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Abstract

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TIN- AND LEAD-ORGANIC DERIVATIVES OF CERTAIN NITROGEN-CONTAINING ACIDS

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Earlier ([1,2]) we studied the synthesis and properties of tin- and lead-organic esters of methacrylic acid, which we called organotin and organolead methacrylates of the general structure $R_3SnOOCC(CH_3) = CH_2$, $R_2Sn(OOCC(CH_3) = CH_2)_2$, $(C_6H_5)_2Pb(OOCC(CH_3) = CH_2)_2$. Polymers and copolymers with a number of unsaturated monomers were also obtained ([1,2]).

It is known that certain nitrogen-containing acids—for example, α-alanine, p-aminobenzoic, nicotinic (β-pyridinecarboxylic, vitamin PP), isocinchomeronic (2,5-pyridinedicarboxylic), orotic (4-uracilcarboxylic, vitamin of the B_{13} group), and uracilacetic acids—play an exceptionally important role in the vital activity of organisms and plants. Orotic acid, which participates in the construction of nucleic acids and is also a growth factor, has been little studied ([3]). Below we present a method for its preparation, based on Hilbert' s procedure but differing in that, instead of the red blood salt, we used a chromium mixture, which considerably facilitates the synthesis of the acid. On the other hand, such organotin compounds as stannols R_3SnOH, acetostannanes $R_3SnOOCCH_3$, and alkyltin esters of nicotinic acid $R_3SnOOCC_5H_4N$ ([8]) possess biocidal properties and inhibit the growth of lower cultures, molds, fungi, etc.

With the aim of synthesizing biologically active organoelement compounds exerting a favorable physiological effect on the organism, we investigated organotin and organolead esters of the indicated nitrogen-containing acids. The corresponding derivatives of α-alanine, nicotinic, isocinchomeronic, p-aminobenzoic, orotic, and uracilacetic acids were obtained according to the reactions:

$$R_3MOH + R'COOH \rightarrow R_3MOOCR' + H_2O;$$

$$2R_3MOH + HOOCR''COOH \rightarrow R_3MOOCR''COOMR_3 + 2H_2O;$$

$$R_2MO + 2R'COOH \rightarrow R_2M(OOCR')_2 + H_2O;$$

$$R_3MOMR_3 + 2R'COOH \rightarrow 2R_3MOOCR' + H_2O, \quad \text{where } M = \text{Sn, Pb.}$$

The reaction of triphenylplumbanol with nicotinic and uracilacetic acids proceeds differently. In these cases diphenyllead esters of the corresponding acids are formed, as in the reaction with methacrylic acid ([2]). Cleavage of a phenyl group is also observed:

$$(C_6H_5)_3PbOH + 2C_5H_4NCOOH \rightarrow (C_6H_5)_2Pb(OOCC_5H_4N)_2 + C_6H_6 + H_2O.$$

$$(C_6H_5)_3PbOH + 2HOOCCH_2C_4H_3N_2O_2 \rightarrow (C_6H_5)_2Pb(OOCC_2H_4H_3N_2O_2)_2 + C_6H_6 + H_2O.$$

We have established ([8]) that these organotin and organolead compounds also possess biocidal properties, strongly dependent on the nature of the alkyl groups in the molecule. Thus, organotin derivatives of nicotinic acid and alanine inhibit, even at insignificant concentrations, the growth of such cultures as *Escherichia coli*, *Streptococcus faecalis*, and *Lactobacillus casei*.

All the organotin and organolead compounds obtained are crystalline substances, sparingly soluble in water and more readily soluble in organic solvents. Trimethylstannyl esters of α-alanine and orotic acid are soluble in water and sparingly soluble in organic solvents.

