate phosphorus. In contrast to the behavior of phosphatrane oxide, the  $^{31}\text{P}$  NMR spectrum of the sulfide is temperature dependent as shown in Figure 6. This is suggestive of an equilibrium for the sulfide as shown below.



As with phosphatrane oxide, protonation can be reversed by removal of the trifluoroacetic acid in vacuo to yield the unprotonated thiophosphate, as the  $^1\text{H}$  and  $^{31}\text{P}$  spectral data of the recovered material are identical to

Figure 6.  $^{31}\text{P}$  NMR spectrum of phosphatrane sulfide as a function of temperature





that of 21. Again, Buck and co-workers<sup>62</sup> have observed the protonation of phosphatrane sulfide in methylene chloride. As in the case of the oxide, only the first protonation of the sulfide is observed in this solvent. In a related study, van Aken et al.<sup>63,64</sup> alkylated the oxide 20 and the sulfide 21 with  $R_3O^+ BF_4^-$  (R = Me or Et). In the case of 20 only a single alkylation of the phosphoryl oxygen was observed. In the alkylation of 21 with  $Me_3O^+ BF_4^-$ , both monoalkylation and dialkylation<sup>62</sup> products were observed. That the first alkylation occurred at sulfur and caused the formation of a P-N bond to occur was confirmed by an X-ray structure determination.<sup>64</sup> The fact that the  $^1H$  and  $^{31}P$  NMR spectra of this alkylated product parallels that observed in the first protonation strongly substantiates our assignments in this case. In the  $^1H$  NMR of the second alkylation product, only a single type of methyl group is observed.<sup>62</sup> An increase in the coupling,  $^3J_{PNCH}$ , from 5.0 to 6.5 Hz, and a downfield shift of the nitrogen methylene group from  $\delta 3.43$  to  $\delta 3.77$  ppm is also observed. They concluded that this species is one in which the sulfur has been dialkylated. The similarities observed in the  $^1H$  NMR spectra of the dialkylated and diprotonated products lends strong support to our conclusion that the phosphoryl oxygen and sulfur are the site of the second protonation.

An attempt was also made to protonate phosphatrane selenide (22) with trifluoroacetic acid. However, a reddish material, most likely selenium, immediately clouded the NMR tube, precluding the possibility of obtaining any meaningful spectral data.

We also investigated the reaction of 20 with triethylsilyl

perchlorate. The NMR data from this study are in Table 12. In a manner similar to that of protonation, one or two triethylsilyl groups can bond to the phosphoryl oxygen causing the formation of a P-N bond. In contrast to protonation, where a large excess of acid is required, silylation is achieved using nearly stoichiometric amounts of  $\text{Et}_3\text{SiClO}_4$ . Also, the  $^{31}\text{P}$  NMR spectrum indicates that removal of the solvent on the vacuum line yields a mixture of the mono and disilylated material, instead of unsilylated phosphatrane oxide.

Addition of  $\text{BF}_3:\text{Et}_2\text{O}$  to a sample of 20 in MeCN causes the formation of the 1:1 adduct. NMR spectral data (Table 3) indicate that a P-N bond is again formed. The further addition of  $\text{BF}_3:\text{Et}_2\text{O}$  causes no subsequent change in either the  $^{31}\text{P}$  or the  $^1\text{H}$  NMR spectral indicative of a bis adduct.

The fact that formation of a complex between phosphatrane oxide and zinc perchlorate did not cause a change in the geometry of the cage to occur is indicated by the small upfield shift in the  $^{31}\text{P}$  NMR spectrum and the absence of an coupling,  $^3\text{J}_{\text{PNCH}}$ , in the  $^1\text{H}$  NMR spectrum.

Delocalization of electrons from the phosphoryl oxygen orbitals into metal orbitals (and vice versa) is thought not to make a significant contribution to the bonding of metal phosphoryl complexes.<sup>65, 66</sup> Rather, it is believed that the positively charged metal polarizes the phosphoryl bond and that the role of the metal is that of orienting the ligands by electrostatic interaction. In a complex with this type of bonding, it might not be surprising that too little electron density is removed from the phosphorus to effect formation of a transannular bond.

Complexes of 20 were also prepared with  $\text{Co}(\text{ClO}_4)_2$  and  $\text{Ni}(\text{ClO}_4)_2$ .

Table 12

$^1\text{H}$  and  $^{31}\text{P}$  NMR data and  $\nu_{\text{P=O}}$  for complexes of  
phosphatrane oxide with  $\text{BF}_3$ ,  $\text{Et}_3\text{SiClO}_4$   
and  $\text{Zn}(\text{ClO}_4)_2$

Compound	$\delta^{31}\text{P}$ (ppm)	$\delta \text{OCH}_2$ (ppm)	$^3\text{J}_{\text{POCH}}$ (Hz)	$\delta \text{NCH}_2$ (ppm)	$^3\text{J}_{\text{PNCH}}$ (Hz)	$^3\text{J}_{\text{HCCH}}$ (Hz)	$\nu_{\text{P=O}}$ (cm)
$\text{OP}(\text{OCH}_2\text{CH}_2)_3\text{N}$	-6.6	4.28 (dt)	15.9	3.24 (t)	--	5.5	1282
$\text{OP}(\text{OCH}_2\text{CH}_2)_3\text{N} + 1\text{BF}_3$	-18.1	4.48 (dt)	16.9	3.51 (td)	3.1	6.1	
$\text{OP}(\text{OCH}_2\text{CH}_2)_3\text{N} + 2\text{BF}_3$	-18.5	4.50 (dt)	16.9	3.51 (td)	3.1	6.1	
$\text{OP}(\text{OCH}_2\text{CH}_2)_3\text{N} + 1\text{Et}_3\text{SiClO}_4$	-18.7	4.35 (dt)	16.9	3.38 (td)	2.0	6.1	
$\text{OP}(\text{OCH}_2\text{CH}_2)_3\text{N} + 2\text{Et}_3\text{SiClO}_4$	-25.6	4.49 (dt)	17.5	3.52 (td)	3.3	6.1	
$\text{OP}(\text{OCH}_2\text{CH}_2)_3\text{N} + \text{Zn}(\text{ClO}_4)_2$	-5.5	4.36 (dt)	17.3	3.24 (t)	--	5.3	1200

Spectral data for the metal complexes are shown in Table 13. The position of the absorption in the UV-vis spectra of these complexes and the shifts in the IR are very similar to those seen for the corresponding complexes of the metals with  $OP(OEt)_3$  and  $OP(OCH_2)_3$  CMe. Based on these data, it is not possible to assign a structure to the phosphatrane oxide ligand, although due to the similarity in the results for all three ligands and the result obtained for  $Zn[OP(OCH_2CH_2)_3N]_5(ClO_4)_2$ , it seems unlikely that a transannular bond is formed in ligated 20.

Compound 20 was also treated with one equivalent of  $SbCl_5$ ,  $PCl_5$  and anhydrous  $H_3PO_4$ . In all three experiments, a fine white precipitate formed which was insoluble in all solvents tried, except DMSO. In the case of the  $SbCl_5$  and  $PCl_5$  adducts, addition of DMSO resulted in a relatively violent reaction which destroyed the phosphatrane oxide, since the  $^1H$  spectrum failed to contain any of the signals characteristic of 20. With the anhydrous phosphoric acid adduct, dissolution in DMSO destroyed the complex, and the  $^1H$  and  $^{31}P$  NMR spectra of this solution showed only peaks for unprotonated phosphatrane oxide. With  $H_3PO_4$ , the white precipitate was most likely the protonated phosphate. This result is supported by the fact that the solid state  $^{31}P$  NMR chemical shift<sup>67</sup> occurs at -11 ppm, a value which compares very well with the solution value of monoprotonated 20.

Attempts were also made to make  $Co^+$ ,  $Co^{+3}$ ,  $Ni^{+2}$  and  $Ag^+$  complexes of  $P(OCH_2CH_2)_2N$ . All of these attempts failed to produce any isolable monomeric materials. The most likely explanation of this failure is the low yield in which phosphatrane is obtained (~8%) and the fact that the polymer produced also has the ability to coordinate. This being the

Table 13

IR and UV data for cobalt complexes of phosphates

Compound	$\lambda$ max (nm)	$\nu_{P=O}$ ( $\text{cm}^{-1}$ )
OP(OCH <sub>2</sub> ) <sub>3</sub> CCH <sub>3</sub>		1210
Co [OP(OCH <sub>2</sub> ) <sub>3</sub> CCH <sub>3</sub> ] <sub>5</sub>	517	1205
OP(OEt) <sub>3</sub>		1270
Co OP(OEt) <sub>3</sub>	530	1260
OP(OCH <sub>2</sub> CH <sub>2</sub> ) <sub>3</sub> N		1276
Co [OP(OCH <sub>2</sub> CH <sub>2</sub> ) <sub>3</sub> N] <sub>5</sub>	575 595 620 643	1260

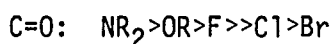
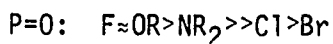
case, statistics would predict that a metal which coordinates to two ligands would only produce a 0.6% yield with two phosphatranes coordinated. With higher coordination, the situation becomes rapidly worse.

PART IV:  $^{17}\text{O}$  NMR OF PHOSPHITES AND PHOSPHATES

## INTRODUCTION

The first  $^{17}\text{O}$  NMR data for phosphorus compounds were published in 1961 by Christ and co-workers.<sup>68</sup> Since then thirteen other papers have appeared which contained  $^{17}\text{O}$  NMR data for phosphorus compounds.<sup>68-81</sup> Five of these references (68, 69, 70, 73, and 75) only reported data for a few phosphorus compounds as part of a study of  $^{17}\text{O}$  NMR of organic compounds. The remaining papers, which dealt primarily with phosphorus compounds are reviewed below.

In 1976, Grossman et al. showed that the shielding of the phosphoryl oxygen was not predominantly affected by the electronegativity of the substituents on phosphorus but was very dependent on the period to which the substituents belonged, such that when the substituents were atoms of the second period, they were much more effective at screening the phosphoryl oxygen than substituents of higher period elements.<sup>71</sup> They also reported that the substituents showed a different ordering of screening ability for phosphoryl and carbonyl oxygens as shown below.



The authors also reported a linear relationship between the value of  $^1J_{\text{P}=\text{O}}$  and the force constants for the phosphoryl bond. From this, they suggested that the value of the phosphorus oxygen coupling constant could be used as a direct measure of the phosphorus-oxygen bond strength. However, this should be viewed with some caution as it was based on only three data points.

Grey and Albright reported the values of  $^1J_{\text{P}=\text{O}}$  for several phosphorus



compounds.<sup>72</sup> They noted that the determination of the coupling constants was hampered by line broadening due to the  $^{17}\text{O}$  quadrupole and that this was quite severe in the case of esteratic oxygens of phosphates. They found that the magnitude of the coupling was very sensitive to the electronegativity of the substituents, such that increasing electronegativity led to an increase in the value of  $^1J_{\text{PO}}$ . (One exception to this rule is that substitution of a fluorine leads to a decrease in the coupling.) This general trend is similar to that observed for P-C,<sup>82</sup> P-H,<sup>83</sup> P-Se,<sup>84</sup> P-W<sup>85</sup> and P-B<sup>86</sup> couplings.

McFarlane and McFarlane reported that the reduced nuclear spin coupling constants between phosphorus and oxygen in three, four, and five coordinate phosphorus compounds have negative values.<sup>74</sup>

Tsai and co-workers observed the  $^{17}\text{O}$  NMR spectrum of ADP and ATP, but were only able to see signals which corresponded to the phosphoryl oxygens.<sup>76</sup> They felt that their inability to observe the signals for the bridging oxygens was due to these oxygens having more restricted rotation, which increases the spin correlation time and causes the signal to broaden.

