SOME PROPERTIES OF BIS(4,6-DIMETHYL-2-PYRIMIDYL)METHYLPHOSPHONATE

V. S. Reznik and N. G. Pashkurov

Khimiya Geterotsiklicheskikh Soedinenii, Vol. 5, No. 1, pp. 129–132, 1969

UDC 547.854.1'547.241:543.422.4

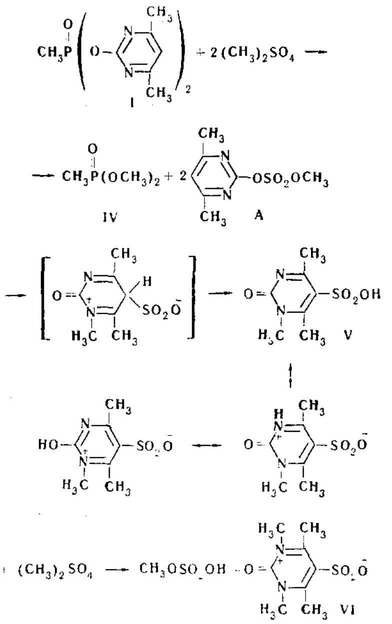
It has been established that bis(4,6-dimethyl-2-pyrimidyl)methylphosphonate (I) is capable of forming a crystalline hydrate with five molecules of water. Compound I reacts with dimethyl sulfate, forming a complex mixture of products from which dimethyl methylphosphonate, 1,4,6-trimethyl-5-sulfo-2-pyrimidinone, the betaine 1,3,4,6-tetramethyl-2-oxodihydropyrimidinium-2-sulfonate, and 4,6-dimethyl-2-hydroxypyrimidine methylphosphonate have been isolated.

We have previously reported [1] the synthesis of bis(4,6-dimethyl-2-pyrimidyl) methylphosphonate (I) by the reaction of the sodium salt of 4,6-dimethyl-2-hydroxypyrimidine and methylphosphonic dichloride. The present work was undertaken in order to study some chemical properties of compound I—its reaction with water and behavior on alkylation.

The ester I is capable of forming a crystalline hydrate (II) containing, according to analysis, five molecules of water of crystallization per molecule of ester. The IR spectrum of the freshly-prepared hydrate taken not more than about an hour after its preparation differs from the spectrum of the initial ester only by the presence of absorption bands in the 1660 and 3400–3600 cm^{-1} regions, just where the vibrations of crystal-bound water appear [2]. If the freshly-prepared hydrate is slowly heated to 100° C in vacuum (8–5 mm), the water distils off and the initial ester I is formed. The hydrate is rapidly hydrolyzed by the water of crystallization. After a day's storage, the hydrolyzed II melted in the range from 168 to 180° C. Fractional crystallization from a mixture of methanol and ether of the hydrolysis product yielded two compounds—4,6-dimethyl-2-hydroxypyrimidine, mp 196–198° C, and 4,6-dimethyl-2-hydroxypyrimidine methylphosphonate (III), mp 153–154.5° C.

We have studied the methylation of the ester I with dimethyl sulfate. The reaction of I with dimethyl sulfate in the absence of a solvent at 60–80° C took place very vigorously and ended, as a rule, in the decomposition of the reaction mixture. Consequently, methylation was subsequently carried out in benzene at 18–20° C in the presence of an excess of dimethyl sulfate, or in nitrobenzene at 110–125° C. From the complex mixture of products of this reaction we isolated, besides dimethyl methylphosphonate (IV), another three compounds to which, on the basis of analytical results and IR spectra, were assigned the structures of 1,4,6-trimethyl-5-sulfo-2-pyrimidinone (V), the betaine 1,3,4,6-tetramethyl-2-oxodihydropyrimidinium-5-sulfonate (VI), and the methyl sulfate derivative of 4,6-dimethyl-2-hydroxypyrimidine (VII).

The formation of compounds IV–VI can be represented by the following scheme:

