Synthesis of Esters of 4-Hydroxy-5-phosphinyl-2-imidazolidinone

John A. Mikroyannidis* and Alexandros K. Tsolis

Chemical Technology Laboratory, University of Patras,
Patras, Greece

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The esters of 4-hydroxy-5-phosphinyl-2-imidazolidinone were prepared by reaction of urea with the esters of 2-hydroxy-2-phosphinylethanal in acidic medium. The ir, ^1H nmr and ^{31}P nmr spectral data of the products are reported. All the isolated products had cis configuration. The stereochemistry of their formation is discussed.

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Introduction.

This article describes the synthesis of the diesters of 4-hydroxy-5-phosphinyl-2-imidazolidinone (**3**). It was undertaken in connection with our interest in the development of new organophosphorus flame retardants (2). The above compounds have been synthesized, because of their promising structural features in order to be employed as flame retardant additives to commercial polymeric materials and as starting materials for the preparation of finishing agents for the improvement of the fire resistance and crease resistance of cotton fabrics.

The flame retarding of cellulose and of man made polymers has been reviewed in various recent monographies (3,4). To date the most widely employed flame retardants are phosphorus compounds and especially those which contain in their structures nitrogen and/or halogen. The most effective finishing agents which impart relatively permanent fire resistance and crease resistance to cotton cellulose are monomers, which are polymerized within the cellulose fiber matrix (5). Some of the commercially available monomers, which impart crease resistance to cotton fabrics, are *N*-hydroxymethyl derivatives of 2-imidazolidinone and its derivatives for example 1,3-di(hydroxymethyl)-2-imidazolidinone and 1,3-di(dihydroxymethyl)-4,5-dihydroxy-2-imidazolidinone (6). They are prefered to the *N,N'*-di(hydroxymethyl)urea because they lack NH groups, which possess the undesirable property to take up chlorine during bleaching (7a).

2-Imidazolidinone is produced commercially by the reaction of urea and ethylenediamine under atmospheric pressure with release of ammonia. It has been also prepared by the reaction of ethylene carbonate with ammonia (8). 4,5-Dihydroxy-2-imidazolidinone has been prepared by the reaction of glyoxal with urea (9-13). The *N*-hydroxymethyl derivatives of the above compounds are prepared by reaction with formaldehyde (14-17).

Results and Discussion.

The synthesis of the diesters of 4-hydroxy-5-phosphinyl-2-imidazolidinone (**3**) has been carried out by reaction of the diesters of 2-hydroxy-2-phosphinylethanal (**1**) with urea.

1 **2** **3**

1a, R = CH_3
1b, R = CH_3CH_2
1c, R = $(CH_3)_2CH$
1d, R = n-C_4H_9
1e, R = $ClCH_2CH_2$
1f, R = C_6H_5

3a, R = CH_3
3b, R = CH_3CH_2
3c, R = $(CH_3)_2CH$
3d, R = n-C_4H_9
3e, R = $ClCH_2CH_2$
3f, R = C_6H_5

The diesters of 2-hydroxy-2-phosphinylethanal (**1**) have been prepared in acidic medium by reacting glyoxal or glyoxal trimer dihydrate, which releases glyoxal *in situ*, or vacuum condensed aqueous glyoxal solutions with phosphorous acid diesters neat or in the presence of solvent (2,18). For the synthesis of **3** crude 2-hydroxy-2-phosphinylethanals **1** obtained from the above reactions after evaporation of the volatile components were employed. Attempts to isolate the phosphinylethanals **1** were unsuccessful due to their isomerization and decomposition when distillation was attempted. The crude reactants have been shown spectroscopically to contain mainly the diester of 2-hydroxy-2-phosphinylethanal (**1**) and minor amounts of formylmethyl phosphates (**4**) arising from

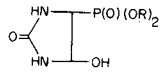
1 **4**

isomerization of **1** as well as some side products arising from the hydrolysis of the phosphinyl ester groups by the water contained in some of the glyoxal starting materials. The reactions of **1** with urea were brought to completion at 50° for 60 minutes, though they were observed to be slightly exothermic.

It has been known (7b) that the reaction of glyoxal with urea leading to the formation of 4,5-dihydroxy-2-imidazo-

Table 1

IR Data of the Esters of 4-Hydroxy-5-phosphinyl-2-imidazolidinone (a)



R	Absorption Bands (μ) C=O	P=O	P-O-C
CH_3	5.88	8.11	9.60
C_2H_5	5.82	8.07	9.68
i-C_3H_7	5.93	8.28	10.10
n-C_4H_9	5.87	8.17	9.85
CH_2CH_2Cl	5.91	8.10	9.82
C_6H_5	5.92	8.40	10.53

(a) All ir spectra were obtained on potassium bromide disks.

