Acta Chemica Scandinavica B 29 (1975) 430—440

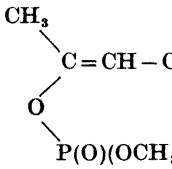
Studies on Organophosphorus Compounds. X.* Phosphorylation of Enolates. Stereochemical Investigations of the Reaction between Salts of β-Dicarbonyl Compounds and *O,O*-Diethyl Phosphorochloridothioate**

H. KOLIND-ANDERSEN and S.-O. LAWESSON

Department of Organic Chemistry, Chemical Institute, University of Aarhus, DK-8000 Aarhus C, Denmark

Sodium salts of β-dicarbonyl compounds are found to yield mainly *Z*-isomers and tetrabutylammonium (TBA) salts mainly *E*-isomers of vinyl phosphorothioates when reacted with *O,O*-diethyl phosphorochloridothioate. The structure of the products is ascribed to the geometry of the anion of the salts: the W-shape yields *E*-isomers and the U-shape *Z*-isomers. At elevated temperature decomposition and *Z/E* isomerization are observed. *O,O*-Diethyl *O*-(2-acetyl-1-phenylvinyl) phosporothioate (*6*) undergoes a thermal rearrangement to *O,O*-diethyl *O*-(2-benzoyl-1-methylvinyl) phosphorothioate (*5*) and the reverse rearrangement is also observed.

Enol phosphates and related compounds are known as powerful insecticides [4-6] and the physiological effect is dependent on the *Z/E* ratio.[5] It is possible to separate the isomers by chromatography,[6] and for Phosdrin the *E*-isomer is found to be the most active one.[5,6] In recent years much effort has been made to design specific reactions, and this has been achieved through variations of solvent, concentration and counter ion of the enolates.

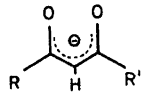


Phosdrin

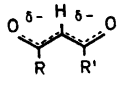
O,O-Diethyl phosphorochloridothioate

Reactions of enolate ions of β-dicarbonyl compounds and similar species with phosphorylating agents such as *O,O*-dialkyl phosphorochloridothioate or *O,O*-dialkyl phosphorochloridate occur solely on oxygen to give stable vinyl phosphorothioates or phosphates [1,4] while normal enolates in few cases give keto phosphonates as co-products.[8] Even metal derivatives of malonic ester are postulated to give diethyl 2-ethoxycarbonyl-1-ethoxyvinyl phosphate by *O*-phosphorylation when reacted with diethyl phosphorochloridate.[16,22] Also the reaction of α-halo ketones with trialkyl phosphites (Perkow reaction) in most cases leads to the *O*-phosphorylated product.[8]

It is found that the ratio of geometrical isomers procuded changes remarkably as the polarity of the solvent is varied.[1] This is accounted for by the shape of the enolate ion. When the enolate ion is U-shaped the phosphorylated product is the *Z*-isomer and when W-shaped,



U-shape



W-shape

* Part IX, Pedersen, E. B. and Lawesson, S.-O. *Acta Chem. Scand. B 28* (1974) 1045.

** Presented in part at the XVth Nordic Chemists Congress, Tammerfors, Finland, June 1974.

the product is the *E*-isomer. In aprotic, polar solvents (DMSO, HMPA) the nucleophilic species is the non-solvated dissociated anion in W-shape.[13] Formation of products of *Z*-configuration in nonpolar, aprotic solvents is due to chelation of the anion in U-shape with the counterion, while formation of *E*-isomers in polar, aprotic solvents is due to reaction of the free, unchelated anions in W-shape.[1,2] The same configuration is achieved if the size of the cation is enlarged to tetrabutylammonium (TBA^+).[2,13] Tetraalkylammonium salts are postulated to exist largely as free ions even in relatively nonpolar solvents. This is concluded from the hypothesis that *E*-isomers exclusively are formed from free anions [1] which should also explain why more dilute solutions give higher percentage of *E*-configuration.[1] However, in relatively nonpolar solvents the presence of the free anions must be questioned and the *E*-isomer must be ascribed to the geometry of an ion pair. The smaller cations give much higher percentages of *Z*-isomers [1,9] due to fixation of the anion in U-shape.

It is postulated that the protonic or non-protonic nature of the solvent should have only little effect on the geometry of the products.[1] That is rejected by Kurts *et al.*,[15] arguing that in polar aprotic solvents W-shape conformations are more stable while in protic solvents enolate ions of β-dicarbonyl compounds adopt the alternative U-shaped conformation. This should be ascribed to hydrogen bond stabilization by the protic solvent of the anionic ground state and it means that the *O*-phosphorylated product in a protic solvent should be the *Z*-isomer.

If the vinyl phosphates are prepared according to the Perkow reaction the products are mixtures of the *Z*- and *E*-isomers.[9]

Previous investigations have supplied us with some helpful spectroscopic tools for the determination of the structure of vinyl phosphates and vinyl phosphorothioates. All compounds assigned to *E*-configuration have the vinyl proton resonance appearing downfield from those assigned to *Z*-configuration [1–3,5,6] and if there is a methyl group attached to the double bond at carbon 1, *e.g.* in the products from alkyl acetoacetate, the methyl proton resonance also occurs at lower field in the *E*- than in the *Z*-isomers.[1,5,6] In some previous investigations [3,6] the coupling constant in the *E*-isomer between the vinylic proton and P is found to be greater than the corresponding constant in the *Z*-isomer and in the products from acetoacetates the coupling constant between the protons in the methyl group and P is found to be greater in the *Z*-isomer than in the *E*-isomer.[3] From the above it is obvious that it should be possible to synthesize *Z*-isomers by reacting the sodium salts of β-dicarbonyl compounds in a suitable alcohol with a suitable electrophilic reagent and the corresponding *E*-isomer by reacting the TBA-salts in methylene chloride. This paper concerns reactions between salts of β-dicarbonyl compounds and *O,O*-diethyl phosphorochloridothioate, $(C_2H_5O)_2P(S)Cl$.

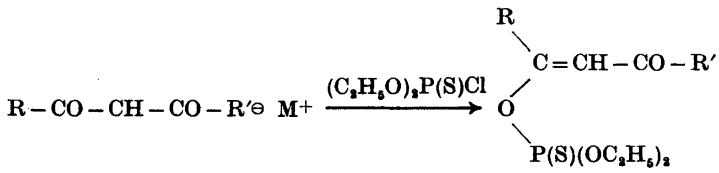
FORMATION OF SALTS OF β-DICARBONYL COMPOUNDS

The TBA-salts of the β-dicarbonyl compounds used in the present investigation (Table 1) were synthesized according to the method described by Brändström and Junggren.[17] However, a more clean reaction was obtained by using methylene chloride instead of chloroform as solvent. The ammonium salts were isolated and, except for III and IV, purified before use. The sodium salts (Table 1) were not isolated before the subsequent reactions and they were generated by adding the β-dicarbonyl compound to a freshly prepared alcoholic solution of sodium alcoholate.

