PHOSPHONEMETHYLATION OF PHOSPHORUS COMPOUNDS WITH LABILE HYDROGEN

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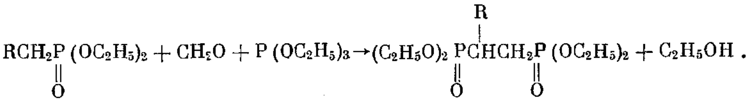
A peculiarity of compounds with a methylenephosphoryl group is the lability of the hydrogen atoms of the methylene group, due to the influence of the P = O group [1]. The lability of the H atoms of the methylene group in such compounds permits them to enter into reactions of the type of the Claisen condensation [2], the crotonic condensation with aldehydes [3, 4], and into reactions of electrophilic addition at double bonds [5], and to readily replace the hydrogen of the methylene group by an alkaline metal [6]. The phosphoryl group activates one hydrogen atom in the adjacent methylene group. If the CH_2 group is between the phosphoryl and some other electron acceptor group ($COCH_3$, COC_6H_5, $COOC_2H_5$, etc.), both hydrogen atoms are active [7].

We were interested in introducing a phosphorus compound with labile hydrogen into a reaction of phosphonemethylation with trialkyl phosphites and aldehydes. We demonstrated that phosphorus compounds containing active hydrogen, with the general formula $RCH_2\underset{\underset{O}{\|}}{P}(OC_2H_5)_2$, where R = CN, $COOC_2H_5$, $COCH_3$, COC_6H_5, enter into a reaction of triple condensation, similarly to malonic and cyanoacetic esters [8], according to the scheme:



$$RCH_2\underset{\underset{O}{\|}}{P}(OC_2H_5)_2 + CH_2O + P(OC_2H_5)_3 \rightarrow (C_2H_5O)_2\underset{\underset{O}{\|}}{P}\overset{\overset{R}{|}}{C}HCH_2\underset{\underset{O}{\|}}{P}(OC_2H_5)_2 + C_2H_5OH\ .$$

The reaction is conducted in an excess of triethyl phosphite, as the solvent. During the reaction, ethanol is distilled off and was demonstrated by the method of gas — liquid chromatography. Conducting the reaction in other solvents, for example, tetralin, lowers the yield of the product. Thus, in triethyl phosphite the yield of 1-cyano-1, 2-bis-(diethylphosphone)-ethane is 37%, while in tetralin it is 18%. The reaction does not take place with the diethyl ester of benzylphosphinic acid and tetraethyldiphosphonemethane.

The reaction of phosphonemethylation of phosphorus compounds with labile hydrogen proceeds under more rigorous conditions and with lower yields than the reaction of condensation in the ternary system malonic (cyanoacetic) ester — trialkyl phosphite — paraform [8], although the diethoxyphosphone group (σ_p = 0.6; σ^* = 2.18), just like the carbethoxy group (σ_p = 0.52; σ^* = 1.87), is a strong electron-acceptor group, capable of activating hydrogen at the α-carbon atom [9].

The structure of the products obtained was confirmed by the analytical data (Table 1), by IR and PMR spectroscopy, and by saponification. The IR spectra of all the products have absorption bands in the region of 1255-1260 cm^{-1} (P = O). In the spectrum of 1-aceto-1, 2-bis-(diethylphosphone)-ethane, there is an absorption band in the region of 1720 cm^{-1} (C = O) of the ketone carbonyl group. In the spectrum of 1-carbethoxy-1, 2-bis-(diethylphosphone)-ethane, there is a band in the region of 1738 cm^{-1} (C = O) of the ester carbonyl group. The spectrum of 1-benzoyl-1, 2-bis-(diethylphosphone)-ethane contains absorption bands in the region of 1685 cm^{-1} (C = O), which is characteristic of a C = O group conjugated with a benzene ring, and 1595 cm^{-1} (C = C), corresponding to the double bond of the benzene ring. In the IR spectra of 1-cyano-1, 2-bis-(diethylphosphone)-ethane there is an absorption band in the region of 2245 cm^{-1} (C ≡ N). In the saponification of 1-carbethoxy-1, 2-bis-(diethylphosphone)-ethane with dilute HCl at 105-110°, 1-carboxy-1, 2-diphosphonethane was isolated and characterized in the form of the aniline salt with mp 214-215° (with decomp.).

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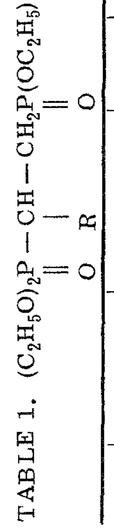
TABLE 1.



$$(C_2H_5O)_2\underset{\substack{\| \\ O}}{P}-\underset{\substack{| \\ R}}{CH}-CH_2\underset{\substack{\| \\ O}}{P}(OC_2H_5)_2$$

Number	R	Bp, °C (p, mm Hg)	n_D^{20}	d_4^{20}	MR		Found, %			Empirical formula	Calculated, %			Yield, %
					found	calculated	C	H	P		C	H	P	
I	CH_3CO	138—139 (0,015)	1,4548	1,1746	79,42	79,36	41,56	7,56	18,31	$C_{12}H_{26}O_7P_2$	41,86	7,55	18,02	55
II	$COOC_2H_5$	147—148 (0,001)	1,4480	1,1692	85,63	85,62	41,37	7,42	16,39	$C_{13}H_{28}O_8P_2$	41,71	7,48	16,57	39
III	CN *	150—152 (0,01)	1,4500	1,1728	75,03	74,50	—	—	18,78	$C_{11}H_{23}O_6NP_2$ †	—	—	18,96	37
IV	C_6H_5CO	175—177 (0,001)	1,5020	1,2098	99,03	98,85	49,87	6,75	15,20	$C_{17}H_{28}O_7P_2$	50,24	6,89	15,27	65

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* According to the data of [10]: bp 173-174° (1 mm); n_D^{20} 1.4508; d_4^{20} 1.1706.