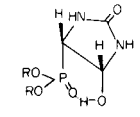
lidinone is a second-order reaction and that it is subject to acid and base catalysis. The reaction rate constant is directly proportional to the amount of acid added except for the region of very small concentrations of acid. The deviation in this region has been attributed to a buffering action and possibly to the inherent acidity of pure glyoxal. The reaction rate constant has been found to increase both above and below pH 4.

In the case of the reactions of **1** with urea base catalysis was precluded, since it caused isomerization of **1** to **4** and other side reactions. Therefore these reactions were carried out at an initial pH of about 2. These acid-catalyzed reactions would be expected to involve initial nucleophilic attack by the neutral amido nitrogen on the previously protonated carbonyl of **1** leading to the formation of the intermediate **2** (19). Cyclization of **2** to 4-hydroxy-5-phosphinyl-2-imidazolidinones **3** follows by a nucleophilic attack of the other amido nitrogen on the carbon atom α to phosphorus. This attack is expected to be facilitated by previous protonation of the hydroxyl group and by the presence of the electron withdrawing phosphinyl group.

The reactions of **1** with urea were carried out in solution and the products **3** precipitated out during the course of the reaction. The prefered solvents were methanol for the preparation of **3a**, ethanol for **3b**, water for **3b**, **3c**, **3e** and **3f** and a mixture of water and acetonitrile for **3d**. When water was employed for the preparation of **3a** appreciable hydrolysis of the phosphinyl ester groups was observed. Wherever it was possible, the alcohol corresponding to the phosphinyl ester moiety was employed in order to avoid transesterification (20). When alcohols were employed as solvents, it was observed that the precipitation of the product **3** was delayed until after the end of the reaction, possibly because of the formation of the acetals of **1** which delays the initial addition reaction towards **2**.

The structures of the diesters of 4-hydroxy-5-phosphinyl-2-imidazolidinone **3** were elucidated by elemental analysis as well as by ir, ^{1}H nmr and ^{31}P nmr spectroscopy. The characteristic infrared absorption bands of the products are given in Table 1. The ^{1}H nmr and ^{31}P nmr assignments for the products are shown in Table 2 and 3 respectively.

It should be noted that the products **3** can exist as two geometric isomers, namely *cis* and *trans*. The careful study of the spectral data has led us to suggest that the analytical samples of **3** we obtained consisted exclusively of one isomer, namely of the *cis* isomer **5** with hydrogen bonding



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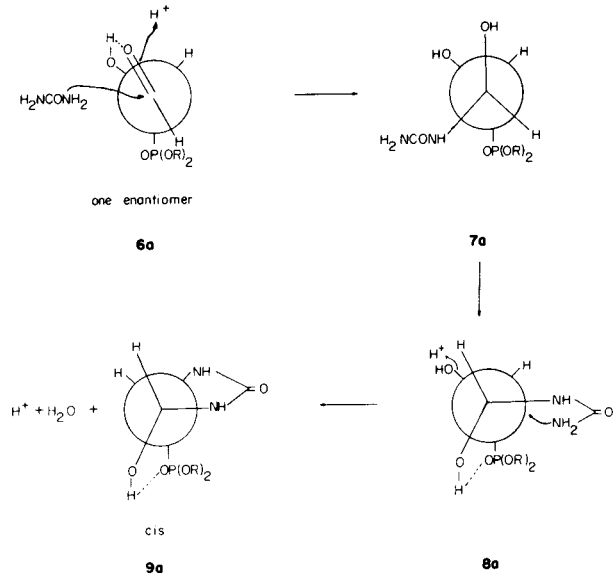
between P=O and OH (21). The *cis* isomer should be the kinetically controlled product (19).

