

The infrared spectrum of the sirup was identical with authentic 1,2,3,5-tetra-*O*-methyl-*D*-xylitol. When examined by gas-liquid partition chromatography, the sirup had the same retention volume as that of the authentic 1,2,3,5-tetra-*O*-methyl-*D*-xylitol.

4-O-p-Nitrobenzoyl-tetra-O-methyl-D-xylitol. The tetra-*O*-methylxylitol (8 mg.) was converted into its *p*-nitrobenzoate by the procedure of Rebers and Smith.¹⁶ The crystals gave the same X-ray diffraction pattern as that from the authentic 4-*O-p*-nitrobenzoyl-tetra-*O*-methyl-*D*-xylitol.

Preparation of 1,2,3,5-tetra-O-methyl-D-xylitol. Beechwood xylan¹⁷ (10 g.) was hydrolyzed with pectinase¹⁸ and the cleavage products were removed by dialysis according to the procedure of Painter.¹⁹ In this way 4.75 g. of monosaccharides and oligosaccharides was obtained. The mixture was resolved by charcoal: Celite chromatography.²⁰ Elution of the column with 5% aqueous ethanol gave two fractions: I, 341 mg., composed of approximately equal amounts of xylose, xylobiose, and xylotriose; and II, 197 mg., predominantly xylotriose.²¹

(16) P. A. Rebers and F. Smith, *J. Am. Chem. Soc.*, **76**, 6097 (1954).

(17) G. A. Adams, *Can. J. Chem.*, **35**, 556 (1957).

(18) A product of Rohm and Haas Co., Philadelphia, Pa.

(19) T. J. Painter, *Can. J. Chem.*, **37**, 497 (1959).

(20) R. L. Whistler and D. F. Durso, *J. Am. Chem. Soc.*, **72**, 677 (1950).

Xylotriose (m.p. 204–205°C., $[\alpha]_D^{25}$ -44° , in water) was reduced with sodium borohydride³ and the product was methylated successively by the Haworth,¹⁰ Purdie,¹² and Kuhn²² procedures. Absence of OH absorption in the infrared spectrum showed that the product was fully methylated.

The methylated xylotriitol was hydrolyzed with *N*-hydrochloric acid at 97° for 12 hr. and the hydrolyzate was oxidized directly with bromine for 48 hr. The sugar acids were adsorbed on Amerlite IR-45(OH) and the effluent was extracted continuously with chloroform to give 1,2,3,5-tetra-*O*-methyl-*D*-xylitol, a sirup which failed to crystallize. The latter was *p*-nitrobenzoylated as described previously to afford crystalline 4-*O-p*-nitrobenzoyltetra-*O*-methyl-*D*-xylitol which was recrystallized from cyclopentane, m.p. 187–189° with preliminary softening or change in crystal form at 165–167°; $[\alpha]_D^{25} \pm 0^\circ$ (*c*, 0.8 in methanol).

Anal. Calcd. for $C_{18}H_{28}O_8N$: C, 53.8; H, 6.49. Found: C, 53.4; H, 6.51.

Acknowledgment. Thanks are due to F. P. Cooper for assistance in the gas liquid chromatography and to A. E. Castagne for microanalyses.

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(21) R. L. Whistler and C. Tu, *J. Am. Chem. Soc.*, **74**, 3609 (1952).

(22) R. Kuhn, H. Trischmann, and I. Löw, *Angew. Chem.*, **67**, 32 (1955).

[CONTRIBUTION FROM THE AGRICULTURAL RESEARCH DIVISION, AND EMERYVILLE RESEARCH CENTER, SHELL DEVELOPMENT CO., A DIVISION OF SHELL OIL CO.]

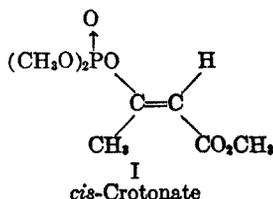
Preparation, Physical Properties, and Configuration of the Isomers in PHOSDRIN® Insecticide

ALAN R. STILES, CHARLES A. REILLY, GLENN R. POLLARD, CHARLES H. TIEMAN, LOYAL F. WARD, JR., DONALD D. PHILLIPS, S. B. SOLOWAY, AND R. R. WHETSTONE

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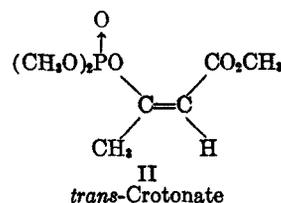
Phosdrin® Insecticide has been separated into its two geometrical isomers I and II by a combination of low temperature fractional crystallization and chromatography. The isomer which predominates in Phosdrin and has the greater toxicity has been assigned the *cis*-crotonate structure on the basis of NMR and infrared absorption spectra as well as other physical evidence. Assignment of structure is also made to a related pair of chlorovinyl phosphates (2-chlorovinyl dimethyl phosphate, V).

Phosdrin® insecticide is prepared by the reaction of trimethyl phosphite with methyl 2-chloroacetate¹ and is essentially a mixture of the two geometrical isomers of methyl 3-(dimethoxyphosphinyloxy)crotonate, I and II.



Partition chromatography with hydrated silica gel and chloroform, carbon tetrachloride and hexane was used by Casida² to separate these isomers.

(1) A. R. Stiles, U. S. Pat. 2,685,552, to Shell Development Co.



The isomer partitioning in favor of the organic phase was removed first and designated as the α -isomer. The isomer partitioning in favor of the water phase, when carbon tetrachloride and hexane were the organic phases, was then designated as the β -isomer. Casida^{2,3} showed that the α -isomer was the more toxic compound to insects and mammals and predominated over the β -isomer in

(2) J. E. Casida, *Science*, **122**, 597 (1955).

(3) J. E. Casida, P. E. Gatterdam, L. W. Getzin, and R. K. Chapman, *J. Ag. Food Chem.*, **4**, 236 (1956).

Phosdrin in the ratio of 3:2. Casida^{2,3} also observed that mixtures rich in the β -form were obtained on ultraviolet irradiation of either α - or β -isomer. He therefore concluded that the β -isomer was the more stable one and assigned to it structure I.

Spencer, Todd, and Webb⁴ separated the isomers from technical Phosdrin by counter-current distribution in an ether-water system. They arrived at the same conclusions as to the configuration of the two isomers from hydrolysis studies. Because the α -isomer was hydrolyzed in 1M sodium carbonate more rapidly at the methoxycarbonyl group than was the β -isomer, they assumed that competitive hydrolysis at phosphorus must be hindered in the α -isomer and, consequently, assigned structure II to the latter.