Vasil'ev et al. recorded the  $^{17}\text{O}$  NMR spectra of a series of acyclic phosphites and acyclic and cyclic chlorophosphites.<sup>77</sup> They found that substitution of a chlorine for an alkoxy group reduces the screening of the remaining oxygens by 18-24 ppm. They also found that oxygens in a five membered ring are less shielded than those in a six-membered ring.

Coderre and co-workers observed that the axial oxygen in cyclic AMP had a further downfield chemical shift, a larger phosphorus oxygen coupling and a narrower line width than the equatorial oxygen.<sup>78</sup> From

this they suggested that  $^{17}\text{O}$  NMR spectroscopy might be a useful probe for making stereochemical assignments in six membered ring phosphorus compounds.

Gerlt et al. observed the  $^{17}\text{O}$  NMR spectrum of several phosphates.<sup>79</sup> They were able to relate the  $^{17}\text{O}$  chemical shift and the value of  $^1J_{\text{pO}}$  to the charge on the phosphoryl oxygen, such that a greater charge led to a more downfield chemical shift and a smaller value of  $^1J_{\text{pO}}$ . They also noted that the observed linewidths showed a strong temperature dependence which is what one would expect since quadrupolar relaxation is the predominant relaxation mechanism.

Gerothanassis and Sheppard reported that the value of  $^1J_{\text{pO}}$  varied with the degree of double bond character in the phosphorus oxygen bond.<sup>80</sup> They also noted that phosphorus oxygen couplings could not be resolved in the case of an oxygen bridging two phosphorus atoms.

Gerlt and co-workers showed that the chemical shifts of the phosphoryl oxygen were pH dependent, with protonation of the oxygen anions resulting in an upfield shift in the  $^{17}\text{O}$  NMR spectrum.<sup>81</sup> The  $\text{pK}_a$  values of several phosphates determined by following the titration by  $^{17}\text{O}$  NMR agreed very well with the values determined by potentiometric titration. They were able to easily identify the different phosphoryl oxygens in adenosine diphosphate and adenosine triphosphate, which may be useful in biological studies of these compounds. They also found a linear dependence between the linewidths of the phosphoryl oxygen and the temperature at which the spectrum was run.

In the present study the effects of conformation and substitution on the  $^{17}\text{O}$  NMR spectrum of acyclic, five- and six-member ring phosphites and phosphates are investigated.

## EXPERIMENTAL

## Techniques

Materials

All solvents were reagent grade or better. Ether, benzene, and toluene were purified by refluxing with and distilling from sodium or sodium potassium alloy. Chloroform and acetonitrile were dried by refluxing with and distilling from  $P_4O_{10}$ . Carbon tetrachloride was dried by storing it over  $MgSO_4$ , followed by distillation from  $P_4O_{10}$ .

Unless noted otherwise, alcohols were reagent grade or better. Methanol was purified by refluxing with and distilling from  $CaSO_4$ . Ethanol was dried by distilling from magnesium ethoxide. Ethylene glycol, glycerol and triethanolamine were purified by azeotropic distillation with benzene, followed by vacuum distillation of the alcohol. Propanol, isopropanol, tert-butanol and 1,2,4-butanetriol were distilled prior to use. 1,3-Propanediol (98%), 1,3-butanediol (99%), 2,2-dimethyl-1,3-propanediol (97%), pinacol and phloroglucinol dihydrate were obtained from Aldrich Chemical Company and were used as received.

Trimethylphosphite (28) and triethylphosphite (29) were refluxed with and distilled from sodium prior to use. Phosphorus trichloride was distilled immediately prior to use. Triphenyl phosphite (30) was obtained from Aldrich Chemical Company and used as received.

Triethylamine was dried by storage over KOH, followed by distillation from BaO. Dinitrogen tetroxide was dried by passing it through a tube of  $P_4O_{10}$  immediately prior to use. Mercuric oxide was obtained from Mallinckrodt and potassium superoxide was obtained from

Alpha Chemical Company. Both were used without further purification.

### NMR Spectroscopy

$^{31}\text{P}$  NMR spectra were obtained on solutions in 10 mm tubes with a Bruker HX-90 spectrometer operating at 36.434 MHz in the FT mode while locked on the  $^2\text{H}$  resonance of the deuterated solvent. The external standard was 85%  $\text{H}_3\text{PO}_4$  sealed in a 1-mm capillary tube held coaxially in the sample tube by a Teflon vortex plug. The spectrometer was interfaced with a Nicolet Instruments 1080 minicomputer system.

$^{17}\text{O}$  NMR spectra were obtained at room temperature on 1 molar  $\text{d}^3$ -acetonitrile solutions in 10-mm tubes with a Bruker WM-300 spectrometer operating at 40.68 MHz in the FT mode while locked on the  $^2\text{H}$  resonance of the deuterated acetonitrile. The external standard was deuterium oxide sealed in a 1-mm capillary tube held coaxially in the sample tube by a Teflon vortex plug. The spectrometer was interfaced with a Bruker ASPECT 2000 minicomputer system.

### Sample Preparation

#### Triethyloxonium tetrafluoroborate

This compound was prepared by the literature procedure of Meerwein.<sup>87</sup>

#### 18-Crown-6 ether

This compound was prepared as described by Gokel and Cram.<sup>88</sup>

meso-1,3-Pentanediol

This diol was prepared by the method of Pritchard and Vollmer<sup>89</sup> as modified by White et al.<sup>16</sup>

Raney nickel W-7

This catalyst was prepared by the method of Adkins and Billica.<sup>90</sup>

cis-1,3,5-Trihydroxycyclohexane

This triol was prepared by the literature method of Stetter and Steinacker<sup>91</sup> as modified by Brown and co-workers.<sup>92</sup>

Triisopropylphosphite (31)

This compound was prepared by the method of Ford-Moore and Williams<sup>93</sup> but with ether in place of light petroleum.

Tri-tert-butylphosphite (32)

This compound was prepared by the method of Cox and Newton.<sup>94</sup>

2-Methoxy-1,3,2-dioxaphospholane (33)

This compound was made by a literature method.<sup>95</sup>

2-Ethoxy-1,3,2-dioxaphospholane (34)

This compound was made by a method previously discussed.<sup>96</sup>

2-Propoxy-1,3,2-dioxaphospholane (35)

This compound was made using the general method of Cason et al.<sup>96</sup>

2-Isopropoxy-1,3,2-dioxaphospholane (36)

This compound was made using the general method of Cason et al.<sup>96</sup>

2-tert-Butoxy-1,3,2-dioxaphospholane (37)

This compound was made using the general method of Cason et al.<sup>96</sup>

2-Phenoxy-1,3,2-dioxaphospholane (38)

The preparation and purification of this phosphite by transesterification of triphenylphosphite has been described.<sup>97</sup>

1-Methoxy-3,3,4,4-tetramethyl-1,3,2-dioxaphospholane (39)

This compound was prepared as described by Denney et al.<sup>98</sup>

1-Ethoxy-3,3,4,4-tetramethyl-1,3,2-dioxaphospholane (40)

This compound was prepared using the general method of Denney et al.<sup>98</sup>

1-Methoxy-1,3,2-dioxaphosphorinane (41)

The synthesis and purification of this six-membered ring phosphite has been described previously.<sup>16</sup>

2-β-Methoxy-4-α-methyl-1,3,2-dioxaphosphorinane (42a)

This six membered ring phosphite was prepared by the method of Bodkin and Simpson.<sup>99</sup>

2-α-Methoxy-4-β-methyl-1,3,2-dioxaphosphorinane (42b)

This compound was prepared by the general method of Mosbo and Verkade.<sup>100</sup>

2-β-Methoxy-4,6,-α,α-dimethyl-1,3,2-dioxaphosphorinane (43a)

This compound was prepared by the method of White et al.<sup>16</sup>

2-α-Methoxy-4,6,-α,α-dimethyl-1,3,2-dioxaphosphorinane (43b)

This compound was prepared as previously described.<sup>100</sup>

2-β-Methoxy-4,4,6,6-tetramethyl-1,3,2-dioxaphosphorinane (44)

The synthesis and purification of this six-membered ring phosphite was carried out by Yilma Gultneh<sup>101</sup> following a known literature procedure.<sup>102</sup>

1-Methoxy-5,5-dimethyl-1,3,2-dioxaphosphorinane (45)

The synthesis and purification of this six-membered ring phosphite has been described previously.<sup>16</sup>



2,5,7-Trioxa-1-phosphabicyclo[2.2.2]heptane (46)

This phosphite was prepared by a slight modification of the procedure described by Denney and Varga.<sup>103</sup> Dow Corning 550 fluid was used in place of SF-96 silicone oil. Purification of the phosphite was carried out as described.<sup>103</sup>

2,7,8-Trioxa-1-phosphabicyclo[3.2.1] octane (47)

This bicyclic phosphite was made by a previously described method.<sup>104</sup>

2,8,9-Trioxa-1-phospha-adamantane (48)

This tricyclic phosphite was prepared by the method of Stetter and Steinacker<sup>91</sup> as modified by Brown and co-workers.<sup>92</sup>

Trimethylphosphate (49)

This phosphate was prepared by  $N_2O_4$  oxidation using the general method described by Keay and Crook.<sup>105</sup>

Triethylphosphate (50)

This phosphate was prepared as previously described.<sup>105</sup>

Triisopropylphosphate (51)

This phosphate was prepared by  $N_2O_4$  oxidation using the general method of Keay and Crook.<sup>105</sup>

Tri-tert-butylphosphate (52)

This phosphate was prepared by air oxidation, by allowing tri-tert-butylphosphite to stand on the lab bench in an open beaker for 24 to 48 hours. It was purified as previously described.<sup>106</sup>

2-Methoxy-2-oxo-1,3,2-dioxaphospholane (53)

The synthesis of this phosphate, by  $N_2O_4$  oxidation, was done using "Method B" as described by Cox and Westheimer.<sup>55</sup>

2-Ethoxy-2-oxo-1,3,2-dioxaphospholane (54)

The synthesis of this phosphate was done using "Method B" described by Cox and Westheimer.<sup>55</sup>

2-Iwopropoxy-2-oxo-1,3,2-dioxaphospholane (55)

The synthesis of this phosphate was done using "Method B" as described by Cox and Westheimer.<sup>55</sup>

2-Methoxy-4,4,5,5-tetramethyl-2-oxo-1,3,2-dioxaphospholane (56)

This compound was prepared by mercuric oxide oxidation as described by Denney et al.<sup>47</sup>

2-Ethoxy-4,4,5,5-tetramethyl-2-oxo-1,3,2-dioxaphospholane (57)

This compound was prepared by mercuric oxide oxidation as described by Denney et al.<sup>47</sup>

1-Methoxy-1-oxo-1,3,2-dioxaphosphorinane (8)

This phosphate was prepared by  $N_2O_4$  oxidation as previously described.<sup>107</sup>

1- $\beta$ -Methoxy-4- $\alpha$ -methyl-1- $\alpha$ -oxo-1,3,2-dioxaphosphorinane (58a)

This phosphate was prepared by  $N_2O_4$  oxidation using the general method described by Mosbo and Verkade.<sup>100</sup>

1- $\alpha$ -Methoxy-4- $\alpha$ -methyl-1- $\beta$ -oxo-1,3,2-dioxaphosphorinane (58b)

This phosphate was prepared by  $N_2O_4$  oxidation using the general method described by Mosbo and Verkade.<sup>100</sup>

1- $\beta$ -Methoxy-4,6,- $\alpha$ , $\alpha$ -dimethyl-1- $\alpha$ -oxo-1,3,2-dioxaphosphorinane (59a)

This phosphate was prepared as described previously.<sup>100</sup>

1- $\alpha$ -Methoxy-4,6,- $\alpha$ , $\alpha$ -dimethyl-1- $\alpha$ -oxo-1,3,2,-dioxaphosphorinane (59b)

This phosphate was prepared by a literature method.<sup>100</sup>

1-Methoxy-5,5-dimethyl-1-oxo-1,3,2-dioxaphosphorinane (60)

This phosphate was prepared by  $N_2O_4$  oxidation as previously described.<sup>107</sup>

