PHOSPHONOMETHYLATION OF ACETOACETIC ESTER AND ACETYLACETONE

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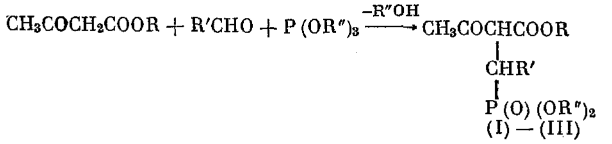
In previous papers [1, 2] we reported the possibility of effecting condensation in the ternary system: trialkyl phosphite – aldehyde – compound containing a labile hydrogen atom. In the present communication we present some data on the reaction of acetoacetic ester and acetylacetone with trialkyl phosphites and aldehydes.

Acetoacetic ester reacts with trialkyl phosphites, formaldehyde or 2-furaldehyde by the usual scheme of the phosphonomethylation reaction [1, 2], with the formation of the esters of 2-aceto-2-carbalkoxyethylphosphonic acids (Table 1).



$$CH_3COCH_2COOR + R'CHO + P(OR'')_3 \xrightarrow{-R''OH} \underset{\substack{| \\ CHR' \\ | \\ P(O)(OR'')_2}}{CH_3COCHCOOR}$$

(I) – (III)

The reactions are run at a temperature of 140-200° for several hours. During reaction the alcohol is distilled off, and then is identified by GLC. Tetralin or excess triethyl phosphite are used as the solvents. In the IR spectra of the products (I)-(III) are present absorption bands (cm^{-1}) in the regions: 1255-1265 ($P = O$), 1635-1645 ($C = C$), 970-1035 ($P - O - C$), and a split doublet at 1712-1720 and 1735-1745 ($C = O$), which is characteristic for the simultaneous presence of keto and ester carbonyl groups in the molecule.

We were unable to isolate the expected esters of 1-alkyl(aryl)-2-aceto-2-carbethoxyethyl-phosphonic acids when acetoacetic ester was reacted with triethyl phosphite, benzaldehydes, propionaldehyde or butyraldehyde under the conditions of the phosphonomethylation reaction. The formation of 2-oxo-2-ethoxy-3-alkyl(aryl)-4-carbethoxy-5-methyl-1-oxa-2-phosphol-4-enes (IV)-(VIII) and the esters of 1-alkyl-2-acetoethylphosphonic acids (IX)-(X) is observed here. Evidently, the esters of 1-alkyl(aryl)-2-aceto-2-carbethoxyethylphosphonic acid are thermally unstable. It is possible to propose the following scheme for the given reaction (on page 108).

Thus, it was shown by B. A. Arbuzov and co-workers [3-5] that the esters of 1-methyl-(phenyl)-2-aceto-2-carbethoxyethylphosphonic acid cannot be distilled without undergoing change, and even in a high vacuum they cleave the alcohol with the formation of 2-oxo-2-alkoxy-3-methyl(phenyl)-4-carbethoxy-5-methyl-1-oxa-2-phosphol-4-enes. The authors postulate that ring closure occurs via the enol form of the ester of 1-methyl(phenyl)-2-aceto-2-carbethoxyethylphosphonic acid. The formation of esters of 1-alkyl-2-acetoethylphosphonic acid (IX)-(X) can be explained by the cleavage of the carbethoxyl group from the initially formed ester of 1-alkyl-2-aceto-2-carbethoxyethylphosphonic acid. The possibility of such cleavage for acetoacetic ester and its derivatives is well-known [6, 7]. The reaction of acetoacetic ester with triethyl phosphite and either propionaldehyde or butyraldehyde is run in sealed tubes. An equimolar mixture of the three components is heated at 175-200° for 8-10 h. The experimental procedure with benzaldehyde is the same as in the case of formaldehyde. Either n-nonane or excess triethyl phosphite is used as the solvent. The GLC data corroborate the presence of diethyl ether and ethanol in the volatile reaction products. Besides the analysis data (see Table 1), the structure of products (IV)-(X) was proved by P^{31} NMR and IR spectroscopy.