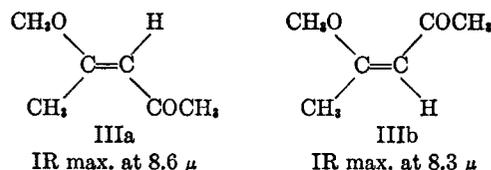
As these assignments of configuration do not depend upon the non-reacting, ground state of the molecules, it was felt important to apply physical methods for an unequivocal means of establishing structure. Consequently, we have used infrared absorption and NMR spectra and other physical evidence in arriving at a structural assignment of these isomers, namely that the α -isomer, the more toxic one predominating in Phosdrin, has structure I and the β -isomer has structure II. This is the opposite of that assumed by both Casida^{2,3} and Spencer *et al.*⁴

Separation of the two Phosdrin isomers. A combination of low temperature crystallization of technical Phosdrin and partition chromatography has been found to be generally satisfactory as a separation method, especially for the higher melting β -isomer. If pure β -isomer is desired, the Schrader synthesis⁵ is carried out with the lithium salt of methyl acetoacetate and dimethyl phosphorochloridate. The product is relatively pure β -isomer and serves as a source of seed crystals. The latter are obtained by vigorous scratching of β -isomer at -78° and may be kept crystalline by storage at -20° . Technical Phosdrin is then dissolved in ether, cooled to -78° , and seeded with the β -isomer. The crop of crystals that precipitates requires only one recrystallization to raise its purity to $>99\%$ β , m.p. 6.9° . The mother liquors are then seeded at -78° with the α -isomer (obtained by vigorous scratching at liquid nitrogen temperatures of α -isomer prepared by Casida's³ procedure) and after two recrystallizations of the crystals that deposit, α -isomer of 90–93% purity is obtained.

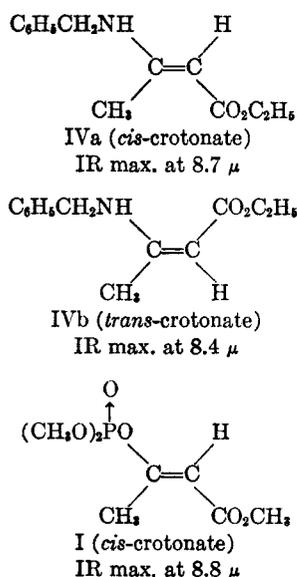
α -Isomer of higher purity is obtained by first freeing the technical material of most of the β -isomer by partitioning the latter into water from a carbon tetrachloride solution, and then subjecting

the crude α -isomer to distillation and recrystallization twice from ether at -78° . A product of 99% purity, m.p. -21° , is thus realized. Alternatively, the α -enriched product remaining after the first crop of β -isomer has been removed by crystallization may be chromatographed in carbon tetrachloride solution on hydrated silica gel. The first fractions that emerge from the column are about 97% pure α -isomer. The experimental section gives details for both of these purification procedures.

Configurational assignments of the Phosdrin isomers. Infrared absorption data. Absorption in the infrared occurs at 8.8 and 8.23 μ for the α - and β -isomers, respectively, presumably due to in-plane wagging of the vinyl hydrogen. Similarly constituted compounds absorb in the same region and may be used as models for assigning stereochemical formulas to the isomers. Thus, the isomer of *O*-methylacetylacetone IIIa in which the methyl and hydrogen are *trans* absorbs at 8.6 μ , whereas the other isomer, IIIb, absorbs at 8.3 μ .⁶ Similarly, ethyl 3-benzylamino-*cis*-crotonate, IVa, absorbs at 8.7 μ whereas the *trans*-crotonate isomer,



IVb, absorbs at 8.4 μ .⁷ The compounds IIIa and IVa are very similar in structure to I, whereas IIIb and IVb strongly resemble II. The parallelism in structure and infrared absorption of these isomers compared to those of Phosdrin suggest that the α -isomer is I and the β -isomer is II.

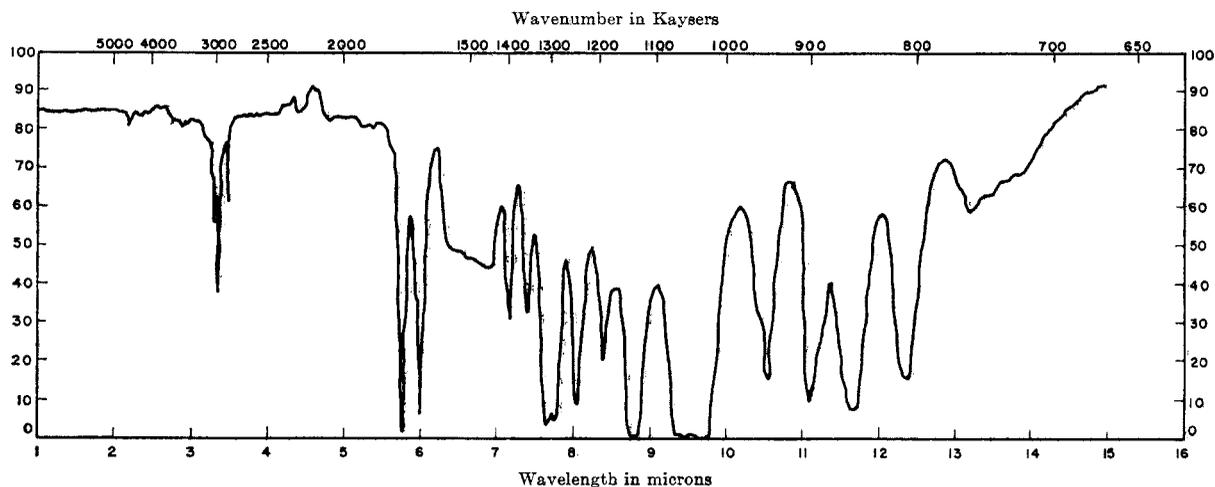
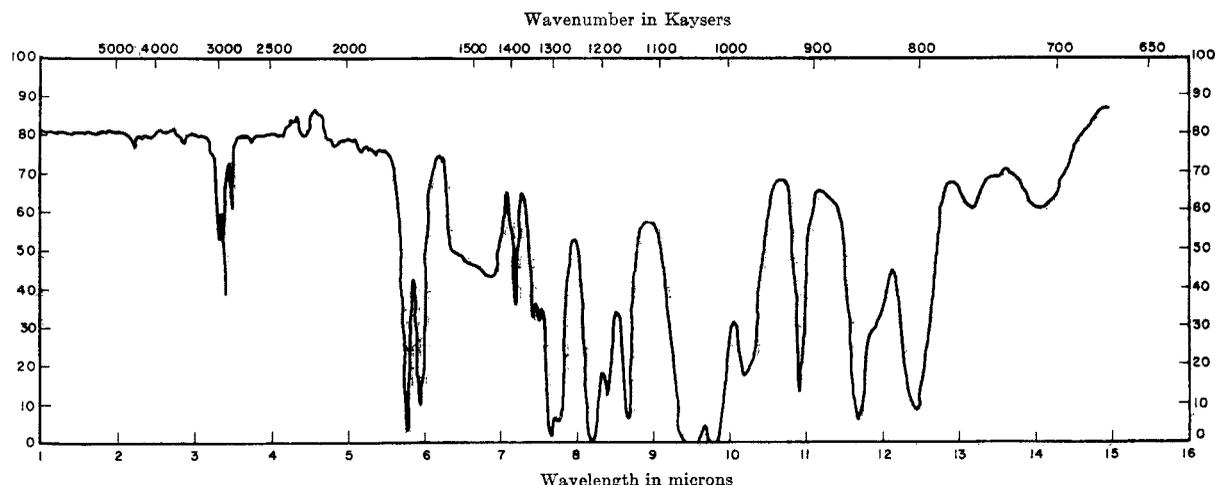
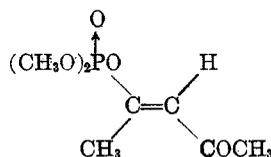
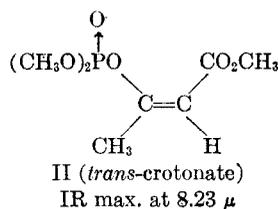
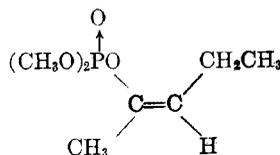