4-Methyl-2,6,7-trioxa-1-oxo-1-phosphabicyclo[2.2.2]octane (6)

This phosphate was prepared by  $N_2O_4$  oxidation following "Method B" as described by Cox and Westheimer.<sup>55</sup> The phosphate was purified by sublimation as previously described.<sup>108</sup>

2,8,9-Trioxo-1-oxo-1-phospha-adamantane (61)

This phosphate was prepared as described in the literature.<sup>91</sup>

1-H-1-Phospha-5-aza-2,6,9-trioxabicyclo[3.3.3]undecane  
tetrafluoroborate (18)

The reaction mixture of (26) was derivatized and purified by the method of Milbrath and Verkade.<sup>47</sup>

## RESULTS AND DISCUSSION

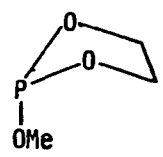
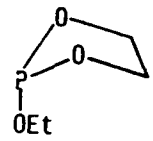
Due to the large bandwidths, the accuracy of the coupling constants is low ( $\pm 10$  Hz for esteratic oxygens and  $\pm 5$  Hz for phosphoryl oxygens). This is reflected by the poor reproducibility between work carried out in different laboratories as seen in Tables 14 and 15. In the phosphates, we were not able to resolve the phosphorus oxygen coupling constants for the esteratic oxygens, although the values for the phosphoryl oxygens were easily determined. This result is in accord with results previously reported.<sup>80, 81</sup> Cheng and Brown determined the nuclear quadrupole coupling constant for the esteratic oxygens of triphenylphosphate to be 9.0 MHz and that of the phosphoryl oxygen to be 3.8 MHz.<sup>109</sup> Since the linewidth should vary directly with the square of the nuclear quadrupole coupling constant,<sup>73</sup> as seen in the equation below, it should not be too surprising that only the coupling to the phosphoryl oxygen was resolvable. It should be pointed out that Elie<sup>110</sup> has been able to

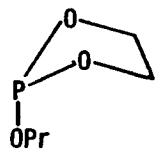
$$\text{Line Width} = \frac{1}{\pi T_2} = \frac{12}{125} \left(1 + \frac{n^2}{3}\right) \left(\frac{e^2 q Q}{h}\right)^2 T_c$$

resolve most of the esteratic couplings by using a higher temperature. This result could not be reproduced here, even though identical conditions and parameters were used. There seems to be no satisfactory explanation for the difference in the results obtained on the two different instruments. There is a relatively large difference in the coupling to axial and equatorial methoxy groups of the phosphites, with the coupling to the equatorial group (166-170 Hz) being larger than that

Table 14

<sup>17</sup>O NMR chemical shifts and coupling constants of phosphites

Compound	$\delta^{17}\text{O}(\text{exo})$ (ppm)	$J_{\text{PO}(\text{exo})}$ (Hz)	$\delta\text{O}(1)$ (ppm)	$J_{\text{PO}(1)}$ (Hz)	$\delta\text{O}(3)$ (ppm)	$J_{\text{PO}(3)}$ (Hz)	Ref
$\text{P}(\text{OMe})_3$	47.7	170.2					This Work
$\text{P}(\text{OEt})_3$	84.9	144.2					This Work
$\text{P}(\text{O-}i\text{-Pr})_3$	114.3	170.1					This Work
$\text{P}(\text{O-}i\text{-Bu})_3$	132	--					This Work
$\text{P}(\text{OPh})_3$	78.5	--					This Work
	67.9	177.6	77.1	133.1			This Work
	67.4	175.8	78.2	156.3			110
	104.6	155.3	78.6	144.3			This Work



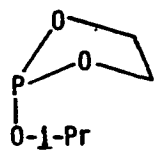
100.0

195.7

78.4

153.9

This Work



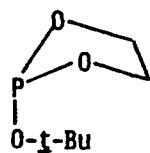
133.4

159.0

79.6

151.7

This Work



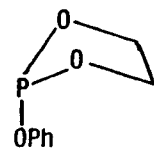
151.0

111.0

79.3

122.1

This Work

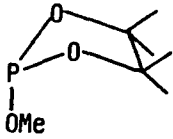
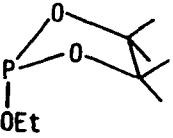
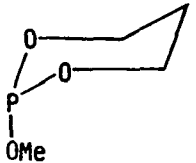


156.0

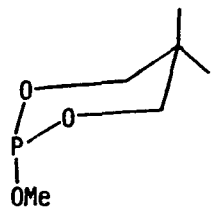
81.0

This Work

Table 14 (continued)

Compound	$\delta^{17}\text{O}(\text{exo})$ (ppm)	$J_{\text{PO}}(\text{exo})$ (Hz)	$\delta\text{O}(1)$ (ppm)	$J_{\text{PO}}(1)$ (Hz)	$\delta\text{O}(3)$ (ppm)	$J_{\text{PO}}(3)$ (Hz)	Ref
	77.0	a	127.0	a			This Work
	125.0	a	125.0	a			This Work
	48.9	136.9	61.3	162.8			This Work
	47.6	149.3	59.2	173.3			110



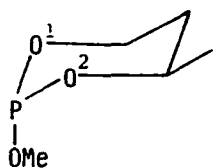


46.0

130

56

This Work



48.7

138

88.8

167

59.9

156

This Work

47.9

142.5

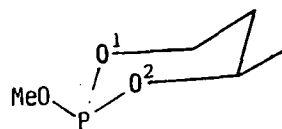
87.7

169.7

58.3

159.5

110



59.4

167

88.3

177

61.9

158

This Work

58.3

169.7

87.6

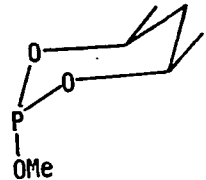
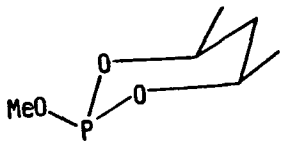
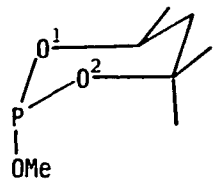
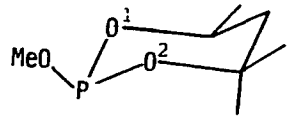
179.9

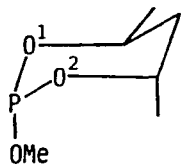
61.5

159.5

110

Table 14 (continued)

Compound	$\delta^{17}\text{O}(\text{exo})$ (ppm)	$J_{\text{PO}}(\text{exo})$ (Hz)	$\delta\text{O}(1)$ (ppm)	$J_{\text{PO}}(1)$ (Hz)	$\delta\text{O}(3)$ (ppm)	$J_{\text{PO}}(3)$ (Hz)	Ref
	48.6	124.3	88.7	153.2			This Work
	48.9	149.9	86.9	173.1			110
	59.6	184.5	88.7	153.2			This Work
	62.6	166.3	88.3	165.8			110
	59.5	155.3	86.5	164.2	99.5	180.8	110
	68.9	144.8	83.3	164.2	102.1	164.8	110



62.9

142.9

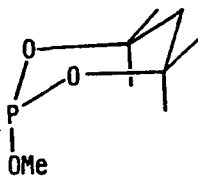
81.6

163.3

86.4

159.9

110



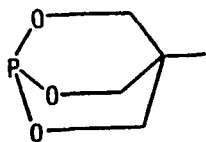
68.8

155

98.6

166

This Work

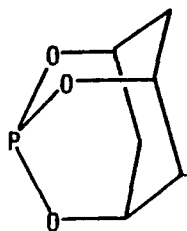


82.7

151.6

This Work

68



82.7

151.6

This Work

Table 14 (continued)

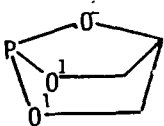
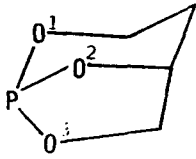
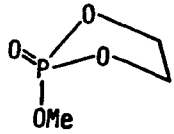
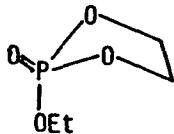
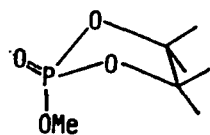
Compound	$\delta^{17}\text{O}(\text{exo})$ (ppm)	$J_{\text{PO}}(\text{exo})$ (Hz)	$\delta\text{O}(1)$ (ppm)	$J_{\text{PO}}(1)$ (Hz)	$\delta\text{O}(3)$ (ppm)	$J_{\text{PO}}(3)$ (Hz)	Ref
	91.6	151.6	116.6	133.1			This Work
	80.0	189.0	104.2	129.4	84.0	170.0	This Work

Table 15

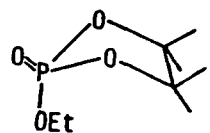
 $^{17}\text{O}$  NMR chemical shifts and coupling constants of phosphates

Compound	$\delta_{\text{P=O}}$ (ppm)	$J_{\text{P=O}}$ (Hz)	$\delta_{\text{O(exo)}}$ (ppm)	$J_{\text{PO(exo)}}$ (Hz)	$\delta_{\text{O(1)}}$ (ppm)	$J_{\text{PO(1)}}$ (Hz)	$\delta_{\text{O(3)}}$ (ppm)	$J_{\text{PO(3)}}$ (Hz)	Ref
$\text{OP(OMe)}_3$	83	156	29.8	58					This Work
$\text{OP(OEt)}_3$	80.7	174	57.0	--					This Work
$\text{OP(O-}i\text{-Pr)}_3$	85	129	85.0	--					This Work
$\text{OP(O-}i\text{-Bu)}_3$	112	162	107.0	--					This Work
	78.9	159	29	--	47	--			This Work
	77.9	166	28.7	78.1	46.1	87.9			110
	80.2	163	60	--	48	--			This Work



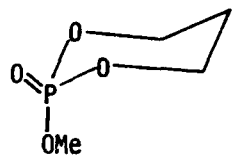
88.8 159 34 -- 96 --

This Work



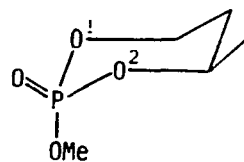
90.6 156 66 -- 98.6 --

This Work



83.9 151.6 23 -- 47 --  
82.4 156.3 21.3 78.1 46.7 78.1

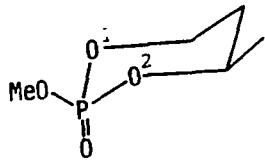
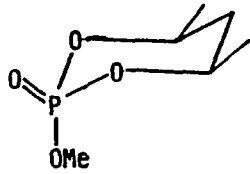
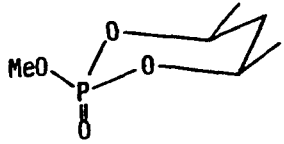
This Work  
110

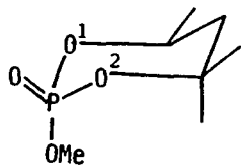


82.7 149.8 24 -- 45 -- 74 --  
82.9 163.6 22.4 67.9 45.2 67.9 76.3 56.7

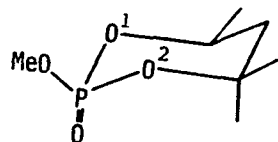
This Work  
110

Table 15 (continued)

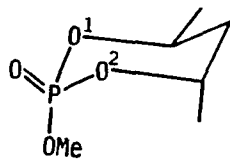
Compound	$\delta_{P=O}$ (ppm)	$J_{P=O}$ (Hz)	$\delta_{O(exo)}$ (ppm)	$J_{PO(exo)}$ (Hz)	$\delta_{O(1)}$ (ppm)	$J_{PO(1)}$ (Hz)	$\delta_{O(3)}$ (ppm)	$J_{PO(3)}$ (Hz)	Ref
	89	151.6	31	--	46	--	72	--	This Work
	87.7	160.7	29.4	74.6	45.8	77.9	73.9	74.6	110
	81.9	160	25	--	74	--			This Work
	81.4	161.5	23.3	91.3	72.9	57.7			110
	88.5	148	29	--	70	--			This Work
	87.6	159.4	28.8	86.8	72.7	88.2			110



88.6 138.4 30.8 87.9 73.7 -- 86.6 -- 110



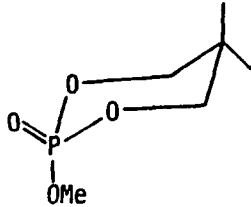
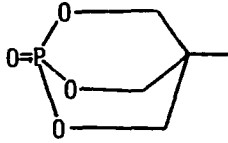
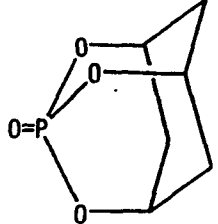
94.4 161.4 34.1 72.5 72.9 -- 88.5 -- 110



89.9 155.9 32.3 74.6 68.9 108.5 72.2 115.3 110



Table 15 (continued)

Compound	$\delta_{\text{P=O}}$ (ppm)	$J_{\text{P=O}}$ (Hz)	$\delta_{\text{O(exo)}}$ (ppm)	$J_{\text{PO(exo)}}$ (Hz)	$\delta_{\text{O(1)}}$ (ppm)	$J_{\text{PO(1)}}$ (Hz)	$\delta_{\text{O(3)}}$ (ppm)	$J_{\text{PO(3)}}$ (Hz)	Ref
	79.2	125.8	22	--	45	--			This Work
	68.4	150	51	--					This Work
	93.0	150	76						This Work

to an axial group (142-150 Hz). The accuracy of the chemical shifts is on the order of  $\pm 2$  ppm or better.