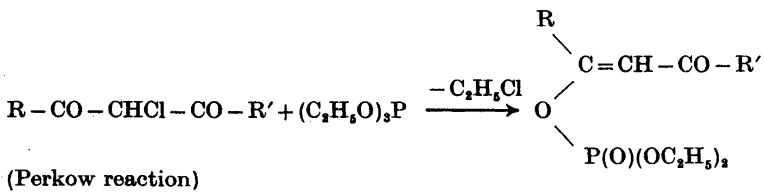
PHOSPHORYLATION, STRUCTURE ELUCIDATION AND REARRANGEMENTS

The phosphorylation reactions were performed by adding $(C_2H_5O)_2P(S)Cl$ to solutions of the salts in the respective solvents. Some of the mixtures were heated to reflux temperature (see experimental). The reactions of the sodium salts in alcoholic solutions yielded the vinyl phosphorothioates in lower yields. Other products isolated were the parent β-dicarbonyl compound and trialkyl phosphorothiates. After workup the product distibution (Table 1) in the reaction mixture was determined by NMR spectroscopy. In Table 2 are shown the NMR chemical shifts and coupling constants of the vinylic and other protons of the vinylic part of the phosphorothioates. Also the products obtained by the Perkow reaction of triethyl phosphite with

Table 1. The product distribution in the vinyl phosphorothioates from the reaction between TBA- and sodium salts of β-dicarbonyl compounds and *O,O*-diethyl phosphorochloridothioate and in the vinyl phosphates from the reaction between triethyl phosphite and 2-chloro-1-phenyl-1,3-butanedione.



Salt No.	R	R′	M+	*Z* (%)	*E* (%)	Prod. No.
I	CH_3	CH_3	TBA^+	30	70	*1*
II	CH_3	OCH_3	TBA^+	~0	100	*2*
III	CH_3	OC_2H_5	TBA^+	~0	100	*3*
IV	C_6H_5	OC_2H_5	TBA^+	25	75	*4*
V	CH_3	C_6H_5	TBA^+	0	100	*5*
	C_6H_5	CH_3	TBA^+	0	0	*6*
VI	CH_3	CH_3	Na^+(EtOH)	90	10	*1*
VII	CH_3	OCH_3	Na^+(EtOH)	90	10	*2* + *3*
			(MeOH)	75	25	*2*
VIII	CH_3	OC_2H_5	Na^+(EtOH)	100	0	*3*
IX	C_6H_5	OC_2H_5	Na^+(EtOH)	100	0	*4*
	CH_3	C_6H_5	Na^+(EtOH)	72	21	*5*
X	C_6H_5	CH_3	Na^+(EtOH)	7	0	*6*



(Perkow reaction)

	CH_3	C_6H_5	Ether	50	10	*7*
	C_6H_5	CH_3		10	30	*8*

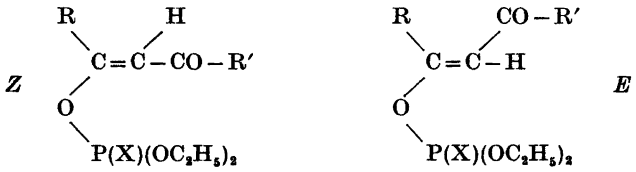
chlorobenzoylacetone (2-chloro-1-phenyl-1,3-butanedione) are included in Tables 1 and 2.

One of the products from the reaction between the TBA-salts and $(C_2H_5O)_2P(S)Cl$ is TBA^+Cl^-. For determination of the yields it is also of interest to isolate this product, but as the chloride is hygroscopic it is converted to the TBA^+I^- by treating the reaction mixture with a water solution of an iodide. For TBA^+Cl^- and TBA^+I^- log E_{TBAX} from the equation

$$\frac{[TBA^+X^-]_{org}}{[TBA^+]_{aq}\,[X^-]_{aq}} = E_{TBAX}$$

is 0.5 and 3.34, respectively, when the organic phase is CH_2Cl_2.[14] According to that, tetra-

Table 2. NMR chemical shifts and coupling constants of the protons from the vinylic part of the vinyl phosphorothioates and phosphates generated by the reactions depicted in Table 1 ($CDCl_3$).



	R	R′	X	R	R′	H_E	H_Z
1E	CH_3	CH_3	S	t, 2.35, (J = ~0.5 Hz)	s, 2.20	m, 6.19	–
1Z	CH_3	CH_3	S	dd, 2.18, (J_1 = ~2.0 Hz, J_2 = ~1.0 Hz)	s, 2.31	–	m, 5.56
2E	CH_3	OCH_3	S	t, 2.38, (J = ~0.5 Hz)	s, 3.71	m, 5.78	–
2Z	CH_3	OCH_3	S	dd, 2.14, (J_1 = ~2.0 Hz, J_2 = ~1.0 Hz)	s, 3.68	–	m, 5.40
3E	CH_3	OC_2H_5	S	t, 2.38, (J = ~0.5 Hz)	CH_2: q, 4.19 (J = 7.1 Hz) CH_3: t, 1.28 J = 7.1 Hz)	m, 5.77	–
3Z	CH_3	OC_2H_5	S	dd, 2.14, (J_1 = ~2.0 Hz, J_2 = ~1.0 Hz)	CH_2: q, 4.17 (J = 7.2 Hz) CH_3: t, 1.26 (J = 7.2 Hz)	–	m, 5.39
4E	C_6H_5	OC_2H_5	S	m, 7.3 – 7.8	CH_2: q, 4.09 (J = 7.0 Hz) CH_3: t, 1.37 (J = 7.0 Hz)	d, 6.06, (J = ~2.2 Hz)	–
4Z	C_6H_5	OC_2H_5	S	m, 7.3 – 7.8	CH_2: q, 4.06 (J = 7.0 Hz) CH_3: t, 1.32 (J = 7.0 Hz)	–	d, 6.00 (J = ~2.2 Hz)
5E	CH_3	C_6H_5	S	t, 2.44 (J = ~0.7 Hz)	2H: m, 7.8 – 8.1 3H: m, 7.4 – 7.7.	m, 6.97	–
5Z	CH_3	C_6H_5	S	dd, 2.23, (J_1 = ~2.0 Hz, J_2 = ~1.0 Hz)	2H: m, 7.8 – 8.1 3H: m, 7.3 – 7.6	–	m, ~6.2
6Z	C_6H_5	CH_3	S	2H: m, 7.8 – 8.1 3H: m, 7.3 – 7.6	s, 2.56	–	m, ~6.2
7E	CH_3	C_6H_5	O	d, 2.46, (J = ~0.8 Hz)	2H: m, 7.8 – 8.1 3H: m, 7.3 – 7.7	m, 7.02	–
7Z	CH_3	C_6H_5	O	dd, 2.29, (J_1 = ~1.5 Hz, J_2 = ~1.0 Hz)	5H: m, 7.3 – 8.0	–	m, ~6.18
8E	C_6H_5	CH_3	O	5H: m, 7.3 – 8.0	s, 2.06	d, 6.40 (J = ~1.9 Hz)	–
8Z	C_6H_5	CH_3	O	5H: m, 7.3 – 8.0	s, 2.44	–	d, 6.18 (J = ~1.0 Hz)