Experimental Part

Trimethylstannyl ester of nicotinic acid $(CH_3)_3SnOOCC_5H_4N$ (10). In a three-necked flask equipped with a stirrer and a reflux condenser were placed 5.4 g (0.03 mole) of trimethylstannol ([1]), 3.7 g (0.03 mole) of nicotinic acid (m.p. 234-237°), and 40 ml of water. The mixture was heated at boiling for 1.5-2 hours and left overnight. The crystals were filtered off on a glass filter and washed several times with hot water. There were obtained 5.9 g (yield 69.1% of theory, calculated on trimethylstannol) of the trimethylstannyl ester of nicotinic acid. After recrystallization from benzene the product had m.p. 188-190°. The substance is sparingly soluble in water and soluble in ordinary organic solvents.

Tri-*n*-propylstannyl ester of nicotinic acid $(*n*-C_3H_7)_3SnOOCC_5H_4N$ (3). Into a flask were placed 2.4 g (0.02 g-mole) of nicotinic acid and 30 ml of water; it was dissolved on heating, and then 2.5 g (0.01 g-mole) of hexa-*n*-propylstannoxane (b.p. 148°, 3 mm, n_D^{20} 1.4915) ([1]) was added from a dropping funnel. The reaction mass was heated with stirring at 70° for 2 hours and left overnight. The precipitate that separated was filtered off and washed with several portions of hot water. There were obtained 2.9 g (yield 79.3% of theory,

calculated on hexapropylstannoxane) of tri-*n*-propylstannyl ester of nicotinic acid. After recrystallization from benzene the substance had m.p. 90–92°.

Dipropylstannylene ester of nicotinic acid $(*n*-C_3H_7)_2Sn(OOCC_5H_4N)_2$ (2). In a three-necked flask were placed 2.2 g (0.01 g-mole) of di-*n*-propylstannone $(*n* -C_3H_7)_2SnO$, obtained by hydrolysis of tri-*n*-propylbromostannane ([1]), 20 ml of water, and 2.7 g (0.02 g-mole) of nicotinic acid. The reaction mixture was heated to boiling for 20 min. At first dissolution of the products occurred, and then a crystalline precipitate began to separate; it was filtered off, washed with several portions of hot water, and dried in vacuo. There were obtained 3.7 g of di-*n*-propylstannylene ester of nicotinic acid. After repeated recrystallizations from chloroform, a product with m.p. 156–158° was obtained.

The trialkylstannyl and dialkylstannylene esters of nicotinic acid indicated in Table 1 were synthesized in an analogous manner. They are solid crystalline white substances, sparingly soluble in water, more readily soluble in benzene, chloroform, and other organic solvents.

Diphenylplumbylene ester of nicotinic acid $(C_6H_5)_2Pb(OOCC_5H_4N)_2$ (12). In a flask were placed 20 ml of alcohol and 4.6 g (0.01 g-mole) of triphenylplumbanol, obtained by hydrolysis of triphenylchloroplumbane with an alcoholic alkali solution ([2]). After dissolution of the triphenylplumbanol, 1.2 g (0.01 g-mole) of nicotinic acid was added, and the reaction mixture was heated to boiling for 1.5–2 hours. Toward the end of boiling, separation of a crystalline precipitate was observed; it was filtered off and washed with hot water. The substance (m.p. 200°) proved to be the diphenylplumbylene ester of nicotinic acid; it is readily soluble in benzene and chloroform, poorly soluble in alcohol, and insoluble in water.

Bis-triethylstannyl ester of isocinchomeronic acid $(C_2H_5)_3SnOOCC_5H_3NCOOSn(C_2H_5)_3$ (6). 2.2 g (0.01 g-mole) of triethylstannol (or, correspondingly, hexaethylstannoxane ([1])), 35 ml of water, and 0.8 g (0.005 g-mole) of isocinchomeronic acid (m.p. 245°) were heated in a three-necked flask at boiling for 3–4 hours. During this, dissolution of the acid and formation of fluffy crystals were observed. The crystalline product, after recrystallization from chloroform, corresponded to the bis-triethylstannyl ester of isocinchomeronic acid. It is sparingly soluble in organic solvents and insoluble in water.