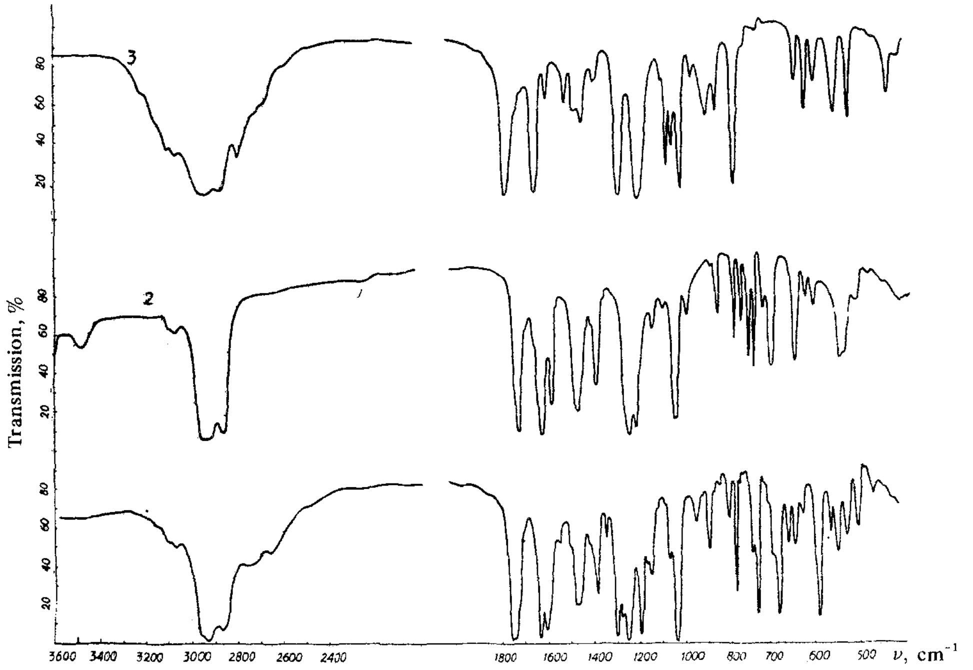


The formation of the small amount of VII can be explained only by the partial hydrolysis of I.

Products V and VI (see figure) have strong bands in the 1190–1250 and 1035–1055 cm^{-1} regions and a number of bands in the 670–690 cm^{-1} region which correspond most closely to the vibrations of SO_2 in sulfonic acids and their salts [3].

In both cases, and also in the methyl sulfate derivative VII, the vibrations of the C=O bond appear in the 1630–1650 and 1730–1770 cm^{-1} regions, the frequencies falling in the sequence VII—V—VI. Such absorption of the carbonyl group is characteristic for salts of 4,6-dimethyl-2-hydroxypyrimidine. Thus, 4,6-dimethyl-2-hydroxypyrimidine hydrochloride absorbs at 1650 and 1765 cm^{-1} (4,6-dimethyl-2-hydroxypyrimidine itself has $\nu_{C=O}$ at 1660–1690 cm^{-1}), which coincides completely with $\nu_{C=O}$ for VII. Alkylation of the nitrogen atom lowers the value of the C=O vibrations. Thus, in N-(β-hydroxyethyl)-4,6-dimethylpyrimidine hydrochloride, $\nu_{C=O}$ appears at 1620 and 1750 cm^{-1}.

In the 2500–3600 cm^{-1} region, products VII and V absorb at 2500–2800 cm^{-1} like 2-hydroxy-4,6-dimethylpyrimidine hydrochloride. This absorption may be ascribed to the vibrations of the N—H bond in ammonium salts. Product VI does not absorb at all in this region, which shows the absence of N—H vibrations and of an OH group capable of tautomerism. The absence of absorption in this region while the C=O absorption characteristic for pyrimidine salts is present



IR spectra (in paraffin oil): 1) 1,4,6-trimethyl-5-sulfo-2-pyrimidinone (V); 2) the hydrated form of the betaine 1,3,4,6-tetramethyl-2-oxodihydropyrimidinium-5-sulfonate (VI); 3) methyl sulfate derivative of 4,6-dimethyl-2-hydroxypyrimidine (VII).

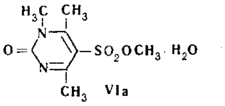
Characteristics of the Compounds Obtained

Compound	Mp, °C	Empirical formula	Found, %			Calculated, %		
			C	H	N	C	H	N
II	77—78	$C_{13}H_{27}N_4O_8P$	—	—	14.25	—	—	14.05
III	153—154.5	$C_7H_{13}N_2O_4P$*	38.96	5.89	13.00 13.03	38.2	5.9	14.1
VII	208—210 (decomp.)	$C_7H_{12}N_2O_5S$	35.56 35.75	5.01 5.09	11.80 11.61	35.6	5.08	11.85
V	221—223 (decomp.)	$C_7H_{10}N_2O_4S$	39.03 39.07	4.91 5.02	12.55 12.78	38.5	4.59	12.83
VI	226—228 (decomp.)	$C_8H_{14}N_2O_5S$	38.55 38.33	5.61 5.70	11.46 11.64	38.4	5.6	11.2

*Found, %: P 14.44. Calculated, %: P 14.10.

can be explained satisfactorily by a betaine-like internal quaternary salt structure. The absorption at 3450–3620 and 1610 cm^{-1} is connected with the water of crystallization, and when the substance is dried in vacuum the intensity of this absorption falls sharply.