butylammonium ion is found as TBA^+I^- in the organic phase when the mixture is treated with iodide. Evaporation of the organic phase followed by treatment with ether yields TBA^+I^- as clean, nonhygroscopic, and white crystals suitable for regeneration of $TBA^+HSO_4^-$. The vinyl phosphorothioate is in the ether phase. That iodide is postulated to be a "catalyst poison" by some authors [11,12] is due to the equilibrium constant above. For chloride and bromide (log $E_{TBABr} = 1.23$ [14]) some TBA^+X^- is found in the water phase and TBA^+ can then serve as catalyst.

The TBA-salt of acetylacetone (I) was refluxed in methylene chloride with $(C_2H_5O)_2P(S)Cl$ yielding 75 % of *1Z* and *1E* (3:7). Distillation enhanced the content of the *E*-isomer to 75 % and the expected conversion [19,26] to products of the type C_2H_5-S-P was also observed. The isomers were separated by column chromatography. Addition of $(C_2H_5O)_2P(S)Cl$ to a solution of the sodium salt of acetylacetone (VI) yielded after a few minutes reflux 90 % of *1Z* and *1E* (9:1).

The reaction of the TBA-salt of methyl acetoacetate (II) with $(C_2H_5O)_2P(S)Cl$ was exothermic and the yields of *2Z* and *2E* were 93 % (apparent ratio 0:100). However, by column chromatography a fraction of 2.13 g containing *2E* and a fraction of 0.08 g containing 50 % *2E* and 50 % *2Z* was isolated from 2.40 g product. This corresponds to less than 2 % of the *Z*-isomer in the crude product. Addition of $(C_2H_5O)_2P(S)Cl$ to the sodium salt generated from methyl acetoacetate in ethanol yielded after reflux for a few minutes 82 % vinyl phosphorothioate (90 % *Z*- and 10 % *E*-isomer). A neat *Z*-fraction containing 43.5 % methyl ester (*2Z*) and 56.5 % ethyl ester (*3Z*) was isolated by column chromatography. Transesterification of the carboxylic ester group has occured. Refluxing diethyl 2-methoxycarbonyl-1-methylvinyl phosphorothioate (*2Z* and *E*) in ethanol did not give diethyl 2-ethoxycarbonyl-1-methylvinyl phosphorothioate (*3*) as shown by gas chromatography. Even ethanolysis of the vinyl phosphorothioate [18] was not observed to any remarkable extent as alkyl acetoacetate or triethyl phosphorothioate were only detected in an amount less than 1 % in the refluxed mixture.

When methanol was used as solvent for the generation and subsequent phosphorylation of the sodium salt of methyl acetoacetate (VII) the product isolated was *2* (75 % *2Z* and 25 % *2E*). If the sodium salt of methyl acetoacetate (VII) was generated in benzene from sodium hydride the yield of the vinyl phosphorothioate after addition of $(C_2H_5O)_2P(S)Cl$ was only 9 % even after reflux for several hours and the added $(C_2H_5O)_2P(S)Cl$ was recovered in 75 % yield. The poor yield must be ascribed to the low solubility of the salt in benzene.[1]

When the TBA-salt of ethyl acetoacetate (III) was reacted with $(C_2H_5O)_2P(S)Cl$ the reaction was exothermic and yielded 84 % of *3E* and *3Z* (apparent ratio 100:0). However, a fraction of 1.23 g *3E* and a fraction of 0.06 g *3Z* was isolated from 1.7 g of product by column chromatography. Addition of $(C_2H_5O)_2P(S)Cl$ to the sodium salt of ethyl acetoacetate (VIII) in hot ethanol yielded *3Z*.

When the TBA-salt of ethyl benzoylacetate (IV) was reacted with $(C_2H_5O)_2P(S)Cl$ at room temperature the product was a mixture of *4Z* (25 %) and *4E* (75 %). The sodium salt of ethyl benzoylacetate (IX) when refluxed with $(C_2H_5O)_2P(S)Cl$ in ethanol gave *4Z* as the only product.

Phosphorylation of salts of benzoylacetone (V,X) can yield two products due to the non-symmetry of the salts. In Table 1, V and X are depicted in two ways to explain the two products *5* and *6*, each with the two possible isomers *Z* and *E*. However, *6E* is not isolated. When the TBA-salt of benzoylacetone (V) was reacted with $(C_2H_5O)_2P(S)Cl$ at room temperature a slight elevation of the temperature was observed. The only product observed was diethyl 2-benzoyl-1-methylvinyl phosphorothioate (*5E*). Distillation of *5E* gave to a great extent new products as shown in Fig. 1. The NMR spectra of the distillation products also showed the expected conversion [19,26] to products of the type C_2H_5-S-P. In Fig. 1 the β-diketone and the monothio-β-diketone are depicted in a similar way rather than necessarily in the most likely form. (About the true structure see Refs. 20 and 23). Simple heating of *5E* in bromobenzene (155 °C) yielded *5E* and *5Z* as well as the rearranged product *6Z* (Fig. 1). The product *6* together with *5E* and *5Z* is only formed from the sodium salt X and only one of the isomers *6E* and *6Z* is found (Table 1). This can be