Diisobutylstannylene ester of *p*-aminobenzoic acid (diisobutylstannylene di-*p*-amino-

Table 1

Preparation no.	Compound	m.p., °C	Yield, %	C found	C calc.	H found	H calc.	N found	N calc.	Sn found	Sn calc.
10	$(CH_3)_3SnOOC$ — pyridine ring	188–190	69.1	37.72, 37.78	37.81	4.70, 4.84	4.85	5.17, 5.19	4.89	41.13, 41.25	41.52
4	$(C_2H_5)_3SnOOC$ — pyridine ring	108–110	85.6	43.91, 43.67	43.93	5.95, 5.96	5.93	4.64, 4.44	4.27	35.78, 35.81	36.19
3	$(n\text{-}C_3H_7)_3SnOOC$ — pyridine ring	90–92	79.3	49.00, 49.15	48.71	7.02, 7.06	6.81	3.74, 3.60	3.71		
5	$(C_2H_5)_2Sn(OOC$ — pyridine ring$)_2$	211–212	85.7	45.34, 45.36	45.65	4.21, 4.20	4.31	6.25, 6.32	6.65	28.00, 27.89	28.20
2	$(n\text{-}C_3H_7)_2Sn(OOC$ — pyridine ring$)_2$	156–158	82.4	47.59, 47.83	48.14	4.81, 4.69	4.94	6.13, 6.16	6.24	26.15, 26.04	26.44
6	$(C_2H_5)_3SnOOCC_5H_3NCOOSn(C_2H_5)_3$	263	50.1	39.25, 39.32	39.56	5.64, 5.85	5.76	2.58, 2.61	2.42	40.95, 41.00	41.15
7	$(n\text{-}C_3H_7)_3SnOOCC_5H_3NCOOSn(C_3H_7\text{-}n)_3$	144–145	31.3	45.18, 45.04	45.03	6.61, 6.85	6.86	2.21, 2.22	2.12	35.53, 35.58	35.91
12	$(C_6H_5)_2Pb(OOC$ — pyridine ring$)_2$	210	70.1	47.76, 47.80	47.59	3.07, 3.12	2.99	10.52, 10.63	[illegible]		
16	$(CH_3)_3SnOOCCH(NH_2)CH_3$	215	40.0	28.47, 28.32	28.61	5.83, 5.76	6.00	5.35, 5.45	5.55	46.93, 46.87	47.12
41	$(CH_3)_3SnOOCC_6H_4NH_2\text{-}m$	258.5–259.5 (decomp.)	30.0	39.87, 39.91	40.04	4.87, 4.93	5.04	4.51, 4.14	4.67	39.12, 39.02	39.55
33	$(CH_3)_2SnOOC$ — uracil residue	302–303	54.1	30.18, 30.09	30.13	3.69, 3.60	3.79	9.12, 9.08	8.78	36.87, 36.93	37.22

Preparation no.	Compound	m.p., °C	Yield, %	C found	C calc.	H found	H calc.	N found	N calc.	Sn found	Sn calc.
34	$(C_6H_5)_2PbOOC$–uracil residue	350	60.25	46.64; 46.05	46.52	3.41; 3.43	3.06	5.00; 5.04	4.72		
35	$(C_6H_5)_2Pb(OOCCH_2$–uracil residue$)_2$	330 (decomp.)	60	40.59; 40.71	41.19	2.86; 2.83	2.88	7.35; 7.48	8.00		
32	$(CH_3)_3Sn(OOCCH_2$–uracil residue	345 (decomp.)		32.17; 32.21	32.47	3.87; 3.94	4.23	8.11; 8.08	8.41	35.00; 35.08	35.66
45	$(iso\text{-}C_4H_9)_2Sn(OOCC_6H_4NH_2\text{-}n)_2$	181–182		52.36; 52.52	52.30	6.06; 6.09	5.98	5.51; 5.53	5.54	23.40; 23.37	23.49

