REACTION OF KETO ALCOHOLS WITH ORGANOPHOSPHORUS COMPOUNDS

COMMUNICATION 4. SYNTHESIS OF ESTERS OF γ-KETOPHOSPHINIC ACIDS

N. I. Rizpolozhenskii and F. S. Mukhametov

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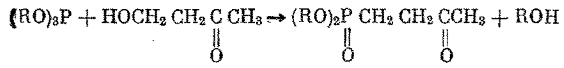
The derivatives of γ-ketophosphinic acids can be obtained by various methods. Thus, according to the method described in [1] the esters of γ-ketophosphonic acids are obtained by the addition of dialkyl phosphites to α,β-unsaturated ketones in the presence of saturated sodium alcoholate solution. Another general method is the reaction of trialkyl phosphites with the hydrochlorides or methiodides of β-dialkylaminoketones [2]. The mixed esters of γ-ketophosphonic acids can be obtained by the alcoholysis of 1,2-oxaphosphol-4-ene derivatives [3]. Other methods are also known for the preparation of derivatives of γ-ketophosphonic acids [4-6], but they have failed to find preparative use.

Continuing our study of the reactions of keto alcohols with various organophosphorus compounds, we established that the esters of γ-ketophosphonic acids are formed in good yields when trialkyl phosphites are heated with 3-ketobutanol at 140-160° in the presence of catalytic amounts of metallic sodium



$$(RO)_3P + HOCH_2CH_2\underset{\overset{\|}{O}}{C}CH_3 \rightarrow (RO)_2\underset{\overset{\|}{O}}{P}CH_2CH_2\underset{\overset{\|}{O}}{C}CH_3 + ROH$$

Triphenyl phosphite reacts with 3-ketobutanol in the same manner as the trialkyl phosphites, but under more drastic conditions.

The reaction of trialkyl phosphites with 3-ketobutanol can also proceed in the absence of a catalyst, provided either the reaction temperature or the time of heating is increased. 3-Ketobutanol reacts much more easily with phosphonites and phosphinites. It is not necessary to add a catalyst in these reactions, and in some cases even a simple mixing of the reactants caused a spontaneous rise in the temperature. In the reactions with phosphonites and phosphinites, in measure with removal of the liberated alcohol by distillation, vigorous reaction sets in and the temperature of the reaction mass rises sharply and exceeds the bath temperature.

Compounds, the constants and analysis results of which are given in Table 1, were obtained as a result of the performed reactions. The structure of the formed products was confirmed by the IR spectra and the hydrolysis results. It should be mentioned that the obtained compounds are hygroscopic and the IR spectra have to be taken immediately after isolating the necessary product. In the opposite case the broad absorption band of the hydroxyl group appears in the IR spectra in the 3400 cm^{-1} region. The IR spectra of a number of products are given in Fig. 1. A comparison of these spectra discloses that an intense absorption band, characteristic for the P=O group, is observed in all cases, in which connection the value of the vibration frequency varies as a function of the type of compound. Thus, in the IR spectrum of di-n-propyl (γ-ketobutyl)phosphonate it has a maximum at 1248 cm^{-1}, in the spectrum of ethyl (γ-ketobutyl)phenylphosphinate at 1236 cm^{-1}, and in the spectrum of γ-ketobutyldiethylphosphine oxide at 1180 cm^{-1}. This change in the frequency of the P=O vibration is associated with the number of electronegative substituents attached to the phosphorus atom [7]. Absorption bands with maxima at 690, 750, and 1605 cm^{-1} are present in the IR spectrum of ethyl (γ-ketobutyl)phenylphosphinate, which can be assigned to a monosubstituted aromatic ring, while the absorption band with a maximum at 1448 cm^{-1} can be assigned to the $P-C_6H_5$ bond [7]. In addition, an intense absorption band in the 1720 cm^{-1} region is observed in all of the IR spectra, which is