In the acyclic phosphites (28-32), one sees a successive downfield shift of the  $^{17}\text{O}$  resonance (Table 14) upon replacement of hydrogen by a methyl group at the  $\alpha$  carbon ( $\beta$  effect). The direction and magnitude of these shifts compare well with those observed in the  $^{17}\text{O}$  NMR spectra of alcohols and ethers.<sup>75,111,112</sup> Only three phosphorus-oxygen couplings were resolved in these compounds and there is no obvious trend in their values.

The 1,3,2-dioxaphospholanes (33-40) show a  $\beta$  effect for the exocyclic group that is essentially identical to that observed for the acyclic compounds (Table 14). Ring substitution also leads to a  $\beta$  shielding of the endocyclic oxygens, and also a fairly large  $\delta$  shielding of the exocyclic oxygen.

While the acyclic and five-membered ring phosphites are conformationally mobile, many of the six-membered ring phosphites are not, and it is possible to relate the observed  $^{17}\text{O}$  chemical shifts and coupling constants in these systems with their configuration and conformation. Phosphites 43a and 43b can be regarded as configurationally fixed as shown in Table 14. In comparing the  $^{17}\text{O}$  spectral data of 43a and 43b, a large difference can be seen between axial and equatorial methoxy groups, with the shift of the axial methoxy occurring 13.7 ppm upfield of the equatorial methoxy group, a trend that is also seen with alcohols and ethers.<sup>113</sup> There is also a difference in the value of  $^1J_{\text{PO}}$ , with the coupling to the equatorial oxygen being significantly larger. The differences in the shifts of the ring oxygens is small (3.6 ppm or

less) implying that the  $\beta_e$  and  $\beta_a$  effects of the methoxy group are similar. For comparison the difference in  $\beta_e$  and  $\beta_a$  for 2-methyl substituted 1,3-dioxanes is 12.1 Hz,<sup>114</sup> a much larger difference than in the present case. It should be pointed out, however, that the difference between  $\beta_e$  and  $\beta_a$  in the  $^{13}\text{C}$  spectra of cyclohexanols (2.4 ppm)<sup>115</sup> is smaller than in methylcyclohexanes (3.6 ppm)<sup>116</sup> but not by as great a factor.

The  $^{13}\text{C}$  spectrum of 42a (Table 16) shows a  $^4J_{\text{PC}(5)}$  value of 4.7 Hz, which falls into the range characteristic of a chair conformation with an axially substituted methoxy group, <sup>117-119</sup> (4-5 Hz for an axial group and 11-14 Hz for an equatorial group). This conformation is also indicated in the  $^{17}\text{O}$  NMR spectrum, since the chemical shift and phosphorus oxygen coupling constant for the methoxy group in 42a agree very well with those of 43a.

On the basis of  $^1\text{H}$  NMR spectroscopy, 42b has been estimated to exist 16% in a diequatorial chair, 44% as a diaxial chair and 40% in the boat form.<sup>120</sup> However, the value of  $^4J_{\text{PC}(5)}$  (Table 16) indicates a much higher population of the diequatorial chair. If the boat form were to have an equatorial methyl group and an axial methoxy group, its effect on  $^4J_{\text{PC}(5)}$  should be similar to a chair with an axial methoxy group, and the value of  $^4J_{\text{PC}(5)}$  would then indicate 42b existing 70-80% in the diequatorial chair form. The  $^{17}\text{O}$  chemical shift of the methoxy group would indicate about 70% diequatorial chair, which is in reasonable agreement with an earlier report.<sup>99</sup> In any case, it is fairly evident that 42b is not conformationally homogeneous.

In the conformationally mobile system, 41, the coupling constants in

Table 16  
 $^{13}\text{C}$  and  $^{31}\text{P}$  NMR data for cyclic phosphites<sup>a</sup>

Compound	Solvent	$\delta^{13}\text{C}(4)$	$\delta^{13}\text{C}(5)$	$\delta^{13}\text{C}(6)$	$\delta^{13}\text{C}(4)$	$\delta^{13}\text{C}(5)$	$\delta^{13}\text{C}(6)$	$\delta^{13}\text{C}(2)$	$\delta^{31}\text{P}$	Ref
<u>41</u>	None	59.5 (1.6)	29.4 (5.5)	59.5 (1.6)				49.8 (17.8)	131.0	93, 117
<u>42a</u>	None	66.0 (2.0)	36.5 (4.7)	60.0 (2.5)	23.4 (3.2)			49.8 (18.0)	129.1	117, 3
<u>42b</u>	None	69.8 (3.6)	34.0 (10.8)	59.0 (1.8)	23.5 (1.6)			49.2 (14.7)	130.3	117, 3
	$\text{CDCl}_2$	69.6	33.6 (12.0)	58.8	23.1			49.3 (15.0)	130.3	110
<u>43a</u>	$\text{CHCl}_3$	65.7	42.7 (4.2)	65.7	22.5 (3.2)		22.5 (3.2)	49.4	127.2	93, 118
<u>43b</u>	$\text{CHCl}_3$	69.7	40.8 (13.5)	69.7	23.3 (1.6)		23.3 (1.6)	48.2	131.5	93, 118
	$\text{CD}_2\text{Cl}_2$	70.2	41.4 (13.8)	70.2	23.7		23.7	48.8 (10.0)		110
<u>59a</u>	$\text{CD}_2\text{Cl}_2$	75.7 (6.0)	46.8 (6.0)	62.3 (2.0)	28.5 eq 33.1 ax		23.1 (3.6)	49.6 (20.0)	129.9	110
<u>59b</u>	$\text{CD}_2\text{Cl}_2$	75.2 (6.0)	44.4 (16.0)	67.3 (6.0)	28.6 eq 32.3 ax		24.1	49.1 (18.0)	131.1	110
<u>61</u>	$\text{CD}_2\text{Cl}_2$	69.3 (6.0)	39.9 (7.0)	61.6	23.0		23.1	49.6 (19.4)	131.9	110

<u>45</u>	CHCl <sub>3</sub>	68.3 (1.3)	32.2 (4.7)	68.3 (1.3)	22.3 eq (1.2) 22.0 ax	49.3 (18.7)	122.6	93, 118
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<sup>a</sup>Values in parentheses are <sup>31</sup>P-<sup>13</sup>C coupling constants in Hz.

the  $^{13}\text{C}$  NMR spectra indicate that it exists essentially exclusively in a chair form with an axial methoxy group.<sup>20,117</sup> This assignment is strongly supported by the comparison of the  $^{17}\text{O}$  chemical shift and coupling of the methoxy group in 41 to those in 42a and 43a and by the similarity of the shift of O(1) in 41 to that in 42a.

On the basis of  $^1\text{H}$  NMR spectroscopy, 45 has been assigned a chair conformation.<sup>16,121</sup> The  $^{31}\text{P}$  spectra indicate that the methoxy group is in an axial position, and the low field value of the shift of C(5) in the  $^{13}\text{C}$  position and also of the  $^{31}\text{P}$  signal have been attributed to increased overlap of the back lobes of the phosphorus and C(5) bonding orbitals when there is an equatorial substituent at C(5).<sup>118</sup> The  $^{17}\text{O}$  chemical shift of the methoxy group is in the normal range for an axial chair conformation (compare to 41, 42a, and 43a). The coupling constant  $J_{\text{P}0(1)}$  also supports this assignment.

In 62a and 62b, the  $^{13}\text{C}$  NMR spectra are consistent with chair configurational isomers differing in their configuration at phosphorus. The O(1) chemical shift of 62a agrees well with that of 43a, and the downfield shift of the methoxy group can be explained by a  $\delta$  compression effect.<sup>113</sup> On the other hand, the O(1) chemical shift of 62b is surprisingly far downfield of that in 43b and the shift of the methoxy group is difficult to explain. If 62b exists in a chair form with an equatorial methoxy group, then it would be necessary to invoke a  $\delta_a$  effect of 5 ppm even though there is no compression. In this geometry, the downfield shift of O(3) can reasonably be ascribed to  $\beta_a$  and  $\beta_{\text{gem}}$  effects, but the upfield shift of O(1), would require an upfield shifting  $\delta$  effect. A second possibility is that 62b exists as a skew boat, as has

been observed in the  $^{13}\text{C}$  NMR of several 1,3-dioxanes.<sup>122</sup> The spectral evidence is neither strongly supportive or decisively against the conformation. A third possibility is that 62b exists as a triaxial chair, which would explain the low field shift of the methoxy group in the  $^{17}\text{O}$  spectrum and the low field shift of Me(6) in the  $^{13}\text{C}$  spectrum. However, this assignment is in conflict with the low field shift of C(6), the fact that the shift of C(4) is nearly the same as in 62a and the large value of  $^4J_{\text{PC}(5)}$ . It also does not account for the fact that O(1) and O(3) shift in opposite directions. Unfortunately, this leaves the  $^{17}\text{O}$  spectrum of 62b largely unexplained.

In 63, the inequality of C(4) and C(6) indicates that this compound does not exist in a twist form nor does it exist as an equal mixture of conformers. The proton spectrum also militates against these possibilities.<sup>110</sup> The value of  $^4J_{\text{PC}(5)}$  is suggestive of a mixture of conformers, in which the chair form with an axial methoxy group is dominant. The resonance of C(5) is somewhat downfield of the position it occupies in trans-4,6-dimethyl-1,3-dioxanes,<sup>122</sup> which is usually true of axial but not equatorially substituted phosphites as can be seen by comparing the chemical shift in 41 with 1,3-dioxane (26.6), 42a and 42b with 4-methyl-1,3-dioxane (33.7), 43a and 43b with cis-4,6-dimethyl-1,3-dioxane (41.1), and 62a and 62b with 4,4,6-trimethyl-1,3-dioxane (44.2).<sup>122</sup> If 63 is a mixture of conformers with the axial form dominant, and the  $\delta$  effect in the absence of compression in 62b is real and is also seen in the equatorial conformer of 63, then the methoxy shift in 61 being intermediate between 62a and 62b is reasonable. In this situation, the upfield shift of C(6) relative to that in 43a can be

explained by a  $\alpha_a$  effect of the C(4) methyl group. The nearly equivalent shifts of the methyl groups could be rationalized as one being mainly equatorial and the other mainly axial and shifted downfield by a  $\delta$ -compression effect of the syn-axial methoxy group. The shifts of the ring oxygens are reasonable, as O(3) compares well with the ring oxygens in 43a and O(1) is upfield of O(3) since  $\alpha_a$  is usually smaller than  $\alpha_e$ .<sup>114</sup>

For the tetrasubstituted compound 44, there is no previous work relating to its conformation. The  $^{17}\text{O}$  spectrum of 44 is indicative of a chair form with an axial methoxy group, as the chemical shift of the endocyclic oxygens compares well with the O(3) shift in 62a and the further downfield shift of the methoxy as compared to 62a can be attributed to an increase in the  $\delta$ -compression effect due to the additional axial methyl group. This conformation is also supported by the similarity in the phosphorus oxygen coupling to the methoxy oxygen between 62a and 44, although the coupling to the ring oxygens would support the other conformer (compare 44 and 62b).