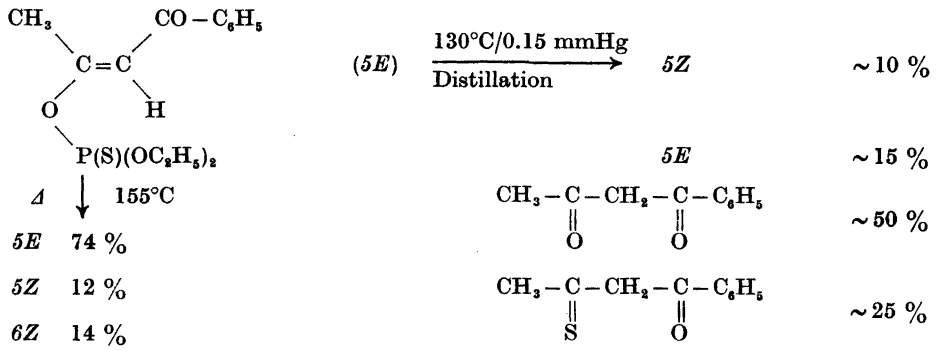


Fig. 1. Rearrangements and decomposition of diethyl 2-benzoyl-1-methylvinyl phosphorothioate (*5E*).

accounted for if *6* is generated only from the U-shaped anion. The product must then be expected to be *6Z* and the NMR data of *6* do also correspond better to *8Z* than to *8E*. Heating a benzene solution of *5Z*, *5E*, and *6Z* shows that *5Z* is transformed to *5E* while *6Z* seems to have reached an equilibrium concentration or to be stable towards rearrangements at that temperature. Heating a chlorobenzene solution of the same compounds gave almost the same product distribution as when neat *5E* was heated in chlorobenzene (Fig. 1). It is thought to be an equilibrium mixture.

Reaction of 2-chloro-1-phenyl-1,3-butanedione with triethyl phosphite (Perkow reaction) yielded the products *7* and *8* (Table 1). By column chromatography *7E* was isolated neat. Refluxing a mixture of *7Z*, *8E*, and *8Z* in chlorobenzene yielded a mixture of benzoylacetone, *7Z*, *7E*, *8Z*, and *8E*, where the *E*-isomers were the most abundant of the vinyl phosphates.

So far only the vinyl phosphorothioates have been looked on as products, but also the parent β-dicarbonyl compounds were isolated together with trialkyl phosphorothioate from the reactions between salts of β-dicarbonyl compounds and $(C_2H_5O)_2P(S)Cl$. In Table 3 is shown the distribution between those products. The trialkyl phosphorothioate is the *O,O,O*-triethyl

Table 3. The yields from the reactions between TBA- and sodium salts of β-dicarbonyl compounds and *O,O*-diethyl phosphorothioate.

Salt	Solvent	Vinyl phosphorothioate %	β-Dicarbonyl compound %	*O,O,O*-Trialkyl phosphorothioate %
I	CH_2Cl_2	75		
II	CH_2Cl_2	93		
III	CH_2Cl_2	84	16	
IV	CH_2Cl_2	95		
V	CH_2Cl_2	85	15	
VI	EtOH	90		
VII	EtOH	82 [a]		18
VII	MeOH	32	37	58
VIII	EtOH	70		30
IX	EtOH	32	64	64
X	EtOH	51	36	48

[a] 2-methoxycarbonyl-1-methylvinyl phosphorothioate (*2*) 27 % 2-ethoxycarbonyl-1-methylvinyl phosphorothioate (*3*) 55 %.

ester except when the solvent was methanol. In this case it was *O,O*-diethyl *O*-methyl phosphorothioate.

DISCUSSION

Polar aprotic solvents and bulky cations should give *E*-isomers when salts of β-dicarbonyl compounds are reacted with diethyl phosphorochloridothioate. In this investigation TBA-salts of β-dicarbonyl compounds produced mainly the *E*-isomers (Table 1), although methylene chloride is not a very polar solvent. If it is only the enolate anion in W-shape that gives the *E*-isomers the anion in the TBA-salts must adopt this W-shape when dissolved in methylene chloride although the ion pair is expected to be maintained. In the introduction it was also mentioned that *Z*-isomers were achieved through phosphorylation of enolate anions in U-shape. This U-shape should be found when the cation was small and nonpolar solvents were used. However, also protic solvents should generate an U-shaped anion. From these predictions the products shown in Table 1 were expected when sodium salts of β-dicarbonyl compounds

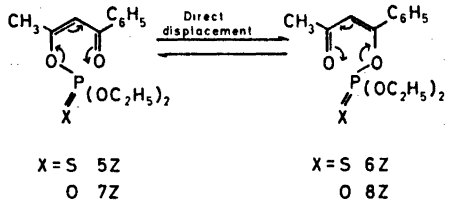


Fig. 2. A mechanism for the rearrangements of diethyl 2-benzoyl-1-methylvinyl phosphorothioate (*5*) to diethyl 2-acetyl-1-phenylvinyl phosphorothioate (*6*) (or vice versa) and of diethyl 2-benzoyl-1-methylvinyl phosphate (*7*) to diethyl 2-acetyl-1-phenylvinyl phosphate (*8*) (or *vice versa*).

were reacted with diethyl phosphorochloridothioate.

In an earlier work [4,18] the structure of the products from the reaction between X and $(C_2H_5O)_2P(S)Cl$, the reaction between X and $(C_2H_5O)_2P(O)Cl$ and the reaction between 2-chloro-1-phenyl-1,3-butanedione and triethyl phosphite are postulated to be *6* and *8*, respectively. This assumption is made from isolating methyl glyoxal and benzoic acid when the products were ozonized. However, the products were purified by distillation before the ozonization and, as shown in the present investigation, this will increase the amounts of the compounds *6* and *8* in the respective mixtures, *i.e.* there is no evidence for the products to have been entirely *6* and *8*.

The rearrangement from *5* to *6* or from *7* to *8* is expected to go *via* the *Z*-isomers as depicted in Fig. 2 (Direct displacement [21]). Two other mechanisms (elimination-addition and addition-elimination) suggested for nucleophilic substitution on phosphorus in phosphates [21] are not considered as likely. The first is excluded because the rearrangements are performed under neutral conditions. The latter involves a charged intermediate probably with a trigonal bipyramidal structure.

The formation of the monothio-β-diketone when diethyl 2-benzoyl-1-methylvinyl phosphorothioate (*5E*) was distilled (Fig. 1) can be expected to go through the intermediate shown in Fig. 3. This is parallel to the finding of products of the type C_2H_5-S-P which are also found after distillation of 1.

The cleavage yielding a β-dicarbonyl compound was also observed when *7* and *8* were heated in chlorobenzene.

