REACTION IN THE SYSTEM TRIALKYL PHOSPHITE - CARBOXAMIDE OR SECONDARY AMINE

B. E. Ivanov and S. S. Krokhina

UDC 542.91:547.1'118

A method is known in the literature for the preparation of the esters of aminomethyl(alkyl)phosphonic acids by the reaction of an amine, an aldehyde and a dialkylphosphorous acid [1]. We ran the condensation in the system: carboxamide-paraform-diethylphosphorous acid. However, we were unable to obtain the esters of N-acylaminomethylphosphonic acids here. The corresponding N,N'-methylenebisamides were isolated as the main product. Previously we had reported that the esters of phosphonic acids can be synthesized by the reaction of trialkyl phosphites, an aldehyde, and compounds containing a labile hydrogen atom [2]. In the present communication are given the results of studying the reaction of trialkyl phosphites with aldehydes and either carboxamides or secondary amines. The main products of these reaction are the corresponding esters of aminomethyl(alkyl)phosphonic acids. The reactions were run either in an Arbuzov flask at 120-150°, or in a sealed ampul at 60-100°. As the amino component we used acetamide, benzamide, methacrylamide, acrylamide, phthalimide, diethylamine, and N-methyl(or ethyl)anilines. The reactions with the carboxamides were accompanied by the formation of 1-2% of the N,N'-methylene-bisamides. A study of the low-boiling products by gas-liquid chromatography (GLC) disclosed that in all the alcohol, containing an alkoxyl radical corresponding to the alkoxyl radical of the phosphite, is liberated

 $\begin{array}{c} & \underset{\|}{\text{CONH}_2} + CH_2O + P(OR')_3 \rightarrow \text{RCONHCH}_2P(OR')_2 + R'OH \end{array}$

The constants of the obtained compounds are given in Tables 1 and 2.

EXPERIMENTAL METHOD

The trialkyl phosphites that were used in the experiments were purified as described in [7]. The lowboiling products were investigated by the GLC method on a KhL-3 chromatograph [7].

Reaction of Diethyl Phosphite, Paraform, and Acetamide. A mixture of 13.8 g of diethyl phosphite, 3.1 g of diethyl phosphite, 3.1 g of paraform and 5.9 g of acetamide was heated in a flask equipped with a Vigreux column at 110-135° for 30 min. Exothermic heat was observed at 110° and the temperature of the reaction mixture rose to 135°, accompanied by the brisk evolution of a low-boiling product. We isolated 4.2 g (42%) of N,N'-methylenebisacetamide with mp 192-194° (from alcohol). Found: C 45.62, 45.88; H 7.99, 8.12; N 21.08, 20.79%. $C_5H_{10}O_2N_2$. Calculated: C 46.15; H 7.46; N 21.53%. From [8]: mp 196°.

Reaction of Diethyl Phosphite, Paraform, and Phthalimide. N,N'-Methylenebisphthalimide was isolated during reaction, the constants of which coincides with those given in [9]. The IR spectrum of N,N'methylenebisphthalimide failed to contain absorption bands in the region of the stretching vibrations of the NH group.

Reaction of Triethyl Phosphite, Paraform, and Benzamide. A mixture of 12.5 g of triethyl phosphite, 2.25 g of paraform and 8.32 g of benzamide was heated in a sealed tube at 100° for 6 h. The reaction mixture was found to contain 1.8 g (1%) of N,N'-methylenebisbenzamide with mp 217-218° (from a mixture of alcohol and water). Found: N 11.19, 11.23%. $C_{15}H_{14}N_2O_2$. Calculated: N 11.76%. From [8]: mp 216-220°. Fractional distillation of the reaction mixture through a molecular-film still in vacuo (0.006 mm) at a heater temperature of 110-120°, followed by the fractional distillation of the still residue from an Arbuzov flask,

A. E. Arbuzov Institute of Organic and Physical Chemistry, Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 12, pp. 2773-2776, December, 1971. Original article submitted March 16, 1970.

© 1972 Consultants Bureau, a division of Plenum Publishing Corporation, 227 West 17th Street, New York, N. Y. 10011. All rights reserved. This article cannot be reproduced for any purpose whatsoever without permission of the publisher. A copy of this article is available from the publisher for \$15.00.

