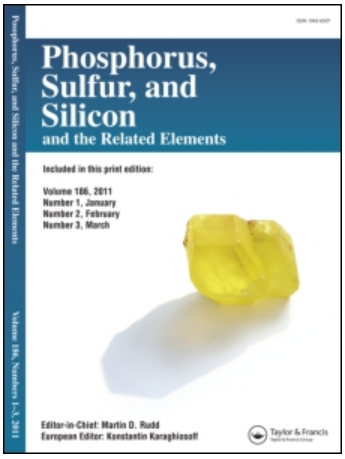


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

5,6-DIHYDRO-2H-OXAPHOSPHORINE-2-OXIDES BY HALOGENATION OF 2-CHLORO-1,3-ALKADIENYLPHOSPHONIC DIALKYL ESTERS

Christo M. Angelov[a]; Valerij Ch. Christov[a]; Jordanka Petrova[b]; Marko Kirilov[b]
[a] Department of Chemistry, Higher Pedagogical Institute, Shoumen, Bulgaria [b] Department of Organic Chemistry, Faculty of Chemistry, Sofia University, Sofia, Bulgaria

To cite this Article Angelov, Christo M. , Christov, Valerij Ch. , Petrova, Jordanka and Kirilov, Marko(1983) '5,6-DIHYDRO-2H-OXAPHOSPHORINE-2-OXIDES BY HALOGENATION OF 2-CHLORO-1,3-ALKADIENYLPHOSPHONIC DIALKYL ESTERS', Phosphorus, Sulfur, and Silicon and the Related Elements, 17: 1, 37 — 45
To link to this Article: DOI: 10.1080/03086648308077522
URL: http://dx.doi.org/10.1080/03086648308077522

Phosphorus and Sulfur, 1983, Vol. 17, pp. 37–45
0308-664X/83/1701-0037/$18.50/0

5,6-DIHYDRO-2H-OXAPHOSPHORINE-2-OXIDES BY HALOGENATION OF 2-CHLORO-1,3-ALKADIENYLPHOSPHONIC DIALKYL ESTERS

CHRISTO M. ANGELOV* and VALERIJ CH. CHRISTOV

Department of Chemistry, Higher Pedagogical Institute 9700 Shoumen, Bulgaria

JORDANKA PETROVA and MARKO KIRILOV

Department of Organic Chemistry, Faculty of Chemistry, Sofia University, 1126 Sofia, Bulgaria

(*Received December 7, 1982; in final form February 9, 1983*)

Halogenation of 3- and 4-substituted 2-chloro-1,3-alkadienylphosphonic dialkyl esters leads to the formation of six-membered heterocycles—derivatives of 5,6-dihydro-2*H*-1,2-oxaphosphorine-2-oxides. The structure of the products was established by ^{1}H- and ^{31}P-nmr. In one case column chromatography allowed isolation of two diastereomeric six-membered heterocycles without any evidence of formation of non-cyclic or five-membered cyclic products.

INTRODUCTION

Although halogenation of 1,3-alkadienes is a well studied reaction there is, however, scant information on this reaction with 1,3-dienic compounds containing electron-withdrawing groups adjacent to the conjugate bond system. Thus, only the halogenation of 1,3-alkadienecarboxylic acids[1–3] and, recently, of their esters[4,5] have been investigated in details.

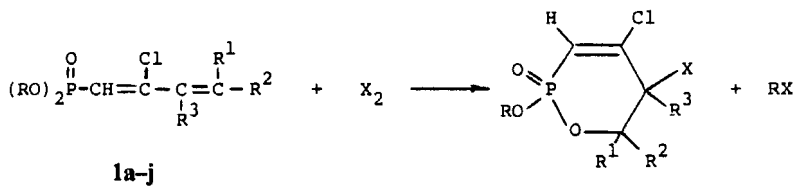
Lately, convenient methods for the preparation of derivatives of 1,3-alkadienephosphonic acids were elaborated, thus making them available for systematic studies of their reactivity. Until now the investigations have shown that, depending on the nature the substituents (usually Cl, R, Ar), including those at the *P*-atom (RO, Cl, NR_2), as well as on their position in the 1,3-diene system, the reaction with halogens leads to formation of adducts,[6] five-[7] or six-membered[8] *P*-containing heterocycles, or mixtures of them,[6] or addition-elimination products via five-membered heterocyclic intermediates.[9]

We now wish to report further investigations on this reaction, undertaken in order to elucidate the influence of the substituents, especially in the 4-position of the 1,3-diene system, on the selectivity of the heterocyclic annulation pathway of the reaction.