As shown in Table 3 phosphorylation of the sodium salts in alcoholic solutions yielded some

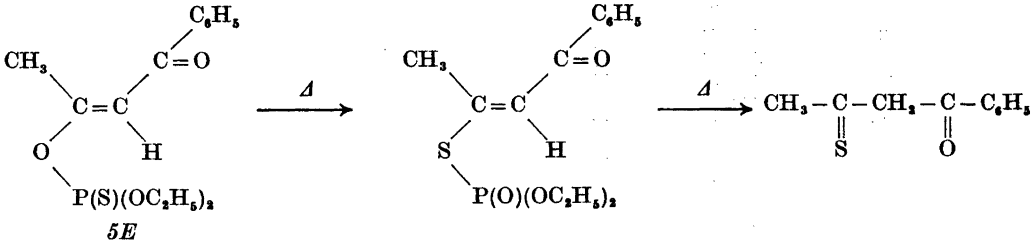


Fig. 3. A reaction sequence for the formation of the monothio-β-diketone from diethyl 2-benzoyl-1-methylvinyl phosphorothioate (*5E*).

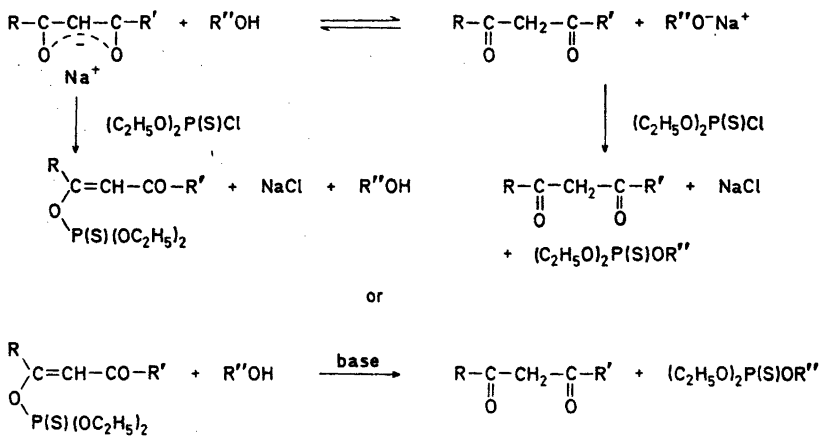


Fig. 4. Reaction sequences for the formation of the products shown in Table 3 from the reaction between $(C_2H_5O)_2P(S)Cl$ and sodium salts of β-dicarbonyl compounds.

trialkyl phosphorothioate and the parent β-dicarbonyl compound. The products can be accounted for by the equilibrium existing between the sodium salt of the β-dicarbonyl compound and sodium alcoholate as shown in Fig. 4. The amounts of β-dicarbonyl compound and *O,O,O*-trialkyl phosphorothioate can also be ascribed to base-catalyzed alcoholysis [18] (Fig. 4), and for the reaction between IX and $(C_2H_5O)_2P(S)Cl$ where the mixture was refluxed for several hours in ethanol, this might account for the poor yields of vinyl phosphorothioate. However, refluxing of *2* in ethanol as mentioned previously only yielded small amounts of the ethanolysis product. The isolation of β-dicarbonyl compound from III and V (Table 3) may be accounted for by hydrolysis of the respective vinyl phosphorothioates (*3* and *5*) during the work-up procedure.

The present investigation shows methods for preparing vinyl phosphorothioates, enriched either in the *Z*- or the *E*-isomer. For the vinyl phosphate phosdrin it is found that the *E*-isomer was 10 to 100 times more toxic to insects and mammals than the *Z*-isomer [5,6] and our procedures should thus prove to be the methods of choice for selective synthesis. Preliminary experiments have been made on the reaction between $(Me_2N)_2P(O)Cl$ and salts of β-dicarbonyl compounds [24] and the results were the same as in the present work.

EXPERIMENTAL

The IR spectra were recorded on a Perkin-Elmer model Infracord Spectrophotometer and the NMR spectra at 60 MHz on a Varian A-60 spectrometer using TMS as internal standard. The chemical shifts are expressed in δ-values. The UV spectra were recorded on a Perkin-Elmer 402 Ultraviolet-Visible Spectrophotometer. Microanalyses were carried out by Micro Analytical Laboratory, Novo A/S, Novo Allé, DK-2880 Bagsvaerd, Denmark, and by Micro Analytical Laboratory, Løvens Kemiske Fabrik, DK-2750 Ballerup, Denmark. Column chromatography was made on silica gel (Kiselgel 60; 0.063 – 0.200 mm; 70 – 230 mesh ASTM; (Merck)). B.p.'s and m.p.'s are uncorrected.

TBA-salt of 2,4-pentanedione (acetylacetone), (I). Compound I was synthesized [17] in 95 % yield. However, methylene chloride was used instead of chloroform. M.p. 151 – 154 °C (acetone).[17]

TBA-salt of methyl acetoacetate, (II). Compound II was synthesized as I in 98 % yield, as yellow crystals, m.p. 87 – 90 °C (AcOEt). (Found: C 69.43; H 12.16; N 3.91. $C_{31}H_{43}NO_3$ requires: C 70.54; H 12.12; N 3.92). IR: ν_{max}($CHCl_3$) 3000, 1655, 1515, 1380, 1150, 1125, 1057, 1000 and 885 cm^{-1}. UV-Visible (EtOH) λ_{max} (log ε): 245 nm (3.031). NMR ($CDCl_3$): δ 0.7 – 1.2 (12 H, m), 1.2 – 2.0 (16 H, m), 2.24 (3 H, broad s), 3.1 – 3.7 (8 H, m), 3.53 (3 H, s), 7.55 (1 H, broad s).

TBA-salt of ethyl acetoacetate, (III). Compound III was synthesized as I in 100 % yield. The compound did crystallize in a deep-freezer and in vacuum, but as it was too soluble in all attempted solvents it could not be recrystallized before use. IR: ν_{max}($CHCl_3$) 2960, 1630, 1505, 1375, 1160, 1065, 1012, 914 and 882 cm^{-1}.

UV (EtOH) λ_{max} (log ε): 210 nm (2.929) and 283 nm (3.441). NMR ($CDCl_3$): δ 0.7 – 1.2 (12 H, m), 1.2 – 1.9 (16 H, m), 1.25 (3 H, t, J 7.1 Hz), 2.34 (3 H, s), 3.0 – 3.5 (8 H, m), 4.10 (2 H, q, J 7.1 Hz), 7.55 (1 H, s).

