SYNTHESIS OF DIALKYL ESTERS OF ARYLAMINO(2-PYRIDYL)METHYL-PHOSPHONIC ACIDS

B. P. Lugovkin

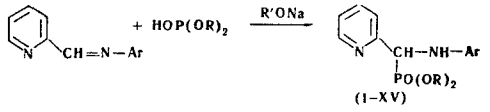
Khimiya Geterotsiklicheskikh Soedinenii, Vol. 4, No. 1, pp. 117–120, 1968

UDC 547.574.4+546.183+547.821

Crystalline dialkyl esters of arylamino(2-pyridyl)methylphosphonic acids have been synthesized by the reaction of 1-pyridylazomethines with dialkyl phosphites in the presence of sodium alkoxides. When α-pyridinealdehyde was condensed with dialkyl phosphites in the presence of sodium alkoxides, dialkyl esters of hydroxy(2-pyridyl) methylphosphonic acids were obtained in the form of viscous liquids. These compounds were identified in the form of the crystalline methiodides.

In a development of an investigation of the properties of 2-pyridylazomethines [1], we have studied their condensation with dialkyl phosphites.

By A. N. Pudovik's reaction [2], we have achieved the addition of dimethyl, diethyl, and diisopropyl phosphites to the azomethine grouping of 2-picolylidene-aniline, 2-picolylidene-m-toluidine, and 2-picolylidene-p-toluidine, and also the addition of dimethyl and diethyl phosphites to the azomethine grouping of 2-picolylidene-o-toluidine, 2-picolylidene-α-naphthylamine, and 2-picolylidene: β-naphthylamine in the presence of sodium alkoxides.

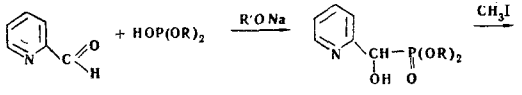


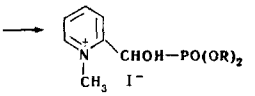
(I–XV)

The dimethyl, diethyl, and diisopropyl esters of arylamino(2-pyridyl)-methylphosphonic acids obtained (I–XV) form crystalline substances stable on storage in the air. They are soluble in organic solvents (sparingly in ether) and insoluble in water; they give picrates in the form of yellow-greenish and yellow crystals. The characteristics of the compounds synthesized are given in Table 1.

Apart from the investigations described above, the reaction of α-pyridinealdehyde with diethyl, diisopropyl, and diisobutyl phosphites has been studied.

The addition of dialkyl phosphites to the carbonyl group [3] of the aldehyde takes place in the presence of sodium alkoxides. The condensation products proved to be viscous noncrystallizing liquids soluble in water. By their reaction with methyl iodide it was possible to identify the diethyl, diisopropyl, and diisobutyl esters of hydroxy(2-pyridyl) methylphosphonic acid in the form of the colorless crystalline methiodides (XVI, XVII, XVIII). These substances are readily soluble in water, methanol, ethanol, and glacial acetic acid, and less readily in acetone, and are insoluble in ether, chloroform, and benzene.





R=C_2H_5 (XVI); i=C_3H_7 (XVII); i-C_4H_9 (XVIII).

The IR spectra of the methiodides XVI, XVII, and XVIII, have strong broad absorption bands characteristic for hydroxy groups (OH) at 3220 cm^{-1} and strong bands (P=O) in the ~ 1252–1270 cm^{-1} region. Table 2 gives the characteristics of the methiodides obtained.

EXPERIMENTAL

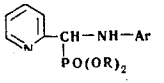
Synthesis of esters of arylamino(2-pyridyl)methylphosphonic acids (I–XV). A saturated anhydrous alcoholic solution of a sodium alkoxide was added to a mixture of a 2-pyridylazomethine and a dialkyl phosphite (~25% excess): for dimethyl and diisopropyl phosphites, 0.2 ml of sodium methoxide in each case; for diethyl phosphite, 0.5 ml of sodium ethoxide. The reaction mixture was stirred, and heat was evolved, (the temperature rose between 30° and 62° C); to complete the condensation the mixture was heated to 85°–90° C for 1–2 mm. The reaction products, in the form of viscous liquids in the majority of the experiments, were dissolved in dry ether (in small amount). On the following day (in some experiments after a long time of standing with cooling), the crystals that had deposited were filtered off and washed. All the esters were recrystallized from xylene with previous filtration from an amorphous residue. Substance XI was heated with activated carbon in xylene; after the solvent had been evaporated, a viscous liquid, which crystallized on standing, was obtained. The picrates of the esters were obtained in ethanolic solution.