(4) E. Y. Spencer, A. Todd, and R. F. Webb, *J. Chem. Soc.*, 2968 (1958).

(5) G. Schrader, *Angew. Chem. Monograph No. 62*, 48 (1952).

(6) V. v. Keussler and G. Rossny, *Z. fur Elektrochemie*, 60, 136 (1956).

(7) H. P. Schad, *Helv. Chim. Acta*, 38, 1117 (1955).

Fig. 1. α -Phosdrin solvent: CS_2 Fig. 2. β -Phosdrin solvent: CS_2 

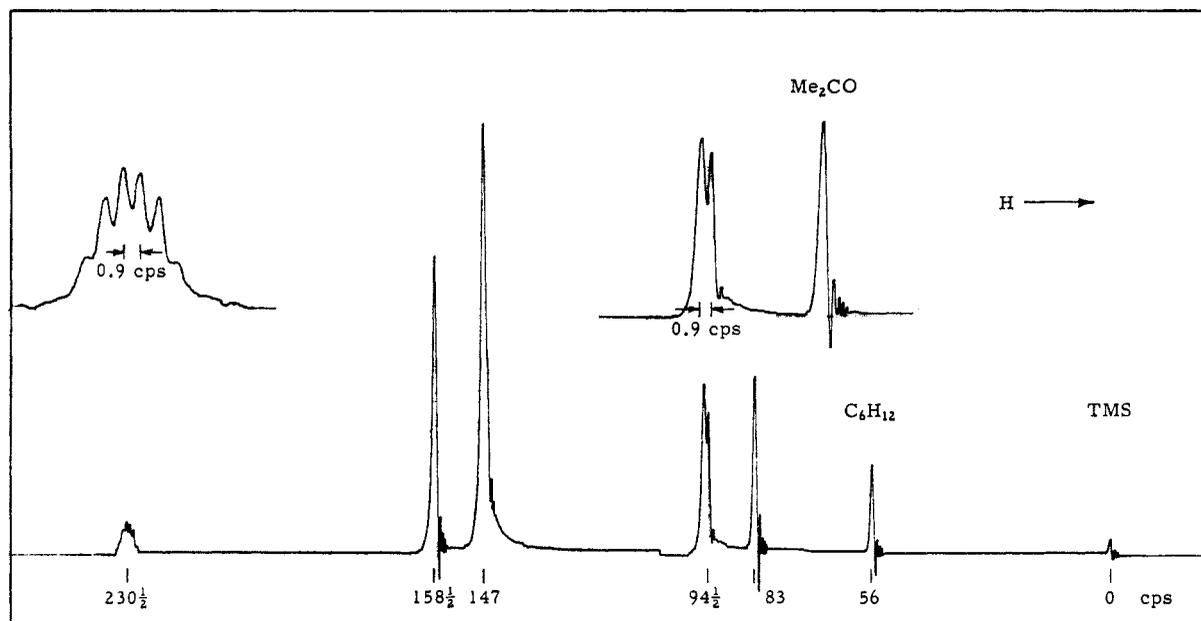
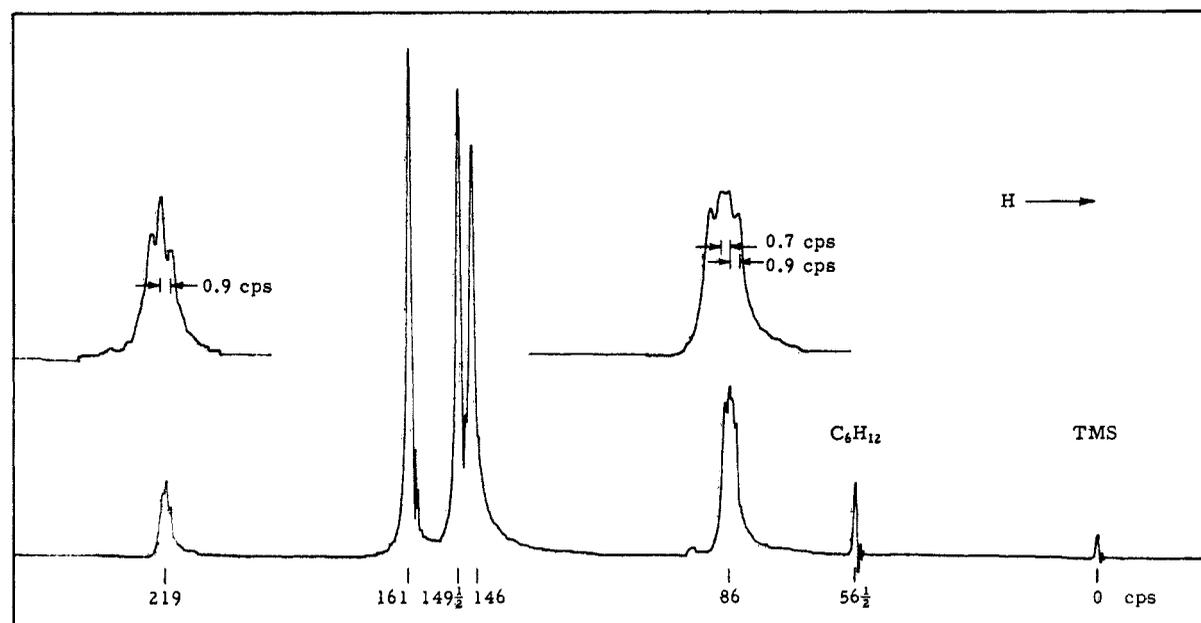
Infrared absorption curves for α - and β -isomers, obtained on a Beckman IR-4 spectrophotometer, are given in Figs. 1 and 2.