TBA-salt of ethyl 3-oxo-3-phenylpropionate (ethyl benzoylacetate), (IV). Compound IV was synthesized as I in almost 100 % yield. As the compound was too soluble in all attempted solvents to be recrystallized it was not further purified before use. NMR ($CDCl_3$): δ 0.8 – 1.6 (31 H, m), 2.9 – 3.3 (8 H, m), 4.02 (2 H, q, J 7.0 Hz), 7.1 – 7.5 (3 H, m), 7.46 (1 H, s), 7.7 – 8.0 (2 H, m).

TBA-salt of 1-phenyl-1,3-butanedione (benzoylacetone), (V). Compound V was synthesized as I in almost 100 % yield. Red-orange crystals, m.p. 100 – 101 °C. (AcOEt). (Found: C 77.26; H 11.31; N 3.48. $C_{26}H_{45}NO_2$ requires: C 77.36; H 11.24; N 3.47). IR: ν_{max}($CHCl_3$) 2950, 1605, 1565, 1495, 1460, 1415, 1370, 1275, 987 and 867 cm^{-1}. ν_{max}(KBr) 2950, 1580, 1555, 1495, 1430, 1380 (sh), 1340, 1295, 1270, 1190, 1172, 1143, 1057, 1021, 987, 880, 865, 798, 758 and 707 cm^{-1}. UV (EtOH) λ_{max} (log ε): 208 nm (3.916), 246 nm (3.803) and 313 nm (4.189). NMR ($CDCl_3$): δ 0.7 – 1.1 (12 H, m), 1.1 – 1.6 (16 H, m), 2.46 (3 H, s), 2.8 – 3.2 (8 H, m), 7.1 – 7.4 (3 H, m), 7.49 (1 H, s), 7.6 – 8.0 (2 H, m).

Phosphorylation of the TBA-salts I-V. Equivalent amounts of TBA-salt and diethyl phosphorochloridothioate were mixed in methylene chloride (25 ml to about 0.01 mol of salt). The product mixture from I was refluxed for about 7 h. The other reactions were observed to be more or less exothermic and therefore only stirred for a couple of hours at room temperature.

I→1. The reaction mixture of 0.0146 mol of I and $(C_2H_5O)_2P(S)Cl$ was treated with a solution of 0.02 mol NaI in water. The methylene chloride phase was separated, dried (Na_2SO_4) and the solvent evaporated. TBA^+I^- (0.0134 mol, 92 %) was then precipitated by adding ether. Evaporation of the ether phase yielded 2.77 g of *1* (75 %) with 30 % *1Z* and 70 % *1E* as confirmed by NMR spectroscopy (Table 2). Distillation enhanced the content of *1E* to 75 % and also small amounts of a product containing the structure element $-P-S-C_2H_5$ were observed in NMR ($CDCl_3$): δ 2.88 (2 H, broad q, J 7.3 Hz). (Found: C 42.69; H 6.86; P 12.26. $C_9H_{17}O_4PS$ requires: C 42.85; H 6.79; P 12.28). The isomers were isolated by column chromatography and the NMR spectra shown in Table 2 were recorded. The groups C_2H_5-O-P- showed the known NMR-patterns.[10] IR(*1E*): ν_{max}(CCl_4) 2985, 1705, 1625, 1410, 1380, 1350, 1210, 1135, 1023, 948 and 862 cm^{-1}. ν_{max}(CS_2) 2980, 1695, 1615, 1375, 1350, 1210, 1135, 1021, 948, 862 and 818 cm^{-1}.

II→2. The reaction mixture was treated as above yielding 93 % of almost neat *2E* and 99 % of TBA^+I^-. A fraction of 2.40 g of the product was separated by silica gel column chromatography (CH_2Cl_2) to yield 2.13 g of neat *2E* and 0.08 g of a mixture of *2E* and *2Z* (1:1). Data of *2E*: (Found: C 39.65; H 6.30; P 11.63. $C_9H_{17}O_5PS$ requires: C 40.29; H 6.39; P 11.55). $n_D^{20.5} = 1.4760$. For NMR data, see Table 2. UV(EtOH) λ_{max} (log ε): 227 nm (3.984). IR: ν_{max}(CCl_4) 3010, 1740, 1665, 1435, 1385, 1335, 1230, 1127, 1025, 965, 944, 891, 853 and 822 cm^{-1}. ν_{max}(CS_2) 3020, 1740, 1665, 1385, 1335, 1230, 1127, 1025, 968, 946, 893, 855 and 822 cm^{-1}.

III→3. The reaction mixture was treated as above and yielded 84 % of almost neat *3E* and 16 % of ethyl acetoacetate, which is likely generated by hydrolysis of *3E*. TBA^+I^- was isolated in 92 % yield. However, by silica gel column chromatography (CH_2Cl_2) 0.06 g of *3Z* and 1.23 g of *3E* was isolated from 1.70 g of *3*. (Found C 42.52; H 6.77; P 11.08. $C_{10}H_{19}O_5PS$ requires: C 42.55; H 6.78; P 10.97). For NMR data, see Table 2. UV(EtOH) λ_{max} (log ε): 225 nm (3.993). IR: ν_{max}(CCl_4) 2970, 1720, 1650, 1430, 1375, 1355, 1325, 1223, 1157, 1120, 1090, 1020, 968, 897, 855 and 822 cm^{-1}. ν_{max}(CS_2) 2975, 1725, 1655, 1380, 1360, 1330, 1225, 1160, 1123, 1093, 1025, 970, 896, 857, 822 and 730 cm^{-1}.

IV→4. The reaction mixture was treated as above and yielded 95 % of *4E* and *4Z* (3:1) and traces of ethyl benzoylacetate which is likely generated by hydrolysis of *4* during work-up. TBA^+I^- was isolated in 88 % yield. Ethyl benzoylacetate was separated from *4* by silica gel column chromatography (CH_2Cl_2), but separation of *4E* and *4Z* did not succeed. The NMR spectra of *4E* and *4Z* are shown in Table 2. They are found to correspond to the spectra of the *Z* and *E* isomers of diethyl 2-ethoxycarbonyl-1-phenylvinyl phosphate.[7] IR(*4E* and *4Z*; 3:1): ν_{max}(CCl_4) 2965, 1725, 1640, 1435, 1385, 1360, 1330, 1265, 1220, 1155, 1087, 1030, 968, 882, 822 and 692 cm^{-1}. ν_{max}(CS_2) 2970, 1725, 1640, 1375, 1355, 1260, 1215, 1155, 1087, 1034(sh), 1018, 968, 882, 822 and 691 cm^{-1}.