.)2	Literature Literence		[3]	[3]	[3]	[3]	[3]	[3]	[3]	1	1	1	1	1
0 ₽(OR	% ,blaiY		22,1	40	29,5	55	63†	33,4	30 15,5	21,5	28,2	20,3	20,2	20,6
-со-NH-СН ₂	Calc., 70	4	17.1	14,97	13,08	11,69	11,44	10,37	9,48 10,44	9,53	8,82	14,02	13,19	10,65
		z	1	6,76	1	1	5,16	1	11	I	I	- {	5,95	4,80
		υ	33,16	ł	45,50	49,81	ł	56,22	5 5 ,45 52,52	55,38	57,62	43,44	1	ł
c Acids R-	Empirical formula		C ₅ H ₁₂ NO ₄ P	C7H16NO4P	C ₉ H ₂₀ NO ₄ P	C11H24NO4P	C ₁₂ H ₁₈ NO ₄ P	C14H22NO4P	CisH26 NO.P CisH26 NO.P	CleH20NO5P	CirHadNO5P	C ₆ H ₁₆ NO4P	CaH18NO4P	ClaH26NO4P
ohosphonic	Found, %	Ч	16,30 16,30	14,56 14,97	$12,88 \\ 13,15$	11,34 11,44	11,09	10,65	66.8 88.8 88.8	10,13	10,25 9,22	9,44 14,39 14,45	12,50 12,68	11,04
		z		6,57	l		5,10	1	11	1	l	1	6,25	4,56
ethyl		υ	33,8 34 ,1	١	45,14 45,85	48,98 49,19	١	55,54 55,64	56,01 56,24 52,52	52,58	55,26	57,50 43,20 43,48	· 1	1
inom	Pp, °C (p,		1797	3839	۱	۱	4041	١	09	١	1	١	١	١
ylam			1,4665	1,4543	1,4568	1,4539	1,5240	1,5095	1,5020	1,5185	1,5105	1,4722	1,4734	1,4640
of N-Ac			117-120 (0,008)	122-123	133-138	139140	170-172	182183	189-191 (0,006) 139-142	(0,006) 153-155	(0,006) 160164	(0,006) 130-133 (0,003)	112 - 13 (0,006)	138139
reparation and Properties of Esters	Reaction products	ំ ទុ យរដ្ឋ	ŝ	9	9	9	9	6 0	3,5	12	9	~~~	~	5
		emper-	100	90-105	110-130	120-150	100	120-134	120160 100140	120135	130150	80-100	100120	150-160
	Reaction products	ч.	CH3*	C ₂ H ₅ *	CaH,*	C ₄ H ₆	C2H5*	CaH7	C4H6 C2H5	CaH,	CaHa	C _a H ₆	C ₂ H ₅	C4H.
		а	O CH ₅ CNH O	CH,CNH O	CH,CNH	CH,CNH	C,H,CNH	C.H.CNH	С. В. В. В. В. В. В. В. В. В. В. В. В. В.	C,H,(CO)2N	C ₆ H ₄ (CO) ₂ N	CH=CHCNH ‡	CH2=C-CNH ‡	CH2=C-CNH ‡
	spunodu	amide	CH ₆ CNH ₂ 0	CH ₆ CNH ₅ O	CH3CNH3	CH ₃ CNH ₃	C.H.CNH.	C,HICNH.	C,H,(GO),NH	C.H.(CO),NH	CeH(CO),NH	CH ₂ =CHCNH2 CH2O	CH1=C-CNH,	CH ₂ =d-CNH2
1. F	ing coi	alde- hyde	CH20	CH20	CH ₂ 0	CH ₂ O	CH20	CH20	CH ₂ O CH ₂ O	CH ₂ 0	CH20	CH ₂ 0	CH ₂ O	CH ₂ 0
TABLE	Start	phos~ phite	P(0CH ₃)3	$P(0C_2H_5)_8$	P(OCaH7)s	P(OC ₄ H ₉)s	P(OC2H5)3	P(OCaH7)a	P(OC4Hs)3 P(OC2H5)3	P(OCaH7)3	P(0C4H9)3	P(0C2H5)3	P(0C ₃ H ₅)s	P(OC4H9)3

*The reaction was run in a sealed tube. *The fractional distillation was run in a molecular-film still; in the other cases it was run using an Arbuzov flask. #The reaction was run in the presence of hydroquinone.