benzoate) $(iso\text{-}C_4H_9)_2Sn(OOCC_6H_4NH_2)_2$ (45). 0.67 g (0.005 g-mole) of diisobutyltin oxide*, 0.62 g (0.005 g-mole) of *p*-aminobenzoic acid, and 50 ml of water were placed in a flask equipped with a reflux condenser and heated at boiling for 5 hours. On the following day the precipitate was filtered off, boiled with 25 ml of water in order to remove traces of *p*-aminobenzoic acid, and after filtration washed with several portions of hot water; the reaction product was then recrystallized from ether, and after evaporation to 1/2 of the volume of the solution a fluffy white precipitate of diisobutyltin di-*p*-aminobenzoate separated (m.p. 181-182°). The substance is soluble in organic solvents and insoluble in water.

Orotic acid $C_4N_2H_3O_2COOH$. 3.5 g of uracilacetic acid (5, 6) was added in portions to an oxidizing mixture of 8.7 g of sodium dichromate, 8.7 ml of H_2SO_4 (d_4^{20} 1.83), and 43 ml of water. The reaction mixture was heated for 5 min at boiling. The precipitate that separated was filtered off. 2.1 g of a yellowish, finely crystalline substance was obtained (m.p. 345°), from which, after recrystallization from water, orotic acid monohydrate with m.p. 300° was obtained (melts with decomposition). Yield 66% of theory.

Found, %: C 34.73; 34.66; H 3.71; 3.62; N 16.00; 15.93
$C_5H_4N_2O_4 \cdot H_2O$. Calculated, %: C 34.46; H 3.47; N 16.15

Orotic acid crystallizes in the form of rhombic plates, dissolves in hot water (1 : 70 at 100°), is insoluble in ordinary organic solvents, and is sparingly soluble in ether.

Diphenyllead ester of uracilacetic acid. $(C_6H_5)_2Pb(OOCCH_2C_4H_3N_2O_2)_2$ (35). A mixture of 3.4 g (0.02 g-mole) of uracilacetic acid and 2.3 g (0.005 g-mole) of triphenyllead hydroxide was dissolved in 60 ml of hot ethyl alcohol and

heated for 5 hours at gentle boiling. The precipitate was filtered off, treated several times with hot water, then with several portions of hot alcohol, and dried to constant weight. 2.1 g was obtained (yield 60% of theory, calculated on triphenyllead hydroxide) of a white substance with m.p. 330° (sinters and decomposes), diphenyllead ester of uracilacetic acid.

Trimethyltin ester of orotic acid. $(CH_3)_3SnOOCC_4H_3N_2O_2$ (33). In a flask were placed 0.54 g (0.003 g-mole) of trimethyltin hydroxide, 0.47 g (0.003 g-mole) of orotic acid, and 35 ml of water. The reaction mixture was heated at boiling for 12 hours. The aqueous solution was then evaporated to 1/7 of the initial volume. White, needle-shaped crystals of the trimethyltin ester of orotic acid separated. The ester is insoluble in ordinary organic solvents and sparingly soluble in water.

1. Tin- and lead-organic esters of amino acids (α-alanine, p-aminobenzoic acid), pyridine acids (nicotinic and isocinchomeronic), and pyrimidine acids (orotic and uracilacetic acids) were synthesized and their biocidal properties toward a number of microorganisms were established.

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* Diisobutyltin oxide (iso-$C_4H_9)_2SnO$ is a white amorphous substance, nonmelting, decomposing when heated in a flame, soluble in alcohol, acetone, and chlo-

roform, less readily in ether, and insoluble in water. It was obtained by hydrolysis of triisobutylbromostannane (iso-$C_4H_9)_3SnBr$ (b.p. 120–123°/5, n_D^{20} 1.5072, d_4^{20} 1.3780), and also by hydrolysis with aqueous alkali of diisobutyldibromostannane (1).

Note: Figure translations are in progress. See original paper for figures.

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