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TABLE 1

Compound	Bp, °C (p, mm Hg)	n_D^{20}	d_4^{20}	Found				Calculated				Yield, %
				MR	C, %	H, %	P, %	MR	C, %	H, %	P, %	
$(C_2H_5O)_2P(O)CH_2CH_2COCH_3$	81—83 (0,05)	1,4380	1,0849	50,30	46,27	8,28	14,70	50,02	46,15	8,17	14,88	71
$(n\text{-}C_3H_7O)_2P(O)CH_2CH_2COCH_3$	95—97 (0,05)	1,4400	1,0465	59,43	50,43	8,94	13,16	59,26	50,84	8,89	13,13	63,5
$(i\text{-}C_4H_9O)_2P(O)CH_2CH_2COCH_3$	104—105 (0,01)	1,4390	1,0106	68,71	54,45	9,47	11,65	68,49	54,54	9,46	11,74	71,2
$(n\text{-}C_4H_9O)_2P(O)CH_2CH_2COCH_3$	180—182 (8)	1,4420	1,0169	68,69	54,31	9,72	11,52	68,49	54,54	9,46	11,74	86,4
$(C_6H_5O)_2P(O)CH_2CH_2COCH_3$	170—172 (0,01)	1,5459	1,2041	79,93	—	—	9,94	79,76	—	—	10,2	49
$CH_3OP(O)(C_2H_5)(CH_2CH_2COCH_3)$	142—144 (10)	1,4610	1,0959	44,61	46,98	8,64	17,26	44,28	47,19	8,48	17,37	40
$C_2H_5OP(O)(C_6H_5)(CH_2CH_2COCH_3)$	129—130 (0,01)	1,5172	1,1273	64,42	59,70	7,35	12,80	64,32	60	7,13	12,89	56
$(n\text{-}C_4H_9O)P(O)(C_2H_5)(CH_2CH_2COCH_3)$	94—95 (0,01)	1,4560	1,0231	58,45	—	—	13,87	58,14	—	—	14,06	82,7
$(C_2H_5)_2P(O)(CH_2CH_2COCH_3)$	163—165 (10)	1,4753	1,0455	47,47	54,41	9,87	17,55	47,90	54,53	9,72	17,58	74
$(C_2H_5)(C_6H_5)P(O)CH_2CH_2COCH_3$	130—131 (0,01)	1,5420	1,1136	63,37	—	—	13,73	63,36	—	—	13,81	72,8

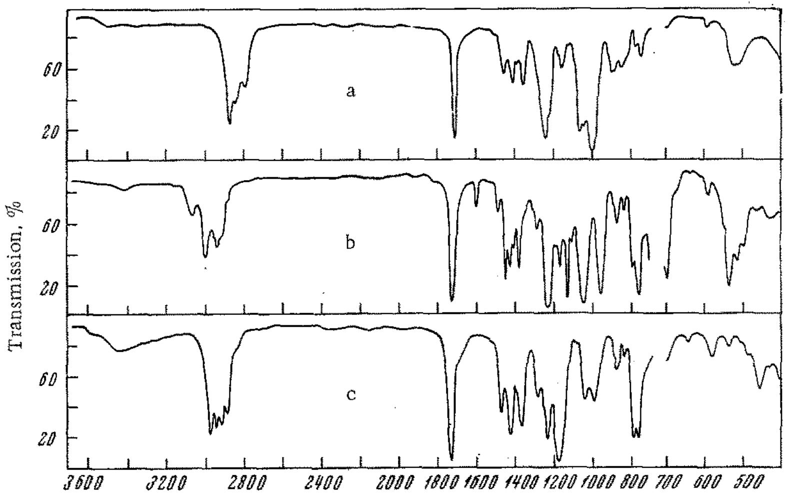
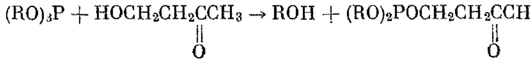


Fig. 1. Infrared spectra: a) di-n-propyl (γ-ketobutyl)phosphonate; b) ethyl (γ-ketobutyl)phenylphosphinate; c) γ-ketobutyldiethylphosphine oxide.

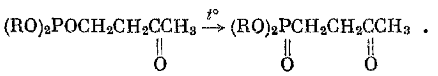
characteristic for the C =O group. The hydrolysis of the reaction product of 3-ketobutanol and triethyl phosphite gave a compound, in whose IR spectrum is present broad diffuse adsorption in the 2200-3300 cm^{-1} region, with a number of submaxima, which absorption can be assigned to the P–OH group, taking part in the formation of a strong hydrogen bond. Also present is an intense band with a maximum at 1718 cm^{-1}, which is characeristic for the C =O group. Based on the data given in [2], the melting point of this product coincided with the melting point for γ-ketobutylphosphonic acid. As a result, a perusal of the IR spectra and the hydrolysis results corroborate the structure assigned the reaction products.