In order to explain how the *cis* isomer may arise preferentially if not exclusively from the reaction of **1** with urea the following plausible Scheme 1 is proposed. It received support from the observation that the reactants 2-hydroxy-

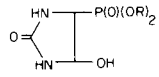
Scheme I



2-phosphinylethanals **6** carry a hydrogen bonded carbonyl absorbing at 1637 cm^{-1} (18). The enantiomer **6a** by entering of the urea from the side shown in Scheme 1 affords the diastereoisomer **7a** which through its rotamer **8a** leads to the *cis* diastereoisomer **9a**. An analogous Scheme 2 shows how the *cis* diastereoisomer **6b**, which is enantiomer of **6a**, may arise. The couple of the *trans* enantiomeric diastereoisomers would be obtained from the enantiomers **6a**

Table 2

^{1}H NMR Data of the Esters of 4-Hydroxy-5-phosphinyl-2-imidazolidinone



R	δ, ppm	Multiplicity of Peak	Number of Protons	Coupling Constant (cps)	Assignment	Solvent
CH_3	8.27	doublet broad	1	10.6	CH of position 5	DMSO-d_6
	7.92	doublet	1	7.0	OH	
	6.68	quartet	1		CH of position 4	
	6.17	broad	2		NH	
	3.53	doublet	6	10.6	CH_3O	
CH_2CH_3	8.23	doublet broad	1	10.6	CH of position 5	DMSO-d_6
	6.67	quartet	1		CH of position 4	
	6.15	broad	2		NH	
	3.93	multiplet	4		CH_2O	
	1.18	triplet	6	6.5	CH_3	
$(CH_3)_2CH$	8.13	doublet broad	1	10.6	CH of position 5	DMSO-d_6
	6.62	quartet	1		CH of position 4	
	6.08	broad	2		NH	
	4.40	multiplet	2		CHO	
	1.30	doublet	12		CH_3	
CH_2CH_2Cl	8.30	doublet broad	1	10.6	CH of position 5	MSO-d_6
	7.98	doublet	1	7.0	OH	
	6.75	quartet	1		CH of position 4	
	6.18	broad	2		NH	
	4.08	multiplet	4		CH_2O	
	3.73	triplet	4	6.0	$ClCH_2$	
C_6H_5	8.47	doublet broad	1	10.6	CH of position 5	DMSO-d_6
	7.25	multiplet	10		C_6H_5	
	6.83	quartet	1		CH of position 4	
	6.23	broad	2		NH	

and **6b** by an attack of urea from the opposite side to the one designated in Schemes 1 and 2.

Scheme 2

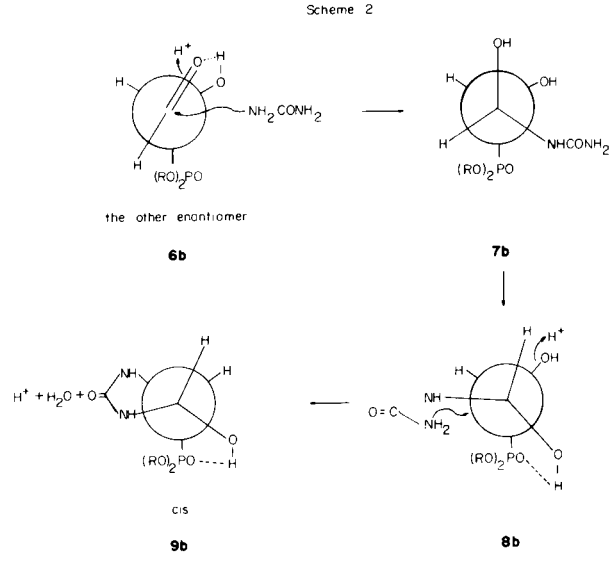
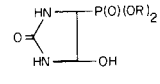


Table 3

^{31}P NMR Data of the Esters of 4-Hydroxy-5-phosphinyl-2-imidazolidinone



R	δ, ppm	Solvent
CH_3	17.2	DMSO-d_6
C_2H_5	15.0	DMSO-d_6
i-C_3H_7	12.4	DMSO-d_6
C_6H_5	10.1	DMSO-d_6

Apparently the prefered side of attack, in this case, is the side of the hydroxyl and $OP(OR)_2$ (of the two bulkiest groups) and not the opposite side, the side of OH and H, which are the two less bulky groups of the assymetric center. This latter side would be the prefered side of the entering group if Cram's rule (22) was applicable in this

case. The results show that it is not.

When **1b** reacted with *N*-methylurea two position isomers were observed in the product by ^{1}H nmr the 1-methyl-4-hydroxy-5-diethoxyphosphinyl-2-imidazolidinone and the 3-methyl-4-hydroxy-5-diethoxyphosphinyl-2-imidazolidinone in a ratio of 18.2:81.8 respectively (21).

