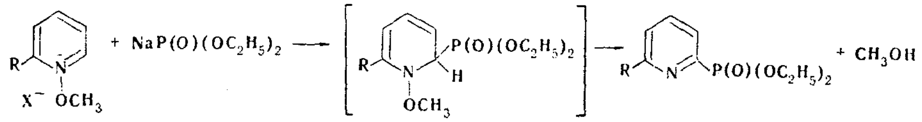
SOME TRANSFORMATIONS IN A NUMBER OF (2-PYRIDYL)PHOSPHONATES

V. N. Eliseenkov, N. V. Bureva, and B. E. Ivanov

UDC 547.821'241

The reaction of sodium diethylphosphite with N-methoxypyridinium methosulfate in a solvent at low temperature makes it possible to obtain diethyl (2-pyridyl)phosphonate in yields up to 75%. The latter was converted to (2-pyridyl)-phosphonic acid dichloride, from which amides, esters, amidochlorides, and (pyridyl)thiophosphonic acid derivatives were obtained.

The most convenient method for the introduction of a phosphone group into the pyridine ring is based on the reaction of the lithium or sodium salt of diethylphosphorus acid with N-methoxypyridinium salts [1].



A

I, II

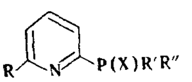
I $R=H$; II $R=CH_3$

The yield of (2-pyridyl)phosphonates ranges from 20 to 67%. The chief reason for the reduction in the yield is the reaction of the resulting methanol with the diethylphosphite anion, which removes the latter from the reaction sphere [2]. A decrease in the temperature of the process and an increase in its duration should therefore raise the yields of products, probably as a consequence of the accumulation of intermediate A. It was found that the reaction between N-methoxypyridinium methosulfate and sodium diethylphosphite is best carried out at −15 to −5°C in an inert solvent (ether, low-boiling petroleum ether), which ensures the preparation of pure sodium diethylphosphite, and, in addition, methanol is partially removed from the reaction phase due to dissolving. Under these conditions, I is formed in 60-75% yield (67% in diethylphosphite as the solvent — to the lithium salt [1]). The yield of dibutyl (2-pyridyl) phosphonate is 45% (as compared with 20% through the sodium salt in diethyl phosphite [1]), while the yield of diethyl (6-methyl-2-pyridyl)phosphonate is 69% (instead of 30% in diethyl phosphite [1]).

Compounds I and II are convenient starting materials for the synthesis of 2-pyridylphosphonates with different environments around the phosphorus atom. The action of phosphorus pentachloride on diesters I and II gives, respectively, (2;pyridyl)-(III) and (6-methyl-2-pyridyl)phosphonic acid dichlorides (IV), during which the transformation proceeds more completely in a solvent. They are readily hydrolyzed in air and react with alcohols and amines to give the corresponding esters, amides, and amidochlorides; when they are treated with phorphorus pentasulfide [3] they give thiophosphonic acid dichlorides. The properties of the compounds obtained are presented in Table 1.

A. E. Arbuzov Institute of Organic and Physical Chemistry, Academy of Sciences of the USSR, Kazan. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1354-1356, October, 1974. Original article submitted April 24, 1973.

TABLE 1.



Compound	R	R′	R″	X	bp, °C (mm)	d_4^{20}	n_D^{20}
III	H	Cl	Cl	O	82 (0,04)	1,4682	1,5608
IV	CH_3	Cl	Cl	O	100—110 (0,1)*	—	—
V	H	Cl	Cl	S	82—84 (0,06)	1,4628	1,6270
VI	H	OCH_3	OCH_3	S	94 (0,03)	1,2433	1,5582
VII	H	Cl	$N(C_2H_5)_2$	O	122 (0,1)	1,1806	1,5300
VIII	CH_3	Cl	$N(C_2H_5)_2$	O	123—125 (0,1)	1,1666	1,5320
IX	H	$N(C_2H_5)_2$	$N(C_2H_5)_2$	O	105 (0,03) †	—	—
X	CH_3	$i\text{-}C_4H_9O$	$i\text{-}C_4H_9O$	O	113—115 (0,05)	1,0463	1,4818