NMR data.⁸ The NMR spectrum of α -isomer is presented in Fig. 3 and that of β -isomer in

Fig. 4. The sample of α -isomer contained a little acetone as well as tetramethylsilane (TMS) and cyclohexane. Separate experiments showed that it had no influence on the α -isomer spectrum.

(8) All NMR spectra in this report were measured at 40 mc./sec. on a modified Varian Model V4300 spectrometer. The samples contained small amounts of tetramethylsilane (TMS) and of cyclohexane as internal references and were degassed by a freeze-pump-thaw technique prior to measurement. The spectra were calibrated in the usual way by the sideband technique.⁹

(9) J. T. Arnold and M. E. Packard, *J. Chem. Phys.*, **19**, 1608 (1951).

Fig. 3. 40 mc./second NMR spectrum of α -PhosdrinFig. 4. 40 mc./second NMR spectrum of β -Phosdrin

The chemical shifts between the various groups of equivalent nuclei are sufficiently greater than the spin-spin coupling constants between these groups of nuclei so that a simple first order perturbation treatment is adequate for the analysis.¹⁰ The location of the center of each band then gives the chemical shift directly. In Figs. 3 and 4 the band locations are given in c.p.s. from tetramethylsilane. It will be noted that the $=\text{CH}-$ resonance is shifted to lower applied field by $11\frac{1}{2}$ c.p.s. in

the α -isomer than in the β -isomer. Similarly, the $=\text{C}-$ resonance in this isomer is shifted by $8\frac{1}{2}$ c.p.s. to lower applied field than in the β -isomer. In the *cis* and *trans* isomers of $\text{CH}_3\text{CCl}=\text{CHCOOR}$ it has been reported¹¹ that the C-methyl resonance occurred at lower field (by several c.p.s.) in the compound with *cis*-relation between the methyl and the $-\text{COOR}$ group. Similar results

(10) J. A. Pople, W. G. Schneider, and H. J. Bernstein, *High Resolution Nuclear Magnetic Resonance*, McGraw-Hill, New York, 1959.

(11) R. Morris, C. A. Vernon, and R. F. M. White, *Proc. Chem. Soc.*, 303 (1958); D. E. Jones, R. O. Morris, C. A. Vernon, and R. F. M. White, *J. Chem. Soc.*, 2349 (1960).

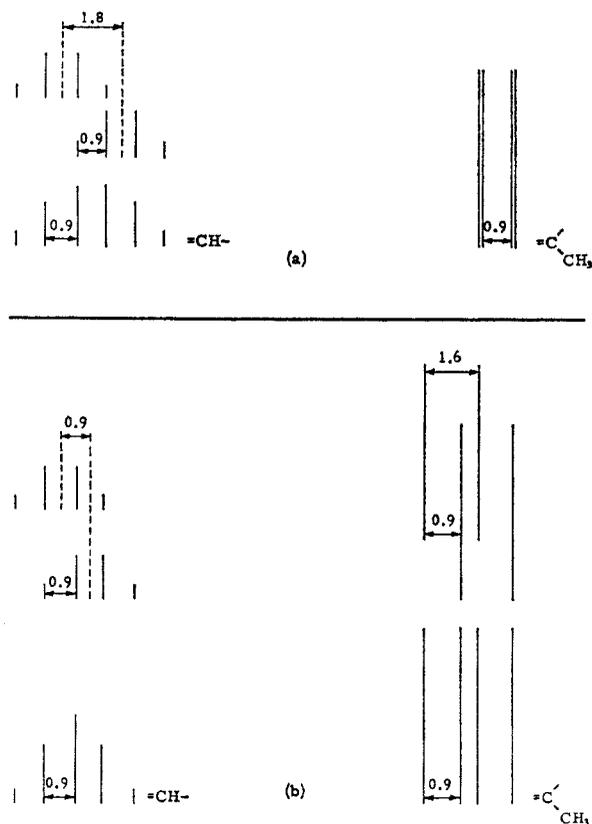


Fig. 5. Origin of fine structure in NMR spectra (a) in α -Phosdrin and (b) in β -Phosdrin

have been reported¹² for both the =C-CH_3 and =CH- groups in several other pairs of related compounds. Hence, assuming the same factors giving rise to the difference in shielding are operative in the Phosdrin isomers, the α -isomer must have the *cis*-crotonate structure I and the β -isomer the *trans* structure II. Although the spin-spin coupling constants in these molecules were not of use in the isomeric assignment, their derivation is of some interest and is presented below.

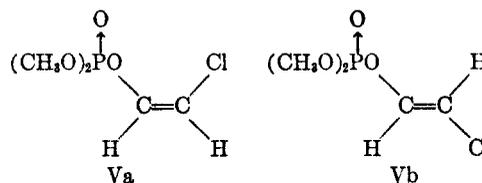
The doubling of the bands at $149\frac{1}{2}$ and 161 c.p.s. and at 147 and $158\frac{1}{2}$ c.p.s. from tetramethylsilane arises from a spin-spin coupling constant of 11.4 c.p.s. between the protons and the phosphorus in the grouping $\text{CH}_3\text{-O-P-O}$ (the resonance at 146 and part of the one at 147 c.p.s. from tetramethylsilane arise from the CH_3 groups in $\text{CH}_3\text{-O-C(=O)-}$). The fine structure in each of the =CH- and =C-CH_3 bands arising from spin-spin coupling is shown under higher resolution conditions as insets in Figs. 3 and 4. This fine structure arises from overlapping lines as indicated

(12) L. M. Jackman and R. H. Wiley, *J. Chem. Soc.*, 196 (1958); 2886 (1960).

in Fig. 5. In both isomers the coupling constant between the =CH- proton and the =C-CH_3 protons is 0.9 c.p.s. This would give rise to a quartet structure in the =CH- resonance and to a doublet structure in the =C-CH_3 resonance. An additional coupling constant of 1.8 c.p.s. in the α -isomer and of 0.9 c.p.s. in the β -isomer between =CH- and P gives rise to the patterns of superimposed quartets as shown in Fig. 5. The coupling constant of ~ 0 c.p.s. in the α -isomer and of 1.6 c.p.s. in the β -isomer between the =C-CH_3 and P gives rise to the fine structure for this group as shown by Fig. 5. The signs of all the coupling constants are indeterminate.