EXPERIMENTAL

The melting points were obtained on a Büchi apparatus and they are uncorrected. The infrared spectra were determined on potassium bromide pellets with a Perkin-Elmer Infracord Spectrometer Model 137. Proton nuclear magnetic resonance spectra were obtained at 60.0 MHz with a Varian T-60A Spectrometer. Tetramethylsilane was used as an internal standard in DMSO-d_6 solutions. Phosphorus nuclear magnetic resonance spectra were obtained at 24.3 MHz with a Varian T-60A spectrometer and are reported with respect to 85% phosphoric acid contained in a capillary. Since the intensity of the signals obtained was weak, a V-2048 NMR Signal Averager of Varian-Tracor was used. All the nmr measurements were made on saturated solutions at 30°, normal probe temperature. Chemical shifts are reported in ppm (δ). Elemental analyses were carried out by Dr. H. Mantzos of the Microanalytical Laboratory of the National Hellenic Research Foundation in Athens, Greece.

4-Hydroxy-5-dimethoxyphosphinyl-2-imidazolidinone (**3a**).

Glyoxal trimer dihydrate and dimethyl phosphite in a molar ratio 0.33:1.1 respectively together with 750 ml of dioxane per mole of glyoxal trimer dihydrate were introduced in a flask equipped with a side condenser. The mixture was boiled under stirring for 25 minutes. During this time the water released was distilled with dioxane at atmospheric pressure in a slow rate. The reaction mixture was cooled to 40° and the volatile components were removed by a rotary evaporator. Methanol (150 ml) and 1.0 mole of urea per mole of crude 2-hydroxy-2-(dimethoxyphosphinyl)ethanal was added and the resulted solution was heated at 50° for 60 minutes. Precipitation of 4-hydroxy-5-dimethoxyphosphinyl-2-imidazolidinone occurred during the course of the reaction and was completed upon cooling, mp 137-138° dec, overall yield 20.0%. Recrystallizations from *N,N*-dimethylformamide-dioxane (1:1 vol/vol) gave an analytical sample, mp 140-141° dec.

Anal. Calcd. for $C_5H_{11}N_2O_5P$: C, 28.58; H, 5.28; N, 13.33. Found: C, 28.71; H, 5.44; N, 13.15.

4-Hydroxy-5-diethoxyphosphinyl-2-imidazolidinone (**3b**).

2-Hydroxy-2-(diethoxyphosphinyl)ethanal was prepared from the reaction of glyoxal trimer dihydrate with diethyl phosphite according to the above procedure with a reaction time of 35 minutes, thus 500 ml of water (or 300 ml of ethanol) and 1.0 mole of urea per mole of crude 2-hydroxy-2-(diethoxyphosphinyl)ethanal was added and the solution was heated at 50° for 60 minutes. Precipitation of 4-hydroxy-5-diethoxyphosphinyl-2-imidazolidinone occurred during the course of the reaction (or by standing overnight at room temperature) and was completed upon cooling; mp 143-145° dec, overall yield 52.0% or 42% respectively when water or ethanol was used as the solvent. Recrystallizations from ethanol-water (4:1 vol/vol) gave an analytical sample, mp 151-152° dec.

Anal. Calcd. for $C_7H_{15}N_2O_5P$: C, 35.29; H, 6.35; N, 11.76. Found: C, 35.53; H, 6.43; N, 12.05.

4-Hydroxy-5-diisopropoxyphosphinyl-2-imidazolidinone (**3c**).

2-Hydroxy-2-(diisopropoxyphosphinyl)ethanal was prepared from the reaction of glyoxal trimer dihydrate with diisopropyl phosphite according to the precedure of 2-hydroxy-2-dimethoxyphosphinyl-2-imidazolidinone with a reaction time of 55 minutes. Water (500 ml) and 1.0 mole of urea per mole of crude 2-hydroxy-2-(diisopropoxyphosphinyl)ethanal was added and the solution was heated at 50° for 60 minutes. Precipitation of 4-hydroxy-5-diisopropoxyphosphinyl-2-imidazolidinone occurred during the course of the reaction and was completed upon cooling, mp 191-193° dec, overall yield 45.0%. Recrystallizations from water-2-propanol (2:1 vol/vol) gave an analytical sample, mp 201-202° dec.

Anal. Calcd. for $C_9H_{19}N_2O_5P$: C, 40.60; H, 7.19; N, 10.52. Found: C, 40.85; H, 6.91; N, 10.24.

4-Hydroxy-5-di(*n*-butoxy)phosphinyl-2-imidazolidinone (**3d**).