Compound	MR_D		Empirical formula	Found, %			Calc., %			Yield, %
	found	calc		Cl	N	P	Cl	N	P	
III	43,68	43,68	$C_5H_4Cl_2NOP$	35,3	—	15,6	35,7	—	15,7	77
IV	—	—	$C_6H_6Cl_2NOP$	33,5	—	14,6	33,8	—	14,7	60
V	51,37	51,17	$C_5H_4Cl_2NPS$	33,1	S 14,9	14,5	33,4	S 15,1	14,6	60
VI	52,71	53,22	$C_7H_{10}NO_2PS$	S 16,0	6,7	16,0	S 15,8	6,9	15,8	71
VII	60,88	60,86	$C_9H_{14}ClN_2OP$	15,5	12,0	13,2	15,2	12,0	13,3	70
VIII	65,39	65,46	$C_{10}H_{16}ClN_2OP$	14,6	11,5	12,6	14,4	11,4	12,6	56
IX	—	—	$C_{13}H_{24}N_3OP$	—	15,6	11,6	—	15,6	11,5	85
X	77,70	78,06	$C_{13}H_{22}NO_3P$	C 58,9	H 8,7	10,8	C 58,9	H 8,5	10,9	60

*This compound had mp 75-81°.

†This compound had mp 50-51° (from ether).

EXPERIMENTAL

Diethyl (2-pyridyl)phosphonate (I). A 110.6-g (0.5 mole) sample of N-methoxypyridinium methosulfate [4] was added dropwise with stirring to sodium diethylphosphite obtained from 83-97 g (0.6-0.7 mole) of diethyl phosphite and 11.5 g (0.5 g-atom) of sodium in 50-100 ml of ether or low-boiling petroleum ether at —15 to —5° in the course of 5 h. The mixture was then stirred at room temperature for 2 h and allowed to stand overnight. The solvent was removed by vacuum distillation, 200 ml of water was added to the residue, and the mixture was extracted with three 200-ml portions of chloroform. The organic layer was separated, and phosphonate I was extracted from it with 4 M hydrochloric acid. The aqueous solution was neutralized with sodium carbonate until it was weakly alkaline, and base I was extracted with chloroform (two 100-ml portions). The chloroform was removed by distillation, and the residue was fractionated with collection of the fraction with bp 100-120° (0.01-0.05 mm). Refractionation gave 65-80 g (60-75%) of I with bp 105-107° (0.03 mm) and n_D^{20} 1.4940.

Diethyl (6-methyl-2-pyridyl)phosphonate (II), with bp 112-115° (0.04 mm), d_4^{20} 1.1375, and n_D^{20} 1.4931 [bp 125-127° (0.1 mm) [1]] was similarly obtained in 69% yield.

2-Pyridylphosphonic Acid Dichloride (III). A total of 90 g (0.215 mole) of phosphorus pentachloride was added in portions at 60-70° to 42 g (0.195 mole) of I in 60 ml of dry benzene, after which the mixture was refluxed for 1 h. The benzene was then removed in vacuo, and the residue was held at 100-130° for 1 h. Fractionation gave 28 g of III.

(6-Methyl-2-pyridyl)phosphonic Acid Dichloride (IV). This compound was similarly obtained.

2-Pyridylthiophosphonic Acid Dichloride (V). An equimolecular mixture of III and phosphorus pentasulfide was heated at 130-140° for 15-20 h with stirring in a stream of carbon dioxide, after which the mixture was fractionated, and V was purified by two vacuum distillations.

Dimethyl(2-Pyridyl)thiophosphonate (VI). A mixture of 1.6 g (50 mmole) of methanol and 5.6 g (55 mmole) of triethylamine in 10 ml of benzene was added dropwise with stirring at 30-50° to 4.8 g (22.6 mmole) of V in 100 ml of dry benzene, after which the mixture was refluxed for 30 min. It was then stirred at room temperature for 2 h, and the triethylamine hydrochloride was removed by filtration. The benzene was removed in vacuo, and the residue was fractionated. Two fractionations gave 2.9 g of VI.

Diethylamido(2-pyridyl)phosphonic acid chloride (VII), diethylamido(6-methyl-2-pyridyl)phosphonic acid chloride (VIII), tetraethylamido(2-pyridyl)phosphonate,(IX), and diisobutyal(6-methyl-2-pyridyl)phosphonate (X) (Table 1) were obtained under similar conditions.

LITERATURE CITED

1. D Redmore, J. Org. Chem., 35, 4114 (1970).
2. K. Moedritzer, J. Inorg. Nucl. Chem., 22, 19 (1961).
3. M. I. Kabachnik and N. N. Godovikov, Dokl. Akad. Nauk SSSR, 110, 217 (1956).
4. W. E. Feely, U.S. Patent No. 2991285 (1961); Ref. Zh. Khim., 20L358 (1962).