The similarity of the methoxy shift in the acyclic and six-membered ring compounds is suggestive of a conformational analogy. The methoxy group in the six-membered rings is usually axially oriented due to the anomeric effect and the same effect leads to a gauche conformation in the acyclic analog. That the endocyclic oxygens resonate downfield of the exocyclic oxygens is most likely due to the  $\beta$  effect of the ring atom, as it has already been shown that the addition of  $\beta$  carbon atoms in acyclic systems results in a downfield shift. Comparison of the shift of the endocyclic oxygens to that in  $\text{P}(\text{OEt})_3$  indicates that the  $\beta$  effect of an



atom in the ring is smaller than that in an acyclic system.

The remaining phosphites are all rigid bicyclic systems. Compound 5, must exist in a boat form, although this would not seem to explain the downfield shift in the  $^{17}\text{O}$  spectrum, relative to that observed in 41, since boat and twist forms usually resonate upfield of the chair conformation in  $^{13}\text{C}$  spectra.<sup>123</sup> The  $^{17}\text{O}$  resonance in 48 is upfield of that in 43a. This is expected since the substituents in 48 are axial and in 43a they are equatorial, and in the 1,3,2-dioxaphosphorinanes it is evident that  $\beta_a$  is less than  $\beta_e$  (note magnitude of shift change in going from 41 to 43a or 43b (~27 ppm) as opposed to going from 43a or 43b to 62a, 62b or 44 (-13 ppm)). In compound 46, the shift of the one-oxygen bridge (116.6 ppm) does not seem far out of line for a five-membered ring with a  $\beta$  substituent (compare to 33 and 34). Also, if the deshielding observed for 5 is indeed due to a boat conformation, then the very low field shift of the other oxygens could be due to the fact that they are in a six-membered ring in the boat conformation and also part of a five-membered ring. In the remaining bicyclic compound 47, the shift at 104.2 ppm is about 20 ppm downfield of that in 48, but this could be due to the fact that it is also in a five-membered ring. The shift of O(3) (84.0 ppm) compares reasonably well with the endocyclic oxygens in unsubstituted five-membered rings (Table 14), however, the remaining oxygen is unexplainably shifted rather far downfield, 80.0 ppm, as compared to the shift in 41 (59.2 ppm).

For the phosphates, there is no clear conformational trend for the couplings to either the ring oxygens or the oxygen of the exocyclic methoxy group. The coupling to the phosphoryl oxygens (156-164 Hz) is

always larger than the coupling to the esteratic oxygens (Table 15).

In the acyclic (49-52) and five-membered ring (53-57) phosphates, just as in the phosphites, there is a downfield  $\beta$  shift for both the exocyclic and endocyclic oxygens. In the tetramethyl substituted phospholanes (56 and 57) the downfield shift of the ring oxygens is quite large. To date, these are the only two compounds which exhibit an esteratic resonance which is downfield of the resonance of the phosphoryl oxygen. The effect of ring substitution on the chemical shift of the exocyclic group is much smaller than in the case of the phosphites.

In the case of the six-membered rings, it is again possible to relate the  $^{17}\text{O}$  chemical shift with structure. As with the phosphites, the structures of the other phosphates will be related to the conformationally rigid compounds 59a and 59b. Again, in these compounds, the  $^{17}\text{O}$  chemical shift of the exocyclic methoxy group are dependent on whether it is axially or equatorially substituted, although the difference is not as large as in the phosphites. In the phosphates, as in the phosphites the equatorial methoxy group appears downfield of an axially oriented methoxy group. Exactly the opposite ordering is seen in the phosphoryl oxygen shifts, where the axial oriented group is now downfield of an equatorial oxygen.

The  $^{13}\text{C}$  and  $^{31}\text{P}$  (Table 17) NMR spectra of the six-membered ring phosphates are not dependent on configuration of the exocyclic group to any great extent. Based on the similarities of the dipole moments (Table 18) of 58a and 59a, it would appear that 58a exists in the chair form with an axial methoxy group. The  $^{17}\text{O}$  chemical shifts of the phosphoryl and methoxy oxygens support this assignment as the values observed in 58a

Table 17

 $^{13}\text{C}$  and  $^{31}\text{P}$  NMR data for cyclic phosphates<sup>a</sup>

Compound	Solvent	$\delta\text{C}(4)$	$\delta^{13}\text{C}(5)$	$\delta\text{C}(6)$	$\delta\text{C}(4\alpha)$	$\delta\text{C}(6\alpha)$	$\delta\text{C}(2\alpha)$	$\delta^{31}\text{P}$	Ref
<u>8</u>	$\text{CDCl}_3$	69.2 (5.7)	26.1 (7.6)	69.2 (5.7)			53.6 (5.7)	-6.7	110
<u>42a</u>	$\text{CDCl}_3$	77.5 (5.7)	33.4 (5.7)	68.3 (5.7)	22.3 (9.5)		53.6 (5.7)	-6.4	110
<u>42b</u>	$\text{CDCl}_3$	76.4 (5.7)	32.6 (5.7)	66.7 (5.7)	21.7 (5.7)		54.6 (5.8)	-4.6	110
<u>43a</u>	$\text{CDCl}_3$	76.1 (7.6)	40.5 (5.7)	76.1 (7.6)	22.1 (9.5)	22.1 (9.5)	53.4 (3.8)	-7.1	110
<u>43b</u>	$\text{CD}_2\text{Cl}_2$	75.1 (7.0)	40.8 (5.8)	75.1 (7.0)	22.2 (8.0)	22.2 (8.0)	54.8 (7.6)	-4.9	110
<u>64a</u>	$\text{CDCl}_2$	82.6 (6.0)	44.6 (8.0)	73.1 (6.0)	30.9 eq (6.0)	22.5 (8.0)	54.5 (6.0)	-6.1	110
					27.3 ax				
<u>64b</u>	$\text{CDCl}_3$	72.9 (7.6)	37.5 (7.6)	74.7 (7.6)	20.5	21.9 (7.6)	53.8 (5.7)	-6.1	110
<u>65</u>	$(\text{CD}_3)_2\text{CO}$	73.7 (6.4)	37.9 (4.1)	75.7 (6.5)	20.7	22.0 (12.3)	53.9 (5.7)		110

<sup>a</sup>Values in parentheses are  $^{31}\text{P}$ - $^{13}\text{C}$  coupling constants in Hz.

Table 18

Dipole moments of cyclic phosphates

Compound	$\mu_D$	Ref
<u>8</u>	5.63	42
<u>58a</u>	4.78	42
<u>58b</u>	4.93	42
<u>59a</u>	6.11 5.43	42 110
<u>59b</u>	4.69 4.73	42 110
<u>60</u>	5.41	42
<u>64a</u>	5.57	110
<u>64b</u>	4.58	110
<u>65</u>	4.88	110

are very close to those in 58a and significantly upfield of 58b.

The dipole moments of 58b and 49b are reasonably close indicating that the dominant conformation should be a diequatorial chair. A value of 60% diequatorial chair, 20% diaxial chair and 20% boat form has been reported earlier based on the coupling constants in the  $^1\text{H}$  NMR.<sup>124</sup> The  $^{17}\text{O}$  chemical shifts of the phosphoryl oxygen and the methoxy group of 58b, agree very well with those of 59b and would indicate that the diequatorial chair probably makes a greater contribution than the earlier proton work indicated.<sup>124</sup>

Earlier work on phosphate 8 indicated that the conformer with an axial methoxy group is either greatly predominant or the only one present.<sup>25</sup> This conformation has also been suggested from  $^{31}\text{P}$  and  $^1\text{H}$  NMR studies of the phenoxy analog,<sup>125</sup> and was seen in the solid state structure.<sup>126</sup> Again, comparison of the  $^{17}\text{O}$  chemical shifts of the methoxy group and phosphoryl oxygen of 8 to those in 58a and 59a supports this conclusion.

Prior IR<sup>127</sup> and NMR<sup>128,129</sup> studies have indicated that phosphate 60 exists in a chair form with the methoxy group in the axial position. This was also the structure found in a crystal structure determination.<sup>130</sup> The  $^{17}\text{O}$  NMR data are also consistent with this form, as chemical shifts of the methoxy and phosphoryl oxygens are close to what is found in 8, 58a, and 59a, although the shifts are at a somewhat higher field than expected.

The analogs of 64a and 64b having an exocyclic phenoxy group are believed to exist in a chair conformation with an axial alkoxy group and a twist form respectively.<sup>125</sup> The dipole moment and  $^{13}\text{C}$  NMR data suggest

that both 64a and 64b are in a chair form. The downfield shift of the methoxy group in 64a relative to 59a can be explained by the  $\delta$ -compression effect. However, the shift to lower field of the methoxy group of 64b and of the phosphoryl group of 64a are very difficult to explain, although this behavior is similar to that found in the analogous phosphite, 62b.

An earlier  $^1\text{H}$  NMR study of the phenoxy analog of 65 indicated that it exists as a mixture of chair conformers, and that the conformer with an axial phenoxy group is dominant.<sup>131</sup> The existence of 65 as a mixture of conformers is consistent with the very similar shifts of C(4) and C(6) and the fact that both methyl group carbons are shifted to high field.<sup>132</sup> The dipole moment of 65 indicates either a predominantly equatorial methoxy group or a twist form. In the  $^{17}\text{O}$ , the facts that the resonances of both the methoxy group and the phosphoryl oxygen are intermediate between those of 64a and 64b and that the ring oxygens have very similar chemical shifts supports the conclusion that 65 is not conformationally homogeneous.

The two caged phosphates 6 and 61 show the same downfield shift of the esteratic oxygens, relative to the model compounds 8 and 59a, that was observed in the phosphite analogs 10 and 11. The phosphoryl oxygens of 6 and 61 show a rather surprising change. The resonance of 6 is shifted upfield of 8 by 14 ppm but the shift of 61 is 12 ppm downfield of 59a. It would seem that the difference must be ascribed to one being in a boat and the other in a chair form, since the phosphorus oxygen couplings,  $^1\text{J}_{\text{PO}}$ , of each (150 Hz) are in the normal range, which argues against a change in hybridization.

In conclusion, it can be seen that the configuration of six-membered ring phosphites and phosphates can be assigned on the basis of chemical shift differences between equatorial and axial alkoxy groups. In the case of the phosphites the magnitude of the phosphorus oxygen coupling may also be used in assigning the configuration.

The effects of substitution can also be seen to be much like those seen in the analogous carbon oxygen compounds, although the difference in the shielding of the ring oxygens by equatorial and axial P-OMe groups is unusually small. Six-membered ring compounds having an axial methyl substituent at the 4 or 6 position show a definite  $\delta$  compression effect on the axially substituted P-OMe group. A downfield shift of equatorial substituted methoxy groups is also seen when the 4 or 6 positions are axially substituted, although this situation is difficult to account for.

From the bicyclic systems, it appears that the phosphoryl oxygen chemical shift in compounds in a boat conformation are well upfield of those in a chair form.