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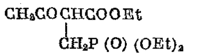
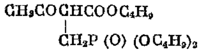
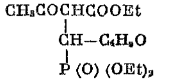
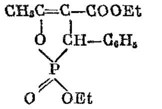
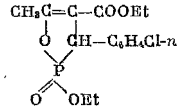
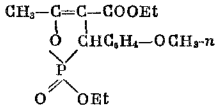
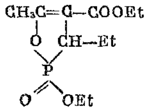
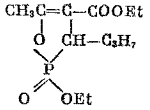
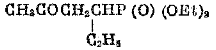
TABLE 1

Number	Formula	Bp, °C (p, mm of Hg)	n_D^{20}	d_4^{20}	*MR*		Found, %			Empirical formula	Calculated, %			Yield, %	δP_{31}, ppm
					found	calculated	C	H	P		C	H	P		
I	 $\mathrm{CH_3CO\underset{\displaystyle CH_2P(O)(OEt)_2}{CH}COOEt}$	123—125 (0,025)	1,4485	1,1455	65,49	65,53	47,49	7,44	11,06	$C_{11}H_{21}O_6P$	47,16	7,50	11,08	80	—
II	 $\mathrm{CH_3CO\underset{\displaystyle CH_2P(O)(OC_4H_9)_2}{CH}COOC_4H_9}$	138—139 (0,008)	1,4522	1,0498	93,57	93,24	55,98	9,08	8,66	$C_{17}H_{33}O_6P$	56,04	9,06	8,51	79,6	—
III	 $\mathrm{CH_3CO\underset{\underset{\displaystyle P(O)(OEt)_2}{\displaystyle CH-C_4H_9O}}{CH}COOEt}$	147—148 (0,001)	1,4905	—	—	—	52,29	6,52	8,97	$C_{15}H_{23}O_7P$	52,02	6,64	8,95	66,5	—22
IV		147—149 (0,007)	1,5152	—	—	—	57,63	6,23	9,65	$C_{15}H_{19}O_5P$	58,06	6,13	10,0	64,5	—40
V*		160—163 (0,001)	1,4970	—	—	—	—	—	8,95	$C_{15}H_{18}O_5PCl$	—	—	8,99	64	—37
VI		170—173 (0,001)	1,5240	—	—	—	—	—	9,03	$C_{16}H_{21}O_6P$	—	—	9,11	41	—36
VII		84—86 (0,01)	1,4550	1,1079	64,41	63,95	50,20	7,01	12,28	$C_{11}H_{20}O_5P$	50,38	7,25	11,83	19	—53,6
VIII		105—108 (0,07)	1,4610	1,0964	69,32	68,68	51,71	8,00	11,27	$C_{12}H_{22}O_5P$	51,98	7,94	11,19	20,7	—45
IX	 $\mathrm{CH_3COCH_2\underset{\displaystyle C_2H_5}{CH}P(O)(OEt)_2}$	91—92 (0,7)	1,4420	1,0509	59,42	59,26	50,97	9,12	12,79	$C_{10}H_{21}O_1P$	50,84	8,89	13,13	67	—35,7
X	 $\mathrm{CH_3COCH_2\underset{\displaystyle C_3H_7}{CH}P(O)(OEt)_2}$	92—93 (0,2)	1,4445	1,0478	63,44	63,87	52,81	9,26	12,24	$C_{11}H_{23}O_4P$	52,8	9,2	12,4	58	—31

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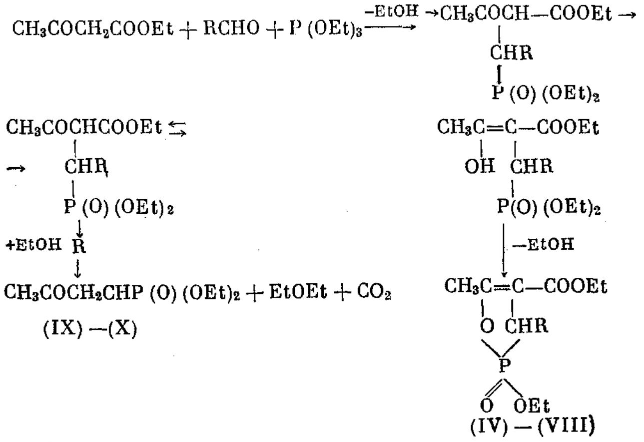
* Found Cl 10.50%. Calculated Cl 10.30%.



$$\mathrm{CH_3COCH_2COOEt + RCHO + P(OEt)_3 \xrightarrow{-EtOH} CH_3COCH(CHRP(O)(OEt)_2)COOEt}$$

