REACTION OF BIS(MERCAPTOMETHYL)PHOSPHONIC ACID WITH ALKYL AND ACYL HALIDES

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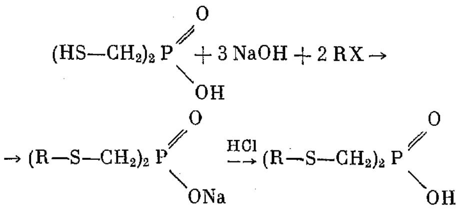
Alkyl(aryl)thiomethyl derivatives of phosphorus are a little studied class of organic compounds, but evidence in the literature indicates that they possess a series of properties which can successfully be used in practice [1-8]. In this connection, it was interesting to synthesize a series of bis(alkylthiomethyl)phosphonic acid derivatives. We prepared these compounds by condensation of bis(mercaptomethyl)phosphonic acid, whose synthesis was reported earlier [9], with alkyl halides by the following scheme:



$$(HS-CH_2)_2\overset{O}{\underset{OH}{P}} + 3\,NaOH + 2\,RX \rightarrow (R-S-CH_2)_2\overset{O}{\underset{ONa}{P}} \xrightarrow{HCl} (R-S-CH_2)_2\overset{O}{\underset{OH}{P}}$$

$R = CH_2{=}CH-CH_2-$, $C_6H_5-CH_2-$, $HOOC-CH_2-$;
$X = Cl$, Br

The reaction proceeds virtually completely; however, the isolation of products in the case of $R = CH_2{=}CH-CH_2-$ and $HOOC-CH_2$ is made difficult because they are viscous, noncrystalline oils which decompose attempts to distill them in vacuum. Bis(allylthiomethyl)phosphonic acid was characterized as its esters. In this case, trialkyl phosphites were used as the esterifying agents. Esterification of bis(β-carboxymethylthiomethyl)phosphonic acid was carried out in two stages: the carboxyl group was esterified with alcohol in benzene solution with azeotropic distillation of water in the presence of p-toluenesulfonic acid as the catalyst, and subsequent esterification of the phosphonic acid group was accomplished by treatment with the trialkyl phosphite. Bis(benzylthiomethyl)phosphonic acid is a crystalline material having mp 87-89°C. The corresponding sulfone was obtained upon its oxidation with peracetic acid.

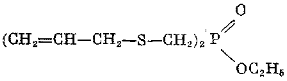
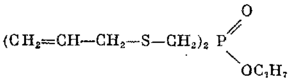
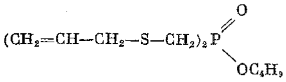
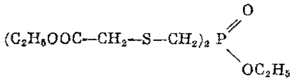
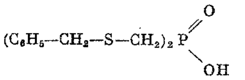
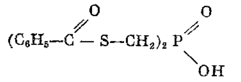
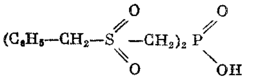
In addition, it was interesting to study the reaction of bis(mercaptomethyl)phosphonic acid with acyl halides. Its reaction with benzoyl chloride was studied in particular, and was carried out at the boundary of phase separation: a water phase of a basic solution of bis(mercaptomethyl)phosphonic acid; the benzoyl chloride in benzene was used as the organic phase. The reaction proceeds sufficiently smoothly and bis(benzoylthiomethyl)phosphonic acid is obtained in a good yield. The properties of all products synthesized are presented in Table 1.

EXPERIMENTAL

Synthesis of Esters of Bis(allylthiomethyl)phosphonic Acid. We dissolved 52 g of bis(mercaptomethyl)phosphonic acid and 40 g of NaOH in 150 ml of water. To the obtained solution was added 100 g of allyl bromide and the reaction mixture was heated with stirring and a temperature of 70° to a neutral reaction (4 h). The upper layer was separated from the reaction mixture and the lower layer was extracted with ether. Then the aqueous layer was acidified with 30 ml of conc. HCl. The upper layer which formed, bis(allylthiomethyl)phosphonic acid, was separated and the water layer after evaporation to 70 ml was filtered from the precipitated salts and extracted with ether. The upper layer and ether extract were combined, and the ether and low-boiling products were distilled in vacuum, during which a precipitate separated. After separation of the precipitate, we obtained 54 g (69%) of bis(allylthiomethyl)phosphonic acid. Found %: C 41.21; H 6.26; P 12.87; S 24.70; acid number 234.9 mg KOH/g. $C_8H_{15}O_2PS_2$. Calculated %: C 40.34; H 6.30; P 13.02; S 26.85; acid number 235.3 mg KOH/g.

A. E. Arbuzov Institute of Organic and Physical Chemistry, Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 10, pp. 2388-2390, October, 1968. Original article submitted April 11, 1968.