RESULTS

For our investigations we have used 2-chloro-1,3-alkadienylphosphonic dialkyl esters **1a–j**, substituted at C^3 and C^4 with different alkyl groups. The reaction with

halogens (Cl_2 or Br_2) proceeds smoothly in an inert solvent but, unlike the case of the more reactive 1,2-alkadienylphosphonic esters,[10] heating (50–60°C) is necessary. In all cases 5,6-dihydro-2*H*-1,2-oxaphosphorine-2-oxides **2a–j**, **3a–c**, **3e** and **3h** were isolated in 77–89% yields, according to Scheme 1:



1a–j

2a–j, 3a–c, 3e, 3h

1,2,3	R	R^1	R^2	R^3
a	Me	H	Me	Me
b	Et	H	Me	Me
c	Me	H	Me	Et
d	Et	H	Me	Et
e	Me	H	Et	Pr^n
f	Et	H	Et	Pr^n
g	Me	Me	Me	Me
h	Et	Me	Me	Me
i	Pr^i	Me	Me	Me
j	Me	Me	Me	Pr^i

X	2	3
	Cl	Br

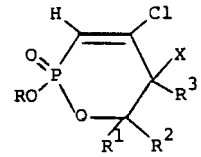
SCHEME 1

In the ^{1}H-nmr spectra of the heterocycles **2a–j**, **3a–h** (Table I) there are weak field doublets from H^3 (δ 6.14–6.30, $^2J_{HP}$ 7.9–9.0 Hz) characteristic of six-membered rings.[6,8] The ^{31}P chemical shifts are in the upfield region (δ 6.1–8.1 ppm) in accordance with literature data[6,8,11] for six-membered phosphorus heterocycles. The formation of ring compounds is evident from the fact that in the ^{1}H-nmr spectra of the crude reaction mixtures of **2c** and **3a** a singlet from methyl halide is observed, and from the fact that the integral over the methoxy group of **2c** and **3a** corresponds to three hydrogens only. Some protons resonate at two frequencies, which is an indication of the existence of diastereoisomers (chirality at P, C^5 or C^6). In Table II physical constants and elemental analysis data are given.

In order to elucidate the course and stereoselectivity of the reaction as well as to isolate the isomers, the reaction products from **1c** and chlorine were chromatographically examined in detail. The crude reaction product was subjected to column chromatography on silica gel Merck 60 (0.063–0.200 mm) using as eluents *n*-hexane–ethylacetate mixtures of increasing polarity, the separation being monitored by thin-layer chromatography. As a result, only two pure diastereoisomeric oxaphosphorins, **2c** α and **2c** β, were isolated in a total yield of 74% (**2c** α—16%; **2c** β—58%), thus indicating a high selectivity of the six-membered annulation pathway of this reaction. No other compounds could be eluted from the column. The ^{1}H-nmr spectrum of the crude reaction product shows (Figure 1) that the two diastereo-