The analytical results and the IR spectrum of the product formed when the reaction is carried out in nitrobenzene agree not only with formula VI but also with VIa.



VIa

However, the poor solubility in nonpolar solvents and the high value of the C=O frequency in the IR spectrum correspond more to structure VI. The characteristics of the compounds studied are given in the table.

EXPERIMENTAL

Bis(4,6-dimethyl-2-pyrimidyl)methylphosphonate hydrate (II). A concentrated benzene solution of bis(4,6-dimethyl-2-pyrimidyl)methylphosphonate was shaken with a small amount of water at 20° C. The white crystals of the hydrate that deposited (yield amost quantitative) were dried in vacuum at room temperature (15 min, 5–7 mm) and analyzed immediately. On slow heating, the substance melted at 76.5–77° C and then became red, solidified, and melted again with decomposition at 105–110° C. On rapid heating, it melted at 77–78° C. After a day, the II was dried in vacuum and recrystallized from a mixture of methanol and ether (3 : 1). On cooling, a precipitate of 4,6-dimethyl-2-hydroxypyrimidine methylphosphonate deposited with mp 153–154.5° C (from methanol). 4,6-Dimethyl-2-hydroxypyrimidine with mp 196–198° C (from methanol) was isolated from the mother liquor. Its IR spectrum was identical with that of an authentic sample of 4,6-dimethyl-2-hydroxypyrimidine.

Reaction of bis(4,6-dimethyl-2-pyrimidyl) methylphosphonate with dimethyl sulfate. a) At 20° C, 40 ml (53.3 g, 0.42 mole) of dimethyl sulfate was added to a solution of 20 g (0.065 mole) of I in a mixture of benzene and chloroform (1 : 1). A white precipitate soon began to deposit. After a month, the precipitate was filtered off and was boiled with a small amount of methanol. From the methanolic extract, 3.5 g of VII was isolated with mp 208–210° C (decomp., from methanol). The substance insoluble in methanol was V, with mp 221–223° C (decomp., from water), yield 75%. When the benzene-chloroform mother liquor was distilled, a 27% yield was obtained of the ester IV, bp 63–64.5° C (10 mm); n_D^{20} 1.4093. Found, %: P 24.7. Calculated for $C_3H_9O_3P$, %: P 25.0. According to the literature [4]: bp 67–68° C (12.5 mm); n_D^{20} 1.4105.

After distillation, a dark viscous noncrystallizing mass remained in the flask from which it was impossible to isolate individual compounds.

b) Twenty grams (0.065 mole) of I was added gradually to a solution of 6.2 ml (8.2 g, 0.065 mole), of dimethyl sulfate in 50 ml of dry nitrobenzene at 100° C. The mixture was heated at 110–125° C for 30 min, cooled, and diluted with ether, and the viscous oil was separated off. This was dissolved in a boiling mixture of ethanol and chloroform (3 : 1). After two weeks, the crystals of VI that had deposited (4 g) were filtered off, decomp. p. 226–228° C (recrystallized three times from methanol and washed with acetone).

1,4,6-Trimethyl-5-sulfo-2-pyrimidinone (V) and the monohydrate of the betaine 1,3,4,6-tetramethyl-2-oxodihydropyrimidinium-5-sulfonate (VI)—colorless crystalline substances very readily soluble in water, moderately soluble in methanol, and practically insoluble in nonpolar solvents. Compound VI is more soluble in methanol than V. The salt VII is very readily soluble in water and methanol. When an aqueous solution of VII was heated with $BaCl_2$, a precipitate of $BaSO_4$ deposited. Even prolonged boiling of aqueous solutions of V and VI with $BaCl_2$ did not lead to the formation of $BaSO_4$.

The IR spectra were recorded on a UR-10 spectrophotometer. The samples were prepared in the form of mulls in paraffin oil, the absorption bands of which are marked in the spectra.

REFERENCES

1. V. S. Reznik and N. G. Pashkurov, KhGS, collection 1, p. 384, 1967.
2. W. West, ed., Chemical Applications of Spectroscopy [Russian translation], IL, Moscow, p. 347, 1959.
3. K. Nakanishi, Infrared Absorption Spectroscopy [Russian translation], Mir, Moscow, p. 67, 1965.
4. B. A. Arbuzov and V. S. Vinogradova, Izv. AN SSSR, OKhN, 459, 1947.

16 October 1967

Arbuzov Institute of Organic
and Physical Chemistry
AS USSR, Kazan