IODONIUM DERIVATIVES OF HETEROCYCLIC COMPOUNDS

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5-Phenyliodonio-2,4-dihydroxypyrimidine tosylate (I) was obtained from the reaction of uracil with phenyl iodosoacetate in the presence of p-toluenesulfonic acid. Treatment of I with alkali gave 5-phenyliodonio-2,4-dihydroxypyrimidine (II). 5-Phenyliodonio-2,4-dihydroxypyrimidine chloride, bromide, iodide, and fluoborate were obtained. The IR and UV spectra were recorded, and the ionization constants were calculated. The phenyliodonium residue increases the acidity of uracil at $N_{(1)}$ by 3.5 orders of magnitude and at $N_{(3)}$ by two orders of magnitude.

Continuing our investigation of aryliodonium derivatives of heterocyclic compounds and taking into account the ever-increasing interest in pyrimidine derivatives as important components of nucleotides, we felt it would be expedient to obtain aryliodonium derivatives of uracil (2,4-dihydroxypyrimidine) and determine the possibility of their use for the synthesis of various uracil derivatives.

We developed a simple and convenient method for the phenyliodonation of uracil; it consists of the reaction of uracil with phenyl iodosoacetate in the presence of p-toluenesulfonic acid in dimethylformamide. The reaction proceeds under extremely mild conditions to give good yields of 5-phenyliodonio-2,4-dihydroxypyrimidine tosylate (I) – a stable crystalline substance. Treatment of I with potassium carbonate solution at room temperature readily gives the betaine of 5-phenyliodonio-2,4-dihydroxypyrimidine (II). This compound is less stable than the tosylate, since it gradually turns yellow on storage in light. It can be stored for a practically unlimited time in the dark at 0-5°.

A number of other 5-phenyliodonio-2,4-dihydroxypyrimidine salts (III) (Table 1) were obtained from betaine II. Thus treatment of II in acetic acid with hydrochloric acid gives the chloride (IIIa), while reaction of II with sodium bromide and potassium iodide in acetic acid gives the bromide (IIIb) and iodide (IIIc), respectively. We also obtained the fluoborate (IIId) in the reaction of II with fluoboric acid. All of the salts obtained are stable crystalline substances.

The IR spectra for the compounds obtained were recorded at 1480-1800 cm^{-1} and 2800-3600 cm^{-1} (Table 2). It must be noted that in comparison with the absorption of the carbonyl groups of unsubstituted uracil, which is observed at 1715 and 1670 cm^{-1} in KBr [2] and at 1722 and 1694 cm^{-1} in dioxane solution [3], there is yet another absorption maximum at 1755-1780 cm^{-1} in this region in the spectra of 5-phenyliodonio-2,4-dihydroxypyrimidine salts. The absorption maxima at 1560-1610 cm^{-1} can be assigned to the absorption of the aromatic ring and the pyrimidine ring. One absorption band of the carbonyl groups is observed in the spectrum of betaine II at 1649 cm^{-1}; this is evidence for the formation of an anionic system and an inner salt.

Compound IIIa was characterized by the electronic absorption spectra of aqueous solutions having different pH values (Fig. 1). The literature contains data on the electronic spectra and tautomeric forms of uracils [2, 4-7]. From the literature data and our data, we suppose that in aqueous alkaline media (pH 8-9.5) III splits out a proton from $N_{(1)}$ and forms monoanion II with a delocalized negative charge. Dianion IV forms at pH > 12. We calculated the acidity constants of IIIa on the basis of the electronic absorption spectra: $pK_1 = 6.04 \pm 0.07$ and $pK_2 = 11.04 \pm 0.07$. A phenyliodonium group in the 5 position of

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TABLE 1. Characteristics of Iodonium Derivatives of Uracil

Compound	mp, °C (crystallization solvent)	Empirical formula	Found, %		Calc., %		Yield, %
			I	N	I	N	
I	226—228 (50%(ethanol)	$C_{17}H_{15}IN_2O_2S \cdot H_2O$	25,0	5,9	25,2	5,6	78
II	206—208 (water)	$C_{10}H_7IN_2O_2$	40,3	8,9	40,4	8,9	72
IIIa	273—275 (water)	$C_{10}H_8ClIN_2O_2$	36,1	8,2	36,2	8,0	74
IIIb	265—267 (water)	$C_{10}H_8BrIN_2O_2$	32,4	7,3	32,1	7,1	86
IIIc	200—202 (water)	$C_{10}H_8I_2N_2O_2$	58,9	6,3	57,4	6,3	86
IIId	180—185 (ethanol–absolute ether)	$C_{10}H_8BF_4IN_2O_2$	31,8		31,6		80

TABLE 2. IR Spectra of Iodonium Derivatives of Uracil*

Compound	1800—1480 cm^{-1}	2800—3600 cm^{-1}
I	1762(47), 1723(66), 1681(78), 1611(71), 1562(52)	3178(53), 3065(56), 2964(39), 2829(33)
II	1649(43), 1598(52), 1566(43), 1528(41), 1512(42)	3345(57), 3129(70), 2974(50), 2923(44)
IIIa	1760(58), 1727(62), 1717(61), 1662(75), 1614(58), 1585(38)	3170(62), 3048(70), 2919(62), 2855(60), 2775(46)
IIIb	1755(58), 1720(60), 1659(72), 1609(58), 1583(38), 1568(35)	3110(70), 3046(48), 2939(54), 2867(50), 2792(44)
IIIc	1754(40), 1718(44), 1661(51), 1594(40), 1576(24), 1563(23)	3153(81), 3045(76), 2934(58), 2877(53)
IIId	1778(22), 1712(77), 1680(78), 1611(51)	3278(67), 3163(65), 3049(67), 2834(50)