TABLE I

NMR and IR data of 2-alkoxy-5,6-dihydro-2*H*-1,2-oxaphosphorine-2-oxides



No.	R (X)	R^1 (R^2)	R^3	Chemical Shifts, δ				Coupl. Const., Hz				IR Spectra, cm^{-1}	
				H	R^1	R^2	R^3	^{31}P	$^2J_{HP}$	$^3J_{HP}$	$^3J_{HH}$	P=O	C=C
2a	Me	H	Me	6.27	4.75	1.62	1.77	6.8	8.5	12.0	6.4	1270	1590
	(Cl)	(Me)		6.30	4.90		1.80						
b	Et	H	Me	6.22	4.61	1.62	1.77	—	8.0	12.4	7.0	1268	1585
	(Cl)	(Me)		6.25	4.90		1.80						
	Me	H					Me 1.07						
c			Et	α 6.24	4.70	1.59	CH_2 2.17		8.5	13.0	6.4		
	(Cl)	(Me)					Me 0.85	7.6				1268	1590
							A 1.91						
				β 6.34	4.90	1.54	CH_2		9.0	11.8	5.8		
							B 2.50						
d	Et	H	Et	6.23	4.65	1.56	Me 0.80	7.2	8.5	12.6	6.5	1290	1600
	(Cl)	(Me)		6.31	4.89	1.61	CH_2 2.24		8.9	11.5	5.9		
e	Me	H	Pr^n	6.24	4.50	Me 1.15	Me 1.04	8.1	8.5	12.2	—	1290	1595
	(Cl)	(Et)		6.30		CH_2 2.27	CH_2CH_2 2.05						

TABLE I (continued)

No.	R (X)	R^1 (R^2)	R^3	Chemical Shifts, δ				Coupl. Const., Hz				IR Spectra, cm^{-1}	
				H	R^1	R^2	R^3	^{31}P	$^2J_{HP}$	$^3J_{HP}$	$^3J_{HH}$	P=O	C=C
f	Et (Cl)	H (Et)	Pr^n	6.22 6.30	4.55	Me 1.22 CH_2 2.17	Me 1.02 CH_2CH_2 1.99	—	8.0	12.0	—	1280	1600
g	Me (Cl)	Me (Me)	Me	6.22 6.27	1.61 1.70	1.61 1.70	1.77 1.83	7.8	8.5	—	—	1278	1590
h	Et (Cl)	Me (Me)	Me	6.23 6.27	1.59 1.71	1.59 1.71	1.73 1.80	7.3	8.5	—	—	1290	1603
i	Pr^i (Cl)	Me (Me)	Me	6.20 6.25	1.63 1.71	1.63 1.71	1.80 1.85	—	8.0	—	—	1290	1605
j	Me (Cl)	Me (Me)	Pr^i	6.36 6.38	1.69 1.75	1.69 1.75	Me 1.31 H 2.56	—	7.9	—	—	1288	1592
3a	Me (Br)	H (Me)	Me	6.14 6.17	4.56 4.90	1.69	1.90 1.94	7.0	8.5	11.6	5.6	1290	1588
b	Et (Br)	H (Me)	Me	6.14 6.20	4.57 4.88	1.70	1.90 1.95	6.1	8.5	11.0	5.8	1276	1585
c	Me (Br)	H (Me)	Et	6.25 6.30	4.52 4.75	1.63	Me 0.92 CH_2 2.24	6.9	8.7	11.2	5.6	1286	1585
e	Me (Br)	H (Et)	Pr^n	6.22 6.31	4.50	Me 1.00 H 2.24	Me 1.19 CH_2CH_2 2.04	6.7	8.5	11.8	—	1290	1595
h	Et (Br)	Me (Me)	Me	6.15 6.19	1.64 1.75	1.64 1.75	1.77 1.95	—	8.0	—	—	1288	1590

TABLE II

Physical constants, yields and elemental analyses of 2-Alkoxy-5,6-dihydro-2*H*-1,2-oxaphosphorine-2-oxides