Synthesis of the methiodides of the dialkyl hydroxy(2-pyridyl)methylphosphonates (XVI–XVIII). With shaking, a saturated alcoholic solution of a sodium alkoxide was added in drops to a mixture of α-pyridinealdehyde and a dialkyl phosphite (~10%): for diethyl phosphite, 0.2 ml of sodium ethoxide, and for diisopropyl and diisobutyl phosphites, 0.2 ml of sodium methoxide in each case. The condensation took place with a rise in the temperature (between 50 and 30°C); to complete the reaction the mixture was heated to 85°–90° C for 1–2 min. The sirupy liquids were dissolved in dry ethyl ether, and 3 ml of methyl iodide was added in each case. After standing for 7 days at room temperature, the crystalline methiodides that had deposited were filtered off, washed, and squeezed out under the press. They were recrystallized from acetone. Colorless crystalline methiodides of the esters were obtained. Additional amounts were isolated from the acetonic mother liquor.

The IR spectra* of the methiodides of the dialkyl hydroxy(2-pyridyl)-methylphosphonates (XVI–XVIII) were taken on a UR-10 spectrophotometer in the form of mulls in paraffin oil.

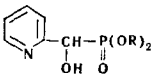
*I thank O. Zolova for recording the IR spectra in the Butlerov Kazan Chemical Institute.

Table 1

Characteristics and Conditions for the Synthesis of Dialkyl Esters of Arylamino(2-pyridyl)methylphosphonic Acids 