V→5E *(and 5Z + 6Z).* The reaction mixture was treated as above and yielded quantitatively a mixture of 85 % *5E* and 15 % benzoylacetone. The yield of TBA^+I^- was 98 %. *5E* was isolated by silica gel column chromatography (CH_2Cl_2). (Found: C 53.53; H 6.05; P 9.85. $C_{14}H_{19}O_4PS$ requires: C 53.50; H 6.09; P 9.85). For NMR-data, see Table 2. IR: ν_{max}(CCl_4) 2970, 1675, 1615, 1440, 1385, 1340, 1235, 1150, 1022, 965, 908 and 697 cm^{-1}. ν_{max}(CS_2) 2970, 1670, 1615, 1380, 1335, 1240, 1150, 1090, 1020, 965, 905, 818 and 698 cm^{-1}. The products obtained when neat *5E* was heated in bromobenzene (155 °C) for 2 h. (*5E*, *5Z*, and *6Z*, Fig. 1) were determined by NMR spectroscopy. Distillation of *5E* onto a cold finger (130 °C/0.15 mmHg) yielded the products shown in Fig. 1 and traces of a product containing the structure element C_2H_5-S-P. They were determined by NMR spectroscopy, also the monothio-β-diketone [20] for which the

molecular weight after separation by silica gel column chromatography (benzene) was determined by MS to be 178. (The mass spectrum was recorded on a CEC 21-104 mass spectrometer operating at 70 eV using the direct inlet). The fragments $C_6H_5-CO^+$ ($m/e=105$) and CH_3-CS^+ ($m/e=59$) were observed in the mass spectrum.

Phosphorylation of the sodium salts VI–X. Equivalent amounts of diethyl phosphorochloridothioate were added to refluxing alcoholic solutions of the sodium salts VI–X. The mixture from IX was refluxed for about 3 h, while the other mixtures were allowed to cool to room temperature after adding $(C_2H_5O)_2P(S)Cl$.

VI→1. Sodium chloride was filtered from the ethanolic reaction mixture of 0.024 mol VI and $(C_2H_5O)_2P(S)Cl$ and the solvent evaporated. The last traces of sodium chloride were precipitated by ether. Evaporation yielded 5.40 g (0.021 mol, 90 %) of *1E* and *1Z* (1:9) as confirmed by NMR spectroscopy (Table 2). IR [*1E* and *1Z* (1:9)]: $\nu_{max}(CCl_4)$ 2985, 1695, 1615, 1430, 1380, 1350, 1155, 1135, 1090, 1023, 963 and 865(sh) cm^{-1}. $\nu_{max}(CS_2)$ 2970, 1695, 1615, 1375, 1345, 1150, 1135, 1090, 1020, 960, 865(sh) and 818 cm^{-1}.

VII→2 *(and 3)*. By the procedure as above from 0.028 mol VII in ethanol was isolated 7.73 g of a mixture of 2-methoxycarbonyl-1-methylvinyl phosphorothioate (2) (27 % yield), 2-ethoxycarbonyl-1-methylvinyl phosphorothioate (3) (55 % yield), and *O,O,O*-triethyl phosphorothioate (18 % yield). The *E*-isomers formed 10 % of the product and the *Z*-isomers 90 %. The *Z*-isomers were isolated neat by silica gel column chromatography (CH_2Cl_2) and the NMR spectrum revealed a distribution between the just mentioned compounds *2Z* and *3Z* which was 43.5 %: 56.5 %. (Found: C 41.55; H 6.60. 43.5 % $C_9H_{17}O_5PS$ and 56.5 % $C_{10}H_{19}O_5$ requires: C 41.57; H 6.61). IR: $\nu_{max}(CCl_4)$ 2965, 1725, 1665, 1430, 1375, 1315, 1205, 1143, 1092, 1046, 1020, 972, 912 and 823 cm^{-1}. $\nu_{max}(CS_2)$ 2965, 1725, 1665, 1375, 1320, 1270, 1205, 1143, 1093, 1046, 1020, 970, 912 and 823 cm^{-1}. Refluxing the mixture of the methyl and ethyl ester in EtOH for 5 3/4 h did not change the ratio of the amounts of the two components as confirmed by GLC (Hewlett-Packard 5711 A Gas Chromatograph, 15 % PEG 4000, 130 °C for 4 min and then 130–200 °C (8 °C/min), N_2-flow: 30 ml/min). However, about 0.5 % of ethyl acetoacetate showed up to be present in the heated solution. Refluxing neat *2E* in EtOH did not give 2-ethoxycarbonyl-1-methylvinyl phosphorothioate (*3*) as confirmed by GLC.

From 0.080 mol of VII prepared in abs. methanol was isolated 18.81 g of a mixture of 0.026 mol 2-methoxycarbonyl-1-methylvinyl phosphorothioate (*2Z*+*2E*) (32 % yield), 0.031 mol methyl acetoacetate (37 % yield), and 0.046 mol *O*-methyl-*O,O*-diethyl phosphorothioate (58 % yield). Most of the two latter compounds were removed by vacuum at room temperature leaving a fraction containing 85 % of *2Z*+*2E* (3:1) and 15 % of *O*-methyl-*O,O*-diethyl phosphorothioate.

The reaction of VII (prepared from sodium hydride and methyl acetoacetate) in benzene with $(C_2H_5O)_2P(S)Cl$ yielded 9 % of *2*, a poor yield corresponding to previous statements.[1]

VIII→3*Z*. By a procedure as above from 0.046 mol VIII in ethanol was isolated 11.82 g of a mixture of 0.032 mol of 2-ethoxycarbonyl-1-methylvinyl phosphorothioate (*3Z*) (70 % yield) and 0.014 mole of triethyl phosphorothioate (30 % yield). For NMR data of *3Z*, see Table 2.

IX→4Z. The refluxed reaction mixture of 0.054 mol of IX and 0.054 mol of $(C_2H_5O)_2P(S)Cl$ in ethanol yielded by the procedure described above 19.32 g of a mixture containing *4Z* (32 % yield), ethyl benzoylacetate (64 % yield) and triethyl phosphorothioate (64 % yield). Distillation of 8 g of this mixture yielded three fractions: 1.59 g (37 °C/0.05 mmHg; triethyl phosphorothioate (confirmed by NMR spectroscopy[10])), 2.54 g (82–83 °C/0.05 mmHg; 39 % triethyl phosphorothioate and 61 % ethyl benzoylacetate) and 2.10 g (115–138 °C/0.08 mmHg; 36 % ethyl benzoylacetate and 64 % *4Z*). By silica gel column chromatography (CH_2Cl_2) 4.15 g of the above mentioned mixture was separated yielding 1.27 g of *4Z*. (Found: C 52.22; H 6.12; P 8.82. $C_{15}H_{21}O_5PS$ requires: C 52.32; H 6.15; P 8.99). IR: $\nu_{max}(CCl_4)$ 2975, 1730, 1645, 1440, 1385, 1355, 1320, 1265, 1153, 1093, 1021, 968, 913, 827 and 692 cm^{-1}. $\nu_{max}(CS_2)$ 2985, 1730, 1645, 1385, 1355, 1320, 1265, 1152, 1092, 1020, 967, 912, 825, 767 and 689 cm^{-1}.