No.	Yield* %	bp,°C mm Hg	d_4^{20}	n_D^{20}	Found % P	Found % Cl, X	Formula	Calculated % P	Calculated % Cl, X
2a	84	121–122/0.5	1.3941	1.5047	12.84	29.32	$C_7H_{11}Cl_2O_3P$	12.64	28.94
b	86	124–125/0.5	1.3784	1.4993	11.80	27.81	$C_8H_{13}Cl_2O_3P$	11.96	27.37
c	88	mp 53–54	—	—	12.09	27.69	$C_8H_{13}Cl_2O_3P$	11.96	27.37
d	89	126–127/0.5	1.2969	1.4968	11.31	26.19	$C_9H_{15}Cl_2O_3P$	11.34	25.96
e	88	134–135/0.5	1.2750	1.4991	10.88	25.02	$C_{10}H_{17}Cl_2O_3P$	10.79	24.69
f	87	133–134/0.5	1.2613	1.4931	10.38	23.90	$C_{11}H_{19}Cl_2O_3P$	10.28	23.53
g	89	118–119/0.5	1.3082	1.5078	12.18	27.53	$C_8H_{13}Cl_2O_3P$	11.96	27.37
h	87	123–124/0.5	1.3025	1.4993	11.52	26.41	$C_9H_{15}Cl_2O_3P$	11.34	25.96
i	85	131–132/0.5	1.3009	1.4981	10.92	24.95	$C_{10}H_{17}Cl_2O_3P$	10.79	24.69
j	86	130–131/0.5	1.3232	1.5102	10.52	24.90	$C_{10}H_{17}Cl_2O_3P$	10.79	24.69
3a	79	137–138/0.5	1.5987	1.5274	10.93	40.32	$C_7H_{11}BrClO_3P$	10.70	39.85
b	77	140–141/0.5	1.5822	1.5186	10.33	38.47	$C_8H_{13}BrClO_3P$	10.20	38.01
c	79	mp 67–68	—	—	10.34	38.51	$C_8H_{13}BrClO_3P$	10.20	38.01
e	81	148–149/0.5	1.4486	1.5148	9.24	34.12	$C_{10}H_{17}BrClO_3P$	9.34	34.79
h	80	134–135/0.5	1.4676	1.5212	9.61	37.02	$C_9H_{15}BrClO_3P$	9.75	36.32

*Purified by distillation.

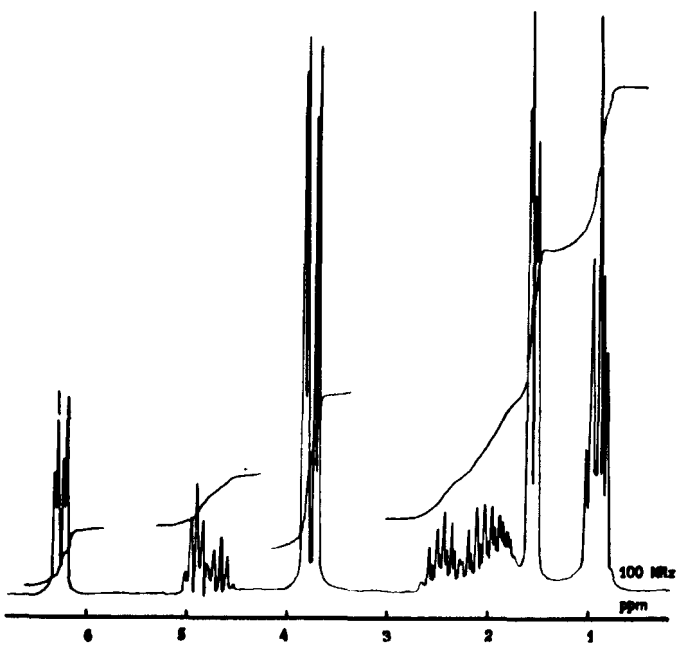


FIGURE 1 ^{1}H-nmr spectrum of the reaction mixture obtained from 3-ethyl-2-chloro-1,3-pentadienylphosphonic dimethyl ester (**1c**) and chlorine.