The NMR parameters for these isomers are summarized in Table I. The chemical shift data have been converted from c.p.s. to parts per million (p.p.m.) from tetramethylsilane by dividing by 40.

NMR Spectra of 2-chlorovinyl dimethyl phosphate (V). Confirming evidence for the structural assignments made above was sought in a similar vinyl phosphate, V. In this instance, analysis of the mixture was possible without isolation of the two individual isomers. The NMR spectrum of the mixture containing unequal amounts of Va and Vb is shown in Fig. 6 and the olefinic region



of the spectrum is shown under higher resolution in Fig. 7.

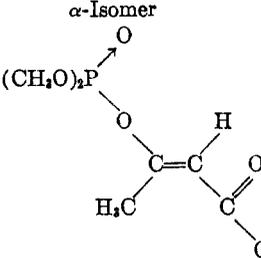
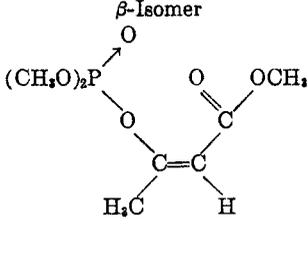
The band at $146\frac{1}{2}$ and 158 c.p.s. from tetramethylsilane comes from the CH_3 groups spin-coupled to P by $11\frac{1}{2}$ c.p.s. This result is practically identical to that found in Phosdrin. A small amount of noninterfering impurity is evidenced by the spectrum in Fig. 6.

The olefinic region of the spectrum (Fig. 7) consists of two overlapping groups of eight lines each. Each group of eight lines can be analyzed as the BA portion of a BAX spectrum¹⁰ (X in this case is the P nucleus). The labeling of the lines in Fig. 7 follows that described recently by one of us¹³ instead of that found in refs. 10 and 14. The spread

(13) C. A. Reilly and J. D. Swalen, *J. Chem. Phys.*, **32**, 1378 (1960).

(14) H. J. Bernstein, J. A. Pople, and W. G. Schneider, *Can. J. Chem.*, **35**, 65 (1957).

TABLE I
SUMMARY OF NMR PARAMETERS FOR THE PHOSDRIN ISOMERS

	α -Isomer	β -Isomer												
														
δ (p.p.m. from TMS)	<table border="1"> <tr><td>$\text{CH}_3\text{C}=\text{C}$</td><td>2.36</td><td>2.15</td></tr> <tr><td>$\text{C}=\text{O}$</td><td>3.68</td><td>3.65</td></tr> <tr><td>$\text{CH}_3\text{O}-\text{P}$</td><td>3.82</td><td>3.88</td></tr> <tr><td>$=\text{CH}-$</td><td>5.76</td><td>5.47</td></tr> </table>	$\text{CH}_3\text{C}=\text{C}$	2.36	2.15	$\text{C}=\text{O}$	3.68	3.65	$\text{CH}_3\text{O}-\text{P}$	3.82	3.88	$=\text{CH}-$	5.76	5.47	
$\text{CH}_3\text{C}=\text{C}$	2.36	2.15												
$\text{C}=\text{O}$	3.68	3.65												
$\text{CH}_3\text{O}-\text{P}$	3.82	3.88												
$=\text{CH}-$	5.76	5.47												
$ J $ (c.p.s.)	<table border="1"> <tr><td>$\text{P}-\text{O}-\text{CH}_3$</td><td>11.4</td><td>11.4</td></tr> <tr><td>$\text{CH}_3-\text{C}=\text{CH}-$</td><td>0.9</td><td>0.9</td></tr> <tr><td>$\text{P}-\text{O}-\text{C}=\text{CH}-$</td><td>1.8</td><td>0.9</td></tr> <tr><td>$\text{P}-\text{O}-\text{C}=\text{CH}_2$</td><td>-0</td><td>1.6</td></tr> </table>	$\text{P}-\text{O}-\text{CH}_3$	11.4	11.4	$\text{CH}_3-\text{C}=\text{CH}-$	0.9	0.9	$\text{P}-\text{O}-\text{C}=\text{CH}-$	1.8	0.9	$\text{P}-\text{O}-\text{C}=\text{CH}_2$	-0	1.6	
$\text{P}-\text{O}-\text{CH}_3$	11.4	11.4												
$\text{CH}_3-\text{C}=\text{CH}-$	0.9	0.9												
$\text{P}-\text{O}-\text{C}=\text{CH}-$	1.8	0.9												
$\text{P}-\text{O}-\text{C}=\text{CH}_2$	-0	1.6												