2630

	Literature reference		[4]	[5]	[5]	i	I.	1	[8]	l	ļ	1	[2]	1	1
R' O ies of Esters of Aminomethylphosphonic Acids R-CH-P(OR") ₂	% ,bIsiY		94,6	72,1	71.7	60,9	45,6	25,5	45,4	35,6	49,1	40	21,4	50,7	51
	89.	Ч	13,9	12,35	11,11	12,06	10,87	9,90	11,43	6,48	13,83	10,36	9,48	8,73	9,30
	alc.	Z	6,27	ł	1	5,44	l	1	I	I	1	1	I	1	1
	0	U,	I	62,59	55,91	t	58,94	61,63	57,56	62,38	48,21	60,20	62,38	64,22	64,86
	Empirical formula		C ₉ H ₂₂ NO ₈ P	C ₁₁ H ₂₆ NO ₃ P	C ₁₃ H ₈₀ NO ₈ P	C ₁₂ H ₂₀ NO ₃ P	C ₁₄ H ₂₄ NO ₃ P	C16H28NO3P	C13H22NO3P	C17H30NO3P	C ₉ H _{z1} O ₄ P	C ₁₄ H ₂₆ NO ₅ P	C17H20NO3P	C ₁₉ Ha,NO ₃ P	C18H24NO3P
	Found, %	പ	13,43 13,59	11,97	11,11	11,60	10,38 10,41	10,10	10,51 10,81	9,59 9,74	12,55	10,11	9,07 9,13	8,35 8,16	9,46 9,47
		. Z	5,42 5,69		I		1	1	1		1	<u> </u>	1	1	
		 U	1	52,85 53,04	55,90 56,14		58,49 58,75	61,58 61,67	56,43	62, 18 62, 38	49,48 49,78	60,02 60,23	63,39 63,01	63,98 64,24	63, 89 64, 12
	MR	calc.	1	67,80	77,04	1	78,05	87,40	73,50	91,9	56,15	82,67	1	101,14	!
		punoj		67,65	77,34	١	79,50	88,55	74,57	93,04	56,47	82,56	1	101,35	1
	d ² 0			0,9704	0,9573	I	1,0719	1,0485	1,0986	1,0367	1,0471	1,0536	1	1,0089	l
	$n_{\rm D}^{20}$		1,4340	1,4370	1,4388	1,5225	1,5105	1,5051	1,5160	1,5028	1,4420	1,4950	1,4925	1,4880	1,5550
	bp, °C (p,		112	77-78 (0,03)	87, 5—88 (0,03)	118 - 120 (0,001)	110-112 (0,003)	120—123 (0,003)	110111 (0,006)	113	103—106 (0,006)	108109 (0,01)	110113 (0,01)	130-131 (0,01)	137139 (0,001)
	Reaction conditions	l 'əmii	-	63	2,5	3.5	2	9	ന	10		4	63	e	3,5
		temper- ature,° C	60100	60100	60100	60100	60—100	60100	100130	100-130		100	100150	100-150	167172
	Reaction products	R.	C2Hs*	CsH,*	C4Ho*	C2H4*	C ₃ H ₃ *	C4H*	C2H,*	C4H,*	*"H"	C2H5*	с,н,	с , Н,	C ₂ H ₅
opert		R	н	H	H	н	Н	н	H	н	H	C,H,	C ₆ H ₅	C ₆ H	CiH,
2. Preparation and Pr		Я	(C2Hs)2 ·	(C2H5)2	(C ₂ H s) ₂	CH3 C6H6	CH3 CeH5	CH _s C ₆ H _s	$C_{\epsilon H_{\delta}}$ N	CeH ₆ N	HO	(C2H ₅)2N	(C2H5)2N	(C2H5),N	CH3 C6H5
	spunc	amino compo- nent	(C2H6)2NH	(C2Hs)2NH	(C2Hs)2NH	C.H.NH	CH ₅ C ₆ H ₅	CH _s CeHs	C2H, NH	C _s H _s		(C ₂ H ₅) ₂ NH	(C2Hs)2NH	(C2Hs)2NH	CH4 CeH6
	ting comp(aldehyde	CH ₂ O	CH,0	CH₂O	CH ₂ O	CH₂O	CH₂O	CH₂O	CH₂O		C,H,CHO	C ₆ H ₈ CHO	C,H,CHO	C,HsCHO
TABLE	Start	phos- phite	P(OC ₂ H ₅) ₈	P(OG ₃ H ₇) ₈	P(OC ₄ H ₀)	P(OC2Hs)3	$P(OC_3H_7)_3$	P(OC4H6)3	P(OC2H6)3	P(OC4H9)3		P(OC ₂ H ₅) ₈	$P(OC_3H_7)_3$	P(OC4Ha)3	P(OC ₂ H ₆) ₃