2-Hydroxy-2-[(*n*-butoxy)phosphinyl]ethanal was prepared from the reaction of glyoxal trimer dihydrate with di(*n*-butyl)phosphite according to the procedure of 2-hydroxy-2-(dimethoxyphosphinyl)ethanal with a reaction time of 60 minutes. Two hundred ml of a mixture of water-acetonitrile (2.3:1.0 vol/vol) and 1.0 mole of urea per mole of crude 2-hydroxy-2-[(*n*-butoxy)phosphinyl]ethanal was added and the solution was heated at 50° for 60 minutes. Precipitation of 4-hydroxy-5-di(*n*-butoxy)phosphinyl-2-imidazolidinone occurred during the course of the reaction and was completed upon cooling, mp 139-141° dec, overall yield 21.0%. Recrystallizations from acetonitrile-dioxane (3:1 vol/vol) gave an analytical sample, mp 146-148° dec.

Anal. Calcd. for $C_{11}H_{23}N_2O_5P$: C, 44.89; H, 7.88; N, 9.52. Found: C, 44.70; H, 7.80; N, 9.32.

4-Hydroxy-5-di(2-chloroethoxy)phosphinyl-2-imidazolidinone (**3e**).

For the preparation of 2-hydroxy-2-[di(2-chloroethoxy)phosphinyl]-ethanal glyoxal trimer dihydrate reacted with di(2-chloroethyl)phosphite according to the procedure of 2-hydroxy-2-(dimethoxyphosphinyl)ethanal with a reaction time of 25 minutes. Water (500 ml) and 1.0 mole of urea per mole of crude 2-hydroxy-2-[di(2-chloroethoxyphosphinyl)]ethanal was added and the solution was heated at 50° for 60 minutes. 4-Hydroxy-5-di(2-chloroethoxy)phosphinyl-2-imidazolidinone precipitated during the course of the reaction and upon subsequent cooling, mp 124-127° dec, overall yield 46.0%. Recrystallizations from ethanol-water (4:1 vol/vol) gave an analytical sample, mp 141-142° dec.

Anal. Calcd. for $C_7H_{13}Cl_2N_2O_5P$: C, 27.39; H, 4. 24; N, 9.13. Found: C, 27.56; H, 4.55; N, 9.05.

4-Hydroxy-5-diphenoxyphosphinyl-2-imidazolidinone (**3f**).

Glyoxal trimer dihydrate (14.01 g, 66.7 mmoles), diphenyl phosphite (56.20 g, 0.24 mole) and 180 ml of dioxane were introduced into a flask equipped with a side condenser. The mixture was stirred under reduced pressure (~ 400 mm Hg) and was heated at about 80° for 65 minutes during which time the water released distilled with dioxane. Subsequently, the mixture was cooled to 40° and the volatile components were removed by a rotary evaporator. Urea (12.01 g, 0.20 mole) and 40 ml of water were added and the resulted solution was heated at 50° for 60 minutes. During the course of the reaction and upon subsequent cooling 4-hydroxy-5-diphenoxyphosphinyl-2-imidazolidinone precipitated, mp 166-169° dec, 10.0 g, overall yield 15.0%. Recrystallizations from *N,N*-dimethylformamide-acetonitrile (1.0:1.3 vol/vol) gave an analytical sample, mp 175-176° dec.

Anal. Calcd. for $C_{15}H_{15}N_2O_5P$: C, 53.89; H, 4.52; N, 8.38. Found: C, 53.98; H, 4.76; N, 8.19.

1-Methyl-4-hydroxy-5-diethoxyphosphinyl-2-imidazolidinone and 3-Methyl-4-hydroxy-5-diethoxyphosphinyl-2-imidazolidinone.

2-Hydroxy-2-(diethoxyphosphinyl)ethanal was prepared from the reaction of 14.0 g (66.7 mmoles) of glyoxal trimer dihydrate with 30.38 g (220 mmoles) of diethyl phosphite. *N*-Methylurea (14.82 g, 200 mmoles) and 45 ml of ethanol was added to the crude 2-hydroxy-2-(diethoxyphosphinyl)ethanal and the resulted solution was heated at 50° for 60 minutes. Addition of ether caused the precipitation of a white solid (19.20 g, overall yield 38.0%, mp 144-145°). Recrystallizations from ethanol-ether (2:1 vol/vol) gave an analytical sample, mp 154-155°.

Anal. Calcd. for $C_8H_{17}N_2O_5P$: C, 38.09; H, 6.79; N, 11.11. Found: C, 37.79; H, 6.48; N, 10.98.