Esters	Ar	R	Amounts of reactants, g (mM)		Mp, °C	Empirical formula	Found, %		Calculated, %		Yield, %	Picrates of the esters					
			Azomethine	Dialkyl phosphite			N	P	N	P		Mp, °C	Empirical formula	Found, %		Calculated %	
														N	P	N	P
I	Phenyl-	CH_3	2.5 (13.7)	1.89 (17.1)	100	$C_{14}H_{17}N_2O_3P$	9.91	10.28	9.59	10.61	82.3	172	$C_{14}H_{17}N_2O_3P \cdot C_6H_3N_3O_7$	13.68	5.67	13.43	5.95
II		C_2H_5	2.7 (14.8)	2.55 (18.4)	106	$C_{16}H_{21}N_2O_3P$	9.16	9.36	8.74	9.68	97.0	175	$C_{16}H_{21}N_2O_3P \cdot C_6H_3N_3O_7$	13.42	5.60	12.75	5.65
III		C_3H_7-iso	2.0 (10.9)	2.28 (13.6)	102	$C_{18}H_{25}N_2O_3P$	8.36	9.34	8.04	8.90	76.3	178	$C_{18}H_{25}N_2O_3P \cdot C_6H_3N_3O_7$	12.49	5.23	12.13	5.37
IV	p-Tolyl-	CH_3	1.5 (7.6)	1.05 (9.5)	112	$C_{15}H_{19}N_2O_3P$	9.47	9.86	9.15	10.13	94.0	164	$C_{15}H_{19}N_2O_3P \cdot C_6H_3N_3O_7$	13.44	5.54	13.08	5.79
V		C_2H_5	1.5 (7.6)	1.31 (9.4)	125	$C_{17}H_{23}N_2O_3P$	8.02	9.14	8.38	9.28	75.2	172	$C_{17}H_{23}N_2O_3P \cdot C_6H_3N_3O_7$	12.32	5.68	12.43	5.57
VI		C_3H_7-iso	1.1 (5.6)	1.16 (6.9)	111	$C_{19}H_{27}N_2O_3P$	7.41	8.91	7.73	8.56	67.0	184	$C_{19}H_{27}N_2O_3P \cdot C_6H_3N_3O_7$	11.53	5.58	11.84	5.24
VII	m-Tolyl-	CH_3	1.7 (8.6)	1.16 (10.5)	102	$C_{15}H_{19}N_2O_3P$	8.86	10.30	9.15	10.13	88.3	169	$C_{15}H_{19}N_2O_3P \cdot C_6H_3N_3O_7$	13.35	5.83	13.08	5.79
VIII		C_2H_5	1.66 (8.4)	1.56 (11.3)	116	$C_{17}H_{23}N_2O_3P$	8.10	8.96	8.38	9.28	95.7	187	$C_{17}H_{23}N_2O_3P \cdot C_6H_3N_3O_7$	12.20	5.50	12.43	5.57
IX		C_3H_7-iso	1.0 (5.1)	1.05 (6.3)	110	$C_{19}H_{27}N_2O_3P$	7.93	8.42	7.73	8.56	67.9	191	$C_{19}H_{27}N_2O_3P \cdot C_6H_3N_3O_7$	10.46	5.05	10.11	5.24
X	o-Tolyl-	CH_3	2.28 (11.6)	1.59 (14.4)	68	$C_{15}H_{19}N_2O_3P$	9.56	9.70	9.15	10.13	70.4	156	$C_{15}H_{19}N_2O_3P \cdot C_6H_3N_3O_7$	13.26	5.83	13.08	5.79
XI		C_2H_5	2.84 (14.4)	2.3 (16.6)	56	$C_{17}H_{23}N_2O_3P$	8.17	9.64	8.38	9.28	94.8	137	$C_{17}H_{23}N_2O_3P \cdot C_6H_3N_3O_7$	12.57	5.68	12.43	5.57
XII	α-Naphthyl-	CH_3	2.1 (9.04)	1.26 (11.4)	131	$C_{18}H_{19}N_2O_3P$	8.47	8.70	8.18	9.06	63.0	158	$C_{18}H_{19}N_2O_3P \cdot C_6H_3N_3O_7$	12.47	5.57	12.26	5.44
XIII		C_2H_5	1.98 (8.53)	1.50 (10.8)	105	$C_{20}H_{23}N_2O_3P$	7.42	8.60	7.56	8.37	38.1	159	$C_{20}H_{23}N_2O_3P \cdot C_6H_3N_3O_7$	11.79	4.84	11.68	5.17
XIV	β-Naphthyl-	CH_3	1.0 (4.30)	0.6 (5.45)	123	$C_{18}H_{19}N_2O_3P$	8.31	9.20	8.18	9.06	75.0	146	$C_{18}H_{19}N_2O_3P \cdot C_6H_3N_3O_7$	11.98	5.14	12.26	5.44
XV		C_2H_5	0.8 (3.44)	0.59 (4.27)	110	$C_{20}H_{23}N_2O_3P$	8.52	8.61	7.56	8.37	47.3	179	$C_{20}H_{23}N_2O_3P \cdot C_6H_5N_3O_7$	11.82	5.33	11.68	5.17

Table 2

Synthesis of Esters of Hydroxy(2-pyridyl)methylphosphonic Acid and the Characteristics of their Methiodides 

Methiodide of the ester	R	Amounts of reactants, g (mM)		Mp, °C, of the methiodide	Empirical formula	Found, %		Calculated, %		Yield, %
		α-pyridinealdehyde	dialkyl phosphate			I	P	I	P	
XVI	C_2H_5	1.5 (14.01)	2.12 (15.34)	111	$C_{11}H_{19}INO_4P$	32.49	8.29	32.78	8.01	24.0
XVII	i-C_3H_7	1.5 (14.01)	2.55 (15.35)	146	$C_{13}H_{23}INO_4P$	30.73	7.50	30.57	7.47	60.8
XVIII	i-C_4H_9	1.5 (14.01)	2.99 (15.39)	151	$C_{15}H_{27}INO_4P$	28.42	7.18	28.64	6.99	64.5

REFERENCES

1. B. P. Lugovkin, KhGS [Chemistry of Heterocyclic Compounds], Coll. 1, 224, 1967.

2. A. N. Pudovik, DAN, 6, 865, 1952.

3. V. S. Abramov, ZhOKh, 22, 647, 1952.

23 March 1966

All-Union Scientific Research Institute for the Protection of Labor, Kazan