R - alkyl or aryl

In the IR spectra of products (IV)-(VIII) are present absorption bands (cm^{-1}) in the regions: 1275-1285 (P = O), 1170-1175 (=C – O), a broad band at 1020-1080, which can be assigned to the vibrations of either the (P) – O – C= or the (C) – O – P group, 1630-1645 (C = C), and 1705-1715 (C = O). A shift of the absorption band of the ester carbonyl group toward longer wavelengths is explained by the presence of a double bond in the α-position to the carbonyl [8]. The absorption intensity of the C = C group increases sharply when compared with the absorption of the C = C group in the acyclic esters of 2-aceto-2-carbethoxyethylphosphonic acid (I-III). The IR spectra of products (IX) and (X) contain absorption bands (cm^{-1}) in the regions: 1245 (P = O) and 1715-1718 (C = O), representing a ketonic carbonyl group. The chemical shifts of the P^{31} nuclei for products (IV-X) (see Table 1), measured relative to 85% H_3PO_4, correspond to the literature data for phosphonates of similar structure [9-11].

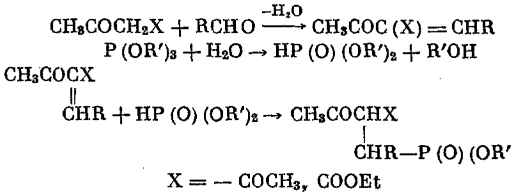
A study of the condensation reaction in the ternary system: triethyl phosphite – formaldehyde – acetylacetone, disclosed that, together with the normal products of the phosphonomethylation reaction, namely the ester of 2,2-diacetoethylphosphonic acids, the esters of 2-acetoethylphosphonic acids are formed. The reaction scheme can be depicted by the equation:

$$\mathrm{CH_3COCH_2COCH_3 + CH_2O + P(OR)_3 \rightarrow CH_3COCH_2CH_2P(O)(OR)_2}$$
$$\mathrm{+ (CH_3CO)_2CHCH_2P(O)(OR)_2 + CH_3COOR + ROH}$$

where R is alkyl. Analysis of the volatile products liberated in the reaction by GLC confirmed the presence of the alcohol and the corresponding acetic acid ester in them.

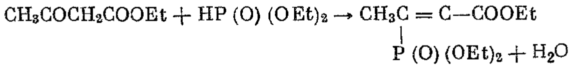
The structure of the products was confirmed by IR spectroscopy. In the IR spectra of the esters of the 2,2-diacetoethylphosphonic acids are present absorption bands (cm^{-1}) in the regions: 1250 (P = O), and a broad band at 1590-1620, which is characteristic for diketones that are capable of enolization and the formation of chelate bonds [8]. The absorption band in the 1710 cm^{-1} region belongs to a ketonic carbonyl group. In the IR spectra of the esters of the 2-acetoethylphosphonic acids are present bands in the regions: 1245 (P = O) and 1715 (C = O), representing a ketonic carbonyl group.

The possibility of forming esters of 2-acetoethylphosphonic acids from the esters of 2,2-diacetoethylphosphonic acids was shown on the example of the reaction of diethyl phosphites with benzylidene- and ethylideneacetylacetone [12]. It is possible to assume that the first step of the phosphonomethylation reaction is the condensation of either acetoacetic ester or acetylacetone with the aldehyde to give the idene derivative. Diethylphosphorous acid, obtained by the isomerization of triethyl phosphite by the water that is liberated here, can react when heated with the idene derivatives of acetoacetic ester and acetylacetone to give the esters of either 2-aceto-2-carbethoxyethylphosphonic or 2,2-diacetoethylphosphonic acids [4, 12, 13], which are capable of undergoing further transformations (intramolecular transesterification, cleavage of acetyl or carbethoxyl groups).



$$\mathrm{CH_3COCH_2X + RCHO \xrightarrow{-H_2O} CH_3COC(X){=}CHR}$$
$$\mathrm{P(OR')_3 + H_2O \rightarrow HP(O)(OR')_2 + R'OH}$$
$$\mathrm{CH_3COCX{=}CHR + HP(O)(OR')_2 \rightarrow CH_3COCHX{-}CHR{-}P(O)(OR')_2}$$
$$\mathrm{X = -COCH_3,\ COOEt}$$

However, the condensation run by us in the system: diethylphosphorous acid – formaldehyde – acetoacetic ester, failed to corroborate the possibility of the initial formation of idene derivatives during condensation in the ternary system. It proved that in this case the diethylphosphorous acid reacted with acetoacetic ester at the carbonyl group, with the subsequent cleavage of water and the formation of the diethyl ester of 1-methyl-2-carbethoxyethylidenephosphonic acid, in which connection formaldehyde does not take part in the given reaction. An analogous product was obtained during condensation in the binary system:



$$CH_3COCH_2COOEt + HP(O)(OEt)_2 \rightarrow \underset{\displaystyle P(O)(OEt)_2}{CH_3C} = C{-}COOEt + H_2O$$

The identity of the products was proved by the analysis data and IR spectroscopy.