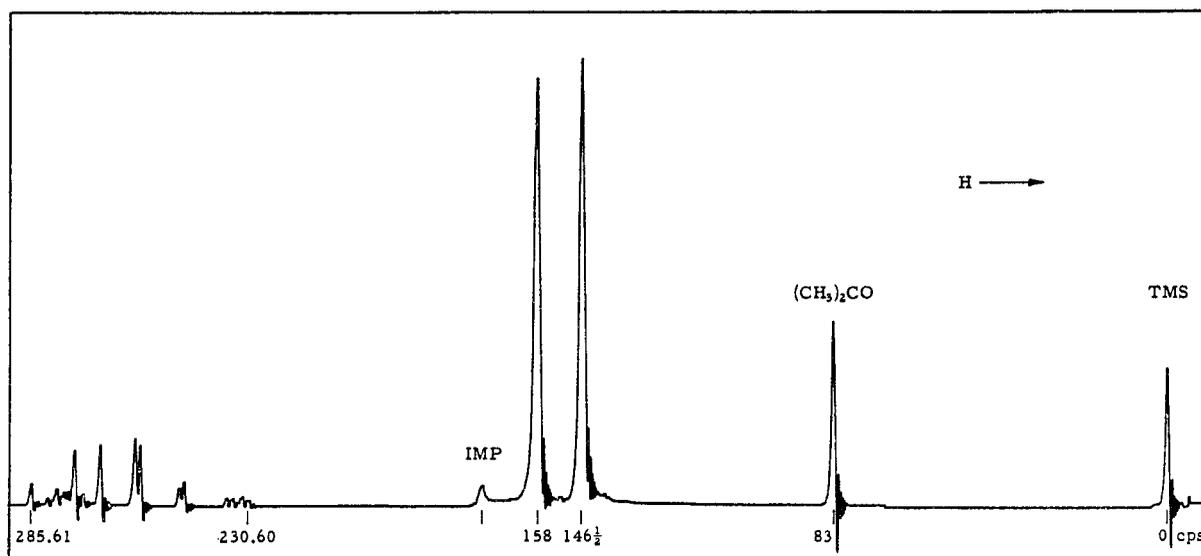


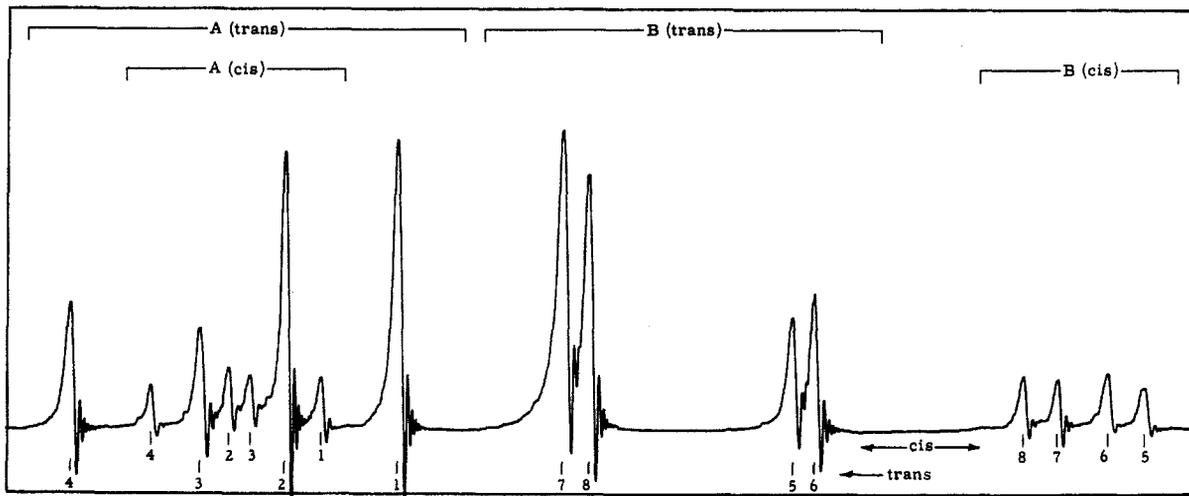
Fig. 6. NMR spectrum of $(\text{CH}_3\text{O})_2\text{POOCH}=\text{CHCl}$

of either the A or the B lines in each isomer is approximately the sum of two coupling constants $J_{AB} + J_{AX}$ or $J_{AB} + J_{BX}$ respectively. As the couplings to the P nucleus (X) can be expected to be small and about the same in both isomers, the larger spread of the A and B lines of the more intense group of lines as compared with that of the less intense groups shows that the coupling constant J_{AB} must be greater for the more abundant isomer. It is well known^{15,16} that the coupling constant between two protons *trans* to one another

across a double bond is invariably greater than when they are *cis*. Hence, it is concluded that the more abundant isomer is the *trans* one. The total intensity of all eight lines in its spectrum is approximately four times that in the spectrum of the *cis* isomer. Thus the two isomers are present in approximately the ratio of four *trans* to one *cis*. This result is in excellent agreement with the gas-

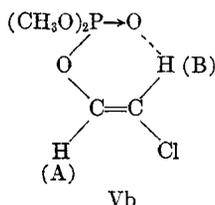
(15) H. M. McConnell, C. A. Reilly, and A. D. McLean, *J. Chem. Phys.*, **24**, 479 (1956).

(16) S. Alexander, *J. Chem. Phys.*, **28**, 358 (1958).

Fig. 7. Olefinic portion of NMR spectrum of $(\text{CH}_3\text{O})_2\text{POOCH}=\text{CHCl}$

liquid chromatography data which indicated a four to one ratio of lower-boiling to higher-boiling component (see Experimental).

Before a detailed analysis of these spectra into the NMR parameters can be made it is necessary to make an assignment. Because of the ease with which intramolecular H-bonding might be expected to occur in the *trans* isomer as compared with the



cis one, it is to be expected that the B proton will show the largest shift from one isomer to the other and that its resonances will occur at higher applied field in the *cis* isomer (when H-bonding occurs the effect is to shift the resonance to lower applied field¹⁰). It might also be expected that the resonances from the A proton would occur at about the same applied field in each isomer. Hence the groups of lines were assigned as shown in Fig. 7.

The labeling of the transitions within each group of lines must be such that, upon completion of the analysis of the spectrum into the parameters using line positions, the relative line intensities can be predicted accurately from these parameters. The labeling shown in Fig. 7 gives results most in agreement with the observed spectra. The parameters derived are given in Table II. It is to be noted that J_{AX} and J_{BX} have opposite signs in the *trans* isomer and the same signs in the *cis* isomer. Except for this result, the signs of all the coupling constants are indeterminate. The chemical shift difference between the *cis* and *trans* positions of the H atom of the $=\text{CH}-$ group relative to the $(\text{CH}_3\text{O})_2\text{POO}-$ group is consistent with that found in the Phosdrin isomers.

The observed and calculated spectra are given in Tables III and IV. For both isomers the calculated spectra agree with those observed about as well as one might expect in view of the lack of experimental precision in the observed spectra. With more precise experimental data, the spectra would undoubtedly show better quantitative agreement.

TABLE II
NMR PARAMETERS FOR $(\text{CH}_3\text{O})_2\text{POOCH}=\text{CHCl}$

	<i>cis</i>	<i>trans</i>																
δ (p.p.m. from TMS)	<table border="1"> <tr><td>(A)</td><td>6.96</td></tr> <tr><td>(B)</td><td>5.84</td></tr> <tr><td>$\text{CH}_3\text{O}-\text{P}$</td><td>3.80</td></tr> </table>	(A)	6.96	(B)	5.84	$\text{CH}_3\text{O}-\text{P}$	3.80	<table border="1"> <tr><td>(A)</td><td>6.87</td></tr> <tr><td>(B)</td><td>6.37</td></tr> <tr><td>$\text{CH}_3\text{O}-\text{P}$</td><td>3.80</td></tr> </table>	(A)	6.87	(B)	6.37	$\text{CH}_3\text{O}-\text{P}$	3.80				
(A)	6.96																	
(B)	5.84																	
$\text{CH}_3\text{O}-\text{P}$	3.80																	
(A)	6.87																	
(B)	6.37																	
$\text{CH}_3\text{O}-\text{P}$	3.80																	
J (c.p.s.)	<table border="1"> <tr><td>AB</td><td>4.1</td></tr> <tr><td>AX</td><td>5.3</td></tr> <tr><td>BX</td><td>1.6</td></tr> <tr><td>$\text{P}-\text{O}-\text{CH}_3$</td><td>11.5</td></tr> </table>	AB	4.1	AX	5.3	BX	1.6	$\text{P}-\text{O}-\text{CH}_3$	11.5	<table border="1"> <tr><td>AB</td><td>11.1</td></tr> <tr><td>AX</td><td>7.0</td></tr> <tr><td>BX</td><td>-1.7</td></tr> <tr><td>$\text{P}-\text{O}-\text{CH}_3$</td><td>11.5</td></tr> </table>	AB	11.1	AX	7.0	BX	-1.7	$\text{P}-\text{O}-\text{CH}_3$	11.5
AB	4.1																	
AX	5.3																	
BX	1.6																	
$\text{P}-\text{O}-\text{CH}_3$	11.5																	
AB	11.1																	
AX	7.0																	
BX	-1.7																	
$\text{P}-\text{O}-\text{CH}_3$	11.5																	