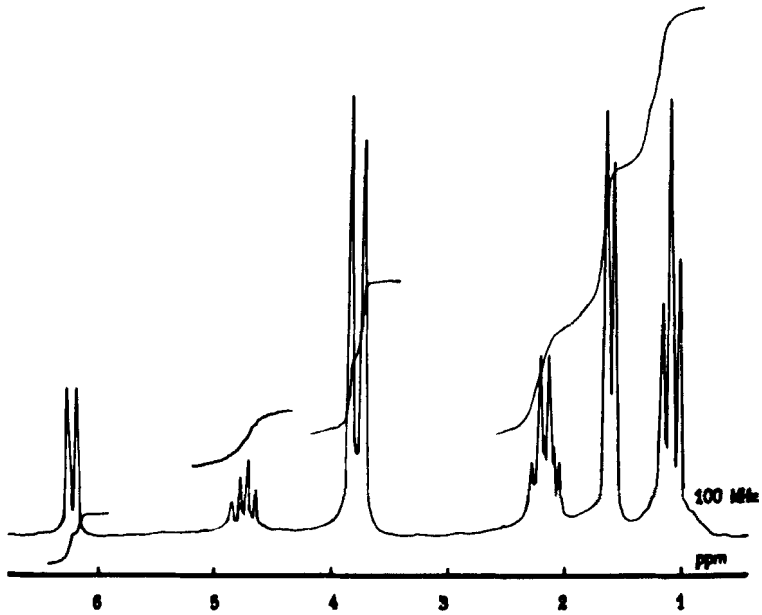


FIGURE 2 ^{1}H-nmr spectrum of 5-ethyl-6-methyl-4,5-dichloro-2-methoxy-5,6-dihydro-2H-oxaphosphorine-2-oxide **2c**; α-isomer (methylene protons of the ethyl group at C-5 are equivalent (δ 2.17 ppm).