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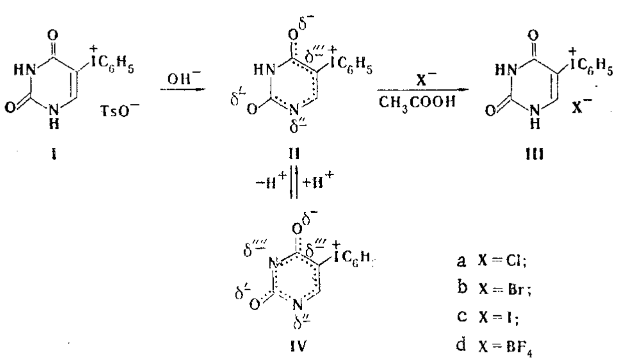
* The percent absorption is given in parentheses.

the uracil ring changes pK_1 of the starting uracil [7] ($pK_1 = 9.5$, $pK_2 = 13$) by 3.5 orders of magnitude. A phenyliodonium group in the 5 position of the uracil ring is in direct conjugation with the $N_{(1)}$ atom, but only the inductive effect of this group acts on $N_{(3)}$.



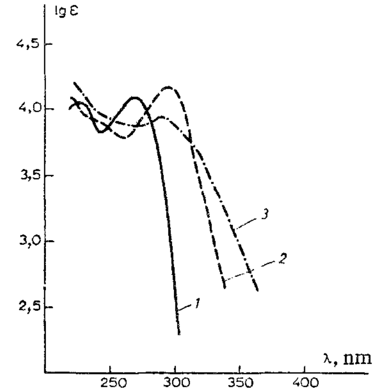


Fig. 1. UV spectrum of IIIa in aqueous solutions: 1) pH ~ 3 (undissociated salt); 2) pH ~ 9 (monoanion); 3) pH ~ 13 (dianion).

EXPERIMENTAL

The UV spectra were recorded with an SFD-2 spectrometer.

The acidity constants were determined by a spectrophotometric method [8]. The pH values of buffer solutions were measured with an LPM-60M pH meter by means of a glass electrode coupled with a flow-type silver–silver chloride electrode. The IR spectra of suspensions of the substances in mineral oil (1480-1800 cm^{-1}) and in hexachlorobutadiene (2800-3600 cm^{-1}) were recorded with an IKS-14A spectrometer.

5-Phenyliodonio-2,4-dihydroxypyrimidine Tosylate (I). A mixture of 1.1 g (0.01 mole) of pulverized uracil, 20 ml of dimethylformamide, 3.22 g (0.01 mole) of phenyl iodosoacetate, and 1.9 g (0.01 mole) of p-toluenesulfonic acid monohydrate was stirred and heated on a water bath as the water was gradually heated to the boiling point. The components dissolved, and I began to precipitate immediately. The mixture was allowed to stand at 0-5° for 12 h, after which the precipitate was removed by filtration and washed with ether.

5-Phenyliodonio-2,4-dihydroxypyrimidine Betaine (II). A 5.05-g (0.01 mole) sample of tosylate I was dissolved by heating in 70 ml of 50% ethanol, after which a solution of 5 g (0.036 mole) of potassium carbonate in 20 ml of water was added, and the mixture was held at 0-5° for 3-4 h. The betaine was then removed by filtration.

5-Phenyliodonio-2,4-dihydroxypyrimidine Chloride (IIIa). A 1.5-ml sample of concentrated hydrochloric acid was added to a filtered solution of 3.2 g (0.01 mole) of II in 15 ml of acetic acid, and a colorless material precipitated immediately. Water (15 ml) was added to the mixture, and it was heated to the boiling point and filtered. Cooling of the filtrate gave IIIa.

5-Phenyliodonio-2,4-dihydroxypyrimidine Bromide (IIIb). A solution of 2.0 g (0.02 mole) of sodium bromide in 15 ml of water was added to a filtered solution of 3.2 g (0.01 mole) of II in 15 ml of acetic acid to give a sticky colorless precipitate of IIIb.

5-Phenyliodonio-2,4-dihydroxypyrimidine Iodide (IIIc). A solution of 3.3 g (0.02 mole) of potassium iodide in 30 ml of water was added to a filtered solution of 3.2 g (0.01 mole) of II in 15 ml of acetic acid. A sticky colorless material precipitated. Water (10 ml) was added, and the mixture was heated until the material dissolved, and the solution was then filtered. The filtrate was cooled, and iodide IIIc was removed by filtration.

5-Phenyliodonio-2,4-dihydroxypyrimidine Fluoborate (IIId). A total of 30 ml of a 1 N solution of fluoboric acid in ethanol (prepared from 19 g of 41% hydrofluoric acid, 6 g of boric acid, and enough ethanol to bring the volume up to 100 ml) was added to 3.2 g (0.01 mole) of II, and the mixture was shaken to dissolve the betaine. The solution was filtered, and the filtrate was vacuum-evaporated to ~5 ml. The precipitate was diluted with 30 ml of ether, and the IIId was removed by filtration after 2 h.

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