*The reaction was run in a sealed tube.

gave 15 g (63%) of the diethyl ester of α -benzamidomethylphosphonic acid, the constants of which are given in Table 1.

Reaction of Triethyl Phosphite, Paraform, and Phthalimide. A mixture of 16.6 g of triethyl phosphite, 3.2 g of paraform and 14.7 g of phthalimide was heated at 100-140° for 10 h. The liberation of 1.2 g (20%) of a low-boiling product occurred during the reaction process, which, based on the GLC data, was ethyl alcohol. Unreacted phthalimide (8 g) remained in the reaction mixture, which was separated by filtration. To the reaction mixture was added 100 ml of absolute ether. We isolated 2.2 g (0.7%) of N,N'methylenebisphthalimide with mp 225-227° (from alcohol). From [9]: mp 224-225° (from alcohol). Found: C 66.01, 66.10; H 3.10, 3.15%. $C_{17}H_{10}NO_4$. Calculated: C 66.6; H 3.26%. The residue from the removal of the ether was fractionally distilled to give 4.6 g (15.5%) of the diethyl ester of α -phthalimidomethylphosphonic acid, the constants of which are given in Table 1.

As a second product we isolated 4.8 g of ethylphthalimide with bp $80-82^{\circ}$ (0.006 mm); mp 75-76° (from alcohol). Found: N 7.88, 7.95%. C₁₀H₉NO₂. Calculated: N 8.00%. From [10]: mp 78-79° (from alcohol).

Reaction of Tributyl Phosphite, Paraform, and N-Ethylaniline. A mixture of 25 g of tributyl phosphite, 3.2 g of paraform and 12.1 g of N-ethylaniline was heated in a sealed tube at $100-130^{\circ}$ for 10 h. Fractional distillation of the reaction mixture gave 3 g (40%) of butyl alcohol with bp $117-118^{\circ}$; n_D^{20} 1.4000; 11 g (35.6%) of the dibutyl ester of N-ethylanilinomethylphosphonic acid, and 11 g (49.1%) of the dibutyl ester of methylolphosphonic acid. The constants of the isolated products are given in Table 2.

CONCLUSIONS

A study was made of reaction in the system: triethyl phosphite-amide (amine)-paraform (benzaldehyde). The reaction leads to the formation of the corresponding esters of aminomethyl(alkyl)phosphonic acids.

LITERATURE CITED

- 1. M. I. Kabachnik, T. Ya. Medved', I. M. Dyatlov, O. T. Arkhipova, and M. V. Rudomino, Usp. Khim., 37, 1161 (1968).
- 2. B. E. Ivanov, L. A. Kudryavtseva, S. S. Krokhina, and S. V. Pasmanyuk, USSR Patent No. 237151; Byul. Izobr., No. 8, 21 (1969).
- 3. B. E. Ivanov and S. S. Krokhina, Izv. Akad. Nauk SSSR, Ser. Khim., 606 (1968).
- 4. Vjekoslav Jagodic, Chem. Ber., 93, 2308 (1960).
- 5. V. P. Evdakov, L. I. Mizrakh, and L. Yu. Sandalova, Dokl. Akad. Nauk SSSR, 162, 573 (1965).
- 6. K. Fields, J. Amer. Chem. Soc., 74, 1528 (1952).
- 7. B. E. Ivanov and S. S. Krokhina, Izv. Akad. Nauk SSSR, Ser. Khim., 424 (1967).
- 8. C. W. Sauer and R. Bruni, J. Amer. Chem. Soc., 77, 2559 (1955).
- 9. H. Bredereck, R. Gompper, H. Herlinger, and E. Woitun, Chem. Ber., 93, 2423 (1960).
- 10. Dictionary of Organic Compounds [Russian translation], IL (1949).