EXPERIMENTAL

Preparation of Diethyl Ester of 2-Aceto-2-carbethoxyethylphosphonic Acid. A mixture of 13 g of acetoacetic ester, 3 g of paraform and 24.9 g of triethyl phosphite was heated at 140-190° for 6.5 h, in which connection ethanol was distilled off. After removal of the excess triethyl phosphite the residue was subjected to two fractional distillations to give 22.4 g of the diethyl ester of 2-aceto-2-carbethoxyethylphosphonic acid.

The dibutyl ester of 2-aceto-2-carbobutoxyethylphosphonic acid and the diethyl ester of 1-furfuryl-2-aceto-2-carbethoxyethylphosphonic acid were obtained in a similar manner.

Reaction of Acetoacetic Ester with Triethyl Phosphite and Propionaldehyde. A mixture of 13 g of acetoacetic ester, 16.6 g of triethyl phosphite and 5.8 g of propionaldehyde was heated in a sealed tube at 175-200° for 10 h. The tube was opened, and the volatile products (ethanol, diethyl ether, unreacted propionaldehyde) were distilled off. Two fractions were isolated when the reaction mass was subjected to fractional distillation: I) bp 90-100° (0.2 mm), n_D^{20} 1.4430, 21.5 g; II) bp 120-130° (0.2 mm), n_D^{20} 1.4530, 7.5 g. Redistillation gave 15.8 g of the diethyl ester of 1-ethyl-2-acetoethylphosphonic acid. From fraction II was isolated 5.0 g of 2-oxo-2-ethoxy-3-ethyl-4-carbethoxy-5-methyl-1-oxa-2-phosphol-4-ene.

Reaction of Acetoacetic Ester with Triethyl Phosphite and Butyraldehyde. A mixture of 13 g of acetoacetic ester, 16.6 g of triethyl phosphite and 7.2 g of butyraldehyde was heated at 175-200° for 10 h. The tube was opened. Removal of the volatile products, followed by fractional distillation of the reaction mass, gave two fractions: I) bp 95-110° (0.2 mm), n_D^{20} 1.4455, 18 g II) bp 110-125° (0.2 mm), n_D^{20} 1.4560, 8 g. The fractional distillation of fraction I gave 14.5 g of the diethyl ester of 1-propyl-2-acetoethylphosphonic acid. From fraction II was obtained 5.6 g of 2-oxo-2-ethoxy-3-propyl-4-carbethoxy-5-methyl-1-oxa-2-phosphol-4-ene.

Reaction of Acetoacetic Ester with Triethyl Phosphite and Benzaldehyde. A mixture of 8.3 g of triethyl phosphite, 5.3 g of benzaldehyde and 6.5 g of acetoacetic ester in 10 ml of n-nonane was heated at 185-190° for 4.5 h. Ethanol (n_D^{20} 1.3665) was distilled off. After removal of the unreacted starting products the reaction mass was subjected to several fractional distillations to give 10 g of 2-oxo-2-ethoxy-3-phenyl-4-carbethoxy-5-methyl-1-oxa-2-phosphol-4-ene.

2-Oxo-2-ethoxy-3-(p-chlorophenyl)-4-carbethoxy-5-methyl-1-oxa-2-phosphol-4-ene and 2-oxo-2-ethoxy-3-(p-methoxyphenyl)-4-carbethoxy-5-methyl-1-oxa-2-phosphol-4-ene were obtained in a similar manner.

Reaction of Acetylacetone with Triethyl Phosphite and Formaldehyde. A mixture of 16.6 g of triethyl phosphite, 3 g of paraform and 10 g of acetylacetone was heated at 140-160° for 5 h; here 5 ml of volatile products was distilled off; n_D^{20} 1.3640. Fractional distillation of the reaction mass gave two fractions: I) bp 98-102° (0.02 mm), n^{20} 1.4470, 8.9 g. II) bp 105-112° (0.02 mm), n_D^{20} 1.4625, 12 g.