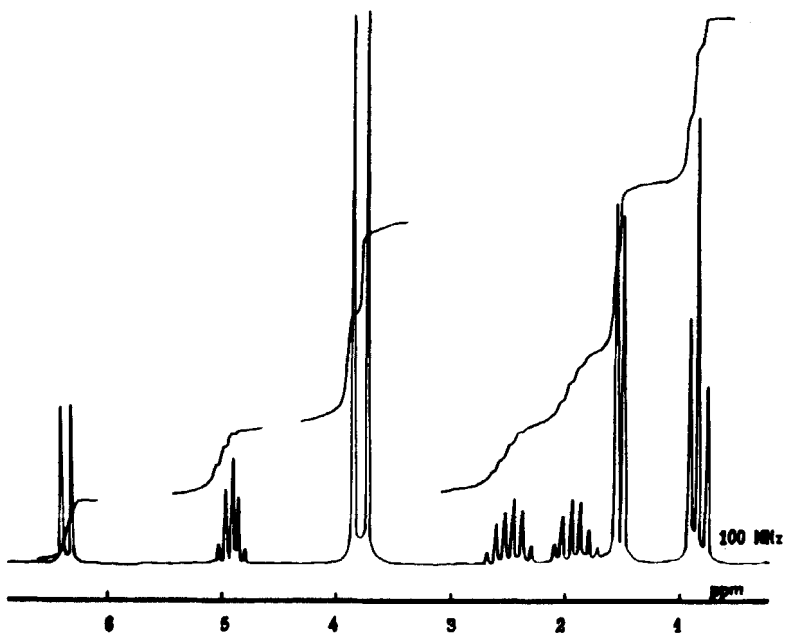


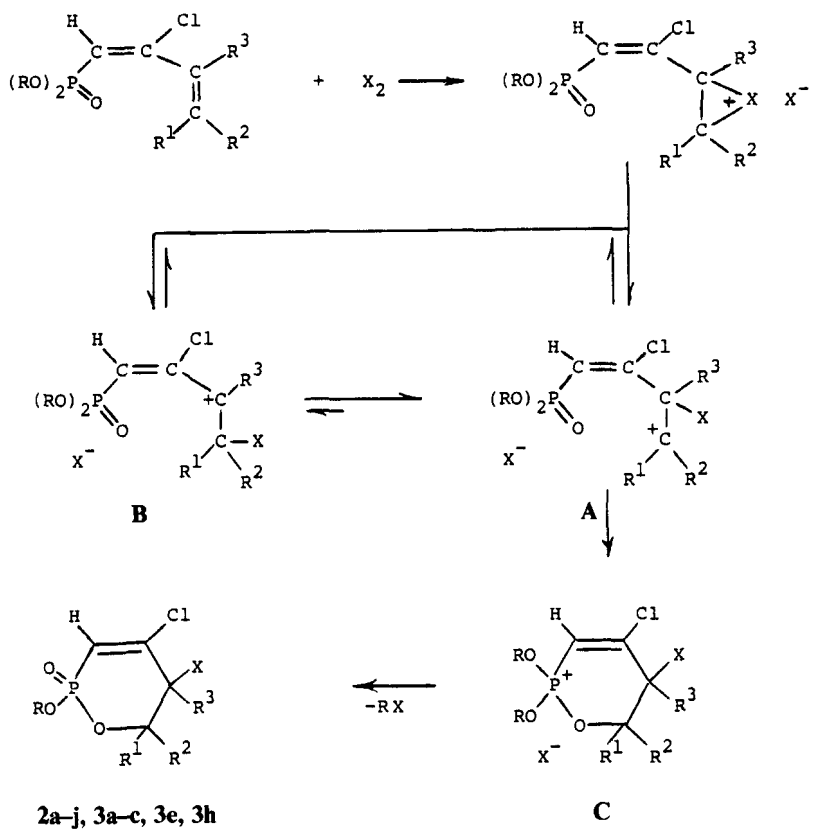
FIGURE 3 ^{1}H-nmr spectrum of 5-ethyl-6-methyl-4,5-dichloro-2-methoxy-5,6-dihydro-2H-1,2-oxaphosphorine-2-oxide, **2c**; β-isomer (in the region 1.90 to 2.30 ppm two multiplets for non-equivalent methylene protons of the ethyl group at C-5 were observed).

isomers are present in the ratio $\alpha : \beta = 1 : 3.5$, which correlates well with the chromatographic data ($\alpha : \beta = 1 : 3.6$). On the other hand the ^{1}H-nmr spectrum of one of the isomers (β) reveals the existence of diastereotopism of the ethyl group methylene protons at the C^5 atom in the ring (Figure 3), while for the other isomer (α) such equivalence is not observed (Figure 2).

DISCUSSION

Recently it was established[12,13] that 2-chloro-1,3-alkadienylphosphonic dialkyl esters synthesized by chlorination of 1,2-alkadienylphosphonic dichlorides[14,15] exist predominantly in the s-cis conformation which is favourable for cyclization reactions. The observed six-membered heterocyclization in our case might be easily explained by the following mechanism of the reaction (Scheme 2).

Halogen attack occurs exclusively at the C^3–C^4 double bond, because of the great destabilizing effect of both the electron-withdrawing phosphonate group and the chlorine atom on a C^1–C^2 onium ion (not shown in Scheme 2), compared with the alkyl substituted C^3–C^4 onium ion shown. This ion, however, exists in equilibrium



SCHEME 2

with the acyclic carbenium ions *A* and *B*. In the case of C^4 mono- and, especially, dialkyl-substituted starting phosphonates **1a–j**, this equilibrium is evidently shifted largely towards the more stabilized carbenium ion *A*, leading, after P=O attack to six-membered heterocyclization (intermediate *C*) with subsequent elimination of alkyl halide and formation of stable products with tetracoordinate phosphorus, **2a–j**, **3a–h**.

EXPERIMENTAL

Methods of Analysis. ^{1}H-nmr spectra were determined on a "Tesla" BS 487 B (80 MHz) and "Jeol" JNM-PS-10 (100 MHz) spectrometers as solutions in CCl_4 or $CDCl_3$ with TMS as internal standard. The ^{31}P chemical shifts were determined on a spectrometer at 24.28 MHz. The ir spectra were run on a IR-72 spectrophotometer (Carl Zeiss Jena, GDR).