TABLE III
OBSERVED AND CALCULATED 40 MC./SEC. NMR SPECTRA FOR *trans* $(\text{CH}_3\text{O})_2\text{POOCH}=\text{CHCl}$

Transition No.	Obs. Position	Calcd. Position	Obs. Relative Int.	Calcd. Relative Int.
6	247.14 c.p.s.	247.01 c.p.s.	0.67	0.59
5	248.35	248.21	0.57	0.43
8	258.24	258.13	1.35	1.41
7	259.43	259.33	1.52	1.57
1	268.01	267.87	1.51	1.57
2	274.37	274.31	1.40	1.41
3	279.07	278.99	0.52	0.43
4	285.61	285.43	0.63	0.59

TABLE IV
OBSERVED AND CALCULATED 40 MC./SEC. NMR SPECTRA
FOR *cis* (CH₃O)₂POOCH=CHCl

Transition No.	Obs. Position	Calcd. Position	Obs. Relative Int.	Calcd. Relative Int.
5	230.60 c.p.s.	230.60 c.p.s.	0.87	0.90
6	232.24	232.25	1.17	0.91
7	234.71	234.72	1.06	1.10
8	236.38	236.37	1.08	1.09
1	272.09	272.08	1.01	1.10
3	276.19	276.20	0.87	0.90
2	277.33	277.35	1.08	1.09
4	281.47	281.47	0.87	0.91

violet. However, both isomers absorb at exactly the same wave length, 215 m μ , with essentially the same extinction coefficient, log ϵ 3.82, so that the information is of no use in establishing structure. Dipole moments of the two isomers were found to be $3.8 \pm 0.2D$ for the α -isomer and $3.4 \pm 0.2D$ for the β -isomer, but these values are also too similar in magnitude to allow definitive conclusions as to spatial configurations.

EXPERIMENTAL

Crystallization of technical Phosdrin. To 1 l. of ether was added 577 g. of technical Phosdrin and the mixture then

TABLE V
PHYSICAL PROPERTIES OF THE PHOSDRIN ISOMERS

Compound	Purity	M.P. ^a	n_D^{20} ^b	d^{20}	MR _D ^c (Calcd.)	MR _D ^d (Obsd.)	ΔY_{vap} (Kcal./Mole)	GLC E.t. ^e (Min.)
α -Isomer	>99%	-21.0	1.4452	1.2345	47.36	48.34	17.1	11.5
β -Isomer	>99%	6.9	1.4524	1.2455	47.36	48.59	18.2	13.0

^a Cryoscopic determination. ^b Spencer *et al.*⁴ found n_D^{20} for α - and β -isomers to be 1.4460 and 1.4505, respectively. ^c Molar refractivity calculated from values in Vogel, *A Textbook of Practical Organic Chemistry*, Longmans, Green and Co., New York (1956) and R. Sayre, *J. Am. Chem. Soc.*, **80**, 5438 (1958). ^d From the Lorenz-Lorentz equation, $MR_D = \left(\frac{n_D^2 - 1}{n_D^2 + 2}\right) \left(\frac{M}{d}\right)$.

^e Emergence time from a Consolidated Electroynamics gas-liquid chromatography instrument using an 18 in. column containing 30 g. of DC710 Silicone oil on 100 g. of GC-22 Supersupport and a helium flow of 50 ml./min.; temp. = 195°.

Physical properties of the Phosdrin isomers. Physical data (see Table V) also support the configurational assignments made above. In agreement with the structures assigned to the Phosdrin isomers, the β -isomer (II, two large groups *cis*) has the higher refractive index, density, and boiling point as suggested by the von Auwers-Skita rule¹⁷. An exception is the melting point, which is higher for the β -isomer, whereas the compound in which the two large groups are *trans* is generally the higher melting of the two isomers. However, there are several exceptions to the von Auwers-Skita rule and, in most cases, the anomaly is confined to the melting point.¹⁸

The partition coefficients for the isomers (Table VI) indicate that the β -isomer partitions into water to a much larger extent than does the α -isomer from chloroform, carbon tetrachloride, and hexane. This higher affinity for water is also to be expected of the β -isomer on the basis of the von Auwers-Skita rule.¹⁷

As expected of α,β -unsaturated esters, the two Phosdrin isomers absorb strongly in the ultra-

TABLE VI
PARTITION COEFFICIENTS OF α - AND β -PHOSDRIN (25°)

Solvent Pair	K_{α} -isomer	K_{β} -isomer
CHCl ₃ :water	80	35
CCl ₄ :water	4	0.8
Hexane:water	0.2	0.04

(17) K. v. Auwers, *Ann.*, **420**, 89 (1920); K. v. Auwers and B. Ottens, *Ber.*, **57**, 437 (1924); A. Skita, *Ber.*, **53**, 1792 (1920); A. Skita and A. Schneck, *Ber.*, **55**, 144 (1922).

was cooled in a Dry Ice-acetone bath. Seeds of β -isomer (from the Schrader⁵ synthesis using the lithium salt of methyl acetoacetate) were added and the mixture was allowed to stand for about 1 hr. at -78°. The first crop of crystals was removed by rapid filtration through a Dry Ice-chilled funnel to yield about 200 g. of solid, slightly contaminated with ether. This material was recrystallized in a similar fashion from 200 ml. of ether to give 127 g. of solid. This was distilled¹⁹ to give 1 g. of forerun and 121 g. (52.5% yield) of a water-white liquid, b.p. 96° (0.1 mm.), and no residue.

Anal. Calcd. for C₇H₁₃PO₆: C, 37.5; H, 5.8; P, 13.8; Cl, 0.0. Found: C, 37.2; H, 5.9; P, 13.4, 13.6; Cl, <0.2.

Infrared analysis indicated this material to be about 99% β -isomer with a barely detectable amount of α -isomer. When a similar crystallization was carried out in slightly more dilute solution (450 g. of technical phosdrin in 900 ml. of ether), a lower yield (73 g.) of a slightly purer product (>99%) was obtained. Physical constants for this sample are given in Table V.