From fraction I was obtained 6.1 g (29.5%) of the diethyl ester of 2-acetoethylphosphonic acid with bp 73-75° (0.015 mm), n_D^{20} 1.4370; d_4^{20} 1.0920. Found: C 45.42; H 8.11; P 14.48%; MR 49.90. $C_8H_{17}O_4P$. Calculated: C 45.9; H 8.15; P 14.90; MR 50.02. From [14]: bp 105-107° (0.3 mm); n_D^{20} 1.4353; [15]: bp 75-78° (0.02 mm); n_D^{20} 1.4388; d_4^{20} 1.0901.

From fraction II was isolated 7.5 g (30%) of the diethyl ester of 2,2-diacetoethylphosphonic acid with bp 125-127° (0.03 mm), n_D^{20} 1.4685, d_4^{20} 1.1644. Found: C 47.65; H 7.31; P 12.79%; MR 59.74. $C_{10}H_{19}O_5P$. Calculated: C 48.00; H 7.60; P 12.40%; MR 59.27.

Reaction of Acetylacetone with Formaldehyde and Tributyl Phosphite. A mixture of 10 g of acetylacetone, 25 g of tributyl phosphite and 3 g of paraform was heated at 140-200° for 7 h; the volatile products (butyl alcohol and butyl acetate) distilled here. Fractional distillation of the reaction mass gave two fractions: I) bp 110-135° (0.01 mm), n_D^{20} 1.4430, 8.1 g. II) bp 135-140° (0.01 mm), n_D^{20} 1.4650, 11.3 g. From fraction I was isolated 6 g (22.8%) of the dibutyl ester of 2-acetoethylphosphonic acid with bp 112-115° (0.02 mm), n_D^{20} 1.4410, d_4^{20} 1.0157. Found: C 54.42; H 9.49; P 11.57%; MR 68.64. $C_{12}H_{25}O_4P$. Calculated: C 54.54; H 9.47; P 11.74%; MR 68.49. From [15]: bp 110-112° (0.05 mm); n_D^{20} 1.4420; d_4^{20} 1.0168. From fraction II was obtained 8 g (26.6%) of the dibutyl ester of 2,2-diacetoethylphosphonic acid with bp 120-122° (0.001 mm); n_D^{20} 1.4690; d_4^{20} 1.0951. Found: C 54.49; H 8.51; P 10.57%; MR 77.82. $C_{14}H_{27}O_5P$. Calculated: C 54.92; H 8.82; P 10.13%; MR 77.74.

Reaction of Diethyl Phosphite with Acetoacetic Ester and Paraform. A mixture of 13.8 g of diethyl phosphite, 13 g of acetoacetic ester and 3 g of paraform was heated at 135-185° for 5 h. After several fractional distillations of the reaction mass we obtained 7.5 g (30%) of the diethyl ester of 1-methyl-2-carbethoxyethylidenephosphonic acid with bp 80-82° (0.02 mm); n_D^{20} 1.4509; d_4^{20} 1.0949. Found: C 48.25; H 7.80; P 12.06%; MR 61.46. $C_{10}H_{19}O_5P$. Calculated: C 48.20; H 7.22; P 12.45%; MR 60.43. From [16]: bp 140° (8 mm); n_D^{20} 1.4482; d_4^{20} 1.0987.

Reaction of Diethyl Phosphite with Acetoacetic Ester. A mixture of 13.8 g diethyl phosphite and 13 g of acetoacetic ester was heated at 140-180° for 7 h. Fractional distillation of the reaction mass gave 7 g (28%) of the ethyl ester of 1-methyl-2-carbethoxyethylidenephosphonic acid with bp 91-92° (0.05 mm); n_D^{20} 1.4490; d_4^{20} 1.0939. Found: C 48.19; H 7.56; P 12.44%; MR 61.31. $C_{10}H_{19}O_5P$. Calculated: C 48.20; H 7.22; P 12.45%; MR 60.43.

CONCLUSIONS

1. The condensation of acetoacetic ester with trialkyl phosphites, formaldehyde or 2-furaldehyde goes with the formation of esters of 2-aceto-2-carbalkoxyethylphosphonic acids.

2. The reaction of acetoacetic ester with benzaldehydes, butyraldehyde or propionaldehyde and triethyl phosphite gave 2-oxo-2-ethoxy-3-alkyl(aryl)-4-carbethoxy-5-methyl-1-oxa-2-phosphol-4-enes and the esters of 1-alkyl-2-acetoethylphosphonic acid.

3. The formation of esters of 2,2-diacetoethylphosphonic acid and 2-acetoethylphosphonic acid is observed during condensation in the ternary system: triethyl phosphite – formaldehyde – acetylacetone.

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