The obtained data do not make it possible to decide unequivocally on the path by which the γ-ketophosphonates are formed. It is possible that transesterification occurs in the first step of the reaction:



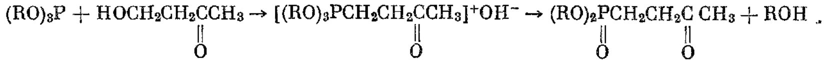
$$(RO)_3P + HOCH_2CH_2\underset{\displaystyle O}{\underset{\|}{C}}CH_3 \rightarrow ROH + (RO)_2POCH_2CH_2\underset{\displaystyle O}{\underset{\|}{C}}CH_3$$

leading to the formation of the 3-ketobutyl dialkyl phosphites, which on heating are isomerized to the esters of γ-ketophosphonic acids [8]



$$(RO)_2POCH_2CH_2\underset{\displaystyle O}{\underset{\|}{C}}CH_3 \xrightarrow{t^\circ} (RO)_2\underset{\displaystyle O}{\underset{\|}{P}}CH_2CH_2\underset{\displaystyle O}{\underset{\|}{C}}CH_3 .$$

The possibility of transesterification can be excluded by acetylating the 3-ketobutanol. However, the formation of diethyl (γ-ketobutyl)phosphonate also occurs when γ-acetoxyethyl methyl ketone is reacted with triethyl phosphite under analogous conditions [9]. In harmony with these data, the mechanism of the Arbuzov rearrangement seems quite probable, similar to that proposed in [10] for the reaction of trialkyl phosphites with methanol



$$(RO)_3P + HOCH_2CH_2\underset{\underset{O}{\|}}{C}CH_3 \rightarrow [(RO)_3PCH_2CH_2\underset{\underset{O}{\|}}{C}CH_3]^+OH^- \rightarrow (RO)_2\underset{\underset{O}{\|}}{P}CH_2CH_2\underset{\underset{O}{\|}}{C}CH_3 + ROH\,.$$

Other routes are also not excluded for the formation of γ-ketophosphonates and, in particular, by the hydrophosphonylation reaction [11].

A study of this reaction is being continued.

EXPERIMENTAL

Reaction of 3-Ketobutanol with Trialkyl Phosphites. In order to remove the dialkyl phosphites the phosphites were distilled twice over Na from a Favorskii flask immediately before experiment. The purity of the phosphites was checked by the IR spectra in the regions 1200 and 2400 cm^{-1}, characteristic for the $P=O$ and $P-H$ groupings, respectively. At the start the experiments were run by heating the mixture of starting materials in sealed glass tubes in a N_2 atmosphere, either in the presence of a catalyst (Na) or without it. It proved that the same results are obtained if the reaction is run in an open vessel, with removal of the liberated alcohol by distillation. This method makes it possible to observe the end of reaction by the fact that the alcohol ceases to distill. Different variations of running the experiments are described on the example of the reaction between triethyl phosphite and 3-ketobutanol.

A mixture of 8.3 g of triethyl phosphite and 4.4 g of 3-ketobutanol was heated in a sealed glass tube in a N_2 atmosphere in the presence of a catalytic amount of Na at 140-150° for 7 h. Distillation of the flask contents from an Arbuzov flask gave 2.1 g (91%) of ethanol with bp 77-79°, n_D^{20} 1.3618, d_4^{20} 0.7896, and 7.4 g (71%) of diethyl (γ-ketobutyl)phosphonate with bp 81-83° (0.05 mm); n_D^{20} 1.4380; d_4^{20} 1.0849. Found: C 46.27; H 8.28; P 14.70%; MR 50.30. $C_8H_{17}O_4P$. Calculated: C 46.15; H 8.17; P 14.88%; MR 50.02. According to [9]: bp 140° (10 mm); n_D^{20} 1.4380; d_4^{20} 1.0910.

A mixture of 16.8 g of triethyl phosphite and 8.9 g of 3-ketobutanol was heated in a sealed glass tube in a N_2 atmosphere at 200° for 7 h. Distillation of the reaction mass from an Arbuzov flask gave 4.4 g (95.6%) of ethanol with bp 76-79°; n_D^{20} 1.3619; d_4^{20} 0.7896, and 15.1 g (72%) of diethyl (γ-ketobutyl)phosphonate with bp 80-81° (0.05 mm); n_D^{20} 1.4387; d_4^{20} 1.0916. Found: C 46.31; H 8.40; P 14.73%; MR 50.09. $C_8H_{17}O_4P$. Calculated: C 46.15; H 8.17; P 14.88%; MR 50.02.

A mixture of 8.3 g of triethyl phosphite and 4.4 g of 3-ketobutanol was heated up to the boil in an Arbuzov flask, in a CO_2 atmosphere, with a catalytic amount of Na. The temperature of heating the reaction mass was raised slowly in measure with removal of the liberated ethanol by distillation. In 30 min 2.15 g (93%) of ethanol had distilled off, in which connection the bath temperature had reached 150° by this time. The fractional distillation of the residue from the same flask gave 7.1 g (68.3%) of diethyl (γ-ketobutyl)phosphonate with bp 143-145° (8 mm); n_D^{20} 1.4380; d_4^{20} 1.4380; d_4^{20} 1.0890. Found: C 46.24; H 8.19; P 14.79%: MR 50.19. $C_8H_{17}O_4P$. Calculated: C 46.15; H 8.15; P 14.88%; MR 50.02.