Starting Materials. 2-Chloro-1,3-alkadienylphosphonic dialkyl esters were synthesized according to the literature.[15]

Chromatographic Investigations. The column chromatography separations were made in a 80 cm column with a diameter of 3 cm. A mixture of *n*-hexane–ethylacetate (10 : 1 through 1 : 1) was used as a solvent and as sorbent-silica gel Merck 60. By means of thin-layer chromatography on alumina (Merck 60 F_{254}), solvent benzene–ethylacetate 2 : 1, the separation of the substances was followed. The plates were developed by sprinkling with 0.06% aqueous solution of rhodamin 6G and irradiation with UV light.

General Method for Preparation of 2-Alkoxy-5,6-dihydro-2H-1,2-oxaphosphorine-2-oxides, **2a–j**, **3a–c**, **3e**, **3h**. A solution of 0.05 mole of the halogen in dry CCl_4 or $CHCl_3$ was slowly added, with stirring, at 50 to 60°C to a solution of 0.05 mole of the 2-chloro-3-alkyl-1,3-alkadienylphosphonic dialkyl ester in the same solvent. Stirring was continued for 3 h and the reaction mixture kept at room temperature overnight. The solvent was removed and the residue was distilled in vacuo or recrystallized from heptane.

ACKNOWLEDGMENT

The authors are indebted to Prof. B. I. Ionin (Lensovet Leningrad Technological Institute, USSR) for the ^{31}P-nmr spectra.

REFERENCES

1. K. V. Auwers and J. Heyna, *Liebigs Ann. Chem.*, **434**, 140 (1923).
2. K. V. Auwers and W. Müller, *Liebigs Ann. Chem.*, **434**, 165 (1923).
3. I. E. Muscat, B. C. Becker and J. S. Lowenstein, *J. Amer. Chem. Soc.*, **52**, 326 (1930).
4. D. F. Shellamer, V. L. Heasley, J. E. Foster, J. K. Luttrull and G. E. Heasley, *J. Org. Chem.*, **42**, 2141 (1977).
5. D. F. Shellamer, V. L. Heasley, J. E. Foster, J. K. Luttrull and G. E. Heasley, *J. Org. Chem.*, **43**, 2652 (1978).
6. A. M. Shekhade, V. M. Ignat'ev, V. I. Zakharov, B. I. Ionin and A. A. Petrov, *Zh. Obshch. Khim.*, **49**, 337 (1979).
7. V. K. Brell, A. V. Dogadina, B. I. Ionin and A. A. Petrov, *Zh. Obshch. Khim.*, **50**, 1652 (1980).
8. Ch. M. Angelov, V. Ch. Christov, B. I. Ionin, M. Kirilov and A. A. Petrov, *Zh. Obshch. Khim.*, **49**, 2381 (1979).
9. V. K. Brell, A. V. Dogadina, B. I. Ionin and A. A. Petrov, *Zh. Obshch. Khim.*, **50**, 1890 (1980).
10. T. S. Mikhailova, Ch. M. Angelov, V. M. Ignat'ev, A. V. Dogadina, V. I. Zakharov, B. I. Ionin and A. A. Petrov, *Zh. Obshch. Khim.*, **47**, 2701 (1977).
11. L. D. Quin, "The Heterocyclic Chemistry of Phosphorus" (John Wiley & Sons, New York, 1981), p. 196.

12. G. A. Berkova, A. M. Shekhade, V. I. Ignat'ev, B. I. Ionin and A. A. Petrov, *Zh. Obshch. Khim.*, **47**, 957 (1977).
13. G. A. Berkova, G. S. Vafina, V. I. Zakharov, L. N. Mashliakovskij and B. I. Ionin, *Zh. Obshch. Khim.*, **51**, 745 (1981).
14. Ch. M. Angelov, T. S. Mikhailova, V. M. Ignat'ev, V. I. Zakharov, A. V. Dogadina, B. I. Ionin and A. A. Petrov, *Zh. Obshch. Khim*, **48**, 1484 (1978).
15. Ch. M. Angelov and V. Ch. Christov, *C. r. Acad. Bulg. Sci.*, **34**, 67 (1981); Chem. Abstr., **95**: 115675c (1981).