As seen in Figure 7, there are a series of linear relationships between the  $^{31}\text{P}$  chemical shift and the  $^{17}\text{O}$  chemical shift of the phosphoryl oxygen of the phosphates. The lines corresponding to the acyclic and five-membered ring phosphates have a negative slope (Table 19) equal to the ratio  $2\langle r^{-3} \rangle_{\text{O}} / \langle r^{-3} \rangle_{\text{P}}$ , (calculated 2.48) where the terms  $\langle r^{-3} \rangle_{\text{O}}$  and  $\langle r^{-3} \rangle_{\text{P}}$  are the inverse cube of the ratios of the valence p orbitals of oxygen and phosphorus respectively.<sup>133</sup> Similar correlations have been reported between  $\delta^{14}\text{N}$  and  $\delta^{17}\text{O}$  for a series of N-O bonds<sup>134</sup> and between  $\delta^{13}\text{C}$  and  $\delta^{17}\text{O}$  for a series of aliphatic ketones and aldehydes.<sup>135</sup> In the two latter cases, the slopes are equal to

Figure 7. Plot of  $^{31}\text{P}$  chemical shift versus the  $^{17}\text{O}$  chemical shift of the phosphoryl oxygen for phosphates



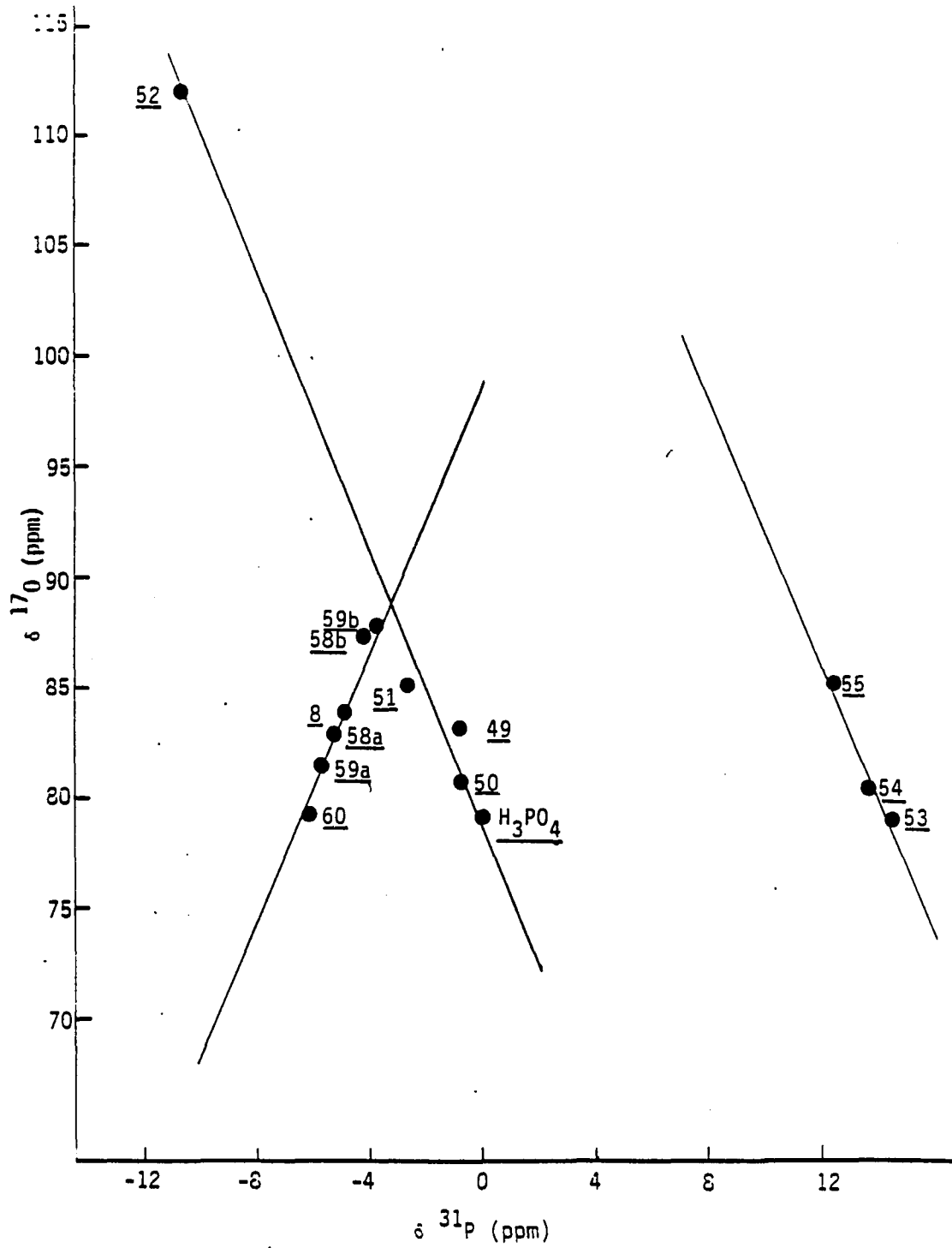


Table 19

Slopes, intercepts and correlation coefficients for plots of  $\delta^{17}\text{O}$  versus  $\delta^{31}\text{P}$  for phosphates

Compounds	Slope	y-Intercept	Correlation Coefficients
Acyclic	-2.48	78.8	0.995
Five-membered ring	-2.41	122.3	0.982
Six-membered ring	3.05	102.9	0.990

$\langle r^{-3} \rangle_{N \text{ or } C} > \langle r^{-3} \rangle_{P}$ . There is no good rationale for the factor of two which appears in the case of the phosphates but not in the other two cases, although it may be due to the fact that phosphorus has 3p valence orbitals as compared to 2p orbitals for all of the other elements.

The behavior of the six-membered rings is quite different. Here, the line has a positive slope, and there is no correlation with the p orbital radius ratio. The reason for this radically different behavior is not clear, although it may be related to the fact that in the first two series the variation in substitution occurs on a non-cyclic group but the substitutions on the six-membered rings is always in a ring position.

In the cases of the carbonyl and N-O compounds, these shifts have been related to changes in the  $\pi$  bond order upon substitution. A decrease in P=O bond order, should lead to increased shielding of the phosphory oxygen and a decrease in the shielding of phosphorus. However, in the case of the six-membered ring compounds, the chemical shift of both the phosphorus and the phosphoryl oxygen change in the same direction. There is also a linear relationship between both  $\delta^{17}O$  and  $\delta^{31}P$  and the value of  $^1J_{PSe}$  of the corresponding selenides (Figures 8 and 9), a parameter which has been related to phosphorus basicity.<sup>136</sup> An increase in the phosphorus basicity should lead to a weaker P=O bond, and a greater shielding of the oxygen. However, a decrease in oxygen shielding with increasing phosphorus basicity is actually observed.

There does not appear to be any correlation between  $^1J_{PSe}$  and the chemical shifts for the acyclic phosphates. This relationship for the five-membered ring compounds could not be checked owing to an absence of the necessary coupling constants in the literature.

Figure 8. Plot of  $^{17}\text{O}$  chemical shift of the phosphoryl oxygen of phosphates versus  $^1\text{J}_{\text{PSe}}$  of the corresponding selenophosphates<sup>136</sup>

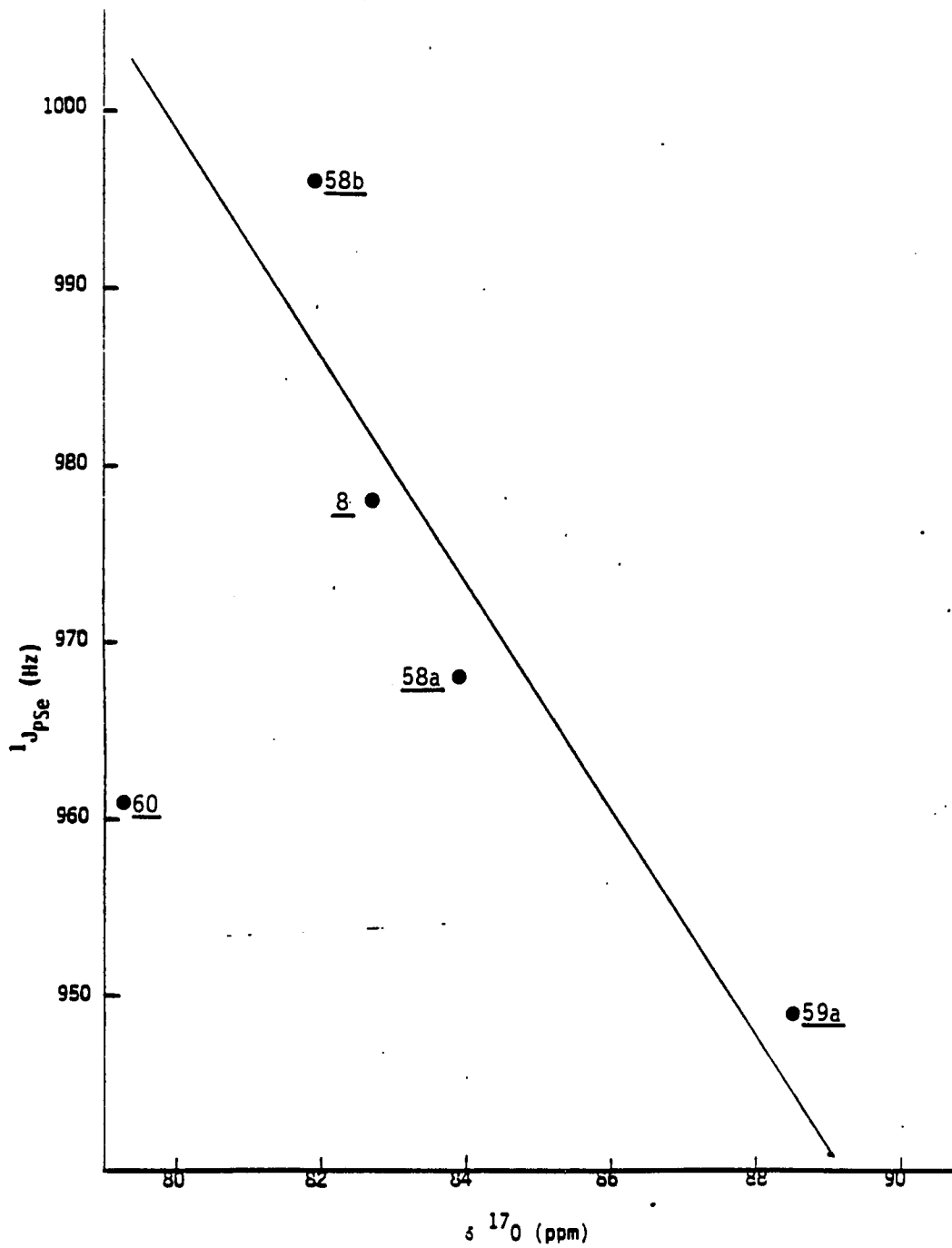
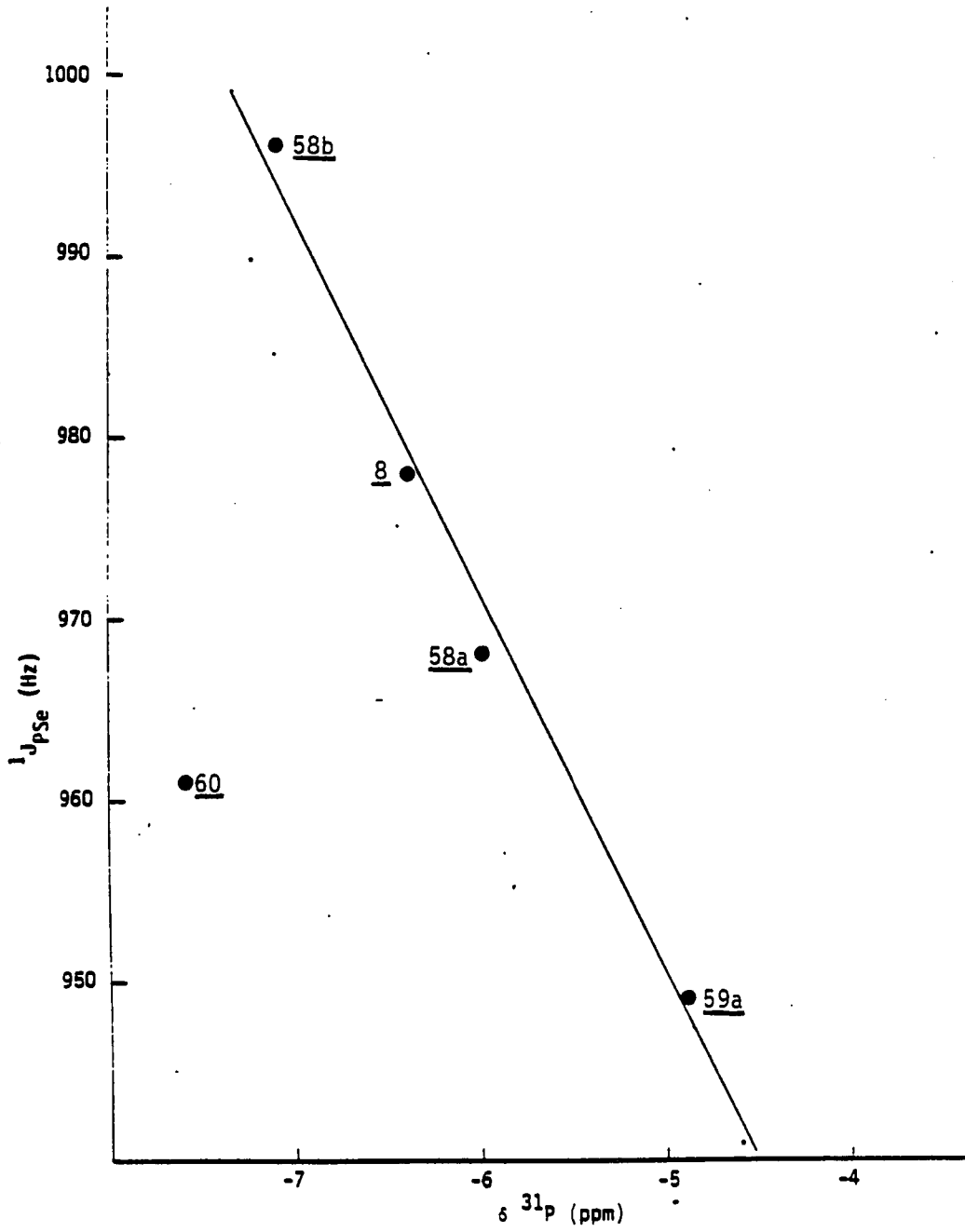