The reaction of 3-ketobutanol with the tri-n-propyl, tri-isobutyl and tri-n-butyl phosphites was run by the third method, and in the case of triphenyl phosphite by the first method at 210°. The constants of the obtained compounds are given in Table 1.

Reaction of 3-Ketobutanol with Phosphonites and Phosphinites. The reaction was run in an Arbuzov flask fitted with a thermometer in order to check the temperature of the reaction medium. All of the operations were carried out in a CO_2 atmosphere.

A spontaneous rise in the temperature up to 42° was observed when 4.7 g of dimethyl ethylphosphonite was mixed with 3.4 g of 3-ketobutanol. The reaction mass was heated up to the boil and the temperature of heating was raised slowly as the liberated methanol was distilled off. Vigorous frothing of the reaction mixture occurred at 100° and rapid distillation of the methanol set in. Distillation of the residue gave 2.75 g (40%) of methyl (γ-ketobutyl)ethylphosphinate with bp 142-144° (10 mm); n_D^{20} 1.4610; d_4^{20} 1.0959. Found: C 46.98; H 8.64; P 17.26%; MR 44.61. $C_7H_{15}O_3P$. Calculated: C 47.19; H 8.48; P 17.39%; MR 44.28.

A mixture of 5 g of diethyl phenylphosphonite and 2.22 g of 3-ketobutanol was heated gradually with a slow distillation of the ethanol. At a bath temperature of 210° the temperature of the reaction medium rose up to 220°, brisk frothing occurred, and rapid distillation of the ethanol began. Fractional distillation from a Favorskii flask gave 3.4 g (56%) of ethyl (γ-ketobutyl)phenylphosphinate with bp 129-130° (0.015 mm); n_D^{20} 1.5172; d_4^{20} 1.1273. Found: C 59.70; H 7.35; P 12.80%; MR 64.42. $C_{12}H_{17}O_3P$. Calculated: C 60; H 7.13; P 12.89%; MR 64.32.

A mixture of 10.3 g of di-n-butyl ethylphosphonite and 4.4 g of 3-ketobutanol was heated gradually with a slow distillation of the n-butanol. Fractional distillation gave 9.1 g (82.7%) of n-butyl (γ-ketobutyl)-ethylphosphinate with bp 94-95° (0.01 mm); n_D^{20} 1.4560; d_4^{20} 1.0231. Found: P 13.87%; MR 58.45. $C_{10}H_{21}O_3P$. Calculated: P 14.06%; MR 58.14.

A mixture of 3.95 g of isopropyl diethylphosphinite and 2.34 g of 3-ketobutanol was heated gradually with a slow distillation of the isopropanol. At a bath temperature of 140° the temperature of the reaction mixture rose up to 180° and vigorous frothing occurred. Fractional distillation gave 3.51 g (74%) of diethyl (γ-ketobutyl)phosphine oxide with bp 163-165° (10 mm); n_D^{20} 1.4753; d_4^{20} 1.0455. Found: C 54.41; H 9.87; P 17.55%; MR 47.47. $C_8H_{17}O_2P$. Calculated: C 54.53; H 9.72; P 17.58%; MR 47.90.

A mixture of 3.6 g of n-propyl ethylphenylphosphinite and 1.62 g of 3-ketobutanol was heated gradually with a slow distillation of the n-propanol. At a bath temperature of 162° the temperature of the reaction mixture rose up to 194° and vigorous frothing occurred. Fractional distillation gave 3 g (72.8%) of ethylphenyl (γ-ketobutyl)phosphine oxide with bp 130-131° (0.01 mm); n_D^{20} 1.5420; d_4^{20} 1.1136. Found: P 13.73%; MR 63.37. $C_{12}H_{17}O_2P$. Calculated: P 13.81%; MR 63.36.

Hydrolysis of Diethyl (γ-Ketobutyl)phosphonate. A mixture of 2.55 g of diethyl (γ-ketobutyl)phosphonate and 13 ml of conc. HCl was heated under reflux at 120° for 4 h. The reaction mass was evaporated in vacuo. The water was removed from the residue by distillation with benzene. Recrystallization from $CHCl_3$ gave 0.6 g of γ-ketobutylphosphonic acid with mp 81-82°. According to [2]: mp 81-82°. Found: C 31.20; H 5.98; P 20.63%. $C_4H_9O_4P$. Calculated: C 31.59; H 5.96; P 20.37%.

CONCLUSIONS

Trialkyl(aryl) phosphites and phosphonites react with 3-ketobutanol to give, respectively, γ-ketobutylphosphonic and phosphinic acids, while the phosphinites react to give the oxides of tertiary phosphines.

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