TABLE 1. Properties of the Synthesized Compounds

Compound	Yield, %	mp °C (solvent) or bp, °C (p, mm Hg)	Acid* no. mg, KOH/g	n_D^{20}	d_4^{20}	MR*	P *, %	S *, %	Empirical formula
 $(CH_2{=}CH{-}CH_2{-}S{-}CH_2)_2P(=O)OC_2H_5$	60	114—116 (10⁻³)	—	1,5280	1,1249	72,83 72,57	11,62 11,65	23,70 24,06	$C_{10}H_{19}O_2PS_2$
 $(CH_2{=}CH{-}CH_2{-}S{-}CH_2)_2P(=O)OC_3H_7$	40	119—120 (10⁻³)	—	1, 5187	1,1082	76,75 77,19	11,04 11,07	22,38 22,86	$C_{11}H_{21}O_2PS_2$
 $(CH_2{=}CH{-}CH_2{-}S{-}CH_2)_2P(=O)OC_4H_9$	40	129—133 (10⁻³)	—	1,5187	1,0933	81,69 81,81	10,32 10,55	21,50 21,95	$C_{12}H_{21}O_2PS_2$
 $(C_2H_5OOC{-}CH_2{-}S{-}CH_2)_2P(=O)OC_2H_5$	—	134—138 (10⁻³)	—	1,5030	1,2306	86,09 86,60	8,49 8,60	17,58 17,88	$C_{12}H_{23}O_6PS_2$
 $(C_6H_5{-}CH_2{-}S{-}CH_2)_2P(=O)OH$	67	87—89 (benzene + pet. ether)	170,0 166,2	—	—	—	9,0 9,17	17,80 17,77	$C_{16}H_{19}O_2PS_2$
 $(C_6H_5{-}C(=O){-}S{-}CH_2)_2P(=O)OH$	68	140—141 (benzene)	155,0 153,0	—	—	—	8,53 8,47	—	$C_{16}H_{15}O_4PS_2$
 $(C_6H_5{-}CH_2{-}S(=O)_2{-}CH_2)_2P(=O)OH$	86	256—257 (alcohol)	137,0 139,3	—	—	—	7,93 7,71	—	$C_{16}H_{19}O_6PS_2$

*Upper value is the found value, and the lower is the calculated value.

A mixture of 10 g of bis(allylthiomethyl)phosphonic acid and 10.2 g of triethyl phosphite was heated for 2 h at a bath temperature of 130-140°. The excess triethyl phosphite and diethylphosphorus acid were distilled in vacuum. After distillation of the reaction mass, 6.6 g of the ethyl ester of bis(allylthiomethyl)-phosphonic acid was obtained. Other esters of bis(allylthiomethyl)phosphonic acid were obtained analogously.

Reaction of Bis(mercaptomethyl)phosphonic Acid with Chloroacetic Acid. To a solution of 17.5 g of bis(mercaptomethyl)phosphonic acid and 26.6 g of NaOH in 100 ml of water was added a solution of 26.2 g of chloroacetic acid in 50 ml of water and the mixture was stirred at a temperature of 68-70° to a neutral reaction (~5 h). The reaction mass was acidified with 40 ml of conc. HCl. The solution was evaporated in vacuum. The NaCl which precipitated according to the degree of evaporation was filtered. As a result of such treatment, 28.0 g (92%) of bis(β-carboxymethylthiomethyl)phosphonic acid was obtained as a yellowish syrupy liquid. Acid number: found, 383 mg KOH/g; calculated, 408.7 mg KOH/g.

We heated 23.5 g of bis(β-carboxymethylthiomethyl)phosphonic acid and 14.2 g of ethyl alcohol in 60 ml of benzene in the presence of 0.46 g of p-toluenesulfonic acid at a temperature of 75-80° with azeotropic distillation of water until its separation ceased (~14 h). After distillation of the benzene and excess alcohol, 22 g (77%) of bis(carbethoxymethylthiomethyl)phosphonic acid was obtained as a yellowish syrupy mass. Acid number: found, 180 mg KOH/g; calculated, 170 mg KOH/g.

We heated 21.5 g of bis(carbethoxymethylthiomethyl)phosphonic acid and 21.6 g of triethyl phosphite at a temperature of 130° to a neutral reaction (~3 h). Then the unreacted triethyl phosphite and diethylphosphorus acid were distilled in vacuum. The yield of crude product was 22 g (94%). After distillation of the reaction mass was isolated 16.9 g of the ethyl ester of bis(carbethoxymethylthiomethyl)phosphonic acid.

Synthesis of Bis(benzylthiomethyl)phosphonic Acid. We dissolved 7.3 g of bis(mercaptomethyl)phosphonic acid and 5.6 g of NaOH in 70 ml of water and added 11.5 g of $C_6H_5CH_2Cl$. The reaction was carried out with stirring at room temperature to a neutral medium (~4 h). Two layers formed. The lower layer was separated, extracted with ether, dissolved in 150 ml of ethanol, and acidified with 20 ml of conc. HCl. The separated precipitate was filtered and recrystallized from a mixture of benzene and petroleum ether. We obtained 10.5 g of bis(benzylthiomethyl)phosphonic acid.

Synthesis of Bis(benzylsulfonylmethyl)phosphonic Acid. To a solution of 4.4 g of bis(benzylthiomethyl)phosphonic acid in 30 ml of $CHCl_3$ at a temperature of 0° was added a solution of 6 g of peracetic acid (volume concentration 0.95) in 20 ml of $CHCl_3$. The formed precipitate was filtered. The weight of crude product was 5 g (95.8%). After recrystallization from alcohol, 45 g (86%) of bis(benzylsulfonylmethyl)phosphonic acid was obtained.

Synthesis of Bis(benzoylthiomethyl)phosphonic Acid. To a solution of 3.4 g of bis(mercaptomethyl)phosphonic acid and 6.1 g of NaOH in 50 ml of water was added with energetic stirring a solution of 11.9 g of C_6H_5COCl in 50 ml of abs. benzene. The mixture was stirred for 0.5 h at 0° to a weakly basic medium. The solution was acidified with 10 ml of conc. HCl. The formed precipitate was filtered and recrystallized from benzene. We obtained 5.2 g of bis(benzoylthiomethyl)phosphonic acid.

CONCLUSIONS

The reactions of bis(mercaptomethyl)phosphonic acid with alkyl and acyl halides were studied and a series of new thiomethyl phosphorus derivatives was synthesized.

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