X→5 *and* 6. By a procedure as above, starting from 0.057 mol X in ethanol was isolated 17.93 g of a mixture of *5E*, *5Z*, and *6Z* (distribution shown in Table 1) (51 % yield), 1-phenyl-1,3-butanedione (36 % yield) and triethyl phosphorothioate (48 % yield). By silica gel column chromatography (CH_2Cl_2) it was possible to get fractions enriched in either of the components of the reaction mixture. A rapid treatment of the mixture with 5 M NaOH + CH_2Cl_2 removed 1-phenyl-1,3-butanedione and triethyl phosphorothioate. Heating a benzene solution of a mixture of *5Z*, *5E*, and *6Z* (77, 6, and 17 %) (80 °C) for 5 1/4 h yielded a mixture of the components with the distribution 47, 37, and 16 %. Heating a chlorobenzene solution of a mixture of *5Z*, *5E*, and *6Z* (10, 71, and 19 %) (132 °C) for 1 h yielded a mixture of the components with the distribution 8, 76, and 16 %.

Preparation of 7 *and* 8. A mixture of *7* and *8* was synthesized [4] from 1-phenyl-2-chloro-1,3-butanedione [25] and triethyl phosphite in 77 % yield without distillation of the product mixture recovering 23 % of 1-phenyl-2-chloro-1,3-butanedione and 15 % of triethyl phosphite. Based on the NMR spectrum *7Z*, *7E*, *8Z*, and *8E* showed 50 %, 10 %, 10 %, and 30 %

appearance. Treatment of the reaction mixture with 5 M NaOH + CH_2Cl_2 removed the β-dicarbonyl compound and triethyl phosphite yielding *7Z*, *7E*, *8Z*, and *8E* with the distribution 11, 45, 33, and 11 %. By silica gel column chromatography (ether) it was possible to isolate neat *7E* from the just mentioned mixture. Refluxing *7* and *8* in chlorobenzene yields 1-phenyl-1,3-butanedione (benzoylacetone): Refluxing a mixture of *7Z*, *8Z*, and *8E* (13, 65, and 22 %) in chlorobenzene (132 °C) for 1 1/4 h yielded benzoylacetone, *7Z*, *7E*, *8Z*, and *8E* (50, 15, 19, 7, and 9 %).

Acknowledgement. A grant from Statens naturvidenskabelige Forskningsråd is gratefully acknowledged. Thanks are expressed to Mrs. Tove Bucholt for her carefully performed NMR-measurements. The supply of *O,O*-diethyl phosphorochloridothioate from Cheminova A/S, Postbox 9, DK-7620 Lemvig, is greatly appreciated.

REFERENCES

1. Miller, B., Margulies, H., Drabb, Jr., T. and Wayne, R. *Tetrahedron Lett.* (1970) 3801, 3805.
2. Gelin, R., Gelin, S. and Galliaud, A. *Bull. Soc. Chim. Fr.* (1973) 3416.
3. Gaydou, E. M. *Can. J. Chem. 51* (1973) 3412.
4. Nishizawa, Y. *Bull. Agr. Chem. Soc. Jap. 24* (1960) 261; *25* (1961) 61, 66 and 150.
5. Fukuto, T. R., Hornig, E. O., Metcalf, R. L. and Winton, M. Y. *J. Org. Chem. 26* (1961) 4620.
6. Stiles, A. R., Reilly, C. A., Pollard, G. R., Tieman, C. H., Ward, L. F., Phillips, D. D., Soloway, S. B. and Whetstone, R. R. *J. Org. Chem. 26* (1961) 3960.
7. Marecek, J. F. and Griffith, D. L. *J. Amer. Chem. Soc. 92* (1970) 917.
8. Borowitz, I. J., Firstenberg, S., Casper, E. W. R. and Crouch, R. K. *J. Org. Chem. 36* (1971) 3282.
9. Fischer, G. W. and Schneider, P. *Chem. Ber. 106* (1973) 435.
10. Williamson, M. P. and Griffin, C. E. *J. Phys. Chem. 72* (1968) 4043.
11. Dockx, J. *Synthesis* (1973) 441.
12. McKillop, A., Fiaud, J.-C. and Hug, R. P. *Tetrahedron 30* (1974) 1379.
13. Bram, G., Guibé, F. and Sarthou, P. *Tetrahedron Lett.* (1972) 4903.
14. Brändström, A. *Private communication.*
15. Kurts, A. L., Macias, A., Beletskaya, I. P. and Reutov, O. A. *Tetrahedron Lett.* (1971) 3037.
16. Kolodyazhnyi, O. I., Kalyagin, G. A. and Gololobov, Yu. G. *J. Gen. Chem. USSR 43* (1974) 1847.
17. Brändström, A. and Junggren, U. *Acta Chem. Scand. 23* (1969) 2203, 2536 and 3585.
18. Lichtenthaler, F. W. *Chem. Rev. 61* (1961) 607.
19. Tammelin, L. E. *Acta Chem. Scand. 11* (1957) 1738.
20. Klose, G., Thomas, Ph., Uhlemann, E. and Märki, J. *Tetrahedron 22* (1966) 2695; Duus, F. and Lawesson, S.-O. *Ark. Kemi 29* (1968) 127; Power, L. F. and Turner, K. E. *Tetrahedron Lett.* (1974) 875; Siiman, O., Fresco, J. and Gray, H. B. *J. Amer. Chem. Soc. 96* (1974) 2347.
21. Walker, B. J. *Organophosphorus Chemistry*, Penguin Books 1972, pp. 108–116.
22. Cramer, F. and Gärtner, K. *Chem. Ber. 91* (1958) 705.
23. Burdett, J. L. and Rogers, M. T. *J. Amer. Chem. Soc. 86* (1964) 2105.
24. Almquist, A., Kolind-Andersen, H. and Lawesson, S.-O. *Unpublished results.*
25. Macbeth, A. K. *J. Chem. Soc. 123* (1923) 1128.
26. Sasse, K. In Houben-Weyl, *Die Methoden der organischen Chemie*, 12/2, pp. 668–671.

Received October 14, 1974.