† Found: N 3.39; calculated: N 4.28%.

The chemical shifts and spin–spin splitting constants of the PMR spectra of 1-aceto-1, 2-bis(diethylphosphone)-ethane and 1-carbethoxy-1, 2-bis-(diethylphosphone)-ethane confirm the structures of these products. The methyls and methylenes of the ethoxy groups at the phosphorus nuclei have chemical shifts of δ_{CH_3} = 1.23 and δ_{CH_2} = 3.94 ppm, respectively, and are split with a spin–spin interaction constant $^2J_{H-H}$ = 6 Hz. The methylene group in the α-position with respect to one of the phosphorus atoms has a distinct quartet with a chemical shift of 2.10 ppm with splitting constants from phosphorus $^2J_{P-H}$ = 18 and $^2J_{H-H}$ = 6 Hz, while the proton at the β-carbon atom is split from the protons of the methylene group into a triplet with constant $^2J_{H-H}$ = 6 Hz; then this triplet is split from the neighboring phosphorus atom into a sextet with spin–spin interaction constant $^2J_{P-H}$ = 18 Hz, which is of very low intensity and almost merges with the noise track.

The chemical shifts and spin–spin splitting constants of the carbethoxy group of 1-carbethoxy-1,2-bis-(diethylphosphone)-ethane coincide with the chemical shifts and interaction constant of the ethoxy group at the phosphorus, i.e., are equal to δ_{CH_3} = 1.23, δ_{CH_2} = 3.94 ppm and $^2J_{H-H}$ = 6 Hz. In the PMR spectrum of 1-aceto-1, 2-bis-(diethylphosphone)-ethane, the peak of the aceto-group with chemical shift 2.27 ppm is superimposed upon the quartet of the methylene group. The remaining picture of splitting of the protons remains the same.

EXPERIMENTAL

The spectra were recorded on an RYa-2303 NMR spectrometer at a working frequency of 60 MHz at room temperature, with tetramethysilane as the internal standard (δ_{TMS} = 0). The samples were 70% solutions in CCl_4.

Production of 1-Aceto-1, 2-bis-(diethylphosphone)-ethane (I). A mixture of 9.7 g diethylphosphoneacetone, 1.5 g paraform, and 12.45 g triethyl phosphite was heated for 6-6.5 h at a temperature of 170-200°. Then 2.3 ml of C_2H_5OH was distilled off (n_D^{20} 1.3650). After removal of the excess triethyl phosphite and distillation of the reaction mass, we obtained 9.5 g (I).

Production of 1-Carbethoxy-1, 2-bis-(diethylphosphone)-ethane (II). A mixture of 22.4 g of the ethyl ester of diethylphosphoneacetic acid, 3.0 g paraform, and 24.9 g triethyl phosphite was heated for 6-7 h at 150-190°. Then 3 ml of ethanol was distilled off (n_D^{20} 1.3640). After removal of the excess triethyl phosphite and distillation of the reaction mixture we obtained 14.5 g (II).

Production of 1-Cyano-1, 2-bis-(diethylphosphone)-ethane (III). A mixture of 8.85 g cyanodiethylphosphomethane, 1.5 g paraform, and 12.45 g triethyl phosphite was heated for 4-5 h at 170-200°. Then 1.2 ml of ethanol was distilled off (n_D^{20} 1.3630). After removal of the excess triethyl phosphite and distillation of the reaction mixture, we obtained 6 g (III).

Production of 1-Benzoyl-1,2-bis-(diethylphosphone)-ethane (IV). A mixture of 12.8 g benzoyldiethylphosphonemethane, 1.5 g paraform, and 12.45 g triethyl phosphite were heated for 4-5 h at 160-200°. Then 3 ml of ethanol was distilled off (n_D^{20} 1.3650). After removal of the excess triethyl phosphite and distillation of the reaction mixture, we obtained 14.75 g (IV).

Saponification of 1-Carbethoxy-1,2-bis-(diethylphosphone)-ethane (II). A mixture of 1.5 g (II) and 2.5 ml dilute HCl (1:1) was heated for 10 h in a sealed tube at 105-110°. After repeated addition of water and evaporation, we obtained 0.8 g (89%) of a crystalline product, to an alcohol solution of which aniline was added to a neutral pH. A white crystalline product was isolated – the aniline salt of 1-carboxy-1,2-diphosphoethane with mp 214-215° (with dec.) after recrystallization from a water – ethanol mixture. Found: P 14.64; N 6.68%. $C_{15}H_{22}O_8N_2P_2$. Calculated: P 14.76; N 6.70%.

CONCLUSIONS

1. The possibility of the reaction of phosphonemethylation for phosphorus compounds containing a labile hydrogen was demonstrated.

2. A series of derivatives of bis-(diethylphosphone)-ethane was produced.

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