The filtrate from the first crop of crystals was seeded at -78° with pure α -isomer (from chromatographically separated α -isomer, see below) and the crystallized solid that precipitated was freed of supernatant by decantation. To the solid was added 500 ml. of dry ether and the mixture was allowed to warm up to room temperature. The solution then was chilled to -78° and seeded with pure α -isomer; 40 g. of recrystallized product was obtained. The filtrate from this recrystallization was dried over sodium sulfate and evaporated at the water pump to 376 g. of residual oil. This was taken up in 500 ml. of ether and seeded as above to obtain a second crop of crystals. This was combined with

(18) G. A. Haggis and L. N. Owen, *J. Chem. Soc.*, 408 (1953); L. N. Owen and P. A. Robins, *J. Chem. Soc.*, 320 (1949).

(19) During the vapor pressure measurements on α - and β -isomers, it was shown that no isomerization of either isomer occurred on heating to 215°; thus, it is safe to assume that distillation is a reasonable purification step in the preparation of the pure isomers.

the 40-g. crop and recrystallized in a similar manner from 300 ml. of ether. A third recrystallization from 150 ml. of ether afforded 62 g., which was distilled to give 57 g., b.p. 90–93° (0.1 mm.). Infrared analysis indicated the distillate to be 93.1% α , 6.9% β .

Further purification of this α -enriched fraction by crystallization could not be effected and a partitioning procedure similar to that employed by Casida³ had to be used for the preparation of pure α -isomer.

Preparation of pure α -isomer. Phosdrin low in chlorine content²⁰ (1033 g., 4.6 moles) was dissolved in 2.5 l. of carbon tetrachloride and extracted seventeen times with 500-ml. portions of water followed by thirteen washings with 1000-ml. portions of water. The organic phase was dried over anhydrous sodium sulfate and the solvent was stripped at the aspirator to leave 146 g. of a yellow liquid residue. This was Claisen-distilled to give 110 g. of product, b.p. 95.5–100° (0.2–0.5 mm.), and then redistilled through a helices-packed column to give 105 g., b.p. 86–89° (0.1 mm.). This was crystallized twice from 200 ml. of ether at –70° and 59 g. of α -isomer melting at about –25° was obtained. Physical constants for this sample are given in Table V.

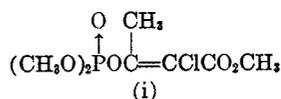
Anal. Calcd. for $\text{PO}_2\text{C}_7\text{H}_{12}$: P, 13.8; C, 37.5; H, 5.8; Cl, 0.0. Found: P, 13.8; C, 37.5; H, 6.1; Cl, <0.2.

Infrared analysis indicated that this material was essentially pure α -isomer with perhaps as much as 1% β -isomer present. Cryoscopic determination of purity indicated a value of 97.48%, but the results were complicated by absorption of water vapor during the seeding process so that purity cannot definitely be stated, but was probably >99%.

Vapor pressure data. Boiling points of the α - and β -isomers at various pressures were obtained using 1.5–3.0 ml. of material in a small, completely enclosed vacuum-jacketed recycle Claisen still. The sample was charged and a pressure of 1 to 3 mm. applied. The liquid was then heated slowly to constant distillation temperature. The voltage input to the heater was varied to eliminate possible super-heating. The pressure was then increased and another boiling point obtained. This process was repeated to give the following boiling points for the isomers.

Some information about the heat stability of these materials was also obtained. The β -isomer is decomposed to a black tar and carbon when heated at atmospheric pressure

(20) As the chlorovinyl analog (i)²¹ behaves similarly to α -isomer in the partitioning procedure, it is important that the Phosdrin be prepared from methyl 2-chloroacetoacetate that is low in dichloroacetoacetate content. This is accomplished by using a 100% excess of methyl acetoacetate in the chlorination step.



(21) R. R. Whetstone and D. Harman, U. S. Pat. 2,956,073 (to Shell Oil Co.).

Boiling Points, (Mm.)	
α -Isomer	β -Isomer
123 (2.0)	126 (1.0)
146 (6.5)	147 (5.0)
155 (11)	160 (10)
175 (30)	171 (20)
189 (50)	188 (40)
200 (75)	204 (71)
208 (100)	213 (100)
220 (150)	272 (760) ^a
266 (760) ^a	

^a Calculated from $\Delta H_{\text{vap}} = 2.303 R \log (P_2/P_1)(1/T_1 - 1/T_2)$; T_1 and T_2 are °K.

(ca. 755 mm.), the maximum temperatures attained being 267°. The α -isomer appears to be the more stable material at these elevated temperatures. Upon heating the pure α -isomer to 259°, the recovered material still contained 63.5% α along with considerable insoluble material, but no β -isomer. It was also noted with one sample of the β -isomer, that heating to 215° does not decompose the material to any great extent (97% β after heating) nor does there appear to be any isomerization to the α -isomer at this temperature.

*Preparation of 2-chlorovinyl dimethyl phosphate (Va and b).*²¹ Freshly distilled dichloroacetaldehyde (50 g., 0.44 mole) of 97% purity was added dropwise with vigorous stirring to 57.5 g. (0.46 mole) of freshly distilled trimethylphosphite. The temperature was maintained at 49–52° by external cooling throughout the addition which required 25 min. After an additional half hour at 45–50°, the reaction mixture was stripped of volatiles at 75° (25 mm.) and the residue was distilled through a 12 × 1.5-in. helices-packed column. After a fore-run of 4.5 g. boiling below 61° (0.1 mm.), there were obtained three fractions: 21.0 g., b.p. 61–62.5° (0.1 mm.); 25.0 g., b.p. 60–61° (0.08 mm.); and 20.0 g., b.p. 60–62.5° (0.08–0.1 mm.); total yield = 80%. Gas-liquid chromatography analysis indicated that these fractions were mixtures of the two isomeric 2-chlorovinyl dimethyl phosphates (Va and Vb) in the following ratios: 85:12; 81:16; 67:32, respectively, the lower boiling component predominating in each case. All fractions were submitted for combustion analysis and the values for the second fraction are listed as being representative of all three.

Anal. Calcd. for $\text{C}_4\text{H}_8\text{PO}_2\text{Cl}$: P, 16.6; Cl, 19.0. Found: P, 16.6; Cl, 19.1.

The sample for NMR analysis was obtained by a careful redistillation of the three fractions above and a center cut was taken (n_D^{25} 1.4359) that analyzed by gas-liquid chromatography for an 80:20 mixture of the lower and higher boiling components, respectively.

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