Figure 9. Plot of  $^{31}\text{P}$  chemical shift of cyclic phosphates against  $^1J_{\text{PSe}}$  of the corresponding selenophosphates<sup>136</sup>



PART V: ATTEMPTED SYNTHESIS OF "ATRAPE" CAGES



## INTRODUCTION

In 1933, Rojahn reported the synthesis of boratrane,  $B(OCH_2CH_2)_3$  N.<sup>137</sup> This led to the extensive study of a new class of caged compounds of the general formula  $M(OCH_2CH_2)_3$  N where M can be boron,<sup>137-171</sup> aluminum,<sup>172-176</sup> silicon,<sup>46, 176-217</sup> phosphorus,<sup>47-51</sup> titanium,<sup>176,218-223</sup> vanadium,<sup>218,224,225</sup> iron,<sup>226,227</sup> zinc,<sup>228</sup> germanium,<sup>229-234</sup> zirconium,<sup>218</sup> molybdenum,<sup>235,236</sup> hafnium,<sup>218</sup> tin,<sup>237-241</sup> lead,<sup>242</sup> bismuth,<sup>243</sup> or samarium.<sup>244</sup>

Of these, by far the most extensively investigated are the boratranes and silatranes. These compounds have been found to be useful for a variety of applications.<sup>245-261</sup>

Because of this and the recent reports in the literature of the synthesis of the triol  $P(CH_2CH_2OH)_3$ ,<sup>262</sup> we decided to attempt to extend the atrane system of compounds to those which would have a phosphorus at the bridgehead in place of the nitrogen,  $M(OCH_2CH_2)_3P$ . In line with the system of nomenclature suggested by Voronkov,<sup>46</sup> these will be named throughout this section as "atrapes" (i.e. boratrape, silatrape, and phosphatrape).

## EXPERIMENTAL

## Techniques

Materials

Triethyl borate, tributyl borate, and dibutyl ether were obtained from Aldrich and used as received. The phenyltrichlorosilane was made by Dow Corning and was used without further purification. Methyltriethoxysilane and phenyltriethoxysilane were distilled prior to use. Tris-2-hydroxyphenylphosphine was purchased from Alfa and used as received.

Preparations

A nitrogen atmosphere was maintained insofar as possible throughout the following preparations.

Phenyltriacetoxysilane

This compound was prepared by the method of Balthis.<sup>263</sup>

Phenyltrichlorosilane Hydrolyzate

This material was prepared by very slowly adding 3.5 g of distilled water to 25.0 g of phenyltrichlorosilane. The resulting white solid was dried on the vacuum line.

2-tert-Butoxyethylchloride

This compound was made by a literature method.<sup>264</sup>

2-tert-Butoxyethylphosphine

This compound was obtained in literature yield by the method of Tzschach et al.<sup>262</sup>

tris-2-tert-Butoxyethylphosphine

This compound was prepared by the method of Tzschach et al.<sup>262</sup>, with the modification that the product was distilled at 83-85<sup>o</sup>/0.01 torr, but could only be made in 4% yield as opposed to the 52% yield reported in the literature.

Triethanolphosphine

This compound was obtained in 50% yield by the method of Tzschach and co-workers.<sup>262</sup> The product was further purified by dissolving in distilled water and extracting with a small amount of CHCl<sub>3</sub>. The water was then removed in vacuo and the resulting oil dissolved in methylene chloride and dried with magnesium sulfate. Following filtration, the methylene chloride was removed on the vacuum line.

Reaction of P(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>3</sub> with B(OH)<sub>3</sub>

This reaction was carried out by a modification of the method of Brown and Fletcher.<sup>138</sup> P(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>3</sub> (0.0100 mole, 1.67 g) and B(OH)<sub>3</sub> (0.0100 mole, 0.618 g) were placed in a 25 ml round bottom flask, equipped with a short path distillation head. The system was slowly evacuated to 1 torr, and the receiver flask was immersed in a liquid nitrogen bath. The temperature of the reaction flask was raised to 112<sup>o</sup>C

over the next 2.3 hours, resulting in 0.17 g of H<sub>2</sub>O being collected in the receiver flask, and a white solid remaining in the reaction flask. The solid proved to be completely insoluble in a variety of solvents and upon attempted sublimation decomposed at 182°/0.01 torr.

Reaction of P(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>3</sub> with B(OH)<sub>3</sub> in dimethylformamide

This reaction was carried out by a modification of the method described by Schlepplik and Gutsche.<sup>143</sup> P(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>3</sub> (0.0100 mole, 1.67 g) and B(OH)<sub>3</sub> (0.010 mole, 0.62 g) and 10 ml of dry dimethylformamide were placed in a 25 ml round bottom flask equipped with a short path distillation column. The reaction mixture was heated to 120° to distill off the water which formed. The white solid which formed was collected by filtration and dried in vacuo. This solid was insoluble in a variety of solvents and decomposed upon attempted sublimation.

Reaction of P(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>3</sub> with B(O-n-Bu)<sub>3</sub>

This reaction was carried out by a modification of the method of Schlepplik and Gutsche.<sup>143</sup> P(CH<sub>2</sub>CH<sub>2</sub>OH)<sub>3</sub> (0.0100 moles, 1.67 g) was added to B(O-n-Bu)<sub>3</sub> (0.0100 moles, 2.30 g) The solution warmed very slightly and a white precipitate formed. The reaction mixture was heated to 130° to distill off the butanol which had formed and the remaining solid was dried in vacuo. This solid was also insoluble in a variety of solvents and decomposed at 211°/0.02 torr upon attempted sublimation.

Reaction of  $P(CH_2CH_2OH)_3$  with  $MeSi(OEt)_3$ 

This reaction was done by a modification of the method of Finestone.<sup>177</sup>  $P(CH_2CH_2OH)_3$  (0.0100 mole, 1.67 g)  $MeSi(OEt)_3$  (0.0100 mole, 1.79 g) and 20 ml of dry benzene were placed in a 50-ml round bottom flask equipped with a Dean-Stark trap. The reaction was brought to reflux and ethanol was azeotropically removed. A white precipitate formed and was collected by filtration. The solid was dried under vacuum. The solid was insoluble in a variety of solvents and decomposed upon attempted sublimation.

Reaction of  $P(CH_2CH_2OH)_3$  and  $Si(OEt)_4$ 

This reaction was done by a modification of the method of Voronkov and Zelcans<sup>190</sup>  $P(CH_2CH_2OH)_3$  (0.010 moles, 1.67 g) and  $Si(OEt)_4$  (0.010 moles, 2.00 g), 15 ml xylene and 0.01 g KOH were placed in a 50 ml round bottom flask equipped with a short path condenser. The reaction was heated to distill off the ethanol and a white solid precipitated. After distillation of about 1.5 ml of ethanol the reaction was cooled, filtered and the solid dried on the vacuum line. The solvent was evaporated to dryness in vacuo, but yielded no residue. The dry solid proved insoluble and decomposed on attempted sublimation.

Reaction of  $P(CH_2CH_2OH)_3$  with  $PhSi(OEt)_3$ 

This reaction was carried out using a modification of the method described by Daneshrad et. al.<sup>186</sup>  $P(CH_2CH_2OH)_3$  (0.010 mole, 1.67 g) and  $PhSi(OEt)_3$  (0.010 mole, 2.40 g) were placed in 15 ml round bottom flask

equipped with a short path distillation head. The reaction was slowly heated to  $125^{\circ}$  and the ethanol which formed was distilled off. When about 1.5 ml of ethanol had been collected, the white solid which had formed was dried on the vacuum line. The resulting material was again insoluble and decomposed upon attempted sublimation.

#### Reaction of $P(CH_2CH_2OH)_3$ with $PhSiCl_3$ hydrolyzate

This reaction was carried out by a modification of the method of Voronkov and Zelcans.<sup>192</sup> Phenyltrichlorosilane hydrolyzate (1.29 g 0.0100 mole), 1.67 g (0.0100 mole) of  $P(CH_2CH_2OH)_3$ , 0.01 g of KOH and 30 ml of dry xylene were placed in a 50 ml round bottom flask equipped with a Dean-Stark trap. The reaction was refluxed for six hours and the water which formed was removed by azeotropic distillation. The reaction mixture was then filtered and the solid dried on the vacuum line. This solid proved insoluble and would not sublime. Evaporating the filtrate to dryness in vacuo showed that nothing remained in solution.

#### Reaction of $PhSi(OAc)_3$ with $P(C_6H_4OH)_3$

This reaction was done by a slight modification of the method of Frye et al.<sup>179</sup> A hot solution of 4.5 g (0.016 mole) of  $PhSi(OAc)_3$  in 25 ml  $CCl_4$  was added to a boiling suspension of 5.0 g (0.016 mole) of tris(2-hydroxyphenyl)phosphine in 70 ml of  $CCl_4$ , the reaction mixture became almost clear momentarily and then a white solid precipitated. This solid was insoluble in a variety of solvents and would not sublime.

Reaction of  $\text{PhSiCl}_3$  with  $\text{P}(\text{C}_6\text{H}_4\text{OH})_3$ 

This reaction was also done by a modification of the method of Frye and co-workers.<sup>179</sup> Tris(2-hydroxyphenyl)phosphine (5.0 g, 0.016 mole) was added to a solution of 3.4 g (0.016 mole) of  $\text{PhSiCl}_3$  in 65 ml of  $\text{Bu}_2\text{O}$  and the mixture was boiled for 4 hours, during which time  $\text{HCl}$  could be detected by litmus paper in the nitrogen flush. The solid which was isolated from the reaction was completely insoluble and would not sublime.