The analytical sample as shown by ^{1}H nmr spectroscopy was a mixture of 18.2% 1-methyl- and of 81.8% 3-methyl-4-hydroxy-5-diethoxyphosphinyl-2-imidazolidinone; ^{1}H nmr (deuterium oxide): δ 7.00 (doublet,

1, J = 6.6 cps, CH of position 4), 4.17 (multiplet, 4, CH_2OP), 2.96 (singlet, 0.54, N-CH_3 of position 1), 2.77 (singlet, 2.46, N-CH_3 of position 3), 1.33 (triplet, 6, J = 7.0 cps, CH_3); ^{31}P nmr (deuterium oxide): 16.8 ppm; ir (potassium bromide): 5.88 (C=O), 8.25 (P=O), 9.47-10.33 (P-O-C).

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REFERENCES AND NOTES

(1) Please address all correspondence to this author.

(2) J. A. Mikroyannidis and A. K. Tsolis, "Symposium on Recent Aspects of Polymer Flammability" at the American Chemical Society 180th National Meeting; Organic Coatings and Plastics Chemistry Preprints, Vol 43, p 195 (1980).

(3) M. Lewin, S. M. Atlas and E. M. Pearce, eds, "Flame-Retardant Polymeric Materials", Vol 1 and 2, Plenum Press, New York, NY, 1978.

(4) W. C. Kuryla and A. J. Papa, eds, "Flame Retardancy of Polymeric Materials", Vol 1-5, Marcel Dekker, Inc., New York, NY.

(5) R. H. Barker and J. E. Hendrix in "Flame Retardancy of Polymeric Materials", Vol 5, W. C. Kuryla and A. J. Papa, eds, Marcel Dekker Inc., New York, NY, 1979, p 39.

(6) Badische Anilin and Soda Fabrik, A. G., British Patent 717,287; *Chem. Abstr.*, **49**, 15976d (1955).; British Patent 720,386 (1954); *Chem. Abstr.*, **49**, 9326g (1955); British Patent 720,387.

(7) H. Mark, N. S. Wooding and S. M. Atlas, eds, "Chemical Aftertreatment of Textiles", John Wiley and Sons, Inc., New York, NY, 1971, (a) pp 296, 570; (b) p 170.

(8) L. Levine, U. S. Patent 2,892,843 (1959) (to Dow Chemical Co.); *Chem. Abstr.*, **53**, 19892e (1959).

(9) H. Pauly and H. Sauter, *Ber.*, **63 b**, 2063 (1930).

(10) Badische Anilin and Soda-Fabrik Akt., British Patent 717,287 (1954); *Chem. Abstr.*, **49**, 15976d (1955).

(11) E. Torke and J. König (to Phrix-Werke A. G.), U. S. Patent 2,876,062 (1959); *Chem. Abstr.*, **53**, 13619f (1959).

(12) H. B. Goldstein and M. A. Silverstri (to Sun Chemical Corp.), U. S. Patent 3,049,446 (1962); *Chem. Abstr.*, **57**, 15390c (1962).

(13) D. D. Gagliardi, W. J. Jutras, Jr. and E. Stern (to Gagliardi Research Corp.), Belgian Patent 616,785 (1962); *Chem. Abstr.*, **68**, 1467 (1963).

(14) E. I. du Pont de Nemours and Co., Inc., U. S. Patent 2,373,136 (1945); *Chem. Abstr.*, **39**, 4763 (1945); Imperial Chemical Industries Ltd., British Patent 577,735; *Chem. Abstr.*, **41**, 2254b (1947).

(15) Phrix-Werke, A. G., British Patent 771,328.

(16) Tootal Broadhurst Lee Co. Ltd., British Patent 831,297; *Chem. Abstr.*, **54**, 18974; (1960).

(17) Sun Chemical Corp., U. S. Patent 3,049,446 (1962); *Chem. Abstr.*, **57**, 15390c (1962).

(18) J. A. Mikroyannidis, A. K. Tsolis and D. J. Gourghiotis, *Phosphorus Sulfur*, in press.

(19) S. L. Vail, R. H. Barker and P. G. Mennitt, *J. Org. Chem.*, **30**, 2179 (1965).

(20) G. M. Kosolapoff and L. Maier, "Organic Phosphorus Compounds", John Wiley and Sons, New York, NY, 1973, p 39.

(21) J. A. Mikroyannidis and A. K. Tsolis, *Appl. Spectros.*, in press.

(22) D. J. Cram and F. A. A. Elhafez, *J. Am. Chem. Soc.*, **74**, 5828 (1952).