Reaction of  $\text{P}(\text{CH}_2\text{CH}_2\text{OH})_3$  with  $\text{P}(\text{NMe}_2)_3$ 

This reaction was run in a manner similar to that previously described for making 26 (vide supra).  $\text{P}(\text{CH}_2\text{CH}_2\text{OH})_3$  (0.010 mole, 1.67 g) was dissolved in 30 ml of  $\text{CHCl}_3$  and placed in a 50 ml syringe.  $\text{P}(\text{NMe}_2)_3$  (0.010 mole, 1.63 g) was dissolved in 30 ml toluene and placed in a second 50 ml syringe. The two reactants were simultaneously added to 250 ml of refluxing toluene by means of the dual syringe drive, over a six hour period. The reaction was allowed to cool to  $45^\circ$  and 0.80 g (0.22 moles) of sublimed sulfur was added. The reaction mixture was slowly heated to reflux and then allowed to cool to room temperature. The reaction mixture was filtered and the solvent removed in vacuo. No material remained in solution. The yellow solid from the filtration was extracted with carbon disulfide to remove unreacted sulfur. The resulting pale yellow solid proved to be insoluble in a variety of solvents and decomposed upon attempted sublimation.

Reaction of  $P(\text{CH}_2\text{CH}_2\text{OH})_3$  with  $\text{OPCl}_3$ 

$P(\text{CH}_2\text{CH}_2\text{OH})_3$  (0.0100 mole, 1.67 g) was dissolved in 30 ml of  $\text{CHCl}_3$  and placed in a 50-ml syringe.  $\text{OPCl}_3$  (0.010 mole, 1.5 g) was dissolved in 30 ml of dry ether and placed in a 50 ml syringe. The two reagents were simultaneously added to 250 ml of dry ether, at  $0^\circ\text{C}$ , over a four hour period by means of a dual syringe drive. The reaction was allowed to warm to room temperature and the white solid that resulted was separated by filtration. This solid also proved to be insoluble and darkened upon attempted sublimation. Evaporating the ether to dryness showed that no material was left in solution.



## RESULTS AND DISCUSSION

All of the reactions failed to yield any of the desired products, which is quite surprising in light of the high yields that are obtained with the nitrogen analogs under the same conditions.

It was felt that this result could be due to the formation of a nitrogen adduct with the boron or silicon, prior to cage closure in one case but not in the case of the phosphorus analogue. To check this hypothesis, the  $^{11}\text{B}$  NMR spectrum of triethylborate with up to three equivalents of  $\text{PEt}_3$  or  $\text{NEt}_3$  was observed. In all cases there was no change in the boron chemical shift, relative to external  $\text{B}(\text{OEt})_3$ , upon addition of either base. Thus, indicating that adduct formation does not precede cage closure in either case.

The inability to form "atrapes" may be related to the higher barrier to inversion of phosphorus. In the absence of a transannular bond, the phosphorus would be forced towards a planar geometry in order to relieve hydrogen-hydrogen interactions, as has been seen for the nitrogen in phosphatranes.<sup>49,50</sup> This is a geometry that phosphorus would most likely be unwilling to adopt, although it should be noted that Diel and Norman<sup>265</sup> have reported the synthesis of  $\text{P}(\text{CH}_2\text{CH}_2\text{CH}_2)_3\text{P}$ , a compound in which hydrogen-hydrogen repulsions should also force the bridgehead atoms towards a planar geometry. If the bicyclic geometry is not stable, then the relative difficulty with which phosphorus inverts, could favor polymer formation, since the correct orientation for cage closure with transannular bond formation would only occur half of the time once two arms of the cage had formed.

Another possibility is that the cage is initially formed, and then a further transesterification occurs to yield polymer. This type of behavior is indicated in the synthesis of phosphatrane by the fact that reaction much longer than twenty four hours results in polymer being obtained as the only product.

PART VI: PROTONATION OF 1-PHOSPHA-5-AZA-2,6,9-TRIOXABICYCLO[3.3.3]  
UNDECANE

## INTRODUCTION

In an attempt to prepare  $RP(OCH_2CH_2)_3N^+BF_4^-$  by treating  $P(OCH_2CH_2)_3N$  with  $R_3O^+BF_4^-$ , R = Me or Et, Milbrath and Verkade<sup>47,48</sup> reported that they obtained  $HP(OCH_2CH_2)_3N^+BF_4^-$ , 18, as the only isolable monomeric product. They speculated that the proton source was either adventitious water or deprotonation of the Meerwein reagent, with an olefin being released into the reaction mixture.<sup>266</sup>

As part of the study on the formation of transannular bond formation in phosphatranes, an attempt was made to make the alkylated phosphatrane  $MeP(OCH_2CH_2)_3N^+CF_3SO_3^-$  by treating 26 with methyl triflate (vide infra). This also resulted in the formation of 18 as the sole isolable monomeric product. At about the same time, an attempt to prepare the tritylated phosphatrane, 19, by the method of Milbrath and Verkade,<sup>47</sup> surprisingly gave 18 rather than the expected product 19. Due to these results, a closer examination of the source of the proton in this reaction seemed in order.

## EXPERIMENTAL

## Techniques

Materials

Heptane was purified by refluxing over and distilling from sodium. Methyl triflate, silver triflate, and deuterated methyl iodide were obtained from Aldrich Chemical Company and used as received. All other reagents were obtained and purified as described in preceding sections.

NMR Spectroscopy

Proton NMR spectra were obtained using a Varian 360 or a Nicolet NT-300 spectrometer in a manner described earlier.

$^{31}\text{P}$  NMR spectra were obtained using a Bruker NX-90 spectrometer as previously described.

Sample PreparationTrimethyloxonium tetrafluoroborate

This compound was prepared by the procedure of Meerwein.<sup>267</sup>

Triphenylmethyl (trityl) tetrafluoroborate

This compound was prepared by the literature method<sup>268</sup> from triphenylcarbinol and fluoroboric acid in acetic anhydride.

 $\text{d}^3$ -Methyl triflate

This compound was prepared by a literature method<sup>269</sup> from silver

triflate and  $d^3$ -methyl iodide.

1-H-1-phospha-5-aza-2,6,9-trioxabicyclo[3.3.3]undecane

This compound was prepared by seven modifications of the method of Milbrath and Verkade<sup>47</sup> as described below.

Method 1

A 1 L three-neck round bottom flask, equipped with a reflux condenser and two bent adaptors with septa, was set up hot from the oven under a nitrogen flush. A solution of 7.5 g (50 mmole) of  $N(CH_2CH_2OH)_3$  in 20 ml of  $CHCl_3$  was diluted to 50 ml with toluene and placed in a 50 ml syringe. Tris-(dimethylamino)phosphine (9.0 g, 55 mmole) was dissolved in enough toluene to make 50 ml of solution and placed in a second 50-ml syringe. The syringes were mounted in a Harvard Apparatus Company dual syringe drive and the needles inserted through the septa in the bent adaptors. Dry toluene (750 ml) was placed in the flask and brought to reflux. The syringe drive was started and the reactants were added simultaneously over a 24 hour period. After completion of the addition, the reaction mixture was allowed to cool to room temperature and trimethyloxonium or triethyloxonium tetrafluoroborate (60 mmoles), dissolved in 100 ml of acetonitrile, was added dropwise. The resulting white solid was filtered and extracted with two 25 ml portions of hot acetonitrile. The acetonitrile was removed in vacuo and the residue extracted with 25-30 ml of acetone.

Further purification was accomplished by the precipitation-filtration procedure described by Milbrath<sup>266</sup> (yield 6%).

Method 2

Method 2 is exactly analogous to Method 1, except that heptane was used as a solvent in place of toluene (yield 4%).

Method 3

Method 3 is the same as described in Method 1, except that methyl triflate (2.5 g, 15 mmole) was added via syringe in place of Meerwein's reagent (yield 7%).

Method 4

Method 4 is the same as Method 3 with the exception that  $d^3$ -methyl triflate was used in place of methyl triflate (yield 6%).

Method 5

Method 5 is the same as Method 3 with the exception that deuteriochloroform was used in place of chloroform (yield 6%).

Method 6

Method 6 is the same as described in Method 3 except that heptane was used as the solvent instead of toluene (yield 5%).

Method 7

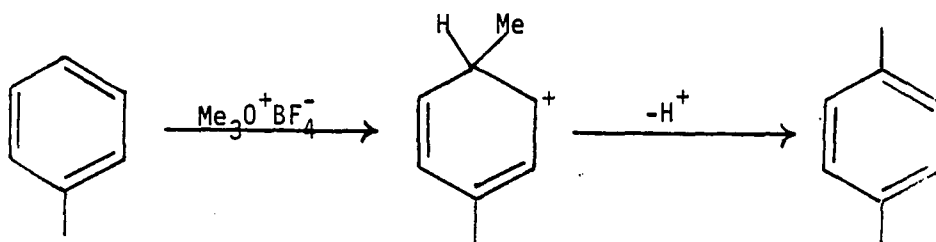
This method was the same as Method 1 except that trityl tetrafluoroborate was used as the derivatizing agent. Formerly, this

reaction yielded tritylated phosphatrane,<sup>47</sup> however, recently only protonated phosphatrane has been obtained (yield 4%).



## RESULTS AND DISCUSSION

There appeared to be four possible proton sources other than adventitious water, an explanation which seemed unlikely since all reagents were carefully dried just prior to use and an inert atmosphere was maintained in the reaction vessel throughout the synthesis. The other sources were proton abstraction from the alkylating agent as previously suggested, proton abstraction from the chloroform, alkylation of the aromatic solvent<sup>269</sup> followed by deprotonation as shown below, or proton abstraction from unreacted hydroxyl groups of the polymer, which is the major product formed in all of the phosphatrane syntheses. It is likely that the polymer contains unreacted hydroxyl groups, as continued heating past the point where the reaction mixture is usually worked up, results in the continued evolution of dimethylamine. However, extending the reaction time till no further amine is evolved, results in polymer being obtained as the only product.



The fact that the use of deuteriochloroform or  $\text{d}^3$ -methyl triflate does not result in a deuterated product or have any significant effect on the yield of the protonated product, eliminates these reagents as the

proton source. Since the use of heptane as a solvent does not affect the course of the reaction, alkylation of the solvent, followed by deprotonation can also be ruled out.

This leaves the polymer as the only remaining proton source. The fact that trityl tetrafluoroborate now yields the protonated product rather than the expected alkylated product is also consistent with this hypothesis, as the tritylated product was always obtained prior to the point in time when the nature of the polymer obtained in the reaction appears to have changed. In the work of Milbrath and in the early part of the present work, the polymer had the form of a white sticky solid. Starting a few years ago, the polymer obtained was in the form of a yellow viscous oil, a result that has not been satisfactorily explained.

## SUMMARY

A crystal structure determination of 4 is reported. The bond lengths and angles of 4 compare favorably with those in 2, thus giving further support to the prior conclusion that 2 is strainless.<sup>7</sup>

The crystal structure determination of 13b confirmed the configurational assignments previously made by White et al.

Evidence is presented for transannular bond upon protonation of 20 and 21. It is also shown that phosphoryl oxygen of 20 or the phosphoryl sulfide of 21 is diprotonated at high acid to substrate ratios.

The <sup>17</sup>O NMR data for a series of phosphites and phosphates is correlated with alkyl substitution and ring conformation.

Unsuccessful attempts to synthesize compounds of the type  $X(\text{OCH}_2\text{CH}_2)_3\text{N}$  (X = B, Si, P) are reported.

Protonation of 26 by trialkyloxonium tetrafluoroborate and methyl triflate was investigated and it was determined that the polymer generated during the formation of 26 was the source of the proton.

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ACKNOWLEDGEMENTS

I would like to thank Dr. John Verkade whose advice and patience has allowed this work to be completed.

I would also like to thank the many friends, that I have made during my graduate career, for their encouragement.

Most importantly, I would like to thank my parents and brothers for the support and encouragement that they have provided throughout my life.